The United States Patent and Trademark Office
PATENT TRIAL AND APPEAL BOARD

DANIELLE L. HERRITT
MCCARTER & ENGLISH LLP,
265 FRANKLIN STREET
BOSTON, MA 02110

Appeal No:	2014-007,671
Appellant:	DANIELLE L. HERRI TT(3RD.PTY.REQ.), BIO
Reexam Control No:	DELIVERY SCIENCE INTERNATIONet al.
Hearing Room:	95/002,170
Hearing Docket:	B
Hearing Date:	A
Hearing Time:	Wednesday, November 05, 2014
Location:	01:00 PM
	Madison Building - East Wing
	600 Dulany Street, 9th Floor
	Alexandria, Virginia 22313-1450

NOTICE OF HEARING
RESPONSE REQUIRED WITHIN 21 DAYS

Your attention is directed to 37 CFR § 41.73. The above identified appeal will be heard by the Patent Trial and Appeal Board on the date indicated. Hearings will commence at the time set, and as soon as the argument in one appeal is concluded, the succeeding appeal will be taken up. **The time allowed for argument is 30 minutes** for each appellant or respondent who has requested an oral hearing, unless additional time is requested and approved before the argument commences. **As the hearing relates to an appeal of a reexamination, the hearing will be open to the public.**

Pursuant to § 41.73(d), if any other party to the appeal desires to participate in the oral hearing, but did not request an oral hearing pursuant to § 41.73(d), i.e., within two months after the mailing date of the Examiner's Answer, then this other party will be permitted to participate in the hearing by filing a separate request for oral hearing and the fee set forth in 37 C.F.R. § 41.20(b)(3) within 21 DAYS of the mailing date of this Notice, as well as a confirmation of attendance at the oral hearing.

CONFIRMATION OF ATTENDANCE OR WAIVER OF THE HEARING IS REQUIRED WITHIN **21 DAYS** OF THE MAILING DATE OF THIS NOTICE. Failure to respond will be treated as a waiver of your request to participate in the oral hearing. If you are no longer interested in participating in the oral hearing, you must still file a waiver of oral hearing with the Board. This allows the panel to promptly act on the appeal without waiting for the oral hearing date.

Confirmation or waiver of the hearing should be indicated by completing the form below and returning it to the Board. This form may be filed with the Board by any one of the following three alternative methods:

1. ***PREFERRED***: Via the USPTO Electronic Filing System (EFS) at

http://www.uspto.gov/patents/process/file/efs/

2. Facsimile transmitted to: The USPTO Central fax number (official copy): **(571) 273-8300**
and the PTAB Hearing fax number (courtesy copy): **(571) 273-9797.**

3. By mail at the PTAB mailing address: Patent Trial and Appeal Board
United States Patent and Trademark Office
P.O. BOX 1450
Alexandria, Virginia 22313-1450

In all communications relating to this appeal, please identify the appeal by its number.

CHECK ONE:
(X) I previously filed my oral hearing request pursuant to 37 C.F.R. § 41.73(b).
( ) I am now filing my initial request to participate in the oral hearing pursuant to 37 C.F. R. § 41.73(d). A request for oral hearing and the fee set forth in 37 C.F.R. § 41.20(b)(3) are either attached to this hearing communication or have already been submitted.

CHECK ONE:
(X) IN-PERSON HEARING - ATTENDANCE CONFIRMED *(EFS-Web selection: Confirmation of Hearing by Appellant)*
( ) TELEPHONIC HEARING - ATTENDANCE CONFIRMED *(EFS-Web selection: Confirmation of Hearing by Appellant)*
( ) VIDEO HEARING - ATTENDANCE CONFIRMED *(EFS-Web selection: Confirmation of Hearing by Appellant)*
( ) HEARING ATTENDANCE WAIVED *(EFS-Web selection: Waiver of Hearing by Appellant)*

To aid the oral hearings staff in scheduling hearing rooms, please indicate the total number of participating and observing attendees if more than three are expected: 5
To aid the judges in determining whether any conflicts exist that may require a recusal, please list in the 'Comments' section the names of any additional person(s) who will be participating in the oral hearing. (Upon arrival, all persons presenting arguments must sign in at the Usher's desk.)

Comments/Special Requests:

Request: ELMO Projector

Participants in Oral Hearing:
Deborah M. Vernon (Reg. No. 55,699)
Kia L. Freeman (Reg. No. 47,577)

Danielle L. Herritt — 43,670

Typed or Printed Name of Attorney/Agent/Appellant — Registration No.

( ) PATENT OWNER (X) THIRD PARTY REQUESTER

/Danielle L. Herritt/ — November 4, 2014

Signature of Attorney/Agent/Appellant — Date

The 'Hearings' tab of the PTAB webpage http://www.uspto.gov/ip/boards/bpai/index.jsp provides additional information about oral hearings.

Please direct other inquiries to the PTAB Hearings Clerk at 571-272-9797.

cc: Patent Owner

HOFFMANN & BARON LLP
6900 JERICHO TURNPIKE
SYOSSET, NY 11791

CERTIFICATE OF SERVICE

The undersigned hereby certifies that a copy of the foregoing Third Updated Third Party Requester's Confirmation of Attendance at Oral Hearing was served on November 4, 2014, by first class mail, directed to the patent owner at the correspondence address of record for the subject patent, that is:

Daniel A. Scola, Jr.

HOFFMANN & BARON, LLP

6900 JERICHO TURNPIKE

SYOSSET, NY 11791

By: /Danielle L. Herritt/
Danielle L. Herritt
Registration No. 43,670
Attorney for Third Party Requester

Electronic Acknowledgement Receipt

EFS ID:	20598225
Application Number:	95002170
International Application Number:	
Confirmation Number:	6418
Title of Invention:	POLYETHYLENE-OXIDE BASED FILMS AND DRUG DELIVERY SYSTEMS MADE THEREFROM
First Named Inventor/Applicant Name:	7897080
Customer Number:	23869
Filer:	Danielle L. Herritt/Maureen Tierney
Filer Authorized By:	Danielle L. Herritt
Attorney Docket Number:	117744-00023
Receipt Date:	04-NOV-2014
Filing Date:	10-SEP-2012
Time Stamp:	11:08:31
Application Type:	inter partes reexam

Payment information:

Submitted with Payment	no

File Listing:

Document Number	Document Description	File Name	File Size(Bytes)/ Message Digest	Multi Part /.zip	Pages (if appl.)
1		080THIRDUpdatedHearingConfirmation2014NOV4.PDF	1084338 cd9572cb8a48233f01ed5ff79fea63522be8c6f7	yes	4

	Multipart Description/PDF files in .zip description		
	Document Description	**Start**	**End**
	Reexam Miscellaneous Incoming Letter	1	3
	Reexam Certificate of Service	4	4

Warnings:	
Information:	
Total Files Size (in bytes):	1084338

This Acknowledgement Receipt evidences receipt on the noted date by the USPTO of the indicated documents, characterized by the applicant, and including page counts, where applicable. It serves as evidence of receipt similar to a Post Card, as described in MPEP 503.

New Applications Under 35 U.S.C. 111
If a new application is being filed and the application includes the necessary components for a filing date (see 37 CFR 1.53(b)-(d) and MPEP 506), a Filing Receipt (37 CFR 1.54) will be issued in due course and the date shown on this Acknowledgement Receipt will establish the filing date of the application.

National Stage of an International Application under 35 U.S.C. 371
If a timely submission to enter the national stage of an international application is compliant with the conditions of 35 U.S.C. 371 and other applicable requirements a Form PCT/DO/EO/903 indicating acceptance of the application as a national stage submission under 35 U.S.C. 371 will be issued in addition to the Filing Receipt, in due course.

New International Application Filed with the USPTO as a Receiving Office
If a new international application is being filed and the international application includes the necessary components for an international filing date (see PCT Article 11 and MPEP 1810), a Notification of the International Application Number and of the International Filing Date (Form PCT/RO/105) will be issued in due course, subject to prescriptions concerning national security, and the date shown on this Acknowledgement Receipt will establish the international filing date of the application.

The United States Patent and Trademark Office
PATENT TRIAL AND APPEAL BOARD

DANIELLE L. HERRITT
MCCARTER & ENGLISH LLP,
265 FRANKLIN STREET
BOSTON, MA 02110

Appeal No:	2014-007,671
Appellant:	DANIELLE L. HERRI TT(3RD.PTY.REQ.), BIO
Reexam Control No:	DELIVERY SCIENCE INTERNATIONet al.
Hearing Room:	95/002,170
Hearing Docket:	B
Hearing Date:	A
Hearing Time:	Wednesday, November 05, 2014
Location:	01:00 PM Madison Building - East Wing 600 Dulany Street, 9th Floor Alexandria, Virginia 22313-1450

NOTICE OF HEARING
RESPONSE REQUIRED WITHIN 21 DAYS

Your attention is directed to 37 CFR § 41.73. The above identified appeal will be heard by the Patent Trial and Appeal Board on the date indicated. Hearings will commence at the time set, and as soon as the argument in one appeal is concluded, the succeeding appeal will be taken up. **The time allowed for argument is 30 minutes** for each appellant or respondent who has requested an oral hearing, unless additional time is requested and approved before the argument commences. **As the hearing relates to an appeal of a reexamination, the hearing will be open to the public.**

Pursuant to § 41.73(d), if any other party to the appeal desires to participate in the oral hearing, but did not request an oral hearing pursuant to § 41.73(d), i.e., within two months after the mailing date of the Examiner's Answer, then this other party will be permitted to participate in the hearing by filing a separate request for oral hearing and the fee set forth in 37 C.F.R. § 41.20(b)(3) within 21 DAYS of the mailing date of this Notice, as well as a confirmation of attendance at the oral hearing.

CONFIRMATION OF ATTENDANCE OR WAIVER OF THE HEARING IS REQUIRED WITHIN **21 DAYS** OF THE MAILING DATE OF THIS NOTICE. Failure to respond will be treated as a waiver of your request to participate in the oral hearing. If you are no longer interested in participating in the oral hearing, you must still file a waiver of oral hearing with the Board. This allows the panel to promptly act on the appeal without waiting for the oral hearing date.

Confirmation or waiver of the hearing should be indicated by completing the form below and returning it to the Board. This form may be filed with the Board by any one of the following three alternative methods:

1. ***PREFERRED***: Via the USPTO Electronic Filing System (EFS) at

http://www.uspto.gov/patents/process/file/efs/

2. Facsimile transmitted to: The USPTO Central fax number (official copy): **(571) 273-8300**
and the PTAB Hearing fax number (courtesy copy): **(571) 273-9797.**

3. By mail at the PTAB mailing address: Patent Trial and Appeal Board
United States Patent and Trademark Office
P.O. BOX 1450
Alexandria, Virginia 22313-1450

In all communications relating to this appeal, please identify the appeal by its number.

CHECK ONE:
(X) I previously filed my oral hearing request pursuant to 37 C.F.R. § 41.73(b).
( ) I am now filing my initial request to participate in the oral hearing pursuant to 37 C.F. R. § 41.73(d). A request for oral hearing and the fee set forth in 37 C.F.R. § 41.20(b)(3) are either attached to this hearing communication or have already been submitted.

CHECK ONE:
(X) IN-PERSON HEARING - ATTENDANCE CONFIRMED *(EFS-Web selection: Confirmation of Hearing by Appellant)*
( ) TELEPHONIC HEARING - ATTENDANCE CONFIRMED *(EFS-Web selection: Confirmation of Hearing by Appellant)*
( ) VIDEO HEARING - ATTENDANCE CONFIRMED *(EFS-Web selection: Confirmation of Hearing by Appellant)*
( ) HEARING ATTENDANCE WAIVED *(EFS-Web selection: Waiver of Hearing by Appellant)*

To aid the oral hearings staff in scheduling hearing rooms, please indicate the total number of participating and observing attendees if more than three are expected: 5
To aid the judges in determining whether any conflicts exist that may require a recusal, please list in the 'Comments' section the names of any additional person(s) who will be participating in the oral hearing. (Upon arrival, all persons presenting arguments must sign in at the Usher's desk.)

Comments/Special Requests:

Request: ELMO Projector

Participants in Oral Hearing:
Danielle L. Herritt (Reg. No. 43,670)
Deborah M. Vernon (Reg. No. 55,699)

Danielle L. Herritt	43,670
Typed or Printed Name of Attorney/Agent/Appellant	Registration No.

( ) PATENT OWNER (X) THIRD PARTY REQUESTER

/Danielle L. Herritt/	November 3, 2014
Signature of Attorney/Agent/Appellant	Date

The 'Hearings' tab of the PTAB webpage http://www.uspto.gov/ip/boards/bpai/index.jsp provides additional information about oral hearings.

Please direct other inquiries to the PTAB Hearings Clerk at 571-272-9797.

cc: Patent Owner

HOFFMANN & BARON LLP
6900 JERICHO TURNPIKE
SYOSSET, NY 11791

CERTIFICATE OF SERVICE

The undersigned hereby certifies that a copy of the foregoing Updated Third Party Requester's Confirmation of Attendance at Oral Hearing was served on November 3, 2014, by first class mail, directed to the patent owner at the correspondence address of record for the subject patent, that is:

Daniel A. Scola, Jr.

HOFFMANN & BARON, LLP

6900 JERICHO TURNPIKE

SYOSSET, NY 11791

By: /Danielle L. Herritt/
Danielle L. Herritt
Registration No. 43,670
Attorney for Third Party Requester

Electronic Acknowledgement Receipt

EFS ID:	20586357
Application Number:	95002170
International Application Number:	
Confirmation Number:	6418
Title of Invention:	POLYETHYLENE-OXIDE BASED FILMS AND DRUG DELIVERY SYSTEMS MADE THEREFROM
First Named Inventor/Applicant Name:	7897080
Customer Number:	23869
Filer:	Danielle L. Herritt/Maureen Tierney
Filer Authorized By:	Danielle L. Herritt
Attorney Docket Number:	117744-00023
Receipt Date:	03-NOV-2014
Filing Date:	10-SEP-2012
Time Stamp:	12:29:39
Application Type:	inter partes reexam

Payment information:

Submitted with Payment	no

File Listing:

Document Number	Document Description	File Name	File Size(Bytes)/ Message Digest	Multi Part /.zip	Pages (if appl.)
1		080UpdatedHearingConfirmation2014NOV3.PDF	1107256 0652a7d5f46dcfac52e946e6140a3301921de2a8	yes	4

	Multipart Description/PDF files in .zip description		
	Document Description	**Start**	**End**
	Reexam Miscellaneous Incoming Letter	1	3
	Reexam Certificate of Service	4	4

Warnings:	
Information:	
Total Files Size (in bytes):	1107256

This Acknowledgement Receipt evidences receipt on the noted date by the USPTO of the indicated documents, characterized by the applicant, and including page counts, where applicable. It serves as evidence of receipt similar to a Post Card, as described in MPEP 503.

New Applications Under 35 U.S.C. 111
If a new application is being filed and the application includes the necessary components for a filing date (see 37 CFR 1.53(b)-(d) and MPEP 506), a Filing Receipt (37 CFR 1.54) will be issued in due course and the date shown on this Acknowledgement Receipt will establish the filing date of the application.

National Stage of an International Application under 35 U.S.C. 371
If a timely submission to enter the national stage of an international application is compliant with the conditions of 35 U.S.C. 371 and other applicable requirements a Form PCT/DO/EO/903 indicating acceptance of the application as a national stage submission under 35 U.S.C. 371 will be issued in addition to the Filing Receipt, in due course.

New International Application Filed with the USPTO as a Receiving Office
If a new international application is being filed and the international application includes the necessary components for an international filing date (see PCT Article 11 and MPEP 1810), a Notification of the International Application Number and of the International Filing Date (Form PCT/RO/105) will be issued in due course, subject to prescriptions concerning national security, and the date shown on this Acknowledgement Receipt will establish the international filing date of the application.

The United States Patent and Trademark Office
PATENT TRIAL AND APPEAL BOARD

DANIELLE L. HERRITT
MCCARTER & ENGLISH LLP,
265 FRANKLIN STREET
BOSTON, MA 02110

Appeal No:	2014-007,671
Appellant:	DANIELLE L. HERRI TT(3RD.PTY.REQ.), BIO
Reexam Control No:	DELIVERY SCIENCE INTERNATIONet al.
Hearing Room:	95/002,170
Hearing Docket:	B
Hearing Date:	A
Hearing Time:	Wednesday, November 05, 2014
Location:	01:00 PM Madison Building - East Wing 600 Dulany Street, 9th Floor Alexandria, Virginia 22313-1450

NOTICE OF HEARING
RESPONSE REQUIRED WITHIN 21 DAYS

Your attention is directed to 37 CFR § 41.73. The above identified appeal will be heard by the Patent Trial and Appeal Board on the date indicated. Hearings will commence at the time set, and as soon as the argument in one appeal is concluded, the succeeding appeal will be taken up. **The time allowed for argument is 30 minutes** for each appellant or respondent who has requested an oral hearing, unless additional time is requested and approved before the argument commences. **As the hearing relates to an appeal of a reexamination, the hearing will be open to the public.**

Pursuant to § 41.73(d), if any other party to the appeal desires to participate in the oral hearing, but did not request an oral hearing pursuant to § 41.73(d), i.e., within two months after the mailing date of the Examiner's Answer, then this other party will be permitted to participate in the hearing by filing a separate request for oral hearing and the fee set forth in 37 C.F.R. § 41.20(b)(3) within 21 DAYS of the mailing date of this Notice, as well as a confirmation of attendance at the oral hearing.

CONFIRMATION OF ATTENDANCE OR WAIVER OF THE HEARING IS REQUIRED WITHIN **21 DAYS** OF THE MAILING DATE OF THIS NOTICE. Failure to respond will be treated as a waiver of your request to participate in the oral hearing. If you are no longer interested in participating in the oral hearing, you must still file a waiver of oral hearing with the Board. This allows the panel to promptly act on the appeal without waiting for the oral hearing date.

Confirmation or waiver of the hearing should be indicated by completing the form below and returning it to the Board. This form may be filed with the Board by any one of the following three alternative methods:

1. ***PREFERRED***: Via the USPTO Electronic Filing System (EFS) at

http://www.uspto.gov/patents/process/file/efs/

2. Facsimile transmitted to: The USPTO Central fax number (official copy): **(571) 273-8300**
and the PTAB Hearing fax number (courtesy copy): **(571) 273-9797.**

3. By mail at the PTAB mailing address: Patent Trial and Appeal Board
United States Patent and Trademark Office
P.O. BOX 1450
Alexandria, Virginia 22313-1450

In all communications relating to this appeal, please identify the appeal by its number.

CHECK ONE:
(X) I previously filed my oral hearing request pursuant to 37 C.F.R. § 41.73(b).
( ) I am now filing my initial request to participate in the oral hearing pursuant to 37 C.F. R. § 41.73(d). A request for oral hearing and the fee set forth in 37 C.F.R. § 41.20(b)(3) are either attached to this hearing communication or have already been submitted.

CHECK ONE:
(X) IN-PERSON HEARING - ATTENDANCE CONFIRMED *(EFS-Web selection: Confirmation of Hearing by Appellant)*
( ) TELEPHONIC HEARING - ATTENDANCE CONFIRMED *(EFS-Web selection: Confirmation of Hearing by Appellant)*
( ) VIDEO HEARING - ATTENDANCE CONFIRMED *(EFS-Web selection: Confirmation of Hearing by Appellant)*
( ) HEARING ATTENDANCE WAIVED *(EFS-Web selection: Waiver of Hearing by Appellant)*

To aid the oral hearings staff in scheduling hearing rooms, please indicate the total number of participating and observing attendees if more than three are expected: 5
To aid the judges in determining whether any conflicts exist that may require a recusal, please list in the 'Comments' section the names of any additional person(s) who will be participating in the oral hearing. (Upon arrival, all persons presenting arguments must sign in at the Usher's desk.)

Comments/Special Requests:

Request: ELMO Projector

Participants in Oral Hearing:
Danielle L. Herritt (Reg. No. 43,670)
Deborah M. Vernon (Reg. No. 55,699)
Kia L. Freeman (Reg. No. 47,577)

Danielle L. Herritt — 43,670

Typed or Printed Name of Attorney/Agent/Appellant — Registration No.

( ) PATENT OWNER (X) THIRD PARTY REQUESTER

/Danielle L. Herritt/ — November 3, 2014

Signature of Attorney/Agent/Appellant — Date

The 'Hearings' tab of the PTAB webpage http://www.uspto.gov/ip/boards/bpai/index.jsp provides additional information about oral hearings.

Please direct other inquiries to the PTAB Hearings Clerk at 571-272-9797.

cc: Patent Owner

HOFFMANN & BARON LLP
6900 JERICHO TURNPIKE
SYOSSET, NY 11791

CERTIFICATE OF SERVICE

The undersigned hereby certifies that a copy of the foregoing Second Updated Third Party Requester's Confirmation of Attendance at Oral Hearing was served on November 3, 2014, by first class mail, directed to the patent owner at the correspondence address of record for the subject patent, that is:

Daniel A. Scola, Jr.

HOFFMANN & BARON, LLP

6900 JERICHO TURNPIKE

SYOSSET, NY 11791

By: /Danielle L. Herritt/
Danielle L. Herritt
Registration No. 43,670
Attorney for Third Party Requester

Electronic Acknowledgement Receipt

EFS ID:	20595766
Application Number:	95002170
International Application Number:	
Confirmation Number:	6418
Title of Invention:	POLYETHYLENE-OXIDE BASED FILMS AND DRUG DELIVERY SYSTEMS MADE THEREFROM
First Named Inventor/Applicant Name:	7897080
Customer Number:	23869
Filer:	Danielle L. Herritt/Maureen Tierney
Filer Authorized By:	Danielle L. Herritt
Attorney Docket Number:	117744-00023
Receipt Date:	03-NOV-2014
Filing Date:	10-SEP-2012
Time Stamp:	20:35:14
Application Type:	inter partes reexam

Payment information:

Submitted with Payment	no

File Listing:

Document Number	Document Description	File Name	File Size(Bytes)/ Message Digest	Multi Part /.zip	Pages (if appl.)
1		080SECONDUpdatedHearingConfirmation2014NOV3.PDF	1106481 7e59f1c3b37be069d63380f35a2829cfff482887	yes	4

	Multipart Description/PDF files in .zip description		
	Document Description	**Start**	**End**
	Reexam Miscellaneous Incoming Letter	1	3
	Reexam Certificate of Service	4	4
Warnings:			
Information:			
	Total Files Size (in bytes):	1106481	

This Acknowledgement Receipt evidences receipt on the noted date by the USPTO of the indicated documents, characterized by the applicant, and including page counts, where applicable. It serves as evidence of receipt similar to a Post Card, as described in MPEP 503.

New Applications Under 35 U.S.C. 111
If a new application is being filed and the application includes the necessary components for a filing date (see 37 CFR 1.53(b)-(d) and MPEP 506), a Filing Receipt (37 CFR 1.54) will be issued in due course and the date shown on this Acknowledgement Receipt will establish the filing date of the application.

National Stage of an International Application under 35 U.S.C. 371
If a timely submission to enter the national stage of an international application is compliant with the conditions of 35 U.S.C. 371 and other applicable requirements a Form PCT/DO/EO/903 indicating acceptance of the application as a national stage submission under 35 U.S.C. 371 will be issued in addition to the Filing Receipt, in due course.

New International Application Filed with the USPTO as a Receiving Office
If a new international application is being filed and the international application includes the necessary components for an international filing date (see PCT Article 11 and MPEP 1810), a Notification of the International Application Number and of the International Filing Date (Form PCT/RO/105) will be issued in due course, subject to prescriptions concerning national security, and the date shown on this Acknowledgement Receipt will establish the international filing date of the application.

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Appeal No. 2014-007671 of	)	
Inter Partes Reexamination of:	)	
US Patent No. 7,897,080	)	Confirmation No.: 6418
	)	
Named Inventor: Robert K. Yang *et al.*	)	Group Art Unit: 3991
	)	
Control No. 95/002,170	)	Examiner: Alan D. Diamond
	)	
Request Filed: September 10, 2012	)	M&E Docket: 117744-00023
	)	
Title: POLYETHYLENE OXIDE-BASED	)	H&B Docket: 1199-26
FILMS AND DRUG DELIVERY	)	RCE/CON/REX
SYSTEMS MADE THEREFROM	)	

PATENT TRIAL and APPEAL BOARD
UNITES STATES PATENT AND TRADEMARK OFFICE
P.O. Box 1450
Alexandria, Virginia 22313-1450

UPDATE ON RELATED APPEAL

Both parties identified the appeal of the *inter partes* reexamination of US Patent No. 7,824,588 as a Related Appeal. See Appellant (MonoSol) Appeal Brief, March 10, 2014, at pp. 1-2 (referencing Appeal No. 2014-000547 of Reexamination Control No. 95/001,753); and BDSI's Respondent Brief in *Inter Partes* Reexamination, April 10, 2014, at p. 2 (with three exceptions, agreeing to Patent Owner's identification of Related Appeals and Interferences). Requester now updates the Board on the resolution of that related appeal and, for the Board's reference, provides the attached Decision on Appeal No. 2014-000547.

The attached Decision issued on April 17, 2014—after the respondent's brief was filed in this appeal. The attached Decision did not become final until June 17, 2014—after the briefing concluded in this appeal. The attached Decision on Appeal is relevant to issues in this appeal.

Respectfully submitted,

Attorneys for Requester, McCarter & English, LLP

Dated: October 17, 2014

By: /Danielle L. Herritt/

Danielle L. Herritt (Reg. No. 43,670)
Kia L. Freeman (Reg. No. 47,577)
Direct Dial: 617-449-6513

CERTIFICATE OF SERVICE

The undersigned hereby certifies that a copy of the Rebuttal Brief was served on October 17, 2014, by first class mail, directed to the patent owner at the correspondence address of record for the subject patent, that is:

Daniel A. Scola, Jr.

HOFFMANN & BARON, LLP

6900 JERICHO TURNPIKE

SYOSSET, NY 11791

By: /Danielle L. Herritt/
Danielle L. Herritt
Registration No. 43,670
Attorney for Respondent

UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
95/001,753	09/12/2011	7,824,588	117744-00016	6620

23869 7590 04/17/2014

Hoffmann & Baron LLP
6900 Jericho Turnpike
Syosset, NY 11791

EXAMINER	
DIAMOND, ALAN D	
ART UNIT	PAPER NUMBER
3991	

MAIL DATE	DELIVERY MODE
04/17/2014	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

PTOL-90A (Rev. 04/07)

UNITED STATES PATENT AND TRADEMARK OFFICE

BEFORE PATENT TRIAL AND APPEAL BOARD

BIODELIVERY SCIENCES INTERNATIONAL, INC.
Requester

v.

MONOSOL RX, LLC
Patent Owner and Appellant

Appeal 2014-000547
Reexamination Control 95/001,753
Patent 7,824,588 B2
Technology Center 3900

Before CHUNG K. PAK, JEFFREY B. ROBERTSON, and RAE LYNN P. GUEST, *Administrative Patent Judges.*

GUEST, *Administrative Patent Judge.*

DECISION ON APPEAL

This is a decision on appeal by the Patent Owner from the Patent Examiner's decision to reject pending claims in an *inter partes* reexamination of U.S. Patent 7,824,588 B2 (herein after the "'588 patent").[1]

[1] The '588 patent issued November 2, 2010, to Robert K. Yang, et al.

The Board's jurisdiction for this appeal is under 35 U.S.C. §§ 6(b), 134, and 315. We AFFIRM.

I. BACKGROUND

A request for *inter partes* reexamination under 35 U.S.C. §§ 311-318 and 37 C.F.R. §§ 1.902-1.997 for the '588 patent was filed on September 12, 2011, by a Third-Party Requester, BioDelivery Sciences International, Inc. (hereinafter "Requester"). *See* Request for *Inter Partes* Reexamination 1 (hereinafter "Request"); Requester's Respondent Brief, dated July 24, 2013 (hereinafter "Res. Br."). The Patent Owner and Appellant is MonoSol Rx, LLC (hereinafter "Patent Owner"). Patent Owner's Appeal Br. 1, dated June 24, 2013 (hereinafter "App. Br.").

The '588 patent is the subject of a litigation proceeding in the United States District Court for the District of New Jersey styled *MonoSol Rx, LLC v. BioDelivery Sciences Int'l, Inc.*, 10-cv-5695. The litigation is currently stayed pending the outcome of this Reexamination proceeding. *See* App. Br. 2.

An oral hearing was held March 26, 2014. A transcript of the hearing will be entered into the record in due course.

The '588 patent is directed to a method for forming a rapidly dissolving film containing an active ingredient evenly or uniformly distributed throughout the film. '588 patent, col. 1, ll. 35-42. According to the '588 patent, "uniform distribution is achieved by controlling one or more parameters, and particularly the elimination of air pockets prior to and during film formation and the use of a drying process that reduces

aggregation or conglomeration of the components in the film as it forms into a solid structure." *Id.* at col. 1, ll. 37-42.

The '588 patent originally contained claims 1-191. During reexamination, Patent Owner amended claim 1 and added new independent claims 192 and 193. Claims 1-193 are currently rejected by the Examiner.

Although Patent Owner appeals the rejection of all of the claims so rejected, with respect to independent claims 25 and 50 and the claims that depend therefrom, Patent Owner does not address the Examiner's specific findings and conclusions articulated in the rejections or explain why these positions are deficient. PO App. Br. 4. Accordingly, we summarily affirm the Examiner's rejections of claims 25 and 50 and the claims that depend therefrom.

Consistent with the arguments presented by Patent Owner, we address the rejections of claims 1-24, 75, 78, 81, 84, 87, 90, 93, 96, 99, 102, 105, 106, 111-132, 177, 178, 183, 186, 189, 192, and 193. *Id.*

Claims 1, 192 and 193 are at issue in this appeal and read as follows (with underlining showing additional language over the original patented claim):

> 1. A method of making a self-supporting therapeutic active-containing film comprising:
>
> (a) Mixing at least one edible polymer component, a therapeutic active composition, and at least one polar solvent to form a matrix;
>
> (b) Forming a wet film from said matrix, <u>said wet film having a substantially uniform content of therapeutic active composition throughout said wet film</u>;
>
> (c) Removing said polar solvent from said matrix with heat and/or radiation energy by exposing said matrix to a

temperature greater than the degradation temperature of said therapeutic active composition to form a self-supporting film;

wherein the temperature of the matrix is 100° C. or less during said step of removing said polar solvent from said matrix;

wherein the resulting self-supporting film maintains the substantially uniform content of therapeutic active composition per unit of film.

192. A method of making a self-supporting therapeutic active-containing film comprising:

(a) Mixing at least one edible polymer component, a therapeutic active composition and at least one polar solvent to form a matrix;

(b) Forming a wet film from said matrix, said wet film having a substantially uniform content of therapeutic active composition throughout said wet film;

(c) Removing said polar solvent from said matrix with heat and/or radiation energy by heating said matrix to a temperature that is less than the boiling point of said at least one polar solvent so as to form a viscoelastic film;

wherein the resulting viscoelastic film maintains the substantially uniform content of therapeutic active composition per unit of film.

193. A method of making a self-supporting therapeutic active-containing film comprising:

(a) Mixing at least one edible polymer component, a therapeutic active composition, and at least one polar solvent to form a matrix;

(b) Forming a wet film from said matrix, said wet film having a substantially uniform content of therapeutic active composition throughout said wet film;

(c) Using heat and/or radiation energy to remove said polar solvent from said matrix to form a self-supporting therapeutic active-containing film without forming bubbles;

wherein the resulting self-supporting film maintains the substantially uniform content of therapeutic active composition per unit of film.

REJECTIONS OF CLAIMS BASED ON SECTION 112

Claims 1-24, 75, 78, 81, 84, 87, 90, 93, 96, 99, 102, 105, 106, 111-132, 177, 178, 183, 186, 189, 192 and 193 stand rejected under 35 U.S.C. § 112, first and second paragraphs as indefinite, lacking in written description support, and lacking an enabling disclosure.

Claim 1 was amended during reexamination to recite a self-supporting therapeutic active-containing film in which there is "a substantially uniform content of therapeutic active composition" in both the wet film and maintained in the resulting self-supporting film "per unit of film." Claims 192 and 193 are new claims and have similar language to that added to claim 1.

The Examiner found that "[i]t is not clear exactly what is encompassed by a substantially uniform content of therapeutic active composition, and the '588 patent does not provide a definition for a substantially uniform content of therapeutic active composition." RAN at 9. The Examiner thus rejects the claim as being indefinite under 35 U.S.C. § 112, second paragraph, and as lacking adequate written descriptive support and lacking an enabling disclosure in the '588 patent under 35 U.S.C. § 112, first paragraph. *Id.* at 9-10. The Examiner further explains that "it is not clear how close to being uniform the product must be in order to be considered 'substantially uniform'. 'Substantially uniform' is not defined in the '588 patent." *Id.* at 68-69.

Patent Owner argues that the phrase "substantially uniform content of therapeutic active composition" means "a film having a degree of uniformity of ± 10% from the FDA label amount for the active per dosage unit." App. Br. 20.[2] In other words, the Patent Owner is arguing that the substantially uniform content must be defined with respect to a particular active content recognized and labeled by the FDA as a proper "dosage."

In support of this meaning, the Patent Owner points to the background of the '588 patent where the process of Fuchs is discussed as follows:

> dosage forms formed by processes such as Fuchs, would not likely meet the stringent standards of governmental or regulatory agencies, such as the U.S. Federal Drug Administration ("FDA"), relating to the variation of active in dosage forms. Currently, as required by various world regulatory authorities, dosage forms may not vary more than 10% in the amount of active present. When applied to dosage units based on films, this virtually mandates that uniformity in the film be present.

'588 patent, col. 2, ll. 25-44.

We disagree with the Patent Owner's interpretation of the phrase "substantially uniform content of therapeutic active composition." The

---

[2] *Cf.* App. Br. 24 (defining the phrase as "a degree of uniformity sufficient to maintain the amount of active in each dosage unit within 10% of the FDA amount of active."); App. Br. 15 (defining only the term *uniformity* as "the amount of active present may not vary more than 10% from amount of the active set by the FDA, for example, in a unit dose (per unit of film, i.e. in a film unit)"); Patent Owner's Rebuttal Brief 3, dated September 9, 2013 (hereinafter "Reb. Br.") (defining the phrase as "a degree of uniformity consistent with FDA pharmaceutical products and must include the limited variation such that the amount of active present may not vary more than 10% from the amount of the active set by the FDA per unit of film, i. e. per therapeutic dosage unit.").

FDA standard identified by Patent Owner in the portion of the '588 patent reproduced supra, is not again referenced. In the remaining parts of the '588 patent, uniformity is characterized not with respect to an FDA recognized dosage, but with respect to the lack of agglomeration of active material in any part of the film. For example, the '588 patent states that the active material is "evenly distributed throughout the film," which is "achieved by . . . the use of a drying process that reduces aggregation or conglomeration of the components in the film as it forms into a solid structure." '588 patent, col. 1, ll. 37-42. An objective of the process is "a substantially non-self-aggregating uniform heterogeneity throughout the area of the films." *Id.* at col. 4, ll. 5-9. The '588 patent further describes "a substantially reduced occurrence of, i.e. little or no, aggregation or conglomeration of components within the film as is normally experienced when films are formed by conventional drying methods." *Id.*, col. 6, ll. 25-32. The process of the '588 patent provides "uniform distribution of components *for any given area in the film*." *Id.* at col. 7, ll. 26-29 (emphasis added).

Requiring a particular film to have an amount of active relative to a FDA recognized dosage considers the active amount in each individual "dosage unit" as compared to a particularly preferred or desired dosage. Patent Owner's interpretation disregards whether or not the active is agglomerated within the film and considers only a total amount of active material per dosage sized film rather than uniformity at *any given area in the film*, be it a small selected area, an area of the film consistent with a particular dosage, or an entire roll of film. Accordingly, the sentence relied

upon by the Patent Owner, stating that uniformity is "virtually mandated" by FDA requirements that the actual dosage be within a range of the labeled dosage, does not provide a definition of what would be considered "uniform," in light of the description of the '588 patent.

Further, the '588 patent describes three tests for determining uniformity. The first test was a visual inspection by "either the naked eye or under slight magnification. By viewing the films it was apparent that they were substantially free of aggregation, i.e. the carrier and the actives remained substantially in place and did not move substantially from one portion of the film to another." *Id.* at col. 28, ll. 1-9. This first test is not consistent with the Patent Owner's interpretation because the test does not measure the active content with respect to any particular desired dosage. Further, Patent Owner's interpretation does not exclude the presence of agglomerated particles, which is the purpose of the visual appearance test.

The second test involved cutting out "dosage forms" "from random locations throughout the film" and additively weighing the randomly selected dosage forms. *Id.* at col. 28, ll. 10-16. Table 2 shows that with each additional dosage form, the weight increased by exactly 0.04g. *Id.* at col. 28, ll. 19-65. The '588 patent explains that "each component has a unique density. Therefore, when the components of different densities are combined in a uniform manner in a film, as in the present invention, individual dosages forms from the same film of substantially equal dimensions, will contain the same mass." *Id.* at col. 29, ll. 3-9. This second test also is not consistent with the Patent Owner's interpretation because the test does not measure the active content with respect to any particular

desired dosage. Rather, the second test is directed towards comparing the active content at various locations on the same film.

The third test involved dissolving "individual doses" and testing for the amount of active in films of particular size. *Id.* at col. 29, ll. 10-12. The '588 patent states that "[t]his demonstrates that films of substantially similar size cut from different locations on the same film contain substantially the same amount of active." *Id.* at col. 29, ll. 13-15. Although the third test determines the actual amount of active within a dosage sized film, the third test also is not consistent with Patent Owner's interpretation because the test does not measure the active content with respect to any particular desired dosage. Rather, the third test is directed towards comparing the active content at various locations on the same film.

Accordingly, we conclude that the term "uniform" in the claims is not directed to uniformity as compared to a particular FDA dosage as proposed by Patent Owner, but rather non-agglomerated and evenly dispersed active content for any area of a given film.

This claim interpretation is more consistent with the Examiner's interpretation of the phrase "unit of film," with which the Patent Owner agrees. App. Br. 17. The Examiner determined that the phrase "unit of film" was broad, but definite, and indicated that "[i]t could be a roll of finished film, it could be a standard area of dried film before being cut, or it could be a dosage unit. Any size can be a unit." RAN 11.

Further, we agree with the Examiner that, while the term "uniform" appears definite in light of the '588 patent, we are not instructed as to the scope to which a film may be "substantially uniform." We are not provided

a degree of agglomeration or an amount of unevenly dispersed active material for which the film would still be acceptable. Considering that the second, additive-weight-based test shows only complete uniformity, with no additional films weighing more or less than exactly 0.04g, we are not instructed as to what deviation in weight would be considered "substantially uniform." Further, we are not provided the results of the dissolution test as evidence of a range of acceptable uniformity.

Words of degree may lack precision, but they do not necessarily render a claim indefinite. *Seattle Box Co., Inc. v. Indus. Crating & Packing, Inc.*, 731 F.2d 818, 826 (Fed. Cir. 1984) (A term of degree is definite if the specification "provides some standard for measuring that degree. . . . that is, whether one of ordinary skill in the art would understand what is claimed when the claim is read in light of the specification."). As discussed above, under the proper interpretation of the term "uniform," the '588 patent provides no standard or guidance by which the term "substantially" can be measured or determined. Nor is there any intrinsic and/or extrinsic evidence relied upon by Patent Owner to show that such term has a known meaning in the art. Thus, we agree with the Examiner that such relative expression, amenable to any number of plausible claim constructions, is deemed indefinite within the meaning of 35 U.S.C. § 112, second paragraph. *Ex parte Miyazaki*, 89 USPQ2d 1207, 1211 (BPAI 2008) ("[During prosecution of a patent application,] if a claim is amenable to two or more plausible claim constructions [upon giving it the broadest reasonable interpretation consistent with the Specification], the USPTO is justified in requiring the applicant to more precisely define the metes and bounds of the

claimed invention by holding the claim unpatentable under 35 U.S.C. § 112, second paragraph, as indefinite."); *see also In re Morris*, 127 F.3d 1048, 1056 (Fed. Cir. 1997) ("It is the applicants' burden to precisely define the invention, not the PTO's. *See* 35 U.S.C. § 112, ¶ 2 . . . . [T]his section puts the burden of precise claim drafting squarely on the applicant.").

Since we are unable to determine an acceptable degree of agglomeration or degree of uniformity for any area of a given film to be considered "substantially uniform," we decline to reach the question of whether the '588 patent provides written descriptive support and an enabling disclosure under 35 U.S.C. § 112, first paragraph. *In re Wilson*, 424, F.2d 1382, 1385 (CCPA 1970); *In re Steele*, 305 F.2d 859, 862 (CCPA 1962). However, we will address the propriety of the certain prior art rejections maintained by the Examiner for the sake of administrative and judicial efficiency because we need not understand the exact scope of "substantially uniform" to resolve certain prior art rejections and/or can give a certain conditional interpretation of "substantially uniform" to resolve certain prior art rejections as is readily apparent from the discussions below. *See, e.g., Ex parte Saceman*, 27 USPQ2d 1472, 1474 (Bd. Pat. App. & Int. 1993); *Ex parte Ionescu*, 222 USPQ 537, 540 (Bd. Pat. App. & Int. 1984).

REJECTIONS BASED ON CHEN

Claims 192 and 193 stand rejected under 35 U.S.C. § 102(b) as being anticipated by Chen.[3] Claim 1 and the claims that depend therefrom stand

[3] WO 00/42992, published July 27, 2000, naming Li-Lan Chen et al. as inventors.

rejected under 35 U.S.C. § 102(b) as anticipated by or, in the alternative, under 35 U.S.C. § 103(a) as obvious over Chen, either alone or view of additional prior art.[4] Patent Owner does not argue for the separate patentability of any dependent claims. Accordingly, the dependent claims stand or fall with claim 1.

Patent Owner contends that Chen fails to disclose a step of removing the polar solvent "by exposing the matrix to a temperature greater than the degradation temperature of said therapeutic active composition," as recited in claim 1.[5] Patent Owner argues that Chen teaches away from drying a film at a temperature above the degradation temperature of the therapeutic active composition. PO App. Br. 25-27. Patent Owner relies on the statement in Chen that the film is "dried under aeration at a temperature between 40-100°C so as to avoid destabilizing the agents contained within the formulation." *Id.* at 27; Chen, p. 15, ll. 19-29. Patent Owner argues that by this statement "Chen says such temperatures should be avoided" and that "Chen is concerned about keeping the temperature low to avoid destabilizing active agents." App. Br. 26 and 27.

---

[4] Other additional art combined with Chen includes Le Person (Le Person, et al., "Near infrared drying of pharmaceutical thin films: experimental analysis of internal mass transport," Chem. Eng. Processing, Vol. 37, pp. 257-263 (1998)), Bernstein (US 5,656,297, issued August 12, 1997), Staab (US 5,393,528, issued February 28, 1995) and Hijiya (US 4,562,020, issued December 31, 1985).

[5] Patent Owner does not present separate the arguments with respect to claims 1, 192, and 193. However, only claim 1 includes a requirement that the temperature be greater than the degradation temperature of the therapeutic active composition.

We disagree with Patent Owner that Chen's statement suggests that higher temperatures "should be avoided" or "keeping the temperature low." Rather, Chen teaches a temperature range in order "to avoid destabilizing the agents contained within the formulation." Chen, p. 15, ll. 28-29. We disagree with Patent Owner that this statement would have suggested the skilled artisan limit the drying temperature to any particular temperature within the recited range of 40-100°C, provided that the film does not, in fact, result in degraded active ingredients. Thus, we find this statement in Chen consistent with the '588 patent. *See* '588 patent, col. 12, ll. 33-43.

Moreover, we agree with the Examiner that the skilled artisan would "have optimized Chen's drying step by using as high a drying temperature as possible within Chen's disclosed the range of 40-100°C without destabilizing the active agent because temperature is a results-effective variable with respect to active agent destabilization as taught by Chen; and so as to dry Chen's film as quickly as possible." RAN 28-29 and 74. We note that the example in Chen of drying for only 9 minutes (Chen, p. 17, ll. 13-15) is consistent with the description in the '588 patent of "drying the film within about 10 minutes or fewer." '588 patent, col. 7, ll. 33-35; *see* RAN 74. Patent Owner has not persuasively rebutted the Examiner's rationale as to the skilled artisan's reasonable optimization of temperatures within the range disclosed in Chen.

With respect to all of the claims on appeal, Patent Owner contends that Chen fails to disclose a film having a "substantially uniform content of therapeutic active composition per unit of film." According to Patent Owner, Chen does "not indicate or establish that the substantially uniform

content of the components is such that, for example, the amount of the active in individual dosage units varies by no more than 10% with respect to the desired/label amount for a particular film." App. Br. 28. Patent Owner argues that "[t]he actual degree of uniformity must be established through a determination of the actual amount of therapeutic active in at least samples of dosage units, which Chen does not disclose." *Id.* at 28 and 31-32. Patent Owner further argues that Figure 5 of Chen demonstrates that "in six instances the amount of active released from Chen's films is greater than 110% of the expected/desired amount." *Id.* at 30; Reb. Br. 5-6.

Initially, we note that Patent Owner's arguments substantially rely on Patent Owner's proposed claim interpretation which emphasizes uniformity with respect to a FDA-recognized dosage. For example, Patent Owner emphasizes a lack of evidence to support that the films of Chen are inherently within 10% of a recognized FDA dosage. Reb. Br. 5-6 Also, Patent Owner's arguments with respect to Figure 5 are exclusively related to release of an amount of active being more than 110% of "an expected/desired amount of pharmaceutical active for that drug." Reb. Br. 5.

We did not adopt the Patent Owner's proposed claim interpretation for the reasons discussed above and determine that the term "uniform content of therapeutic active composition" means non-agglomerated and evenly dispersed active content for any area of a given film, with the qualifier "substantially" expanding the scope to encompass some undefined agglomeration or some undefined degree of unevenly dispersed active material to also be acceptable. Accordingly, we do not find Patent Owner's arguments, including those regarding the release data over time in Figure 5

of Chen, to be compelling of a lack of uniformity. Figure 5 does not suggest agglomerated or unevenly dispersed active content for any area of a given film. Figure 5 merely indicates that different amounts of active material releases from the Chen films at various times, which is not shown to be an indicator that the active material is agglomerated or unevenly dispersed.

We agree with the Examiner that there is sufficient evidence to find that Chen inherently discloses a film with a substantially uniform content of therapeutic active composition per unit of film. RAN 21, 69-73, and 75.

In a case such as this where patentability rests upon a property of the claimed material not disclosed within the art, the PTO has no reasonable method of determining whether there is, in fact, a patentable difference between the prior art materials and the claimed material. Therefore, where the claimed and prior art products are identical or substantially identical, or are produced by identical or substantially identical processes, the PTO can require an applicant to prove that the prior art products do not necessarily possess the characteristics of his claimed product. *In re Spada*, 911 F.2d 705, 708 (Fed. Cir. 1990); *In re Best*, 562 F.2d 1252, 1255 (CCPA 1977). However, the initial burden of presenting a case of unpatentability remains with the Requester and Examiner. If that burden is met, only then does the burden of coming forward with evidence or argument shift to the Patent Owner. *See In re Oetiker*, 977 F.2d 1443, 1445 (Fed. Cir. 1992).

Although Patent Owner argues that the drying process of Chen is a conventional drying method that is distinguishable from the drying process of the '588 patent (App. Br. 29; Reb. Br. 14-15), we find that Chen describes

a substantially identical process to that described in the '588 patent. RAN 70 and 75.

Claim 1 does not recite any particular film drying steps. The evidence does not support Patent Owner's contention that the processes disclosed in Chen and in the '588 patent are clearly distinguishable. The '588 patent describes its drying process generally and does not clearly identify how a drying step can vary from a conventional drying process and avoid agglomerations of the active ingredients. For example, the '588 patent states that agglomerations form from "conventional drying methods such as a high-temperature air-bath using a drying oven, drying tunnel, vacuum drier, or other such drying equipment." However, the description of non-agglomerating drying methods in the '588 patent does not clearly distinguish such drying equipment. *See* col. 14, ll. 13-14 ("the inventive process is not limited to any particular apparatus for the above-described desirable drying."). The '588 patent is not limited to any particular drying methods but rather includes a variety of drying methods. *Id.* col. 7, ll. 6-25; col. 25, ll. 15-16 ("When a controlled or rapid drying process is desired, this may be through a variety of methods."). The only process clearly distinguished by the '588 patent is "uncontrolled air currents, either above or below the film" which "can create non-uniformity in the final film product." *Id.*, col. 7, ll. 19-21; *see also* col. 6, ll. 50-61; col. 12, ll. 47-57 ("The films are Controllably dried to prevent aggregation and migration of components, as well as preventing heat build up within."); col. 10, l. 67-col. 11, l. 4; col. 13, ll. 13-15; col. 25, ll. 2-8. The '588 patent does not exclude top air flow (*id.* at col. 11, ll. 6-23) nor does the '588 patent require bottom directed

drying, since it only describes this process as either exemplary or preferable. *See id.* at col. 6, ll. 53-58; col. 7, ll. 6-8; col. 12, ll. 56-57; col. 25, ll. 22-23.

Chen describes a process in which a film is dried in a "drying oven with aeration controller" as illustrated in Figure 2. Chen, p. 6, l. 2. Figure 2 is reproduced below.

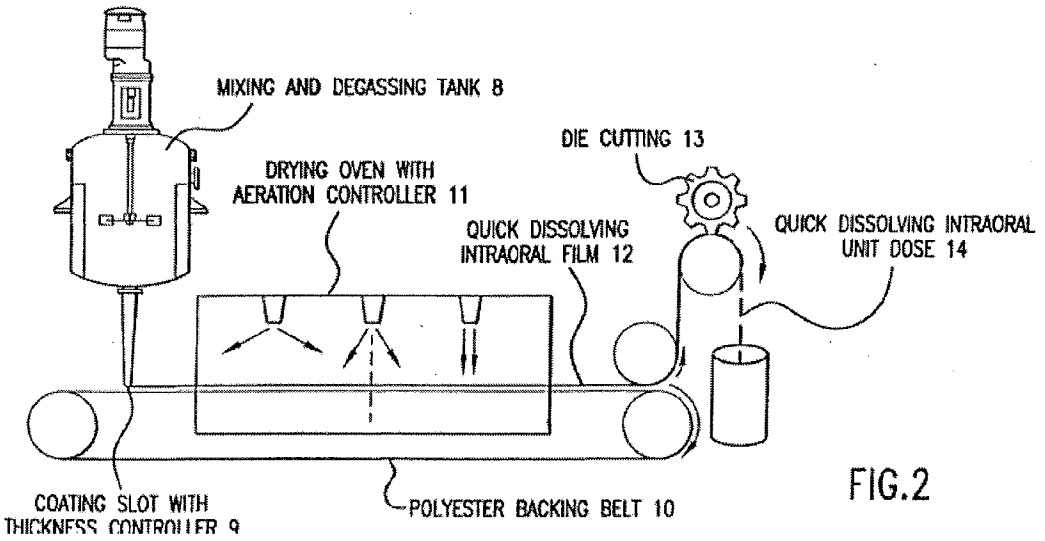


Figure 2 depicts a schematic of a manufacturing process for a dosage unit. Chen, p. 5, l. 31-p. 6, l. 3.

Figure 2 shows that at the initial drying stage, air currents are not directed onto the top of the film. Thus, we find that Chen teaches controlled drying and avoiding air currents directed onto the top surface of a film. The drying process of Chen is not sufficiently distinguished from the general drying method of the '588 patent.

Patent Owner's position is supported by the testimony of Dr. Rounds,[6] who testifies that Chen uses "a high presence of air flowing over the surface(s) of the wet film product" and that "uneven air currents flow[ing] over the wet film surface . . . can cause disruption of the fluid matrix and the components held therein, causing compositional non-uniformity of active content in the final, resulting film product." Rounds Decl. ¶ 16. We give little weight to Dr. Rounds' testimony because neither the "hot air circulating oven" nor the controlled air flow of Chen is distinguished from the equipment of the '588 patent. Dr. Rounds does not address Figure 2 which appears to show air diverted from the wet film surface consistent with the requirement for "controlled drying" in the '588 patent.

Moreover, the Examiner also finds that Chen's Table 4 describes weight per dosage film, thickness, density and water content measurements with minimal deviation as evidence that substantially uniform content of therapeutic active is inherent in the films described by Chen. RAN 15 and 71; *see* Chen p. 20, Table 4. The measured weight per dosage film as described in Chen is consistent with the additive weight test described in the '588 patent for determining uniformity. Specifically, the '588 patent states: "when the components of different densities are combined in a uniform manner in a film, as in the present invention, individual dosages forms from the same film of substantially equal dimensions, will contain the same mass." '588 patent, col. 29, ll. 4-9. Because the claims require only a "substantially uniform" film, which is broader than complete uniformity, but

[6] Declaration of Rhyta S. Rounds, dated January 9, 2012 and entered into the record on January 10, 2012 with Patent Owner's Response (hereinafter "Rounds Declaration" or "Rounds Decl.").

indefinite as to the degree of agglomeration or unevenly dispersed active material that would still be considered substantially uniform, for the purpose of applying art to the claims, we find that a weight deviation of ± 0.001 satisfies the limitation of "substantially uniform" active content. This amount is well within the less than 10% variation of active content per film unit requirement of claim 3.[7] Patent Owner does not persuasively show a distinction between the additive weight test of the '588 patent and the consistent weight measurements of Chen.

Accordingly, the Examiner's finding of inherency based on the processes of Chen and the '588 patent being "substantially identical" is supported by the evidence of record, as well as the Examiner's finding that Chen teaches films with consistent weight per unit film. Accordingly, the burden was properly shifted to Patent Owner to demonstrate that the process of Chen does not, in fact, teach a film having a substantially uniform content of therapeutic active composition per unit of film.

REJECTIONS BASED ON PEH

Claims 192 and 193 stand rejected under 35 U.S.C. § 102(b) as being anticipated by or, in the alternative, under 35 U.S.C. § 103(a) as obvious over Peh,[8] either alone or in view of additional prior art.[9]

---

[7] While Patent Owner does not clearly argue the limitation of claim 3 separately from independent claims 1, 192 and 193, we note that Patent Owner refers to claim 3 in distinguishing the scope over that of claim 1. App. Br. 23; Reb. Br. 3.

[8] Kok Khiang Peh et al., "Polymeric Films as Vehicle for Buccal Delivery: Swelling, Mechanical, and Bioadhesive Properties," J. Pharm. Pharmaceut. Sci., Vol. 2, No. 2, pp. 53-61 (1999).

In affirming the rejection of claims 192 and 193 as anticipated by Chen under 35 U.S.C. § 102(b) and as unpatentable under 35 U.S.C. § 112, it is unnecessary to address the additional rejections maintained by the Examiner for claims 192 and 193. *See In re Gleave*, 560 F.3d 1331, 1338 (Fed. Cir. 2009) (holding that obviousness rejections need not be reached upon affirming a rejection of all claims as anticipated).

SUMMARY

For the reasons discussed above, we affirm the Examiner's rejections of:

1. Claims 1-24, 75, 78, 81, 84, 87, 90, 93, 96, 99, 102, 105, 106, 111-132, 177, 178, 183, 186, 189, 192, and 193, under 35 U.S.C. § 112, as being indefinite;
2. Claims 25-28, 30-33, 35, 36, 40, 42-53, 55-58, 60, 61, 65, 67-74, 76, 77, 79, 80, 82, 83, 85, 86, 88, 89, 91, 92, 94, 95, 97, 98, 100, 101, 103, 104, 107-110, 133-139, 141-143, 155-161, 163-165, 179-182, 184, 185, 187, 188, 190-193 under 35 U.S.C. § 102(b) as being anticipated by Chen;
3. Claims 1-3, 5-8, 10, 11, 15, 17-24, 75, 78, 81, 84, 87, 90, 93, 96, 99, 102, 105, 106, 111-117, 119-121, 177, 178, 183, 186, and 189 under 35 U.S.C. § 102(b) as anticipated by or, in the alternative, under 35 U.S.C. § 103(a) as obvious over Chen;
4. Claims 4, 14, 29, 39, 54, 64, 118, 140, and 162 under 35 U.S.C. § 103(a) as being unpatentable over Chen;
5. Claims 1, 122-132, 144-154 and 166-176 under 35 U.S.C. § 103(a) as being unpatentable over the combination of Chen and Le Person;
6. Claims 2, 5, 8, 9, 12, 15, 16, 18, 34, 37, 41, 59, 62, 66, 84, 99, 113, and 121 under 35 U.S.C. § 103(a) as being unpatentable over the combination of Chen and Bernstein;

---

[9] Other additional art combined with Peh includes Le Person, Staab, Chen, Strobush (U.S. 5,881,476, issued March 16, 1999), Bernstein, and Hijiya.

7. Claims 13, 14, 17, 38, 39, 42, 63, 64 and 67 under 35 U.S.C. § 103(a) as being unpatentable over Chen in combination with Staab or Hijiya;
8. Claims 2, 5, 8, 15, 84, 99 and 113 under 35 U.S.C. § 103(a) as being unpatentable over the combination of Chen and Hijiya.

For the reasons discussed above, we do not reach the Examiner's rejections based on 35 U.S.C. § 112, first paragraph, or the Examiner's rejections based on the teachings of Peh alone or in view of additional prior art.

TIME PERIOD FOR RESPONSE

In accordance with 37 C.F.R. § 41.79(a)(1), the "[p]arties to the appeal may file a request for rehearing of the decision within one month of the date of: . . . [t]he original decision of the Board under § 41.77(a)." A request for rehearing must be in compliance with 37 C.F.R. § 41.79(b). Comments in opposition to the request and additional requests for rehearing must be in accordance with 37 C.F.R. § 41.79(c) & (d), respectively. Under 37 C.F.R. § 41.79(e), the times for requesting rehearing under paragraph (a) of this section, for requesting further rehearing under paragraph (d) of this section, and for submitting comments under paragraph (c) of this section may not be extended.

An appeal to the United States Court of Appeals for the Federal Circuit under 35 U.S.C. §§ 141-144 and 315 and 37 C.F.R. § 1.983 for an *inter partes* reexamination proceeding "commenced" on or after November 2, 2002 may not be taken "until all parties' rights to request rehearing have been exhausted, at which time the decision of the Board is final and appealable by any party to the appeal to the Board." 37 C.F.R.

§ 41.81. *See also* MPEP § 2682 (8th ed., Rev. 7, July 2008). In the event neither party files a request for rehearing within the time provided in 37 C.F.R. § 41.79, and this decision becomes final and appealable under 37 C.F.R. § 41.81, a party seeking judicial review must timely serve notice on the Director of the United States Patent and Trademark Office. *See* 37 C.F.R. §§ 90.1 and 1.983.

AFFIRMED

ak

PATENT OWNER:

Hoffmann & Baron, LLP
6900 Jericho Turnpike
Syosset, NY 11791

THIRD-PARTY REQUESTER:

McCarter & English, LLP
265 Franklin Street
Boston, MA 02110

Electronic Acknowledgement Receipt

EFS ID:	20450825
Application Number:	95002170
International Application Number:	
Confirmation Number:	6418
Title of Invention:	POLYETHYLENE-OXIDE BASED FILMS AND DRUG DELIVERY SYSTEMS MADE THEREFROM
First Named Inventor/Applicant Name:	7897080
Customer Number:	23869
Filer:	Danielle L. Herritt/Maureen Tierney
Filer Authorized By:	Danielle L. Herritt
Attorney Docket Number:	117744-00023
Receipt Date:	17-OCT-2014
Filing Date:	10-SEP-2012
Time Stamp:	16:52:15
Application Type:	inter partes reexam

Payment information:

Submitted with Payment	no

File Listing:

Document Number	Document Description	File Name	File Size(Bytes)/ Message Digest	Multi Part /.zip	Pages (if appl.)
1	Miscellaneous Incoming Letter	080UpdateOnRelatedAppealW588DecisionFINAL2014OCT17.PDF	1226067 41527131f7d795e12ccf33e7528a9e99bd58d6ba	no	26

Warnings:	
Information:	

Total Files Size (in bytes):	1226067

This Acknowledgement Receipt evidences receipt on the noted date by the USPTO of the indicated documents, characterized by the applicant, and including page counts, where applicable. It serves as evidence of receipt similar to a Post Card, as described in MPEP 503.

New Applications Under 35 U.S.C. 111

If a new application is being filed and the application includes the necessary components for a filing date (see 37 CFR 1.53(b)-(d) and MPEP 506), a Filing Receipt (37 CFR 1.54) will be issued in due course and the date shown on this Acknowledgement Receipt will establish the filing date of the application.

National Stage of an International Application under 35 U.S.C. 371

If a timely submission to enter the national stage of an international application is compliant with the conditions of 35 U.S.C. 371 and other applicable requirements a Form PCT/DO/EO/903 indicating acceptance of the application as a national stage submission under 35 U.S.C. 371 will be issued in addition to the Filing Receipt, in due course.

New International Application Filed with the USPTO as a Receiving Office

If a new international application is being filed and the international application includes the necessary components for an international filing date (see PCT Article 11 and MPEP 1810), a Notification of the International Application Number and of the International Filing Date (Form PCT/RO/105) will be issued in due course, subject to prescriptions concerning national security, and the date shown on this Acknowledgement Receipt will establish the international filing date of the application.

The United States Patent and Trademark Office
PATENT TRIAL AND APPEAL BOARD

DANIELLE L. HERRITT
MCCARTER & ENGLISH LLP,
265 FRANKLIN STREET
BOSTON, MA 02110

Appeal No:	2014-007,671
Appellant:	DANIELLE L. HERRI TT(3RD.PTY.REQ.), BIO
Reexam Control No:	DELIVERY SCIENCE INTERNATIONet al.
Hearing Room:	95/002,170
Hearing Docket:	B
Hearing Date:	A
Hearing Time:	Wednesday, November 05, 2014
Location:	01:00 PM Madison Building - East Wing 600 Dulany Street, 9th Floor Alexandria, Virginia 22313-1450

NOTICE OF HEARING
RESPONSE REQUIRED WITHIN 21 DAYS

Your attention is directed to 37 CFR § 41.73. The above identified appeal will be heard by the Patent Trial and Appeal Board on the date indicated. Hearings will commence at the time set, and as soon as the argument in one appeal is concluded, the succeeding appeal will be taken up. **The time allowed for argument is 30 minutes** for each appellant or respondent who has requested an oral hearing, unless additional time is requested and approved before the argument commences. **As the hearing relates to an appeal of a reexamination, the hearing will be open to the public.**

Pursuant to § 41.73(d), if any other party to the appeal desires to participate in the oral hearing, but did not request an oral hearing pursuant to § 41.73(d), i.e., within two months after the mailing date of the Examiner's Answer, then this other party will be permitted to participate in the hearing by filing a separate request for oral hearing and the fee set forth in 37 C.F.R. § 41.20(b)(3) within 21 DAYS of the mailing date of this Notice, as well as a confirmation of attendance at the oral hearing.

CONFIRMATION OF ATTENDANCE OR WAIVER OF THE HEARING IS REQUIRED WITHIN **21 DAYS** OF THE MAILING DATE OF THIS NOTICE. Failure to respond will be treated as a waiver of your request to participate in the oral hearing. If you are no longer interested in participating in the oral hearing, you must still file a waiver of oral hearing with the Board. This allows the panel to promptly act on the appeal without waiting for the oral hearing date.

Confirmation or waiver of the hearing should be indicated by completing the form below and returning it to the Board. This form may be filed with the Board by any one of the following three alternative methods:

1. ***PREFERRED***: Via the USPTO Electronic Filing System (EFS) at

http://www.uspto.gov/patents/process/file/efs/

2. Facsimile transmitted to: The USPTO Central fax number (official copy): **(571) 273-8300**
and the PTAB Hearing fax number (courtesy copy): **(571) 273-9797.**

3. By mail at the PTAB mailing address: Patent Trial and Appeal Board
United States Patent and Trademark Office
P.O. BOX 1450
Alexandria, Virginia 22313-1450

In all communications relating to this appeal, please identify the appeal by its number.

CHECK ONE:
(X) I previously filed my oral hearing request pursuant to 37 C.F.R. § 41.73(b).
( ) I am now filing my initial request to participate in the oral hearing pursuant to 37 C.F. R. § 41.73(d). A request for oral hearing and the fee set forth in 37 C.F.R. § 41.20(b)(3) are either attached to this hearing communication or have already been submitted.

CHECK ONE:
(X) IN-PERSON HEARING - ATTENDANCE CONFIRMED *(EFS-Web selection: Confirmation of Hearing by Appellant)*
( ) TELEPHONIC HEARING - ATTENDANCE CONFIRMED *(EFS-Web selection: Confirmation of Hearing by Appellant)*
( ) VIDEO HEARING - ATTENDANCE CONFIRMED *(EFS-Web selection: Confirmation of Hearing by Appellant)*
( ) HEARING ATTENDANCE WAIVED *(EFS-Web selection: Waiver of Hearing by Appellant)*

To aid the oral hearings staff in scheduling hearing rooms, please indicate the total number of participating and observing attendees if more than three are expected: _____
To aid the judges in determining whether any conflicts exist that may require a recusal, please list in the 'Comments' section the names of any additional person(s) who will be participating in the oral hearing. (Upon arrival, all persons presenting arguments must sign in at the Usher's desk.)

Comments/Special Requests:

Request: ELMO Projector

Danielle L. Herritt	43,670
Typed or Printed Name of Attorney/Agent/Appellant	Registration No.

( ) PATENT OWNER (X) THIRD PARTY REQUESTER

/Danielle L. Herritt/	October 2, 2014
Signature of Attorney/Agent/Appellant	Date

The 'Hearings' tab of the PTAB webpage http://www.uspto.gov/ip/boards/bpai/index.jsp provides additional information about oral hearings.

Please direct other inquiries to the PTAB Hearings Clerk at 571-272-9797.

cc: Patent Owner

HOFFMANN & BARON LLP
6900 JERICHO TURNPIKE
SYOSSET, NY 11791

UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
95/002,170	09/10/2012	7897080	117744-00023	6418

23869 7590 09/16/2014

Hoffmann & Baron LLP
6900 Jericho Turnpike
Syosset, NY 11791

EXAMINER	
DIAMOND, ALAN D	
ART UNIT	PAPER NUMBER
3991	

MAIL DATE	DELIVERY MODE
09/16/2014	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

CERTIFICATE OF SERVICE

The undersigned hereby certifies that a copy of the foregoing Third Party Requester's Confirmation of Attendance at Oral Hearing was served on October 2, 2014, by first class mail, directed to the patent owner at the correspondence address of record for the subject patent, that is:

Daniel A. Scola, Jr.

HOFFMANN & BARON, LLP

6900 JERICHO TURNPIKE

SYOSSET, NY 11791

By: /Danielle L. Herritt/
Danielle L. Herritt
Registration No. 43,670
Attorney for Third Party Requester

Electronic Acknowledgement Receipt

EFS ID:	20310915
Application Number:	95002170
International Application Number:	
Confirmation Number:	6418
Title of Invention:	POLYETHYLENE-OXIDE BASED FILMS AND DRUG DELIVERY SYSTEMS MADE THEREFROM
First Named Inventor/Applicant Name:	7897080
Customer Number:	23869
Filer:	Danielle L. Herritt/Maureen Tierney
Filer Authorized By:	Danielle L. Herritt
Attorney Docket Number:	117744-00023
Receipt Date:	02-OCT-2014
Filing Date:	10-SEP-2012
Time Stamp:	13:48:05
Application Type:	inter partes reexam

Payment information:

Submitted with Payment	no

File Listing:

Document Number	Document Description	File Name	File Size(Bytes)/ Message Digest	Multi Part /.zip	Pages (if appl.)
1	Reexam Miscellaneous Incoming Letter	080IPRxConfirmationOfAttendance2014OCT2.PDF	1107471 a223e7546a38b22d80e91a09f55dfb35ef776fed	no	4

Warnings:

Information:

2	Reexam Certificate of Service	080COSforConfirmationOfHearing2014OCT2.PDF	16036 03be71507f275d2cd70eea60aacac82e1e3f332f	no	1

Warnings:	
Information:	
Total Files Size (in bytes):	1123507

This Acknowledgement Receipt evidences receipt on the noted date by the USPTO of the indicated documents, characterized by the applicant, and including page counts, where applicable. It serves as evidence of receipt similar to a Post Card, as described in MPEP 503.

New Applications Under 35 U.S.C. 111
If a new application is being filed and the application includes the necessary components for a filing date (see 37 CFR 1.53(b)-(d) and MPEP 506), a Filing Receipt (37 CFR 1.54) will be issued in due course and the date shown on this Acknowledgement Receipt will establish the filing date of the application.

National Stage of an International Application under 35 U.S.C. 371
If a timely submission to enter the national stage of an international application is compliant with the conditions of 35 U.S.C. 371 and other applicable requirements a Form PCT/DO/EO/903 indicating acceptance of the application as a national stage submission under 35 U.S.C. 371 will be issued in addition to the Filing Receipt, in due course.

New International Application Filed with the USPTO as a Receiving Office
If a new international application is being filed and the international application includes the necessary components for an international filing date (see PCT Article 11 and MPEP 1810), a Notification of the International Application Number and of the International Filing Date (Form PCT/RO/105) will be issued in due course, subject to prescriptions concerning national security, and the date shown on this Acknowledgement Receipt will establish the international filing date of the application.

The United States Patent and Trademark Office
PATENT TRIAL AND APPEAL BOARD

HOFFMANN & BARON LLP
6900 JERICHO TURNPIKE
SYOSSET, NY 11791

Appeal No:	2014-007,671
Appellant:	MONOSOL RX, LLC(OWNER), et al.
Reexam Control No:	95/002,170
Hearing Room:	B
Hearing Docket:	A
Hearing Date:	Wednesday, November 05, 2014
Hearing Time:	01:00 PM
Location:	Madison Building - East Wing 600 Dulany Street, 9th Floor Alexandria, Virginia 22313-1450

NOTICE OF HEARING
RESPONSE REQUIRED WITHIN 21 DAYS

Your attention is directed to 37 CFR § 41.73. The above identified appeal will be heard by the Patent Trial and Appeal Board on the date indicated. Hearings will commence at the time set, and as soon as the argument in one appeal is concluded, the succeeding appeal will be taken up. **The time allowed for argument is 30 minutes** for each appellant or respondent who has requested an oral hearing, unless additional time is requested and approved before the argument commences. **As the hearing relates to an appeal of a reexamination, the hearing will be open to the public.**

Pursuant to § 41.73(d), if any other party to the appeal desires to participate in the oral hearing, but did not request an oral hearing pursuant to § 41.73(d), i.e., within two months after the mailing date of the Examiner's Answer, then this other party will be permitted to participate in the hearing by filing a separate request for oral hearing and the fee set forth in 37 C.F.R. § 41.20(b)(3) within 21 DAYS of the mailing date of this Notice, as well as a confirmation of attendance at the oral hearing.

CONFIRMATION OF ATTENDANCE OR WAIVER OF THE HEARING IS REQUIRED WITHIN **21 DAYS** OF THE MAILING DATE OF THIS NOTICE. Failure to respond will be treated as a waiver of your request to participate in the oral hearing. If you are no longer interested in participating in the oral hearing, you must still file a waiver of oral hearing with the Board. This allows the panel to promptly act on the appeal without waiting for the oral hearing date.

Confirmation or waiver of the hearing should be indicated by completing the form below and returning it to the Board. This form may be filed with the Board by any one of the following three alternative methods:

1. ***PREFERRED***: Via the USPTO Electronic Filing System (EFS) at

http://www.uspto.gov/patents/process/file/efs/

2. Facsimile transmitted to: The USPTO Central fax number (official copy): **(571) 273-8300**
and the PTAB Hearing fax number (courtesy copy): **(571) 273-9797.**

3. By mail at the PTAB mailing address: Patent Trial and Appeal Board
United States Patent and Trademark Office
P.O. BOX 1450
Alexandria, Virginia 22313-1450

In all communications relating to this appeal, please identify the appeal by its number.

CHECK ONE:
(X) I previously filed my oral hearing request pursuant to 37 C.F.R. § 41.73(b).
( ) I am now filing my initial request to participate in the oral hearing pursuant to 37 C.F. R. § 41.73(d). A request for oral hearing and the fee set forth in 37 C.F.R. § 41.20(b)(3) are either attached to this hearing communication or have already been submitted.

CHECK ONE:
(X) IN-PERSON HEARING - ATTENDANCE CONFIRMED *(EFS-Web selection: Confirmation of Hearing by Appellant)*
( ) TELEPHONIC HEARING - ATTENDANCE CONFIRMED *(EFS-Web selection: Confirmation of Hearing by Appellant)*
( ) VIDEO HEARING - ATTENDANCE CONFIRMED *(EFS-Web selection: Confirmation of Hearing by Appellant)*
( ) HEARING ATTENDANCE WAIVED *(EFS-Web selection: Waiver of Hearing by Appellant)*

To aid the oral hearings staff in scheduling hearing rooms, please indicate the total number of participating and observing attendees if more than three are expected: 6
To aid the judges in determining whether any conflicts exist that may require a recusal, please list in the 'Comments' section the names of any additional person(s) who will be participating in the oral hearing. (Upon arrival, all persons presenting arguments must sign in at the Usher's desk.)

Comments/Special Requests:

ADDITIONAL PARTICIPANT: MICHAEL I. CHAKANSKY (REG. No. 31,600)
REQUEST: USE OF AN ELMO PROJECTOR & AV EQUIPMENT TO DISPLAY POWERPOINT SLIDES WITH USB CONNECTION

DANIEL A. SCOLA, JR. — 29,855
Typed or Printed Name of Attorney/Agent/Appellant — Registration No.

(X) PATENT OWNER ( ) THIRD PARTY REQUESTER

Signature of Attorney/Agent/Appellant

9/22/14
Date

The 'Hearings' tab of the PTAB webpage http://www.uspto.gov/ip/boards/bpai/index.jsp provides additional information about oral hearings.

Please direct other inquiries to the PTAB Hearings Clerk at 571-272-9797.

cc: Third Party Requester

DANIELLE L. HERRITT
MCCARTER & ENGLISH LLP,
265 FRANKLIN STREET
BOSTON, MA 02110

UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
95/002,170	09/10/2012	7897080	117744-00023	6418

23869 7590 09/16/2014

Hoffmann & Baron LLP
6900 Jericho Turnpike
Syosset, NY 11791

EXAMINER	
DIAMOND, ALAN D	
ART UNIT	PAPER NUMBER
3991	
MAIL DATE	DELIVERY MODE
09/16/2014	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

CERTIFICATE OF FIRST CLASS SERVICE

It is certified that a copy of the foregoing Patent Owner's Confirmation of Attendance at Oral Hearing was served, by first class mail, postage prepaid, on September 22, 2014, in its entirety on the Respondent, Third Party Requester (Respondent) as provided in 37 CFR § 1.903, 37 CFR § 1.248 and 37 C.F.R. § 41.73(b) at the address below.

DANIELLE L. HERRITT
McCARTER & ENGLISH LLP
265 FRANKLIN STREET
BOSTON, MASSACHUSETTS 02110

/Michael I. Chakansky/
Michael I. Chakansky
Registration No.: 31,600
Attorney for the Patentee/Appellant

Electronic Acknowledgement Receipt

EFS ID:	20200964
Application Number:	95002170
International Application Number:	
Confirmation Number:	6418
Title of Invention:	POLYETHYLENE-OXIDE BASED FILMS AND DRUG DELIVERY SYSTEMS MADE THEREFROM
First Named Inventor/Applicant Name:	7897080
Customer Number:	23869
Filer:	Michael I. Chakansky
Filer Authorized By:	
Attorney Docket Number:	117744-00023
Receipt Date:	22-SEP-2014
Filing Date:	10-SEP-2012
Time Stamp:	12:00:11
Application Type:	inter partes reexam

Payment information:

Submitted with Payment	no

File Listing:

Document Number	Document Description	File Name	File Size(Bytes)/ Message Digest	Multi Part /.zip	Pages (if appl.)
1	Confirmation of Hearing by Appellant	PatentOwnersConfirmation.pdf	1722712 1f3252299a946da668adf805ff5a386f146a9a2b	no	5

Warnings:	
Information:	

Total Files Size (in bytes):	1722712

This Acknowledgement Receipt evidences receipt on the noted date by the USPTO of the indicated documents, characterized by the applicant, and including page counts, where applicable. It serves as evidence of receipt similar to a Post Card, as described in MPEP 503.

New Applications Under 35 U.S.C. 111

If a new application is being filed and the application includes the necessary components for a filing date (see 37 CFR 1.53(b)-(d) and MPEP 506), a Filing Receipt (37 CFR 1.54) will be issued in due course and the date shown on this Acknowledgement Receipt will establish the filing date of the application.

National Stage of an International Application under 35 U.S.C. 371

If a timely submission to enter the national stage of an international application is compliant with the conditions of 35 U.S.C. 371 and other applicable requirements a Form PCT/DO/EO/903 indicating acceptance of the application as a national stage submission under 35 U.S.C. 371 will be issued in addition to the Filing Receipt, in due course.

New International Application Filed with the USPTO as a Receiving Office

If a new international application is being filed and the international application includes the necessary components for an international filing date (see PCT Article 11 and MPEP 1810), a Notification of the International Application Number and of the International Filing Date (Form PCT/RO/105) will be issued in due course, subject to prescriptions concerning national security, and the date shown on this Acknowledgement Receipt will establish the international filing date of the application.

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
95/002,170	09/10/2012	7897080	117744-00023	6418

23869 7590 09/16/2014

Hoffmann & Baron LLP
6900 Jericho Turnpike
Syosset, NY 11791

EXAMINER	
DIAMOND, ALAN D	

ART UNIT	PAPER NUMBER
3991	

MAIL DATE	DELIVERY MODE
09/16/2014	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

The United States Patent and Trademark Office
PATENT TRIAL AND APPEAL BOARD

DANIELLE L. HERRITT
MCCARTER & ENGLISH LLP,
265 FRANKLIN STREET
BOSTON, MA 02110

Appeal No:	2014-007,671
Appellant:	DANIELLE L. HERRI TT(3RD.PTY.REQ.), BIO
Reexam Control No:	DELIVERY SCIENCE INTERNATIONet al.
Hearing Room:	95/002,170
Hearing Docket:	B
Hearing Date:	A
Hearing Time:	Wednesday, November 05, 2014
Location:	01:00 PM Madison Building - East Wing 600 Dulany Street, 9th Floor Alexandria, Virginia 22313-1450

NOTICE OF HEARING
RESPONSE REQUIRED WITHIN 21 DAYS

Your attention is directed to 37 CFR § 41.73. The above identified appeal will be heard by the Patent Trial and Appeal Board on the date indicated. Hearings will commence at the time set, and as soon as the argument in one appeal is concluded, the succeeding appeal will be taken up. **The time allowed for argument is 30 minutes** for each appellant or respondent who has requested an oral hearing, unless additional time is requested and approved before the argument commences. **As the hearing relates to an appeal of a reexamination, the hearing will be open to the public.**

Pursuant to § 41.73(d), if any other party to the appeal desires to participate in the oral hearing, but did not request an oral hearing pursuant to § 41.73(d), i.e., within two months after the mailing date of the Examiner's Answer, then this other party will be permitted to participate in the hearing by filing a separate request for oral hearing and the fee set forth in 37 C.F.R. § 41.20(b)(3) within 21 DAYS of the mailing date of this Notice, as well as a confirmation of attendance at the oral hearing.

CONFIRMATION OF ATTENDANCE OR WAIVER OF THE HEARING IS REQUIRED WITHIN **21 DAYS** OF THE MAILING DATE OF THIS NOTICE. Failure to respond will be treated as a waiver of your request to participate in the oral hearing. If you are no longer interested in participating in the oral hearing, you must still file a waiver of oral hearing with the Board. This allows the panel to promptly act on the appeal without waiting for the oral hearing date.

Confirmation or waiver of the hearing should be indicated by completing the form below and returning it to the Board. This form may be filed with the Board by any one of the following three alternative methods:

1. ***PREFERRED***: Via the USPTO Electronic Filing System (EFS) at

   http://www.uspto.gov/patents/process/file/efs/

2. Facsimile transmitted to: The USPTO Central fax number (official copy): **(571) 273-8300**
   and the PTAB Hearing fax number (courtesy copy): **(571) 273-9797.**

3. By mail at the PTAB mailing address: Patent Trial and Appeal Board
   United States Patent and Trademark Office
   P.O. BOX 1450
   Alexandria, Virginia 22313-1450

In all communications relating to this appeal, please identify the appeal by its number.

CHECK ONE:
( ) I previously filed my oral hearing request pursuant to 37 C.F.R. § 41.73(b).
( ) I am now filing my initial request to participate in the oral hearing pursuant to 37 C.F. R. § 41.73(d). A request for oral hearing and the fee set forth in 37 C.F.R. § 41.20(b)(3) are either attached to this hearing communication or have already been submitted.

CHECK ONE:
( ) IN-PERSON HEARING - ATTENDANCE CONFIRMED *(EFS-Web selection: Confirmation of Hearing by Appellant)*
( ) TELEPHONIC HEARING - ATTENDANCE CONFIRMED *(EFS-Web selection: Confirmation of Hearing by Appellant)*
( ) VIDEO HEARING - ATTENDANCE CONFIRMED *(EFS-Web selection: Confirmation of Hearing by Appellant)*
( ) HEARING ATTENDANCE WAIVED *(EFS-Web selection: Waiver of Hearing by Appellant)*

To aid the oral hearings staff in scheduling hearing rooms, please indicate the total number of participating and observing attendees if more than three are expected: _____
To aid the judges in determining whether any conflicts exist that may require a recusal, please list in the 'Comments' section the names of any additional person(s) who will be participating in the oral hearing. (Upon arrival, all persons presenting arguments must sign in at the Usher's desk.)

Comments/Special Requests:

_____

_____

Typed or Printed Name of Attorney/Agent/Appellant	Registration No.

( ) PATENT OWNER ( ) THIRD PARTY REQUESTER

Signature of Attorney/Agent/Appellant	Date

The 'Hearings' tab of the PTAB webpage http://www.uspto.gov/ip/boards/bpai/index.jsp provides additional information about oral hearings.

Please direct other inquiries to the PTAB Hearings Clerk at 571-272-9797.

cc: Patent Owner

HOFFMANN & BARON LLP
6900 JERICHO TURNPIKE
SYOSSET, NY 11791

UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
95/002,170	09/10/2012	7897080	117744-00023	6418

23869 7590 09/16/2014

Hoffmann & Baron LLP
6900 Jericho Turnpike
Syosset, NY 11791

EXAMINER	
DIAMOND, ALAN D	

ART UNIT	PAPER NUMBER
3991	

MAIL DATE	DELIVERY MODE
09/16/2014	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

The United States Patent and Trademark Office
PATENT TRIAL AND APPEAL BOARD

HOFFMANN & BARON LLP
6900 JERICHO TURNPIKE
SYOSSET, NY 11791

Appeal No:	2014-007,671
Appellant:	MONOSOL RX, LLC(OWNER), et al.
Reexam Control No:	95/002,170
Hearing Room:	B
Hearing Docket:	A
Hearing Date:	Wednesday, November 05, 2014
Hearing Time:	01:00 PM
Location:	Madison Building - East Wing 600 Dulany Street, 9th Floor Alexandria, Virginia 22313-1450

NOTICE OF HEARING
RESPONSE REQUIRED WITHIN 21 DAYS

Your attention is directed to 37 CFR § 41.73. The above identified appeal will be heard by the Patent Trial and Appeal Board on the date indicated. Hearings will commence at the time set, and as soon as the argument in one appeal is concluded, the succeeding appeal will be taken up. **The time allowed for argument is 30 minutes** for each appellant or respondent who has requested an oral hearing, unless additional time is requested and approved before the argument commences. **As the hearing relates to an appeal of a reexamination, the hearing will be open to the public.**

Pursuant to § 41.73(d), if any other party to the appeal desires to participate in the oral hearing, but did not request an oral hearing pursuant to § 41.73(d), i.e., within two months after the mailing date of the Examiner's Answer, then this other party will be permitted to participate in the hearing by filing a separate request for oral hearing and the fee set forth in 37 C.F.R. § 41.20(b)(3) within 21 DAYS of the mailing date of this Notice, as well as a confirmation of attendance at the oral hearing.

CONFIRMATION OF ATTENDANCE OR WAIVER OF THE HEARING IS REQUIRED WITHIN **21 DAYS** OF THE MAILING DATE OF THIS NOTICE. Failure to respond will be treated as a waiver of your request to participate in the oral hearing. If you are no longer interested in participating in the oral hearing, you must still file a waiver of oral hearing with the Board. This allows the panel to promptly act on the appeal without waiting for the oral hearing date.

Confirmation or waiver of the hearing should be indicated by completing the form below and returning it to the Board. This form may be filed with the Board by any one of the following three alternative methods:

1. ***PREFERRED***: Via the USPTO Electronic Filing System (EFS) at

http://www.uspto.gov/patents/process/file/efs/

2. Facsimile transmitted to: The USPTO Central fax number (official copy): **(571) 273-8300**
and the PTAB Hearing fax number (courtesy copy): **(571) 273-9797.**

3. By mail at the PTAB mailing address: Patent Trial and Appeal Board
United States Patent and Trademark Office
P.O. BOX 1450
Alexandria, Virginia 22313-1450

In all communications relating to this appeal, please identify the appeal by its number.

CHECK ONE:
( ) I previously filed my oral hearing request pursuant to 37 C.F.R. § 41.73(b).
( ) I am now filing my initial request to participate in the oral hearing pursuant to 37 C.F. R. § 41.73(d). A request for oral hearing and the fee set forth in 37 C.F.R. § 41.20(b)(3) are either attached to this hearing communication or have already been submitted.

CHECK ONE:
( ) IN-PERSON HEARING - ATTENDANCE CONFIRMED *(EFS-Web selection: Confirmation of Hearing by Appellant)*
( ) TELEPHONIC HEARING - ATTENDANCE CONFIRMED *(EFS-Web selection: Confirmation of Hearing by Appellant)*
( ) VIDEO HEARING - ATTENDANCE CONFIRMED *(EFS-Web selection: Confirmation of Hearing by Appellant)*
( ) HEARING ATTENDANCE WAIVED *(EFS-Web selection: Waiver of Hearing by Appellant)*

To aid the oral hearings staff in scheduling hearing rooms, please indicate the total number of participating and observing attendees if more than three are expected: ____
To aid the judges in determining whether any conflicts exist that may require a recusal, please list in the 'Comments' section the names of any additional person(s) who will be participating in the oral hearing. (Upon arrival, all persons presenting arguments must sign in at the Usher's desk.)

Comments/Special Requests:

_____

_____

_____ _____
Typed or Printed Name of Attorney/Agent/Appellant Registration No.

( ) PATENT OWNER ( ) THIRD PARTY REQUESTER

_____ _____

Signature of Attorney/Agent/Appellant Date

The 'Hearings' tab of the PTAB webpage http://www.uspto.gov/ip/boards/bpai/index.jsp provides additional information about oral hearings.

Please direct other inquiries to the PTAB Hearings Clerk at 571-272-9797.

cc: Third Party Requester

DANIELLE L. HERRITT
MCCARTER & ENGLISH LLP,
265 FRANKLIN STREET
BOSTON, MA 02110

UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
95/002,170	09/10/2012	7897080	117744-00023	6418

23869 7590 07/12/2014

Hoffmann & Baron LLP
6900 Jericho Turnpike
Syosset, NY 11791

EXAMINER	
DIAMOND, ALAN D	
ART UNIT	PAPER NUMBER
3991	
MAIL DATE	DELIVERY MODE
07/12/2014	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

United States Patent and Trademark Office

Under Secretary of Commerce for Intellectual Property and
Director of the United States Patent and Trademark Office
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

HOFFMANN & BARON LLP
6900 JERICHO TURNPIKE
SYOSSET, NY 11791

Appeal No: 2014-007671
Inter Partes Reexamination
Control No: 95/002,170
Appellant: 7897080 et al.

Patent Trial and Appeal Board Docketing Notice

Inter Partes Reexamination Control No. 95/002,170 was received from the Technology Center at the Board on July 08, 2014 and has been assigned Appeal No: 2014-007671.

In all future communications regarding this appeal, please include both the Inter Partes Reexamination Control Number and the appeal number.

The mailing address for the Board is:

PATENT TRIAL and APPEAL BOARD
UNITED STATES PATENT AND TRADEMARK OFFICE
P.O. BOX 1450
ALEXANDRIA, VIRGINIA 22313-1450

Telephone inquiries can be made by calling 571-272-9797 and referencing the appeal number listed above.

By order of the Patent Trial and Appeal Board.

JAG

cc: Third Party Requester

DANIELLE L. HERRITT
MCCARTER & ENGLISH LLP,
265 FRANKLIN STREET

BOSTON, MA 02110

PTO/AIA/32 (03-13)
Approved for use through 03/31/2013. OMB 0651-0031
U.S. Patent and Trademark Office; U.S. DEPARTMENT OF COMMERCE

REQUEST FOR ORAL HEARING BEFORE THE PATENT TRIAL AND APPEAL BOARD

Docket Number (Optional): 117744-00023

I hereby certify that this correspondence is being facsimile transmitted to the USPTO, EFS-Web transmitted to the USPTO, or deposited with the United States Postal Service with sufficient postage in an envelope addressed to "Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450" [37 CFR 1.8(a)]

on June 25, 2014.

Signature /Danielle L. Herritt/

Typed or printed name Danielle L. Herritt

In re Application of
Yang et al. (USPN 7,897,080)

Application Number	Filed
95/002,170	September 10, 2012

For
POLYETHYLENE-OXIDE BASED FILMS AND DRUG DELIVERY SYSTEMS MADE THEREFROM

Art Unit	Examiner
3991	Alan D. Diamond

Applicant hereby **requests an oral hearing** before the Patent Trial and Appeal Board in the appeal of the above-identified application.

The fee for this Request for Oral Hearing is (37 CFR 41.20(b)(3)) $ 1,300.00

☐ Applicant asserts small entity status. See 37 CFR 1.27. Therefore, the fee shown above is reduced by 50%, and the resulting fee is: $ _____

☐ Applicant certifies micro entity status. See 37 CFR 1.29. Therefore, the fee shown above is reduced by 75%, and the resulting fee is: $ _____
Form PTO/SB/15A or B or equivalent must either be enclosed or have been submitted previously

☐ A check in the amount of the fee is enclosed.

☐ Payment by credit card. Form PTO-2038 is attached.

☐ The Director has already been authorized to charge fees in this application to a Deposit Account.

☑ The Director is hereby authorized to charge any fees which may be required, or credit any overpayment to Deposit Account No. 50-4876.

☐ Payment made via EFS-Web.

☐ A petition for an extension of time under 37 CFR 1.136(b) (PTO/SB/23 or equivalent) is enclosed.
For extensions of time in reexamination proceedings, see 37 CFR 1.550.

WARNING: Information on this form may become public. Credit card information should not be included on this form. Provide credit card information and authorization on PTO-2038.

I am the

☐ applicant ☑ attorney or agent of record Registration number 43,670 ☐ attorney or agent acting under 37 CFR 1.34 Registration number _____

Signature /Danielle L. Herritt/

Typed or printed name Danielle L. Herritt

Telephone Number 617-449-6513

Date June 25, 2014

NOTE: This form must be signed in accordance with 37 CFR 1.33. See 37 CFR 1.4 for signature requirements and certifications. Submit multiple forms if more than one signature is required, see below*.

☑ * Total of 1 forms are submitted.

This collection of information is required by 37 CFR 41.20(b)(3). The information is required to obtain or retain a benefit by the public which is to file (and by the USPTO to process) an application. Confidentiality is governed by 35 U.S.C. 122 and 37 CFR 1.11, 1.14 and 41.6. This collection is estimated to take 12 minutes to complete, including gathering, preparing, and submitting the completed application form to the USPTO. Time will vary depending upon the individual case. Any comments on the amount of time you require to complete this form and/or suggestions for reducing this burden, should be sent to the Chief Information Officer, U.S. Patent and Trademark Office, U.S. Department of Commerce, P.O. Box 1450, Alexandria, VA 22313-1450. DO NOT SEND FEES OR COMPLETED FORMS TO THIS ADDRESS. **SEND TO: Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450.**

If you need assistance in completing the form, call 1-800-PTO-9199 and select option 2.

Privacy Act Statement

The **Privacy Act of 1974 (P.L. 93-579)** requires that you be given certain information in connection with your submission of the attached form related to a patent application or patent. Accordingly, pursuant to the requirements of the Act, please be advised that: (1) the general authority for the collection of this information is 35 U.S.C. 2(b)(2); (2) furnishing of the information solicited is voluntary; and (3) the principal purpose for which the information is used by the U.S. Patent and Trademark Office is to process and/or examine your submission related to a patent application or patent. If you do not furnish the requested information, the U.S. Patent and Trademark Office may not be able to process and/or examine your submission, which may result in termination of proceedings or abandonment of the application or expiration of the patent.

The information provided by you in this form will be subject to the following routine uses:

1. The information on this form will be treated confidentially to the extent allowed under the Freedom of Information Act (5 U.S.C. 552) and the Privacy Act (5 U.S.C 552a). Records from this system of records may be disclosed to the Department of Justice to determine whether disclosure of these records is required by the Freedom of Information Act.
2. A record from this system of records may be disclosed, as a routine use, in the course of presenting evidence to a court, magistrate, or administrative tribunal, including disclosures to opposing counsel in the course of settlement negotiations.
3. A record in this system of records may be disclosed, as a routine use, to a Member of Congress submitting a request involving an individual, to whom the record pertains, when the individual has requested assistance from the Member with respect to the subject matter of the record.
4. A record in this system of records may be disclosed, as a routine use, to a contractor of the Agency having need for the information in order to perform a contract. Recipients of information shall be required to comply with the requirements of the Privacy Act of 1974, as amended, pursuant to 5 U.S.C. 552a(m).
5. A record related to an International Application filed under the Patent Cooperation Treaty in this system of records may be disclosed, as a routine use, to the International Bureau of the World Intellectual Property Organization, pursuant to the Patent Cooperation Treaty.
6. A record in this system of records may be disclosed, as a routine use, to another federal agency for purposes of National Security review (35 U.S.C. 181) and for review pursuant to the Atomic Energy Act (42 U.S.C. 218(c)).
7. A record from this system of records may be disclosed, as a routine use, to the Administrator, General Services, or his/her designee, during an inspection of records conducted by GSA as part of that agency's responsibility to recommend improvements in records management practices and programs, under authority of 44 U.S.C. 2904 and 2906. Such disclosure shall be made in accordance with the GSA regulations governing inspection of records for this purpose, and any other relevant (*i.e.*, GSA or Commerce) directive. Such disclosure shall not be used to make determinations about individuals.
8. A record from this system of records may be disclosed, as a routine use, to the public after either publication of the application pursuant to 35 U.S.C. 122(b) or issuance of a patent pursuant to 35 U.S.C. 151. Further, a record may be disclosed, subject to the limitations of 37 CFR 1.14, as a routine use, to the public if the record was filed in an application which became abandoned or in which the proceedings were terminated and which application is referenced by either a published application, an application open to public inspection or an issued patent.
9. A record from this system of records may be disclosed, as a routine use, to a Federal, State, or local law enforcement agency, if the USPTO becomes aware of a violation or potential violation of law or regulation.

CERTIFICATE OF SERVICE

The undersigned hereby certifies that a copy of the foregoing Respondent's Request for Oral Hearing (PTO/AIA/32) was served on June 25, 2014, by first class mail, directed to the patent owner at the correspondence address of record for the subject patent at the following address:

Daniel A. Scola, Jr.

HOFFMANN & BARON, LLP

6900 JERICHO TURNPIKE

SYOSSET, NY 11791,

By: /Danielle L. Herritt/
Danielle L. Herritt
Registration No. 43,670
Attorney for Respondent

ME1 18412323v.1

Electronic Patent Application Fee Transmittal

Application Number:	95002170
Filing Date:	10-Sep-2012
Title of Invention:	POLYETHYLENE-OXIDE BASED FILMS AND DRUG DELIVERY SYSTEMS MADE THEREFROM
First Named Inventor/Applicant Name:	7897080
Filer:	Danielle L. Herritt/Maureen Tierney
Attorney Docket Number:	117744-00023

Filed as Large Entity

inter partes reexam Filing Fees

Description	Fee Code	Quantity	Amount	Sub-Total in USD($)
Basic Filing:				
Pages:				
Claims:				
Miscellaneous-Filing:				
Petition:				
Patent-Appeals-and-Interference:				
Request for Oral Hearing	1403	1	1300	1300
Post-Allowance-and-Post-Issuance:				
Extension of Time:				

Description	Fee Code	Quantity	Amount	Sub-Total in USD($)
Miscellaneous:				
		Total in USD ($)		**1300**

Electronic Acknowledgement Receipt

EFS ID:	19406732
Application Number:	95002170
International Application Number:	
Confirmation Number:	6418
Title of Invention:	POLYETHYLENE-OXIDE BASED FILMS AND DRUG DELIVERY SYSTEMS MADE THEREFROM
First Named Inventor/Applicant Name:	7897080
Customer Number:	23869
Filer:	Danielle L. Herritt/Maureen Tierney
Filer Authorized By:	Danielle L. Herritt
Attorney Docket Number:	117744-00023
Receipt Date:	25-JUN-2014
Filing Date:	10-SEP-2012
Time Stamp:	13:49:55
Application Type:	inter partes reexam

Payment information:

Submitted with Payment	yes
Payment Type	Deposit Account
Payment was successfully received in RAM	$1300
RAM confirmation Number	13453
Deposit Account	504876
Authorized User	

The Director of the USPTO is hereby authorized to charge indicated fees and credit any overpayment as follows:

Charge any Additional Fees required under 37 C.F.R. Section 1.16 (National application filing, search, and examination fees)

Charge any Additional Fees required under 37 C.F.R. Section 1.17 (Patent application and reexamination processing fees)

Charge any Additional Fees required under 37 C.F.R. Section 1.19 (Document supply fees)

Charge any Additional Fees required under 37 C.F.R. Section 1.20 (Post Issuance fees)

Charge any Additional Fees required under 37 C.F.R. Section 1.21 (Miscellaneous fees and charges)

File Listing:

Document Number	Document Description	File Name	File Size(Bytes)/ Message Digest	Multi Part /.zip	Pages (if appl.)
1	Oral Hearing Request - Third Party Requester	080RequestforOralHearing2014JUN25.PDF	321333 43fe781ca644cca14239ba2f398ed58fa230adec	no	2
Warnings:					
Information:					
2	Reexam Certificate of Service	080COSforRequestforOralHearing2014JUN25.PDF	5691 c36aa7cf417168fcc2463514a000816c4d2076ae	no	1
Warnings:					
Information:					
3	Fee Worksheet (SB06)	fee-info.pdf	30054 44af82b34f1a4f2912ed6da07701f202596b0214	no	2
Warnings:					
Information:					
		Total Files Size (in bytes):	357078		

This Acknowledgement Receipt evidences receipt on the noted date by the USPTO of the indicated documents, characterized by the applicant, and including page counts, where applicable. It serves as evidence of receipt similar to a Post Card, as described in MPEP 503.

<u>New Applications Under 35 U.S.C. 111</u>
If a new application is being filed and the application includes the necessary components for a filing date (see 37 CFR 1.53(b)-(d) and MPEP 506), a Filing Receipt (37 CFR 1.54) will be issued in due course and the date shown on this Acknowledgement Receipt will establish the filing date of the application.

<u>National Stage of an International Application under 35 U.S.C. 371</u>
If a timely submission to enter the national stage of an international application is compliant with the conditions of 35 U.S.C. 371 and other applicable requirements a Form PCT/DO/EO/903 indicating acceptance of the application as a national stage submission under 35 U.S.C. 371 will be issued in addition to the Filing Receipt, in due course.

<u>New International Application Filed with the USPTO as a Receiving Office</u>
If a new international application is being filed and the international application includes the necessary components for an international filing date (see PCT Article 11 and MPEP 1810), a Notification of the International Application Number and of the International Filing Date (Form PCT/RO/105) will be issued in due course, subject to prescriptions concerning national security, and the date shown on this Acknowledgement Receipt will establish the international filing date of the application.

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Inter Partes Reexamination of Yang et al.	Examiner: Alan D. Diamond
U.S. Patent No. 7,897,080	Group Art Unit: 3991
Reexamination Control No. 95/002,170	Confirmation No. 6418
Filed: September 10, 2012	H&B Docket: 1199-26 RCE/CON/REX M&E Docket: 117744-00023

For: POLYETHYLENE-OXIDE BASED FILMS AND
DRUG DELIVERY SYSTEMS MADE THEREFROM

REQUEST FOR ORAL HEARING

Mail Stop *Inter Partes* Reexam
Central Reexamination Unit
Commissioner for Patents
U.S. Patent and Trademark Office
P.O. Box 1450
Alexandria, VA 22313-1450

Certificate of EFS-Web Transmission
I hereby certify that this correspondence is being transmitted via the U.S. Patent and Trademark Office electronic filing system (EFS-Web) to the USPTO on June 17, 2014.

Signed: Michael I. Chakansky /Michael I Chakansky/Reg. No. 31,600

Dear Madame:

Patent owner MonoSol Rx, LLC (Appellant) hereby requests an oral hearing in the above-captioned proceeding. Appellant considers an oral hearing necessary and desirable for a proper presentation of its appeal. 37 C.F.R. § 41.73(a). This request is being timely submitted within two months after the examiner's answer, which was dated April 25, 2014, and includes a certification that same was served in its entirety on all other parties to the proceeding. Authorization is hereby provided to charge the fees due in connection with this submission to Deposit Account No. 08-2461. 37 C.F.R. § 41.73(b) and 37 C.F.R. § 41.20(b)(3).

Dated: June 17, 2014

Respectfully submitted,

/Daniel A. Scola, Jr./
Daniel A. Scola, Jr.
Registration No. 29,855

Michael I. Chakansky
Registration No. 31,600

HOFFMANN & BARON, LLP

6900 Jericho Turnpike
Syosset, New York 11791
(973) 331-1700

Attorneys for the Appellant, Patent Owner

CERTIFICATE OF FIRST CLASS SERVICE

It is certified that a copy of this **REQUEST FOR ORAL HEARING** has been served, by first class mail, postage prepaid, on June 17, 2014, in its entirety on the Respondent, Third Party Requester (Respondent) as provided in 37 CFR § 1.903, 37 CFR § 1.248 and 37 C.F.R. § 41.73(b) at the address below.

DANIELLE L. HERRITT
McCARTER & ENGLISH LLP
265 FRANKLIN STREET
BOSTON, MASSACHUSETTS 02110

/Michael I. Chakansky/
Michael I. Chakansky
Registration No.: 31,600
Attorney for the Patentee/Appellant

Electronic Patent Application Fee Transmittal

Application Number:	95002170
Filing Date:	10-Sep-2012
Title of Invention:	POLYETHYLENE-OXIDE BASED FILMS AND DRUG DELIVERY SYSTEMS MADE THEREFROM
First Named Inventor/Applicant Name:	7897080
Filer:	Michael I. Chakansky
Attorney Docket Number:	117744-00023

Filed as Large Entity

inter partes reexam Filing Fees

Description	Fee Code	Quantity	Amount	Sub-Total in USD($)
Basic Filing:				
Pages:				
Claims:				
Miscellaneous-Filing:				
Petition:				
Patent-Appeals-and-Interference:				
Request for Oral Hearing	1403	1	1300	1300
Post-Allowance-and-Post-Issuance:				
Extension-of-Time:				

Description	Fee Code	Quantity	Amount	Sub-Total in USD($)
Miscellaneous:				
			Total in USD ($)	**1300**

Electronic Acknowledgement Receipt

EFS ID:	19331811
Application Number:	95002170
International Application Number:	
Confirmation Number:	6418
Title of Invention:	POLYETHYLENE-OXIDE BASED FILMS AND DRUG DELIVERY SYSTEMS MADE THEREFROM
First Named Inventor/Applicant Name:	7897080
Customer Number:	23869
Filer:	Michael I. Chakansky
Filer Authorized By:	
Attorney Docket Number:	117744-00023
Receipt Date:	17-JUN-2014
Filing Date:	10-SEP-2012
Time Stamp:	17:11:14
Application Type:	inter partes reexam

Payment information:

Submitted with Payment	yes
Payment Type	Credit Card
Payment was successfully received in RAM	$1300
RAM confirmation Number	4100
Deposit Account	
Authorized User	

File Listing:

Document Number	Document Description	File Name	File Size(Bytes)/ Message Digest	Multi Part / .zip	Pages (if appl.)

1	Oral Hearing Request-Owner	080RequestOralHearing.pdf	162438 7aea2ba861c83b6838d1be13a807bbc454ce6c3d	no	3
Warnings:					
Information:					
2	Fee Worksheet (SB06)	fee-info.pdf	30269 e84ebb6dafe6497274479287ef98d314af2efbf3	no	2
Warnings:					
Information:					
		Total Files Size (in bytes):	192707		

This Acknowledgement Receipt evidences receipt on the noted date by the USPTO of the indicated documents, characterized by the applicant, and including page counts, where applicable. It serves as evidence of receipt similar to a Post Card, as described in MPEP 503.

New Applications Under 35 U.S.C. 111
If a new application is being filed and the application includes the necessary components for a filing date (see 37 CFR 1.53(b)-(d) and MPEP 506), a Filing Receipt (37 CFR 1.54) will be issued in due course and the date shown on this Acknowledgement Receipt will establish the filing date of the application.

National Stage of an International Application under 35 U.S.C. 371
If a timely submission to enter the national stage of an international application is compliant with the conditions of 35 U.S.C. 371 and other applicable requirements a Form PCT/DO/EO/903 indicating acceptance of the application as a national stage submission under 35 U.S.C. 371 will be issued in addition to the Filing Receipt, in due course.

New International Application Filed with the USPTO as a Receiving Office
If a new international application is being filed and the international application includes the necessary components for an international filing date (see PCT Article 11 and MPEP 1810), a Notification of the International Application Number and of the International Filing Date (Form PCT/RO/105) will be issued in due course, subject to prescriptions concerning national security, and the date shown on this Acknowledgement Receipt will establish the international filing date of the application.

UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
95/002,170	09/10/2012	7897080	117744-00023	6418

23869 7590 06/04/2014

Hoffmann & Baron LLP
6900 Jericho Turnpike
Syosset, NY 11791

EXAMINER	
DIAMOND, ALAN D	

ART UNIT	PAPER NUMBER
3991	

MAIL DATE	DELIVERY MODE
06/04/2014	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

UNITED STATES DEPARTMENT OF COMMERCE
U.S. Patent and Trademark Office
Address : COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450

APPLICATION NO./ CONTROL NO.	FILING DATE	FIRST NAMED INVENTOR / PATENT IN REEXAMINATION	ATTORNEY DOCKET NO.
95/002,170	10 September, 2012	7897080	117744-00023

		EXAMINER	
Hoffmann & Baron LLP 6900 Jericho Turnpike Syosset, NY 11791		Alan Diamond	
		ART UNIT	PAPER
		3991	20140530

DATE MAILED:

Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner for Patents

The rebuttal brief filed May 27, 2014 by Patent Owner Appellant has been entered.

The rebuttal brief filed May 27, 2014 by Third Party Requester Appellant has been entered.

No further response by the specialist is appropriate. Any further reply/comments by any party will be not be considered, and may be returned to the party that submitted it. The reexamination proceeding is being forwarded to the Patent Trial and Appeal Board for decision on the appeal(s).

/Alan Diamond/
Patent Reexamination Specialist
Central Reexamination Unit 3991

PTO-90C (Rev.04-03)

Transmittal of Communication to Third Party Requester *Inter Partes* Reexamination	Control No.	Patent Under Reexamination	
	95/002,170	7897080	
	Examiner	Art Unit	
	Alan Diamond	3991	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address. --

(THIRD PARTY REQUESTER'S CORRESPONDENCE ADDRESS)

Danielle L. Herritt
McCarter & English LLP
265 Franklin Street
Boston, MA 02110

Enclosed is a copy of the latest communication from the United States Patent and Trademark Office in the above-identified reexamination proceeding. 37 CFR 1.903.

Prior to the filing of a Notice of Appeal, each time the patent owner responds to this communication, the third party requester of the *inter partes* reexamination may once file written comments within a period of 30 days from the date of service of the patent owner's response. This 30-day time period is statutory (35 U.S.C. 314(b)(2)), and, as such, it cannot be extended. See also 37 CFR 1.947.

If an *ex parte* reexamination has been merged with the *inter partes* reexamination, no responsive submission by any *ex parte* third party requester is permitted.

All correspondence relating to this inter partes reexamination proceeding should be directed to the **Central Reexamination Unit** at the mail, FAX, or hand-carry addresses given at the end of the communication enclosed with this transmittal.

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re *Inter Partes* Reexamination of:	)	
	)	
US Patent No. 7,897,080	)	Confirmation No.: 6418
	)	
Named Inventor: Robert K. Yang *et al.*	)	Group Art Unit: 3991
	)	
Control No.: 95/002,170	)	Examiner: Alan D. Diamond
	)	
Request Filed: September 10, 2012	)	M&E Docket: 117744-00023
	)	
Title: POLYETHYLENE OXIDE-BASED FILMS AND DRUG DELIVERY SYSTEMS MADE THEREFROM	)	H&B Docket: 1199-26 RCE/CON/REX

Mail Stop *Inter Partes* Reexam
Attn: Central Reexamination Unit
Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

REBUTTAL BRIEF

BioDelivery Systems, Inc. ("BDSI") respectfully submits this rebuttal brief pursuant to 37 CFR 41.66 and 37 CFR 41.71 within one month of the Examiner's Answer.

Certificate Regarding Word Count Pursuant to 37 CFR 1.943(c)

I hereby certify that this Brief does not exceed 7,000 words in total length, based on WORD's count of the words beginning on page 1 and continuing through the end of the signature page in this brief.

Signed: Danielle L. Herritt /Danielle L. Herritt/ Reg. No. 43,670 Dated: May 27, 2014

Table of Contents

INTRODUCTION

In its April 10, 2014 Patent Owner's Cross-Respondent's Brief, MonoSol attempts to demonstrate that the newly-added recitations in the '080 patent are clear, enabled and/or supported by written description. But it does not do so by relying on the specification. Instead, MonoSol relies on unsupported attorney argument (*see*, *e.g.*, Section A below), third party declarations (*see*, *e.g.*, Section C), and/or inherency (*see*, *e.g.*, Section D). In other words, MonoSol has failed to present any arguments or rely on any evidence relevant to the proposed rejections under 35 USC 112. And MonoSol's interpretation of the claims, and in particular its interpretation of the newly-added recitations, has changed throughout this proceeding—making it difficult for the Office, and others, to understand how MonoSol's amended or new claims relate to, or are supported by, the specification of the '080 patent.

A. Claims Reciting the Term "*Suitable for Commercialization…*" Lack Clarity, Written Description, and Enablement.

MonoSol does not address BDSI's proposed rejections of the '080 claims containing the term "*suitable for commercialization and regulatory approval … including analytical chemical testing which meets the standards of the U.S. Food and Drug Administration relating to variation of an active in individual dosage*

units" under 35 USC 112. MonoSol instead relies on several irrelevant arguments based on a mischaracterization of the Examining Panel's construction of this term. Nowhere does MonoSol identify the support from the '080 specification necessary to satisfy the requirements of Section 112.

1. MonoSol's shifting claim construction demonstrates the lack of clarity of the "*suitable for commercialization…*" term.

The newly-added claim term "*suitable for commercialization …*" is indefinite. *See* BDSI March 10, 2014 Appeal Brief in *Inter Partes* Reexamination ("Cross-Appeal Brief"), at 14-17, 20-21. By introducing yet another proposed construction of this added term, MonoSol further demonstrates the lack of clarity of this term.

a. *MonoSol's current proposed construction is inconsistent with the Panel's construction.*

In responding to BDSI's proposed rejection for lack of clarity, MonoSol mischaracterizes the Panel's construction of the "*suitable for commercialization…*" term. MonoSol claims "there is only one interpretation set forth by both the Examiner and MonoSol." MonoSol's April 10, 2014 Patent Owner's Cross-Respondent's Brief ("Cross-Respondent's Brief"), at 12:11-12.

However, as illustrated in the table below, the construction now proposed by MonoSol is not the Panel's construction.

Panel's Construction	MonoSol's Current Construction
"[T]he bright line test for such suitability is based on performing analytical chemical tests for uniformity of content of active, said tests showing a particular variation of active, for example, not more than 10%." RAN at 14:3-5.	"[S]uitability for commercialization and FDA approval in the context of the present invention is clearly directed to maintaining the uniformity of content of the pharmaceutical active from start to finish in the manufacture of the pharmaceutical resulting film. Moreover, commercialization inherently requires the ability to mass produce the films at scale and that film products from different manufacturing runs will fall within the FDA uniformity requirements." Cross-Respondent's Brief at 12:22-13:3.

There are multiple critical differences between MonoSol's current proposed construction and the Panel's construction. For example, the Panel's construction does not mention "mass production" or uniformity between "manufacturing runs." Neither the Panel's construction nor the claims mentions "maintaining the

uniformity of content of the pharmaceutical active" and the Panel's construction does not mention "maintaining" at all.[1]

b. *MonoSol's current proposed construction is inconsistent with its own previously proposed constructions.*

In its Cross-Respondent's Brief, MonoSol proposes a construction that is inconsistent with previous constructions it proposed during reexamination. Although MonoSol now argues that the term does not require that all requirements for FDA approval be met, MonoSol previously argued, in an attempt to distinguish the prior art, that the term should be construed to require compliance with FDA requirements. *See* March 13, 2013 Reply ("Reply-2") at 66:16-20 ("[BDSI] has not provided any proof that Chen's process examples … will provide a process suitable for commercial manufacture, a process which produces products which are regulatory approvable by the FDA…").

---

[1] MonoSol criticizes the Clevenger Declaration for "not discussing suitability for FDA approval and commercialization in connection with *maintaining* the uniformity of content in the amount of active." Cross-Respondent's Brief at 15:2-5 (emphasis added). This criticism is misplaced. The Panel never defined "suitable for commercialization …" in terms of "maintaining" anything.

MonoSol's shifting and inconsistent construction of this term supports, rather than rebuts, BDSI's proposed rejection of the "*suitable for commercialization …*" term for lack of clarity under Section 112.

2. Lack of Written Description

MonoSol has not responded in substance to BDSI's proposed rejection for lack of written description for the "*suitable for commercialization…*" term. *See* Cross-Respondent's Brief at 12-15. MonoSol fails to identify any language in the '080 specification, examples, figures, or original claims purportedly supporting this newly-added recitation. *See id.*

For the sake of completeness, BDSI notes that MonoSol cites a single sentence from the '080 specification as alleged support for this recitation[2], which sentence reads "[o]ther factors, such as mixing techniques, also play a role in the manufacture of pharmaceutical film suitable for commercialization and regulatory approval." '080 patent at 3:58-60, *quoted in* Cross-Respondent's Brief at 8. This sentence by no means provides written description of "*suitable for commercialization …*," in particular in light of the Panel's construction of this term

[2] In addition to the preamble, MonoSol also relies on this single sentence as support for newly-added steps (e) and (f).

involving a "bright line test … based on performing analytical chemical tests." *See* RAN at 14:3-5.

3. Lack of Enablement

MonoSol has not responded in substance to BDSI's proposed rejection for lack of enablement for the newly-added term "*suitable for commercialization …*". *See* Cross-Respondent's Brief at 12-15.

Instead, MonoSol devotes over three pages of its Cross-Respondent's Brief to arguing that BDSI's interpretation of the Lin Declaration, together with its claim construction, is "absurd." *Id.* at 12-15. But MonoSol has failed to explain why. For example, BDSI has demonstrated that, when applying the standard outlined in the Lin Declaration—which mandates compliance with FDA requirements—the '080 patent is not enabled. Cross-Appeal Brief at 17-19. In response, MonoSol disavows its previous proposed construction, and does not explain how the '080 specification enables the newly-recited term under *any* construction. *See* Cross-Respondent's Brief at 12-15.

BDSI's proposed rejections based upon the newly-added "*suitable for commercialization…*" term are proper. The Panel erred by not adopting these rejections, as this newly-added term is not clear, is not described, and is not

enabled. MonoSol's Cross-Respondent Brief does not effectively rebut the lack of clarity, but demonstrates the lack of clarity by proposing yet another construction of this term.

B. Claims Reciting the Term "*Analytical Chemical Tests*" Lack Clarity and Written Description.

1. Lack of Clarity

MonoSol has not addressed BDSI's proposed rejection for lack of clarity of the "*analytical chemical tests*" term. *See* Cross-Appeal Brief at 16-19. Instead, MonoSol repeats and reproduces block quotations of the RAN. *Id.*

In the quoted passage from the RAN, the Panel found that the difference between chemical and physical testing is that chemical testing involves "direct testing for the amount of active." RAN at 16:24-26 *quoted in* Cross-Respondent's Brief at 17. MonoSol argues that Example M of the '080 patent is an example of analytical chemical testing because Example M describes the use of a spectrophotometer to measure light absorption, which produces measurements "directly related to the amount of active present." Cross-Respondent's Brief at 19. But MonoSol does not even say that the Example M testing is "direct *testing* for the amount of active." Accordingly, this passage does not support MonoSol's position or justify the Panel's failure to adopt this rejection.

2. Lack of Written Description

The term "*analytical chemical tests*" does not appear in the specification, a point which MonoSol does not dispute. *See* Cross-Respondent's Brief at 16-19.

MonoSol quotes several passages from the '080 specification, but none discusses the combination of "analytical" and "chemical" together in the context of testing for uniformity. Instead of demonstrating how the '080 patent provides written description, MonoSol merely relies upon the Panel's finding that "*analytical chemical tests*" requires direct testing for the amount of the claimed pharmaceutical and/or bioactive active. *Id.* at 17. MonoSol has failed to point out how the specification conveys to one of ordinary skill in the art this narrow definition of "*analytical chemical tests*." *See* MPEP 2163.02.

Further, in an attempt to distinguish the prior art, MonoSol argued for a narrower construction of "*analytical chemical tests*," one that excludes visual inspection and weight measurement. Reply-2 at 53-59. But MonoSol has not identified a single test in the '080 specification that meets its newly-invented criteria.

Instead, MonoSol only points to the use of a spectrophotometer to test for the concentration of dye in Example M. *See* Cross-Respondent's Brief at 19:4-5.

But it is undisputed that a dye is not a pharmaceutical or bioactive active, as claimed. *See* MonoSol September 3, 2013 Response to ACP, at 66. MonoSol has not explained how a test for the concentration of a dye would be useful in direct testing for a pharmaceutical or bioactive active, as claimed. Accordingly, MonoSol has failed to identify any written description in the '080 specification that supports the Examiner's non-adoption of BDSI's proposed rejection.

MonoSol claims that BDSI somehow admits that Example M "provides an actual example of using a chemical analytical test to determine directly the amount of active in films made by the '080 Patent processes." *See* Cross-Respondent's Brief at 19. BDSI admitted no such thing. It is unclear how MonoSol can make such a leap from the quoted language. A sentence stating that measuring active content would have been obvious does not support—or even suggest—that Example M of the '080 patent provides an example of "analytical chemical tests."

BDSI's proposed rejections based upon the newly-added term "analytical chemical tests" are proper. The Examiner erred by not adopting these rejections, as this newly-added term is neither clear nor described in the specification. For the reasons stated above, all claims should have been rejected under Section 112.

C. Claims Requiring that in a Film "*Active…Varies by No More Than 10%*" and "*Less than 5%| 2%|1%| 0.5%*" Lack Written Description, Clarity, and Enablement.

1. Lack of Written Description

MonoSol makes no substantive argument challenging BDSI's proposed rejection based on lack of written description for the recitations that "*active…varies by no more than 10%*" and "*less than 5%|2%|1%| 0.5%.*" *See* Cross-Respondent's Brief at 19:18-20:2. Instead, MonoSol alleges that BDSI raised this argument for the first time on appeal. This allegation is not true. BDSI made this argument during reexamination. *Compare* Apr. 12, 2013 Comment at 17:3-5 ("In over 100 examples, the '080 Patent never demonstrates that any disclosed method results in a film that satisfies the recited active variation limitation as determined by analytical chemical testing."), *with* Cross-Appeal Brief at 30:14-17 ("Again, despite over 100 examples and 150 total original pages of specification, the '080 patent discloses no method that results in a film that satisfied the new variation/uniformity recitation as verified by analytical chemical testing.").

Because MonoSol has not substantively addressed this proposed rejection, BDSI's arguments are apparently unopposed.

2. Lack of Clarity and Enablement

Although MonoSol purports to substantively challenge BDSI's proposed lack of enablement and clarity rejections based on recitations that active varies by no more than 10% and/or by less than 5%, 2%, 1%, or 0.5%—it does not make any arguments relevant to these proposed rejections. *See* Cross-Respondent's Brief at 19-26. Instead, MonoSol makes three irrelevant arguments: (a) that *Chen* allegedly teaches a process for producing films with 30% variation in weight, (b) that *Staab* allegedly teaches films that lack uniformity, and (c) that the Declaration of MonoSol's expert, Dr. Bogue, exemplifies the use of analytical chemical tests to show films with uniformity of content in the amount of active. *Id.* None of these arguments addresses BDSI's proposed lack of enablement and clarity rejections. Neither the teachings of the prior art references nor an expert's post-grant opinions cure the lack of enablement and clarity of the claims of the '080 patent.

a. Chen *does not cure the lack of clarity and enablement of claimed degrees of active uniformity within a film.*

MonoSol argues that *Chen* teaches that films made according to *Chen*'s process have a 30% variation in the amount of active between "separately manufactured films." Cross-Respondent's Brief at 22:2-4. This argument is irrelevant to the limitations at issue. The limitations at issue do not concern a

comparison between "separately manufactured films."[3] *See, e.g.*, step (f) of claim 1 and step (e) of claim 82.

Further, *Chen* discloses processes for manufacturing film with the recited "uniformity of content of said active in substantially equal sized individual dosage units of said visco-elastic film is such that the amount of the active varies by no more than 10%." *See Chen* Table 4, at 20 (disclosing that the dried film of *Chen*'s Example 1, when rounded to two decimal places, as in Table 2 of the '080 patent, is 0.03 g/ dosage film with a variation of 0%). Moreover, Dr. Reitman confirmed that film manufactured according to *Chen*'s Example 7 process featured that recited uniformity. *See* Declaration of Dr. Maureen Reitman, Exhibit 2 to Cross-Appeal Brief ("Reitman Decl."), at ¶7.

Most importantly, MonoSol's premise is flawed. Even if *Chen* did teach a manufacturing process that did not result in film with the recited uniformity, such teaching would not cure the lack of enablement and indefiniteness in the '080 patent claims.

---

[3] The comparison is addressed with respect to the relevant limitation in section D below.

b. Staab *does not cure the lack of clarity and enablement of claimed degrees of active uniformity within a film.*

Similarly, MonoSol contends that *Staab* demonstrates film lacking the recited uniformity. Cross-Respondent's Brief at 23-24. Again, MonoSol's premise is flawed. Whether or not *Staab* discloses non-uniform films, the claims of the '080 patent reciting the claimed degrees of active uniformity within a film are still indefinite and not enabled.

Taking one line out of context in its effort to distinguish *Staab*, MonoSol extracts an incorrect desired amount of active for *Staab*. *See* Cross-Respondent's Brief at 23-24. MonoSol then argues that there is a 100% variation from that incorrect "desired" amount. *See id.* This is a new argument, which was never presented to the Panel.[4] But in any event, any difference with respect to a desired amount of active is not relevant because the limitation at issue is not directed to active variation *from a desired amount*.

MonoSol argues that *Staab* intended the exemplary film to contain 5% active (*i.e.*, 9.5 mg)—based on a misreading of the third line in the table on column 11 of *Staab*. *See* Cross-Respondent's Brief at 23 (relying on the line in *Staab*

[4] On the contrary, MonoSol argued to the Panel that *Staab*'s "perfect yield" was suspect. *See* Reply-2 at 69 (emphasis omitted).

"benzalkonium chloride (50% aqueous) … 10%"). But the sentence that introduces the relevant example in *Staab* identifies the intended amount as "19 mg of benzalkonium chloride." *Staab* at 11:24-25. And the following paragraph confirms that the amount intended was obtained: "[t]his procedure was utilized to produce two[-]inch square films each containing 19 mg benzalkonium chloride and about 190 mg in weight." *Id.* at 11:49-51. Thus, not only did *Staab* obtain 19 mg films, but *Staab* intended to do so.

According to *Staab*'s disclosure, the film dosages each contained 10% active—that is, the same active percentage. And importantly, by only addressing a difference from an alleged target, MonoSol does not dispute that the active in *Staab*'s film varies by no more than 10%, and/or by less than 5%, 2%, 1%, or 0.5%. *See* Cross-Respondent's Brief at 23-24.

c. *Example M and the declaration of MonoSol's expert cannot cure the lack of enablement and indefiniteness of the claims of the '080 patent.*

The third irrelevant argument raised by MonoSol, in an attempt to demonstrate clarity and/or enablement, is based upon an expert declaration submitted during the reexamination proceeding. Specifically, MonoSol relies upon the March 13, 2013 Declaration of Dr. Bogue to somehow support the Panel's non-

adoption of this rejection. Cross-Respondent's Brief at 25-26. It is unclear how this expert declaration providing uniformity data collected after the filing of the '080 patent could establish clarity or enablement.

Neither does MonoSol's reliance on Example M provide clarity and/or enablement for the multiple different degrees of uniformity of active claimed. *See, e.g.*, independent claims 1, 82, 315, and 318. Example M does not include a pharmaceutical and/or bioactive active and thus cannot enable the degrees of such active uniformity claimed.

For the reasons set forth in BDSI's Cross-Appeal Brief, the Panel erred by not adopting these rejections, as this newly-added term is not clear and is not enabled.

D. Claims Reciting the Term "*Repeating Steps (a) Through (e) to Form Additional Resulting Films…*" Lack Written Description, Enablement, and Clarity.

After MonoSol amended two of its claims to include a new step, step (f), wherein other methods steps are repeated to form additional films such that the active content in the resulting film and the additional films varies no more than 10% from the desired amount (*see* claims 82 and 315), BDSI properly raised

Section 112 rejections. This new step is not described anywhere in the '080 specification.

1. Lack of Written Description and Enablement

MonoSol neither addresses BDSI's proposed rejections nor demonstrates how the Panel's non-adoption is proper. Instead, MonoSol relies on irrelevant arguments that do not address written description and enablement.

a. *MonoSol fails to demonstrate written description or enablement.*

In an attempt to demonstrate written description and enablement, MonoSol cites a single passage from the background of the '080 specification. Cross-Respondent's Brief at 27. The passage reads: "[c]urrently, as required by various world authorities, dosage forms may not vary more than 10% in the amount of active present. When applied to dosage units based on films, this virtually mandates that uniformity in the film be present." '080 patent at 2:42-46, *quoted in* Cross-Respondent's Brief at 27. But this passage provides neither written description nor enablement for the "*repeating*" term, which includes the requirement that the resulting films and the additional films vary no more than 10% from the desired amount of active as indicated by analytical chemical tests. *See* '080 claims 82 and 315 at step (f).

MonoSol does not dispute BDSI's argument that there is no support in the '080 patent for a method that achieves one variation percentage within a resulting film, and second variation percentage between resulting films. *See* Cross-Appeal Brief at 34. This appears to be a post-grant idea.

Further, with respect to the lack of enablement, MonoSol cites part of claim 1 to somehow address the problem of maintaining uniformity. Cross-Respondent's Brief at 27-28 ("Moreover, the pending claims do enable by addressing the problem of maintaining uniformity. For example, claim 1 recites, *inter alia*, casting a flowable polymer matrix…"). With respect to enablement, MonoSol insists "No more is required." *Id.* at 28:7.

As an initial matter, claim 1 does not include the "*repeating*" step, which is the subject matter of this proposed 35 USC 112 rejection. Therefore, it is unclear how claim 1 enables this element or how, in MonoSol's words, "[n]o more is required." Specifically, if MonoSol's arguments or conclusion were true, then MonoSol has conceded that any prior art reference that discloses the claimed steps, such as *Chen*, is enabled and anticipates or renders obvious MonoSol's claims. In any event, as claim 1 does not enable this repeating step, MonoSol has failed to provide any explanation of why its claims are enabled.

As another irrelevant argument with respect to lack of enablement and written description, MonoSol appears to suggest that written description or enablement is not needed as it is inherent to its disclosure. Specifically, MonoSol states:

> Because the '080 Patent discloses processes which are suitable for commercialization, including scaling up and reproducibility, it is inherent that the process provides the same degree of uniformity in amount of active in dosage units produced from one manufacture of a resulting film to another manufacture of a resulting film and that the resulting films would be tested and should fall within the stated degree of uniformity.

Cross-Respondent's Brief at 28:13-18. As an initial matter, it is unclear how written description or enablement can be "inherent," and MonoSol fails to cite any authority for this proposition.

Further, this passage contains two apparent admissions. First, MonoSol appears to admit that any prior art reference that discloses the claimed materials and steps, such as *Chen*, inherently discloses the recited desired uniformity results between different manufacturing runs. Second, MonoSol appears to concede that the "analytical chemical testing" step implied in step (f) can be satisfied by performing the operative film-making process steps, without conducting an actual

analytical test. This is directly contrary to other arguments MonoSol has made. *See, e.g.*, MonoSol's March 10, 2014 Appeal Brief at 17:9-11 ("Only by analytical chemical testing is it possible to determine the actual amount of active present and hence whether uniformity of active content has been maintained during processing. This is the essence of the '080 Patent claims.").

b. Chen *does not cure the lack of written description and enablement of claimed active uniformity of separately manufactured films as compared to a target.*

MonoSol suggests that the newly-added "*repeating*" step is somehow enabled or described by the prior art *Chen* reference or the declaration of Dr. Reitman. Cross-Respondent's Brief at 27-28. This cannot be true. Prior art references and post-grant declarations do not provide written description or enablement for newly-added recitations to patents.

While more relevant to claims requiring separately manufactured films, MonoSol's misleading comparison of active in the *Chen* and Reitman films (*see* Cross-Respondent's Brief at 22:2-4) remains irrelevant to written description and enablement of those claims. MonoSol assumes a non-existent specific desired dosage weight for *Chen*'s Example 7—in its effort to distinguish *Chen*. *See* Cross-Respondent's Brief at 20-22. But *Chen* does not identify a desired dosage weight

for Example 7. On the contrary, *Chen* explains that "[t]he size of the film may be varied according to the dosage required." *Chen* at 16:5-6. *Chen* notes that "[t]he dosage form was 25-250 mg in various, shapes, sizes, and thicknesses." *Chen* at 17:18-19. In short, there is no basis for MonoSol's direct dosage weight comparison.

As a result, the only legitimate basis for comparison is the target active percentage, as recited in the limitation at issue. *See*, *e.g.*, '080 claims 82 and 315 at step (f). *Chen* discloses that the Example 7 coating solution includes 3.71% oxybutynin and 70.72% water. *See Chen* at 21:5-17, Table 5. *Chen* discloses that, after drying, the Example 7 film included 2.32% water. *See Chen* at 15:5, Table 6. The Example 7 film thus included 12.38% oxybutynin,[5] which may be considered the target oxybutynin percentage.

---

[5] $composition_{film}$ = (other $ingredients_{solution}$ – $H_2O_{solution}$)+H_2O_{film}

= (100 – 70.72) + H_2O_{film} = 29.28 + H_2O_{film}

H_2O_{film} = 0.695 because 2.32% = H_2O_{film} / (29.28 + H_2O_{film})

$composition_{film}$ = 29.28 + 0.695 = 29.975

oxybutynin % = $oxybutynin_{film}$ / $composition_{film}$ = 3.71 / 29.975 = 12.38%

The oxybutynin percentage in each film that Dr. Reitman produced using *Chen*'s Example 7 process may be calculated for each sample, using the measured oxybutynin and the consistent sample weight. *See* Reitman Decl. ¶¶6-7 (for data). Dr. Reitman's samples A-E featured 12.94%[6], 12.94%, 12.65%, 12.94%, and 12.06% oxybutynin, respectively. *See id.* (for data). A comparison of the oxybutynin dosage percentages calculated from Dr. Reitman's data to the target oxybutynin percentage inferred from *Chen*'s Example 7 shows that Dr. Reitman's samples were each within 90 percent and 110 percent of the target (*i.e.*, within 11.14% and 13.61%). Indeed, the available data indicates that *Chen*'s process produces film featuring uniformity measures that are similar to those Dr. Bogue reported for SUBOXONE film lots. In short, Dr. Reitman's declaration provides additional objective evidence that film manufactured using *Chen*'s process features the active uniformity that MonoSol attempts to rely on to distinguish its claims.

In view of the foregoing, it was improper for the Panel not to adopt BDSI's proposed rejections for lack of enablement and written description. MonoSol's irrelevant arguments do not change this.

[6] 4.4 mg oxybutynin / 0.034 g total sample weight (1000 mg / 1 g) = 12.94%.

2. Lack of Clarity

MonoSol has not responded in substance to BDSI's proposed rejection for lack of clarity for the "*repeating*" recitation. *See* Cross-Respondent's Brief at 27-28.

Further, MonoSol's apparent admission described above—that step (f) can be satisfied without conducting an actual analytical test—further illustrates MonoSol's confusion and the resulting lack of clarity of this recitation. On one hand, when attempting to distinguish prior art, MonoSol argues that using analytical chemical tests to determine that the uniformity of active content has been maintained is the "essence" of the '080 patent. MonoSol's March 10, 2014 Appeal Brief at 17:9-11. On the other hand, when attempting to rebut rejections under Section 112, MonoSol argues that it is "inherent" that the claimed process produces uniformity of active content. *See* Cross-Respondent's Brief at 28:13-18. Either the act of analytical chemical testing is the "essence" of the claims or it is unnecessary. It cannot be both. MonoSol's inconsistent arguments further demonstrate the lack of clarity of claims reciting the "*repeating*" term.

E. Claims Reciting the Term "*Rapidly Increasing the Viscosity of Said Flowable Polymer Matrix*" Lack Clarity.

As explained in BDSI's Cross-Appeal Brief, the newly-added term "*rapidly increasing the viscosity of said flowable polymer matrix*" fails to recite any actual method step and creates ambiguity and confusion in the claims in which it appears. Cross-Appeal Brief at 35-37. MonoSol does not substantively address this proposed rejection.

Rather, MonoSol pastes into its Cross-Respondent's Brief the passage from the RAN describing the non-adoption of this proposed rejection, without any further explanation and without identifying any support for the Panel's decision. Cross-Respondent's Brief at 29:10-19. Then, after concluding without explanation that a case cited by BDSI is distinguishable, MonoSol cites another case for the proposition that "a comparative term…requires a reference point." *Id.* at 29:22-30:6 *quoting Playtex Prods., Inc. v. Procter & Gamble, Co.*, 400 F.3d 901, 908 (Fed. Cir. 2010). Finally, MonoSol concludes, without explanation, that "[i]n the instant claim recitation, rapidly's reference point is 'within about the first 4 minutes' of the start of evaporation of the solvent, and is therefore definite." Cross-Respondent's Brief at 30:6-8 (emphasis omitted). But simply referring to original claim language does not illuminate the meaning of the added claim language or somehow render it definite.

Because MonoSol has not substantively addressed this proposed rejection, BDSI's arguments are apparently unopposed.

F. Claims Reciting the Term "*Controlling Drying … During Said Drying Said Flowable Polymer Matrix Temperature is 100ºC or Less*" Lack Clarity.

During reexamination, the "controlling drying" step was amended to recite "*controlling drying … to form a visco-elastic film … wherein during said drying said flowable polymer matrix temperature is 100ºC or less.*" As explained in BDSI's Cross-Appeal Brief, it is unclear whether the "100ºC or less" recitation applies only the beginning or throughout the "controlling drying" step and therefore claims reciting that recitation lack clarity. Cross-Appeal Brief at 37-38. MonoSol has not substantively disputed this proposed rejection.

Instead, MonoSol quotes the passage of the RAN regarding the non-adoption of this proposed rejection and then reiterates the Panel's reasoning. Cross-Respondent's Brief at 31:8-13.[7] MonoSol does not offer support for the Panel's finding or dispute any of BDSI's arguments, instead concluding that the "claim language makes this clear." Cross-Respondent's Brief at 31:17-18.

[7] The relevance of MonoSol's comment—"[i]mportantly, the Examiner did not define visco-elasticity in terms of viscosity" (Cross-Respondent's Brief at

Because MonoSol has not substantively addressed this proposed rejection, BDSI's arguments are apparently unopposed.

G. (Adopted)

H. The Multiple New Expressions of Desired Variation/Uniformity Added to Different Steps and Combinations of Steps During Reexamination Lack Clarity, Written Description, and Enablement.

MonoSol does not dispute that the '080 patent includes no evidence or verification of uniformity of content of a pharmaceutical and/or bioactive active in the final step or in any of the intermediate steps where its new recitations require a specific uniformity. *Compare* Cross-Appeal Brief at 43 *with* Cross-Respondent's Brief at 34-35. It is true that working examples generally are not required, as noted correctly in the underlying reexamination. RAN at 21:27-28. But the '080 patent's failure to demonstrate the alleged key point of novelty creates problems in clarity, written description, and enablement because, in this case, MonoSol argues that its claims require a higher degree of uniformity than produced by the prior art, which disclose the same methods using the same materials and reporting the same uniformity using the same criteria as the instant claims. RAN at, *e.g.*, 82 (finding

---

31:14)—is unclear. BDSI has not argued that visco-elastic and viscosity are identical.

Chen discloses the same methods using the same materials); *id.* at 77 (finding *Chen* achieves uniformity to the same degree using the same criteria set forth in the '080 patent). The alleged higher degree of uniformity is neither described nor demonstrated in the '080 patent specification. And it is unclear how the scope of the claimed methods differs from the methods disclosed in *Chen* and *Staab*.

1. Lack of Clarity

First, MonoSol states that "there are two ways to compare the amounts and both are correct depending upon the circumstance." Cross Respondent's Brief at 35. By that statement, MonoSol admits that there are at least two interpretations of their desired variation recitations. MonoSol's attorney argument about what "scientists" would know "depending upon the circumstance" is unsupported by evidence. *See id.* Because there are at least two interpretations of the desired variation recitations—recitations that MonoSol relies upon heavily in its arguments—claims containing this recitation lack clarity.

Second, MonoSol does not clarify whether the claims require testing with respect to the new recitations of uniformity in various intermediate steps, and if so, whether such testing may be analytical, visual or any other methods known in the art. *See* Cross Respondent's Brief at 34-35. This is especially important because

MonoSol has argued both for and against the criticality of directly measuring the amount of active.

Third, MonoSol did not clarify what "*indicating…*" in step (e) means or requires in the context of the uniformity recited thereafter. *Compare* Cross-Appeal Brief at 40:3-8 *with* Cross-Respondent's Brief at 34-35.

Finally, MonoSol has failed to point to any description of "additional films" or "resulting film" or how they relate to any methods or uniformity requirements, yet they have recited these features. *Compare* Cross-Appeal Brief at 40:9-18 *with* Cross-Respondent's Brief at 34-35.

2. Lack of Written Description

According to MonoSol, "[t]he '080 Patent expressly recognizes the need to test for uniformity by any and all means at various steps during the manufacturing process." Cross-Respondent's Brief at 34, *citing* '080 patent at 29:6-52. This statement has at least three problems.[8]

[8] Another problem is that it is unclear which discussion "supra" MonoSol references for support.

First, none of the claims broadly recite "testing by *any and all* means." MonoSol's statement, suggesting various uniformity recitations require testing by any and all means, introduces yet another clarity problem.

Second, "any and all means" is inconsistent with MonoSol's narrow definition of analytical chemical testing.

Third, again contrary to MonoSol's argument, this cited passage does not teach testing during intermediate steps. This passage clearly states that all samples are cut from the film *after drying*:

> A method for testing uniformity in accordance with the present invention includes conveying a film through a manufacturing process. This process may include subjecting the film to drying processes … the cut film *then* [*i.e.* after drying] may be sampled … [t]his can save time and expense because the process may be altered prior to completing an entire manufacturing run. For example, the drying conditions … may be changed. Altering the drying conditions may involve changing the temperature, drying time, moisture level, and dryer positioning, among others.

'080 Patent at 29:7-47 (emphasis added). The same is true for the block quotation at the bottom of page 34 of MonoSol's Cross Respondent's Brief, citing '080 patent at 29:47-52. This second quotation is completely silent with respect to testing for uniformity at intermediate steps.

In addition, MonoSol does not dispute the lack of written description for the claimed variation between "resulting" films and "additional" films. *Compare* Cross-Appeal Brief at 44 *with* Cross Respondent's Brief at 34-35. MonoSol fails to cite written support for "resulting" and "additional" films and other recitations identified at pages 43 and 44 in BDSI's Cross-Appeal Brief, such as "varying by no more than 10% from a desired target."

3. Lack of Enablement

First, apparently in an attempt to identify support for written description and/or enablement, MonoSol argues that testing at various steps "is an obvious step to add, for example, to ensure early on in the manufacturing process that the degree of uniformity is being maintained." Cross-Respondent's Brief at 35:13-17. This contrasts with MonoSol's amendment and arguments during the reexamination where MonoSol amended every independent claim and proposed four new independent claims with this "obvious" testing step, in an effort to overcome the prior art. *See* MonoSol's March 10, 2014 Appeal Brief at 17:9-11 ("*Only by analytical chemical testing* is it possible to determine the actual amount of active present and hence whether uniformity of active content has been maintained during processing. This is the essence of the '080 Patent claims.") (emphasis added); *see also* Reply-2 at 69:1-4.

Second, MonoSol does not dispute that it has added multiple new expressions of variation/uniformity to the claims, without reciting what new and non-obvious methods steps or conditions achieve them. *Compare* Cross-Appeal Brief at 38-39, *with* Cross-Respondent's Brief at 34-35. MonoSol does not dispute that, although the claimed methods have different uniformity requirements at different steps, there are no discernible operative process differences. *Compare* Cross-Appeal Brief at 39:6-8 *with* Cross Respondent's Brief at 34-35. For example, claim 16 recites "varies by no more than 10% " and claim 315 recites "varies by no more than 10% from the desired amount." But these two claims do not have different operative, film-making process steps: claims 315 and 316 are identical, except that 315 has the repeating step (which provides more films, but does not provide different films) and recites "desired amount." And these claims have no operative, film-making process steps that are not in the cited prior art.

Finally, MonoSol again does not dispute that the '080 patent lacks results of analytical chemical tests (as defined by MonoSol, *e.g.*, a dissolution test) measuring a pharmaceutical and/or bioactive active. *Compare* Cross-Appeal Brief at 43 *with* Cross Respondent's Brief at 34-35. Whether examples are required or optional (*see* Cross-Respondent's Brief at 35:12-13) is not relevant. MonoSol has (erroneously) criticized the prior art for not demonstrating the recited desired

results by direct measurement of pharmaceutical and/or bioactive active by assaying. Reply-2 at 51:4-8, 69:1-6. MonoSol has insisted that methods taught and exemplified in the '080 specification—visual inspection and dosage unit weights—"cannot be relied upon." *See* Reply-2 at 51:6. Therefore, according to MonoSol's own statements and definition, none of the '080 claims is enabled.

CONCLUSION

Because MonoSol has not substantively addressed the issues raised by BDSI in this Appeal, they are apparently unopposed.

In the event that any fee has been overlooked and is required, Commissioner is hereby authorized to charge all necessary fees to Deposit Account No. 50-4876 under Attorney Docket No. 117744-00023.

Respectfully submitted,

Attorneys for Requester, McCarter & English, LLP

Dated: May 27, 2014

By: /Danielle L. Herritt/

Danielle L. Herritt (Reg. No. 43,670)
Kia L. Freeman (Reg. No. 47,577)
Direct Dial: 617-449-6513

CERTIFICATE OF SERVICE

The undersigned hereby certifies that a copy of the Rebuttal Brief was served on May 27, 2014, by first class mail, directed to the patent owner at the correspondence address of record for the subject patent, that is:

Daniel A. Scola, Jr.

HOFFMANN & BARON, LLP

6900 JERICHO TURNPIKE

SYOSSET, NY 11791

By: /Danielle L. Herritt/
Danielle L. Herritt
Registration No. 43,670
Attorney for Respondent

Electronic Acknowledgement Receipt

EFS ID:	19138882
Application Number:	95002170
International Application Number:	
Confirmation Number:	6418
Title of Invention:	POLYETHYLENE-OXIDE BASED FILMS AND DRUG DELIVERY SYSTEMS MADE THEREFROM
First Named Inventor/Applicant Name:	7897080
Customer Number:	23869
Filer:	Kia L. Freeman
Filer Authorized By:	
Attorney Docket Number:	117744-00023
Receipt Date:	27-MAY-2014
Filing Date:	10-SEP-2012
Time Stamp:	19:09:37
Application Type:	inter partes reexam

Payment information:

Submitted with Payment	no

File Listing:

Document Number	Document Description	File Name	File Size(Bytes)/ Message Digest	Multi Part /.zip	Pages (if appl.)
1	Rebuttal Brief - Requester	27March2014_BDSI080RebuttalBrief.pdf	142835 e5a414cd12f1d08147150e28fcc60e69ef0ef4ef	no	35

Warnings:

Information:

Total Files Size (in bytes):	142835

This Acknowledgement Receipt evidences receipt on the noted date by the USPTO of the indicated documents, characterized by the applicant, and including page counts, where applicable. It serves as evidence of receipt similar to a Post Card, as described in MPEP 503.

New Applications Under 35 U.S.C. 111

If a new application is being filed and the application includes the necessary components for a filing date (see 37 CFR 1.53(b)-(d) and MPEP 506), a Filing Receipt (37 CFR 1.54) will be issued in due course and the date shown on this Acknowledgement Receipt will establish the filing date of the application.

National Stage of an International Application under 35 U.S.C. 371

If a timely submission to enter the national stage of an international application is compliant with the conditions of 35 U.S.C. 371 and other applicable requirements a Form PCT/DO/EO/903 indicating acceptance of the application as a national stage submission under 35 U.S.C. 371 will be issued in addition to the Filing Receipt, in due course.

New International Application Filed with the USPTO as a Receiving Office

If a new international application is being filed and the international application includes the necessary components for an international filing date (see PCT Article 11 and MPEP 1810), a Notification of the International Application Number and of the International Filing Date (Form PCT/RO/105) will be issued in due course, subject to prescriptions concerning national security, and the date shown on this Acknowledgement Receipt will establish the international filing date of the application.

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Inter Partes Reexamination of Yang et al.	Examiner: Alan D. Diamond
U.S. Patent No. 7,897,080	Group Art Unit: 3991
Reexamination Control No. 95/002,170	Confirmation No. 6418
Filed: September 10, 2012	H&B Docket: 1199-26 RCE/CON/REX M&E Docket: 117744-00023

For: POLYETHYLENE-OXIDE BASED FILMS AND
DRUG DELIVERY SYSTEMS MADE THEREFROM

PATENT OWNER'S APPELLANT'S REBUTTAL BRIEF

Mail Stop *Inter Partes* Reexam
Central Reexamination Unit
Commissioner for Patents
U.S. Patent and Trademark Office
P.O. Box 1450
Alexandria, VA 22313-1450

Certificate of EFS-Web Transmission
I hereby certify that this correspondence is being transmitted via the U.S. Patent and Trademark Office electronic filing system (EFS-Web) to the USPTO on May 27, 2014.

Signed: Michael I. Chakansky /Michael I Chakansky/Reg. No. 31,600

I hereby certify that, pursuant to 37 CFR § 1.943(c), based on the WordPerfect word count of 5868 words, plus a hand count of 362 words for the images on pages 18 and 19, for a total of 6230 words, Appellant's brief, counting the words on those pages beginning at page 1 (entitled Patent Owner's Appellant's Rebuttal Brief) and continuing through and including all words of the signature page (entitled Conclusion), does not exceed 7,000 words in length.

Signed: Michael I. Chakansky /Michael I Chakansky/Reg. No. 31,600

Dear Madame:

Patent owner MonoSol Rx, LLC (Appellant), pursuant to 37 C.F.R. § 41.71 and MPEP § 2678, hereby responds to the Examiner's Answer dated April 25, 2014, incorporating in its entirety the Right of Appeal Notice mailed December 6, 2013 (RAN), and BDSI's Respondent Brief in *Inter Partes* Reexamination mailed April 10, 2014 (BDSI's RB). This response (MRB)

filed and served on May 27, 2014, is timely as May 25, 2014 was a Sunday, and May 26, 2014 was Memorial Day, a federal holiday.

No fees are believed to be due. If however, there are any fees due in connection with this submission, authorization to charge such fees and authorization to credit any overpayments, to Deposit Account No. 08-2461, is hereby provided.

TABLE OF CONTENTS

PATENT OWNER'S APPELLANT'S REBUTTAL BRIEF

I. PRELIMINARY STATEMENT[1]

As noted in MonoSol's Appellant's Brief (MAB), the invention in U.S. Patent No. 7,897,080 (the " '080 Patent") is directed to novel and non-obvious processes for manufacturing pharmaceutical and bioactive active-containing films suitable for commercialization and regulatory approval by the U.S. Food and Drug Administration ("FDA"). The suitability is with respect to uniformity of content in the amount of active in the resulting films, such that:

(i) the degree of uniformity of content of the amount of active (*e.g.*, where the amount of active varies by no more that 10% between equally sized dosage units) throughout a single manufactured roll (lot) of resulting film can also be strictly maintained through the claimed processes; and

(ii) the degree of uniformity of content in the amount of active in individual dosage units (*e.g.*, where the amount of active in any equally sized dosage unit varies by no more than 10% from the expected or desired amount) taken from different manufactured rolls (lots) of resulting films can also be strictly maintained through the claimed processes.

---

[1] This Rebuttal Brief offers additional arguments addressing the rejections and arguments set forth in the (i) Examiner's Answer dated April 25, 2014, which expressly incorporated in its entirety the Examiner's Right of Appeal Notice mailed December 6, 2013 (RAN), and (ii) BDSI's Respondent Brief in *Inter Partes* Reexamination mailed April 10, 2014 (BDSI's RB or BDSI's Respondent Brief). "The rebuttal brief of the owner may be directed to the examiner's answer and/or any respondent brief." 37 C.F.R. § 41.71(b)(1). As the Examiner's Answer incorporated the RAN in its entirety, MonoSol may and does direct the rebuttal brief herein to the RAN as well.

Moreover, commercialization requires the ability to mass produce the films at scale and to ensure that resulting film products from different manufactured lots (runs) reproducibly meet the requisite degree of uniformity in amount of drug.

As noted in Bogue Declaration I, EA-1, ¶ 4, **one manufactured lot of resulting film can contain 2,000,000 individual dosage units**. The claimed processes accomplish this feat while providing the necessary narrow ranges in variation of the amount of active in individual dosage units across all lots, *i.e.*, multiple rolls of resulting films and even narrower ranges of uniformity of content in amount of active within a single lot, *i.e.*, a single roll of resulting film. Thus, as claimed, the '080 Patent requires a uniformity of content in amount of active (i) in individual dosage units sampled from a single lot of resulting film of 10% or less (independent claims 1, 161 and 316-318, see Appendix A, Bogue Declaration I, EA-1), and (ii) in individual dosage units sampled from two or more lots of resulting films of +/-10% of the pre-determined desired amount (independent claims 82 and 315, see Appendix B, Bogue Declaration I, EA-1).

Processes for such control of content uniformity are not present in or taught or suggested by the prior art. The Examiner and BDSI both wrongly assumed the '080 Patent's claimed uniformity in the distribution of active, *e.g.*, was present in the prior art and thus provided a basis for the claims being rejected. As shown again below, the Examiner's and BDSI's assumed uniformity is not present in or taught or suggested by the prior art.

BDSI's Respondent Brief (BDSI's RB) focuses on the alleged findings in the RAN at pp. 30-44 (Chen), pp. 52-62 (Staab), pp. 63-71 (Le Person); Reitman Declaration; and Cohen

Declaration.[2] BDSI's RB, p. 7. However, the primary references **Chen, Staab and Le Person do not support a *prima facie* case of obviousness**. All three are relied on to support the claim that the prior art disclosed methods of achieving the degrees of uniformity claimed by the '080 Patent. All three were taken on their face as demonstrating such uniformity. However, a closer look at all three shows the exact opposite -- **the prior art did not teach nor achieve the '080 Patent's claimed uniformity**.

First, BDSI and the Examiner have both relied on the false assumption that uniformity of weight of equally sized film samples in Chen, *e.g.*, is, by itself, sufficient to demonstrate that the amount of active present in prior art references meets the '080 Patent's claimed uniformity of active. As a consequence of this improper assumption, BDSI's Reitman Declaration demonstrates that samples taken from Chen's Example 7, and samples taken from Reitman's declared exact copying of Chen's Example 7 process, differed in weight by 30% from the expected or desired sample weight and thus exhibited a 30% non-uniformity in weight of pharmaceutical active from the expected or desired amount as well. Uniformity in amount of active of +/- 10% from the desired amount of drug is necessary in order to be suitable for regulatory approval– outside the scope of the '080 Patent claims.

Second, BDSI and the Examiner have both relied on the false assumption that uniformity of weight of equally sized film samples in Staab, *e.g.*, is, by itself, sufficient to demonstrate that the amount of active present in prior art references meets the '080 Patent's claimed uniformity of

---

[2] Chen (WO 00/42992) ("Chen"); Staab (U.S. 5,393,528) ("Staab"); and Le Person (*"Near infrared drying of pharmaceutical thin films: experimental analysis of internal mass transport,"* Chemical Engineering and Processing, Vol. 37, pp. 257-263 (1998)) ("Le Person").

active and that Staab's reported 0% variation on uniformity of active is sufficient to demonstrate that Staab meets the '080 Patent's claimed uniformity of active. However, Staab disclosure actually demonstrates non-uniformity of content in weight of active of between 90 and 100% from the expected or desired amount of active– again, outside the scope of the '080 Patent claims.

Third, Le Person demonstrates a maldistribution of active ranging from over 20% to over 150% when measured as the percent difference in amount of active, as disclosed in Example M of the '080 Patent, col. 33, l. 20 - col. 34, l. 24 – again, outside the scope of the '080 Patent claims.

Thus, as will be shown again *infra,* the primary references **Chen, Staab and Le Person do not support a *prima facie* case of obviousness**, which MonoSol herein further rebuts with **factually supported objective evidence gleaned from the very prior art references** used by the Examiner to support the *prima facie* case of obviousness. It was error for the Examiner to rely on Chen, Staab and Le Person for *prima facie* obviousness. In fact, on their own or even in combination with BDSI's Reitman Declaration, these references clearly and unambiguously demonstrate **the non-obviousness of the '080 Patent claims** subject to this reexamination (hereinafter the " '080 Patent claims").

Finally, as supported by the Bogue Declarations, the 1 billion dollars in sales of Suboxone in 2012 alone, demonstrates the commercial success of the '080 Patent's claimed invention, which provides for the first time for the sublingual oral drug delivery in a film format, capable of being mass produced with the necessary uniformity (quality) to meet regulatory

requirements.

Neither the Examiner nor BDSI have met their burden of proving anticipation or obviousness and the rejections set forth in the RAN should be reversed.

II. CLAIM REJECTIONS ADDRESSED HEREIN.

The following claim rejections and associated errors in rejecting same that are directly and/or indirectly addressed herein are listed below. Moreover, Appellant maintains all its early arguments addressing same.

A. Claims 1-11, 13-15, 17-71, 82-90, 92-94, 96-150, 161-172, 174-176, 178-232, 243-253, 256, 258-271, 274, 276-289, 292 and 294-318 stand rejected under 35 U.S.C. § 103(a) as being unpatentable over Chen (RAN, pp. 29-44).

B. Claims 2, 3, 32, 55, 72-81, 111, 134, 151-160, 193, 216 and 233-242 stand rejected under 35 U.S.C. §103(a) as being unpatentable over the combined teaching of Chen and Staab (RAN, pp. 45-48).

C. Claims 317 and 318 stand rejected under 35 U.S.C. § 103(a) as being unpatentable over the combined teachings of Chen and Arter (RAN, pp. 48-50).

D. Claims 317 and 318 stand rejected under 35 U.S.C. § 103(a) as being unpatentable over the combined teachings of Chen and Strobush (RAN, pp. 50-52).

E. Claims 1-5, 10, 13-15, 21, 24, 25, 32, 44-46, 54, 55, 59, 63-70, 72-75, 78-84, 89, 92-94,100,103,104,111,123-125,133,134,138, 142-149, 151-154, 157-166,171, 174-176, 182, 185, 186, 193, 205-207, 215, 216, 220, 224-231, 233-236, 239-242,

249-252, 258-260, 267-270, 276-278, 285-288 and 294-318 stand rejected under 35 U.S.C. § 102(b) as anticipated by or, in the alternative under 35 U.S.C. § 103(a) as being obvious over Staab (RAN, pp. 52-62).

F. Claims 8, 9, 76, 77, 87, 88, 155, 156, 169, 170, 237 and 238 stand rejected under 35 U.S.C. § 103(a) as being unpatentable over Staab are (RAN, pp. 62-63).

G. Claims 82, 89, 90, 92, 161, 171, 172, 174, 274, 292, 304-311 and 313-318 stand rejected under 35 U.S.C. § 103(a) as being unpatentable over Le Person (RAN, pp. 63-71).

III. RESPONDENT'S REITMAN DECLARATION DEMONSTRATES THAT **CHEN'S PROCESSES PRODUCE FILMS WHICH ARE 30% FROM THE EXPECTED OR DESIRED DOSAGE WEIGHT** AND **NOT** THE 10% OR LESS RELIED ON BY THE EXAMINER AND BDSI FOR PRIMA FACIE OBVIOUSNESS (RAN, pp. 36-37, 44, 74-75, 77, 85, 88, 97, 100, 104, etc.; BDSI's RB, pp. 7, 8, 9, 17-28, etc.).

BDSI and the Examiner have both relied on the false assumption that uniformity of weight of equally sized film samples in Chen, *e.g.*, is, by itself, sufficient to demonstrate that the amount of active present in prior art references meets the '080 Patent's claimed uniformity of active. *See, e.g.*, RAN, pp. 36-37, 44, 74-75, 77, 85, 88, 97, 100, 104, etc.; and BDSI's RB, pp. 7, 9, 17-18, 22, etc. As a consequence of this improper assumption, BDSI's Reitman Declaration (EA-3) instead clearly **demonstrates the inability of Chen to provide** film dosage units meeting the '080 Patent's claimed substantial uniformity across different manufactured resulting films (lots).

BDSI's Reitman declares that she and her team "**manufactured a film in accordance with Example 7 of *Chen***", *i.e.*, Chen Example 7 film (Reitman Declaration, EA-3, p. 2, ¶ 3, emphasis supplied).

Reitman further declares that her 5 cm^2 dosage unit samples of **Reitman's Chen Example 7 film ("Reitman's Chen Example 7 film") all weighed exactly 34 mg.** *See* Reitman Declaration, EA-3, Table 2, page 4, ¶ 6.

Chen provides all the information necessary to calculate the weight of the 5 cm^2 dosage unit samples of Chen's Example 7 film. Indeed, **Chen's 5 cm^2 dosage unit sample of Example 7 film ("Chen's Example 7 film") weighed 48.8 mg.**[3]

According to the Examiner and BDSI, Chen's process provides for the production of uniform films. Moreover, in accordance with the Examiner's and BDSI's "assumption" that the same size films should have the same distribution of components and thus weigh the same, any replication of Chen's Example 7 must, in accordance with this "assumption", result in the same size films having the same weight. Yet, instead of **Chen's Example 7 film weighing the same as Reitman's Chen Example 7 film, they differ in weight by 30%.**[4]

The findings of obviousness and inherency are based on this erroneous "assumption", *e.g.*, that purely physical characteristics, *e.g.,* weight, can determine the degree of uniformity of content in the amount of active. There is a **30% weight difference between Chen's Example 7 film samples and Reitman's Chen's Example 7 film samples**. The "assumption" requires there to be a 30% difference in the weight (amount) of active between Chen's and Reitman's samples. Thus, **Chen's Example 7 and Reitman's Chen's Example 7 demonstrate a lack of**

---

[3] Chen provides the following information regarding its film formed in Chen Example 7 (Chen, p. 22, Table 6, and p. 16, l. 5): Thickness = 3.2 mil = 0.008128 cm (3.2 mil x 0.00254 cm/mil = 0.008128 cm.); Size = 5 cm^2; and Density = 1.2 gm/cm^3. From this information the weight of the dosage sample can be calculated. Area x Thickness x Density = Weight of Film Sample. 5 cm^2 x 0.008128 cm x 1.2 gm/cm^3 = 0.0488 gm = 48.8 mg. Thus, the weight of Chen's 5 cm^2 Example 7 sample is **48.8 mg**, and any duplication of this example is expected to produce same size samples having the same weight.

[4] Chen's Example 7 Weight of Samples was 48.8 mg. Reitman's Example 7 Weight of Samples was 34 mg. ((48.8 mg - 34 mg)/(48.8 mg)) = (14.8 mg)/(48.8 mg) = 30%.

active content uniformity of 30% between their separately manufactured films. This degree of dis-uniformity does not meet the claimed uniformity limitation, which requires that all dosage units vary by no more than 10% from a desired amount of the active, *i.e.*, contain amounts of active within +/- 10% of the desired amount for the particular drug for all manufactured films. Nor would the 30% degree of dis-uniformity from the desired amount meet the limitation that the amount of active varies by no more than 10% in dosage units taken from a single manufactured film.

Thus, the factual basis for the Examiner's determination of *prima facie* obviousness in connection with Chen's alleged demonstration of uniformity of content in amount of active has been overcome as incorrect based on factual and objective evidence. "The examiner bears the initial burden of factually supporting any *prima facie* conclusion of obviousness. If the examiner does not produce a *prima facie* case, the applicant is under no obligation to submit evidence of nonobviousness." MPEP § 2142. The Examiner's and BDSI's allegations of obviousness and inherency cannot stand, and the rejections should be removed.

The claims of the '080 Patent are not obvious in view of Chen.

IV. **STAAB'S EXAMPLE DEMONSTRATES A 100% - 90% DIFFERENCE IN UNIFORMITY** AND **NOT** THE 10% OR LESS RELIED ON BY THE EXAMINER AND BDSI FOR PRIMA FACIE OBVIOUSNESS (RAN, pp. 54, 56-59, 62, 75, 85, 95, 113-114, etc.; BDSI's RB, pp. 7, 8, 17, 18, 23, 29-32, etc.).

BDSI and the Examiner have again both relied on the false assumption that uniformity of weight of equally sized film samples in Staab, *e.g.*, is, by itself, sufficient to demonstrate that the amount of active present in prior art references meets the '080 Patent's claimed uniformity of active. *See, e.g.*, RAN, pp. 54, 56-59, 62, 75, 85, 95, 113-114, etc.; BDSI's RB, pp. 7, 8, 18, 29-32, etc. However, this "assumption" is incorrect. At best, Staab's ability to double the amount of its starting active which, if believed on its face, is an example of the application of alchemy or, more likely, is merely a bad prophetic example. Staab demonstrates the lack of uniformity of content in amount of active exceeding 90% - 100% and thus cannot be relied upon as a reference to reject the current claims.

Staab states (Staab, col. 11, l. 22 to col. 12, l. 3) that, when he incorporated 10% of a 50% by weight benzalkonium chloride aqueous solution into a film-forming mixture, he obtained, after drying, a film product having exactly 19 mg benzalkonium chloride ("active") in all film samples weighing 190 mg each. According to BDSI and the Examiner, because all the film samples had 19 mg of active, this demonstrated a 0% variation in uniformity of content in the active, and the Examiner relied on this 0% in his rejections. The Examiner's and BDSI's conclusion of **0% is wrong! Staab's lack of degree of uniformity of active content is actually 100% from the desired amount**.

The following is based on Staab, col.11, lines 22-51, and assumes no water is driven off. Staab starts with **10% by weight of benzalkonium chloride (50% aqueous)**. Thus, Staab starts

with **5% by weight of benzalkonium chloride active and 5% by weight of water**.[5] Staab and any reader/POSA would expect that the resulting film would maintain the 5% by weight of benzalkonium chloride active.[6] This is the desired amount of active. Staab cut out 190 mg samples from his resulting film. If Staab maintained the 5% by weight of active, the expected or desired amount of active in a 190 mg film sample would be 9.5 mg of benzalkonium chloride active.

190 mg x 5% = **9.5 mg**[7] **= Staab's desired amount of active**.

Instead Staab's 190 mg samples each contained 19 mg of benzalkonium chloride active.

19 mg is Staab's "reported" amount of active.

---

[5] The Examiner also relied on Staab starting with 5% water in his obviousness analysis. "The ingredients blended to prepare the film are 52.5% HPMC, 37.5% glycerin and 10.0% of a 50% aqueous solution of the benzalkonium chloride (see col. 11, lines 30-34). Since **the water content before drying is 5%** (i.e., half of the 10% of the 50% aqueous solution of benzalkonium chloride), the dried film must have a water content of 10% or less as here claimed." RAN, p. 55 (emphasis supplied).

[6] This is assuming that everything else stays the same except, perhaps, for the water content. In the extreme example where the 5% by weight of water is removed, the expected, desired amount of active becomes 5.26% (.0526) by weight of benzalkonium chloride. (5)/(100-5) = (5)/(95) = .0526.

[7] **So far we have assumed that no water was driven off because Staab says nothing about the water content of his films. But even if we assume that all the water is driven off, then the difference is still too much at 90%.** If all the 5% by weight of water was driven off, then 10.0 mg of active would be the desired amount of active (190 mg x .0526 = 9.994 mg), and Staab's 19 mg of active results in a 90% difference from the 10 mg desired amount. A 90% difference would not meet regulatory requirements either.

The variation in uniformity of distribution of benzalkonium chloride active in Staab's resulting films was 100% from the desired amount.

$$\frac{\text{19.0 mg (actual amount of active) - 9.5 mg (desired amount of active)}}{\text{9.5 mg (desired amount of active)}}$$

$$= (9.5)/(9.5) = \mathbf{100\%}.$$

Nor would the 100% (or even the 90%) degree of dis-uniformity from the desired amount meet the limitation that the amount of active varies by no more than 10% in dosage units taken from a single manufactured film.

Thus, the factual basis for the Examiner's determination of *prima facie* obviousness in connection with Staab's alleged demonstration of uniformity of content in amount of active has been overcome as incorrect based on factual and objective evidence. "The examiner bears the initial burden of factually supporting any prima facie conclusion of obviousness. If the examiner does not produce a *prima facie* case, the applicant is under no obligation to submit secondary evidence to show nonobviousness." MPEP § 2142. The Examiner's and BDSI's allegations of obviousness and inherency cannot stand, and the rejections should be removed.

The claims of the '080 Patent are neither anticipated by, nor obvious in view of, Staab.

V. LE PERSON FIGURE 10 DEMONSTRATES A DEGREE OF **MALDISTRIBUTION OF ACTIVE OF FROM OVER 20% TO OVER 150%** AND NOT THE 10% OR LESS RELIED ON BY THE EXAMINER AND BDSI FOR PRIMA FACIE OBVIOUSNESS (RAN, pp. 63-71, 75, 85, 95, 115-117, etc.; BDSI's RB, pp. 32-35, etc.).

Le Person has not been used to reject claim 1 or its dependencies.[8] As MonoSol has argued from the beginning, Le Person demonstrates the maldistribution of active in thin films.[9] The Examiner and BDSI allege that Le Person's maldistribution is irrelevant because Le Person only discusses and provides data on the maldistribution of active in the depth (Z-axis) of the films tested. But the Examiner has not considered two important facts. First, the degree of maldistribution in Le Person is enormous. Second, Le Person discusses the large degree of shrinkage (50%) of the film as components evaporate. Contractive forces attendant to such shrinkage can cause significant movement of the active in virtually any direction. The Examiner's disregard of the lack of uniformity in Le Person was thus clear error.

Moreover, the '080 Patent claims all require that the process ensures that the "substantially uniform distribution of said active by locking-in or substantially preventing migration of said active within said visco-elastic film" is maintained throughout the manufacturing process. Substantial uniformity is not limited to uniformity only in the X-Y plane of the film, but the Z-axis as well. The fact that the testing steps are for total amount of active in

---

[8] Also, "[n]either in the request for reexamination nor in the Comments filed 04/12/13 has Third Party Requester shown how Le Person alone teaches or renders obvious all the limitations in claim 1." RAN, p. 64.

[9] Please note that Le Person uses the term "enduction" which, according to an online dictionary, means "coating" in French.

individual dosage units is related to the need for its application as a delivery system for bioactives and pharmaceutical actives regulated by the FDA.

Moreover, as the Examiner premises his case for *prima facie* obviousness on the conclusion that MonoSol's claimed uniformity would necessarily result from Le Person's disclosure, the Examiner's distinction that Le Person's examination and disclosure of the maldistribution of active (lack of substantial uniform distribution of active) in its films was limited to the Z-axis is without merit and cannot be disregarded.

Certainly, Le Person's disclosure of the maldistribution in active in the Z-axis as determined by analytical chemical testing, with the concomitant 50% shrinkage, must reflect maldistribution in the X-Y plane of Le Person's films as well. "The coupling between studies performed, on the one hand on a temporal basis (chromatographic and coulometric analysis), and on the other hand on a spatial basis (LSCM) allows to propose a model of the constituent transports inside the film whose thickness shrinks from 100 to 50 μm during drying." Le Person, p. 263. Common sense dictates that the 50% reduction in thickness of the film causes the active to move not only in the Z-axis but in the X-Y plane as well. Such contractive forces are clearly not limited to a single axis. There is certainly no reason or evidence to believe that such enormous maldistribution is limited to the Z-axis, especially as the film shrinks and the active is forced to find a place to reside.

MonoSol provides herein, based on Le Person's own data, a quantitative aspect to the degree of maldistribution or lack of uniformity in the distribution of active in Le Person's films. The quantitative data from Le Person demonstrates that: (i) at 5 minutes, Le Person's films

exhibited a maldistribution of active of over **80%**; (ii) at 10 minutes, Le Person's films exhibited a maldistribution of active of over **150%**; and (iii) at 15 minutes, Le Person's films exhibited a maldistribution of active of over **20%**.

Thus, Le Person's films significantly exceed the claimed "**substantially uniform distribution of said active**" of the '080 Patent, as demonstrated by analytical chemical tests which clearly **do not indicate** that the "uniformity of content in the amount of the active varies by no more than 10% ". Finally, the '080 Patent claims explicitly provide for "locking-in" uniformity "within about the first 4 minutes." MonoSol has consistently and repeatedly emphasized the importance of this claim language in achieving its degree of uniformity. Neither Le Person, Chen, Staab, nor any other prior art reference recognizes this important claim feature, which clearly further distinguishes the references in so far as their inability to "lock-in" within "about the first 4 minutes." This is clearly established by Le Person's demonstration of the continual movement of the active mass during at least the first 15 minutes of drying. **Le Person Figure 10 unequivocally demonstrates that Le Person's films could not lock-in uniformity within 5 or even 10 minutes.**

A. Development of Le Person's quantitative disclosure of the maldistribution of active in its films.

Figure 10 of Le Person (Le Person, p. 262) shows the mass fraction of the active substance relative to the complete film coating measured at 2 micron intervals from the bottom of the film (the left side of Figure 10) to the top of the film (see "exposed surface" all the way to the right of Figure 10). Le Person prepared three films which were analyzed for variation in active relative to the Z-axis of the films. These films, indicated on Figure 10 by "◊", "□", and "**X**", were dried for 5 minutes, 10 minutes and 15 minutes, respectively. Figure 10 provides the mass fraction of active for each of the films at various depths of the films. Those data points appear in Chart I below. As a measure of quality control to ensure that the correct numbers were used for each data point, Appellant inputted the Chart I data into a Microsoft Excel spreadsheet and had Excel generate its own figure based on the data in Chart I. The Excel generated figure appears below a copy of Le Person Figure 10 on the next page and, as can be seen, both exactly match each other with respect to the data points. Hence, the data in Chart I accurately reflects the information provided in Le Person's Figure 10.

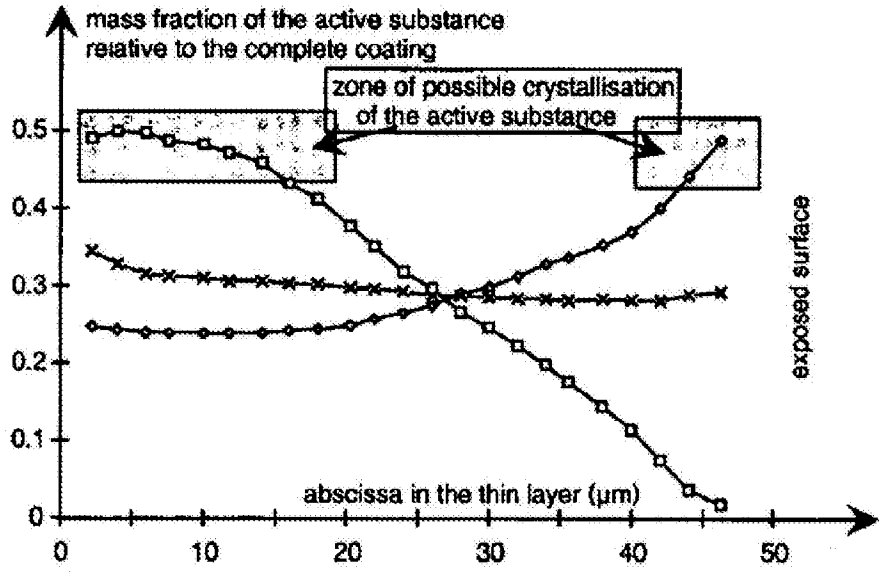
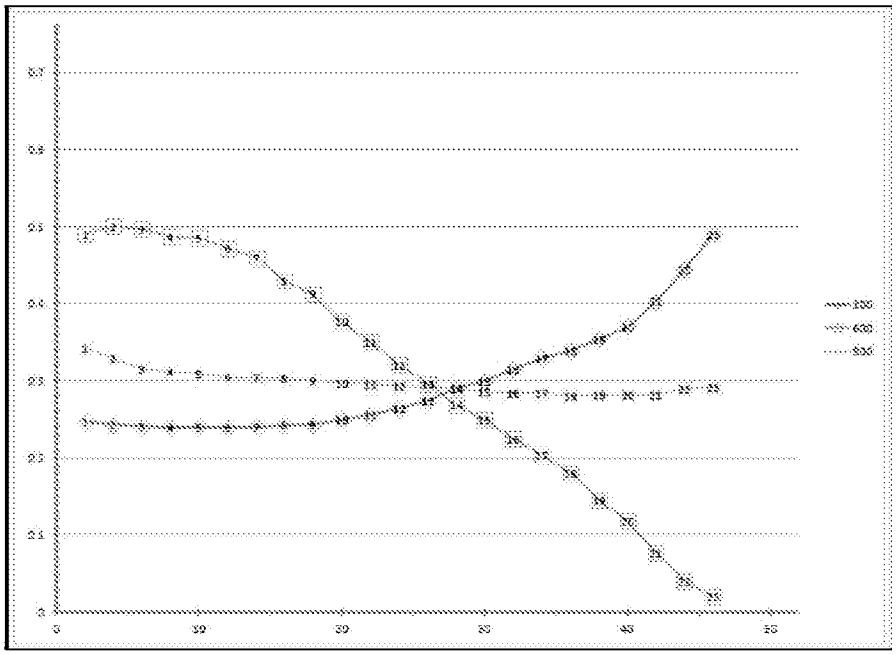


Fig. 10. Mass fraction fields of the active substance at three drying times (300 ◇, 600 □, 900 s x) during drying of a 100 µm thick coating under Short Infra Red drying process. Indications of the possible zones of crystallisation.



B. Le Person Figure 10 & Excel Reproduction of Le Person Figure 10 from Data Points in Chart I

C. Chart I - Data Points from Le Person Figure 10

Le Person Figure 10 Demonstrates Maldistribution of Active

Data Point	300 seconds 5 minutes ◊	600 seconds 10 minutes □	900 seconds 15 minutes X
1	0.247	0.490	0.343
2	0.244	0.500	0.329
3	0.241	0.497	0.315
4	0.240	0.487	0.312
5	0.240	0.485	0.309
6	0.240	0.472	0.305
7	0.240	0.460	0.304
8	0.243	0.430	0.303
9	0.244	0.413	0.301
10	0.250	0.377	0.297
11	0.256	0.350	0.296
12	0.265	0.330	0.293
13	0.275	0.296	0.292
14	0.291	0.269	0.290
15	0.299	0.250	0.286
16	0.315	0.225	0.284
17	0.329	0.204	0.284
18	0.339	0.180	0.281
19	0.354	0.145	0.282
20	0.370	0.118	0.282
21	0.403	0.077	0.282
22	0.445	0.040	0.285
23	0.490	0.020	0.292
MAX	0.490	0.500	0.343
MIN	0.240	0.020	0.281
AVG	0.298	0.309	0.298
(Max-Min)/Avg.	83.82%	155.38%	20.81%

As referred to above, these data points provide a quantitative measure to the degree of maldistribution of active in Le Person's films. The maldistribution differed for different drying times. The maldistribution of active of >80%, >150%, and >20% for films dried at 5 minutes, 10 minutes, and 15 minutes, respectively, clearly demonstrates that a "substantially uniform distribution of active" in Le Person's films had not been achieved within about 4 minutes as required by the '080 Patent claims. Moreover, even the film with the least maldistribution of active, the film dried for 15 minutes, namely >20%, does not support a degree of uniformity of active in individual dosage units which varies by no more than 10%.

Thus, the factual basis for the Examiner's determination of *prima facie* obviousness in connection with Le Person's alleged demonstration of uniformity of content in amount of active has been overcome as incorrect based on factual and objective evidence. "The examiner bears the initial burden of factually supporting any *prima facie* conclusion of obviousness. If the examiner does not produce a *prima facie* case, the applicant is under no obligation to submit evidence of nonobviousness." MPEP § 2142. The Examiner's and BDSI's allegations of obviousness and inherency cannot stand and the rejections should be removed.

The claims of the '080 Patent are not obvious in view of Le Person.

VI. THUS, CHEN AND/OR STAAB AND/OR LE PERSON DO NOT RENDER THE '080 PATENT CLAIMS UNPATENTABLE.

Thus, Chen and/or Staab and/or Le person do not render the following '080 Patent claims unpatentable: claims 1-11, 13-15, 17-71, 21, 24, 25, 32, 44-46, 54, 55, 59, 63-70, 72-81, 82-84, 82-90, 92-94, 96-150, 151-160, 161-172, 174-176, 178-232, 233-242, 243-253, 256, 258-271, 274, 276-289, 292 and 294-318. It was error to reject same.

VII. ARTER AND STROBUSH DO NOT SUPPLY THE MISSING CLAIM ELEMENTS OF CHEN, STAAB AND LE PERSON (RAN, pp. 48-50, 50-52; BDSI's RB, 23-28)

Arter and Strobush[10] do not disclose the claim elements absent from Chen, Staab and/or Le Person and thus do not remedy their defects as references. Moreover, as noted above, Appellant maintains all its prior arguments regarding Arter and Strobush. *See, e.g.*, discussions in Appeal Brief.

A. Arter

The claim elements missing in Chen are not provided by Arter. Arter is cited for its disclosure of foraminous shields which form a "quiescent region" between the shields and the coated surface. Arter is a customized process and apparatus useful for making photographic coatings. Such a process and apparatus are not at all transferrable to drying methods for pharmaceutical films and, particularly, pharmaceutical films which are aqueous-based and self-supporting.

Arter is only concerned about the coatings appearance, not the degree of uniformity. At the very least, Arter is devoid of any suggestion whatsoever of the "locking-in" within "about the first 4 minutes" or the degree of uniformity as claimed.

B. Strobush

The claim elements missing in Chen are not provided by Strobush. Strobush teaches that evaporation of the solvent must be performed very slowly (low $h\Delta T$), in multiple stages, so that the silver atoms lined up on the coating's surface are not disturbed so as not to cause a mottled

---

[10] Arter (U.S. 4,365,423) ("Arter"); and Strobush (U.S. 5,881,476) ("Strobush")

appearance to the photographic coating. Strobush states "increasing the initial rate of heat transfer to the film ($h\Delta T_i$), increased the severity of mottle." Strobush, col. 20, ll. 39-41.

In contradistinction, the '080 Patent claims require **rapid evaporation of at least a portion of the solvent within about 4 minutes** so as to maintain the substantial uniformity in the distribution of active.

> "(c) controlling drying through a process comprising conveying said flowable polymer matrix through a drying apparatus using air currents, which have forces below a yield value of said flowable polymer matrix during drying, to **evaporate at least a portion of said solvent** to form a visco-elastic film, having said active substantially uniformly distributed throughout, **within about the first 4 minutes** by rapidly increasing the viscosity of said flowable polymer matrix upon initiation of drying **to maintain said substantially uniform distribution of said active by locking-in or substantially preventing migration of said active within said visco-elastic film**, such that uniformity of content in the amount of said active in substantially equal sized individual dosage units, sampled from different locations of said visco-elastic film, varies by no more than 10%, and wherein during said drying said flowable polymer matrix temperature is 100 °C or less;".
>
> '080 Patent, claim 317, Appellant Brief, p. CA-39 (emphasis supplied).

See also, '080 Patent, claim 318, Appellant Brief, p. CA-40-41.

Again, as previously argued, Strobush is concerned about eliminating mottle to achieve a good appearance and is devoid of any teaching regarding "locking-in" within "about the first 4 minutes" or achieving the degree of uniformity claimed.

Thus, claims 317 and 318 are not rendered obvious over the combined teachings of Chen and Arter and/or Strobush. The Examiner's and BDSI's allegations of obviousness should and cannot stand and the rejections should be removed.

VIII. BOGUE DECLARATIONS AND COMMERCIAL SUCCESS – THE APPROPRIATE NEXUS TO THE CLAIMED INVENTION IS PRESENT (RAN, pp. 74, 78-80; BDSI's RB, pp. 10-18)

The Bogue Declarations provide ample evidence of the nexus between the commercially manufactured resulting films discussed in his declarations and the claimed invention as well as the commercial success of the claimed invention as exemplified by the sales of Suboxone. It was error not to do so. As set forth in Section II of Bogue Declaration I (AB, EA-1):

> II. Producing resulting films in accordance with the '080 Patent
>
> 4. Each of the 73 lots of resulting films (Lots 1-73) containing approximately 2,000,000 individual dosage units per lot discussed herein were manufactured: (i) for commercial use and regulatory approval; (ii) in compliance with U.S Food and Drug Administration ("FDA") standards and regulations, including those relating to analytical chemical testing for variation in active in individual dosage units; and (iii) in accordance with the invention disclosed in the '080 Patent, and as claimed by the '080 Patent both as issued and as amended in the Patentee's Reply to the Office Action; by:
>
> (a) forming a flowable polymer matrix comprising a water-soluble polymer, a solvent and a pharmaceutical active, said matrix having a substantially uniform distribution of said active;
>
> (b) casting said flowable polymer matrix, said flowable polymer matrix having a viscosity from about 400 to about 100,000 cps;
>
> (c) controlling drying through a process comprising conveying said polymer matrix through a drying apparatus and evaporating at least a portion of said solvent to form a visco-elastic film, having said active substantially uniformly distributed throughout, within about the first 4 minutes by rapidly increasing the viscosity of said polymer matrix upon initiation of drying to maintain said substantially uniform distribution of said active by locking-in or substantially preventing migration of said active within said visco-elastic film wherein the polymer matrix temperature is 100 °C or less;

(d) forming the resulting pharmaceutical film from said visco-elastic film, wherein said resulting pharmaceutical film has a water content of 10% or less and said substantially uniform distribution of active by said locking-in or substantially preventing migration of said active is maintained, such that uniformity of content in the amount of the active in substantially equal sized individual dosage units, sampled from different locations of said resulting pharmaceutical film, varies by no more than 10%; and

(e) performing analytical chemical tests for uniformity of content of said active in substantially equal sized individual dosage units of said sampled resulting pharmaceutical film, said tests indicating that uniformity of content in the amount of the active varies by no more than 10%, [see Appendix A] said resulting pharmaceutical film suitable for commercial and regulatory approval, wherein said regulatory approval is provided by the U.S. Food and Drug Administration.

5. Additionally, the uniformity of content in the amount of active as sampled from the 73 lots of resulting film varies no more than 10% from the desired amount of the active as indicated by said analytical chemical tests from 4(e) above. [See Appendix B]

Bogue Declaration I, ¶¶ 4 & 5, AB, EA-1.

In accordance with the process steps above, the ability to manufacture up to 2,000,000 films per lot of pharmaceutical-containing active with prescribed amount of active per unit dose provides the ability, for the first time, to provide a commercially viable FDA approved product, **(i) in a sub-lingual oral drug delivery film, (ii) in commercially sufficient quantities, and (iii) of sufficient quality (uniformity of active)** to enable Suboxone to have had sales of 1 billion dollars in 2012 alone. The combination of items (i), (ii) and (iii) alone at least provide the necessary nexus. Those sales figures have continued to increase, notwithstanding the entry into the marketplace of generic Suboxone tablets.

But for the process of the present invention as currently claimed, these sales would not be possible. Unless the uniformity of content in the amount of active as claimed is present, films

produced by the process claimed would not be marketable. The commercial success of the claimed film is directly related and conditioned upon achieving the claimed uniformity of active content in equally sized dosage units. These films were the first pharmaceutical sublingual film dosage units ever sold in the United States. Absent the ability to achieve the claimed uniformity, no pharmaceutical film could be commercially sold.

MonoSol submits that a clear nexus exists between the claims of the '080 Patent and its commercial success. Such evidence deserves full consideration and further supports secondary considerations relevant to the patentability of the claims.

IX. CONCLUSION

For the reasons set forth herein, all rejections should be withdrawn and a reexamination certificate issued.

If a reexamination certificate is not issued, Appellant requests that prosecution in this reexamination should be reopened and/or remanded, and the Examiner directed to respond with a non-final office action.

Appellant authorizes the Commissioner to charge all fees, if any, associated herewith to Deposit Account No. 08-2461.

Dated: May 27, 2014 Respectfully submitted,

/Daniel A. Scola, Jr./
Daniel A. Scola, Jr.
Registration No. 29,855

Michael I. Chakansky
Registration No. 31,600

HOFFMANN & BARON, LLP
6900 Jericho Turnpike
Syosset, New York 11791
(973) 331-1700

Attorneys for the Appellant

EVIDENCE APPENDIX

The below Reitman declaration was submitted by Third-Party Requester/Cross-Appellant. It was admitted in the record, and referred to in the Examiner's Right of Appeal Notice, mailed December 6, 2013, *see*, *inter alia*, pp. 2, 14, 75,77, 87-92, 94, 97, 100, 105.

3 BDSI's/Respondent's Declaration by Maureen Reitman, Sc.D. Under 37 C.F.R. § 1.132, dated February 28, 2013, filed April 12, 2013 ("Reitman Declaration")

3 BDSI's/Respondent's Declaration by Maureen Reitman, Sc.D. Under 37 C.F.R. § 1.132, dated February 28, 2013, filed April 12, 2013 ("Reitman Declaration")

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re *Inter Partes* Reexamination of:	)
US Patent No. 7,897,080	)
Issued: March 1, 2011	) Confirmation No.: 6418
Named Inventor: Robert K. Yang *et al.*	) Group Art Unit: 3991
Control No.: 95/002,170	) Examiner: Diamond, Alan D.
Filed: September 10, 2012	) M&E Docket: 117744-00023
Title: POLYETHYLENE-OXIDE BASED FILMS AND DRUG DELIVERY SYSTEMS MADE THEREFROM	) H&B Docket: 1199-26 RCE/CON/REX

Mail Stop *Inter Partes* Reexam
Attn: Central Reexamination Unit
Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

DECLARATION BY MAUREEN REITMAN, SC.D.
UNDER 37 CFR § 1.132

Sir/Madam:

I, Maureen Reitman, do hereby make the following declaration:

I. Technical Background

1. I am a Principal and the Director of the Polymer Science and Materials Chemistry Practice at Exponent. I hold two academic degrees: (1) a Bachelor of Science in Materials Science and Engineering from the Massachusetts Institute of Technology (MIT), and (2) a Doctor of Science in Materials Science and Engineering, with a thesis in the field of polymers, from MIT. I have been practicing in the field of polymer science and engineering for more than 20 years as a researcher at MIT, in a variety of technical roles at the 3M Company, and as a consultant with Exponent. I provide consulting engineering services in all aspects of polymer science and engineering including, but not limited to material selection, product design and development, mechanical and chemical testing, failure analysis, polymer chemistry, polymer

physics, and polymer processing. My specialties include formulation, processing and performance evaluation of polymeric materials, including films, coatings, adhesives and transdermal drug delivery systems. I have been directly involved in product development, product line extensions, transfer of new products to manufacturing, qualification of alternative materials and manufacturing equipment, evaluating field performance, and assessing intellectual property. I am a past chairman and continue to serve as a member of the board of directors of the Medical Plastics Division of the Society of Plastics Engineers. My *curriculum vitae* is provided in Appendix A.

2. While Exponent is being paid for my time, I am not an employee of, nor do I have any financial interest in, BioDelivery Sciences International, Inc.

3. I have been asked to carefully review International Publication No. WO 00/42992 ("*Chen*"), and manufacture a film as described in *Chen*. I carefully reviewed *Chen*. Under my direction, my team manufactured a film in accordance with Example 7 of *Chen*. I have also been asked to take samples and perform various analytical tests to confirm the uniform distribution of the pharmaceutical active in substantially equal sized individual dosage units of the film, which we did.

4. Manufacturing Example 7 of *Chen*

Chen states: "According to Examples 1-8, the hydrocolloid [Methocel E5(HPMC)] was dissolved in water under agitated mixing to form a uniform and viscous solution." Chen 17:7-8.

- Methocel E5(HPMC) was dissolved in water under agitated mixing to form a uniform and viscous solution, by my team.

Chen states: "Additional ingredients were then added sequentially to the viscous solution such as peppermint, aspartame, propyl[ene] glycol, benzoic acid and citric acid under agitated mixing until they were uniformly dispersed or dissolved in the hydrocolloid." Chen 17:8-11.

- Additional ingredients were then added sequentially to the viscous solution including peppermint oil, aspartame, propylene glycol, benzoic acid and citric acid under agitated mixing until they were uniformly dispersed or dissolved in the hydrocolloid, by my team.

- Kolliphor EL was also added to the viscous solution.

Chen states: "Therapeutic agents were added to the homogeneous mixture (coating solution) prior to forming the film." *Chen* 20:19-20.

- Oxybutynin chloride (the therapeutic agent of Example 7) was added to the homogeneous mixture (coating solution) prior to forming the film, by my team.

Chen's Table 5 specifies the composition for Example 7.

- We used the ingredients in the amounts identified in *Chen*'s Table 5. *See* Table 1.

Table 1			
Formulation, Ex. 7, Table 5, *Chen*	% Weight	Formulation, Prepared by Maureen Reitman Team	% Weight
Oxybutynin	3.71	Oxybutynin chloride	3.71
Methocel E5 (HPMC)	21.06	Methocel E5 Premium LV	21.06
Water	70.72	Water, distilled	70.72
Cremophor EL40	1	Kolliphor EL[1]	1
Propylene glycol	1	Propylene glycol	1
Peppermint	1	Peppermint oil	1
Aspartame	0.8	Aspartame	0.8
Benzoic acid	0.013	Benzoic acid	0.013
Citric acid	0.7	Citric acid, monohydrate	0.7

Chen states: "The resultant mixture was degassed in a vacuum chamber until trapped air bubbles were removed." Chen 17:11-12.

- The resultant mixture was degassed in a vacuum chamber until trapped air bubbles were removed, by my team.

Chen states: "The formulation was then coated on the non-siliconized side of a polyester film at a wet thickness of 10 mil and dried in a hot air circulating oven at 50°C for 9 minutes." Chen 17:13-15.

- The formulation was then coated on a non-siliconized side of a polyester film at a wet thickness of 10 mil and dried in a hot air circulating oven at 50°C for up to 9 minutes, on commercial manufacturing equipment by my team.

Chen states: "Methods for manufacturing the dosage unit include the solvent casting methods as shown in Figure 2." Chen 15:13-14. "The manufacturing process for forming the dosage unit is illustrated in Figure 2. The dry film formed by this process is a glossy, stand alone, self supporting, non-tacky and flexible film (12)." Chen 15:29-31.

- A solvent casting manufacturing process for forming the dosage unit as illustrated in Figure 2 was used[2], by my team.

[1] The Cremophor line of products now owned by BASF and renamed Kolliphor. Based on the naming convention of the Cremophor/ Kolliphor products, EL40 is Polyoxyl 40 Castor Oil and EL is Polyoxyl 35 Castor Oil (*i.e.*, they are based on a 1:40 and 1:35 ratio, respectively, of castor oil:ethylene oxide). They are different materials. However, one of skill in the art would recognize Kolliphor EL as an appropriate substitute, as Cremophor EL40 is no longer available.

- The film was manufactured using a controlled drying process.
- As illustrated in Figure 2, the drying oven featured aeration controller with 3 zones set such that in each successive zone air impingement on the surface of the film increased.
- The dry film formed by the process is a glossy, stand alone, self-supporting, non-tacky and flexible film.

Chen states: "A glossy, substantially transparent, stand alone, self-supporting, non-tacky and flexible film was obtained after drying." Chen 17:15-16.

- A glossy, substantially transparent, stand alone, self-supporting, non-tacky and flexible film was obtained after drying, by my team.

5. Verification of Content Uniformity – Visual Inspection

- By examination with the naked eye, uniformity was verified by my team.

6. Verification of Content Uniformity – Unit Dose Weight

- By weighing individual dosage units of substantially identical size, uniformity was verified by my team. *See* Table 2.

Table 2	
Sample	Weight of 5 cm[2] dosage unit (grams)
1	0.034
2	0.034
3	0.034
4	0.034
5	0.034
6	0.034
7	0.034

7. Verification of Content Uniformity – Dissolution Test (HPLC)

- By dissolution of individual dosage units of substantially identical size and analysis by High Performance Liquid Chromatography (HPLC) active content uniformity was verified by my team. *See* Table 3.

[2] Our backing was not looped and we did not die cut in line, but the solvent casting and drying under aeration is matched.

Table 3	
Sample	Oxybutynin weight (mg)
A	4.4
B	4.4
C	4.3
D	4.4
E	4.1

- As can be seen in Table 3, the active varies by less than 10%.

8. Additional Observations

   - The components of the formulation, including the active component, were uniformly distributed in the viscous solution, which was used to cast the film, as was verified by my team.

   - The viscous solution, which was used to cast the film, exhibited the flow properties of honey (around 10,000 cps), as observed by my team.

   - Water content of the film was less than 10%, as verified by my team.

   - Within about 4 minutes after initiation of drying, the film was self-supporting, non-tacky, flexible and viscoelastic, as verified by my team.

9. I hereby declare that all statements made herein of my own knowledge are true and that all statements made on information and belief are believed to be true; and further that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine, or imprisonment, or both, under section 1001 of Title 18 of the United States Code, and that such willful statements may jeopardize the validity of the application or any patents issued thereon.

Dated: February 28, 2013

Maureen Reitman, Sc.D.

Appendix A

Exponent
Failure Analysis Associates

Exponent
[illegible]
Suite 700
Boston, Maryland 02215

[illegible]
[illegible]
[illegible]

Maureen T. F. Reitman, Sc.D.
Principal and Practice Director

Professional Profile

Dr. Maureen Reitman is a Principal and the Director of Exponent's Polymer Science and Material Chemistry practice. Her expertise includes polymer and composite technology, mechanics of materials, adhesion science, fiber mechanics, history and technology of plastics, and material failure analysis. She is skilled in the development and use of testing tools and methods and has applied them to plastic, rubber, textile, metal, glass, ceramic, and composite materials and systems. She is experienced in major aspects of product development, including materials selection, formulation, scale-up, end-use testing, failure analysis, certification procedures and issues related to intellectual property.

Dr. Reitman has conducted research in the areas of packaging and barrier materials; paints and coatings; plastic pipes; transdermal drug delivery; adhesives, sealants, and encapsulants; molding compounds; high temperature resins; nanoparticles; fibers and textiles; protective coatings and finishes; polymer chemical resistance; plastic insulation; connectors and splices; plastic packaging; medical devices; environmental effects on durability; and product aging. She has used her expertise to solve a broad range of problems related to coatings, fibers, films, and extruded and molded products, and their use in the telecom, electronics, electrical, transportation, construction, fire protection, medical, and consumer products markets.

Dr. Reitman is a member of the Board of Directors of the Medical Plastics Division of the Society of Plastics Engineers and an active member of two Underwriters Laboratories Standard Technical Panels, addressing Polymeric Materials (UL 94, UL 746, UL 1694) and Appliance Wiring (UL758).

Prior to joining Exponent, Dr. Reitman worked for the 3M Company in both research and management roles. Her activities included technology identification, materials selection and qualification, product development, customer support, program management, acquisition integration, intellectual property analysis, and patent litigation support.

Academic Credentials and Professional Honors

Sc.D., Materials Science and Engineering/ Program in Polymer Science and Technology, Massachusetts Institute of Technology, 1993
B.S., Materials Science and Engineering, Massachusetts Institute of Technology, 1990

National Academy of Engineering Frontiers of Engineering, 2009; Tau Beta Pi; Sigma Xi
John Wulff Award; Carl Loeb Fellowship; NCAA Postgraduate Scholarship;
Malcolm G. Kispert Award; GTE Academic All-American

02/13

Patents

Patent 6,311,524: Accelerated Method for Increasing the Photosensitivity of a Glassy Material, issued November 6, 2001.

European Patent EP0830428: Tackified Polydiorganosiloxane Polyurea Segmented Copolymers and a Process for Making Same, published March 25, 1998.

Patent 5,371,051: Fiber Optic Fusion Splice Protector Sleeve, issued March 24, 1998.

Publications

Kurtz S, Siskey R, Reitman M. Accelerated aging, natural aging, and small punch testing of gamma-air sterilized polycarbonate urethane acetabular components. Journal of Biomedical Materials Research Part B: Applied Biomaterials 2010 May; 93B(2):422–447.

Hoffman JM, Reitman M, Donthu S, Ledwith P. Complimentary failure analysis methods and their application to CPVC pipe. Proceedings, ANTEC 2010, Society of Plastics Engineers, Orlando, FL, May 2010.

Hoffman JM, Reitman M, Donthu S, Ledwith P, Wills D. Microscopic characterization of CPVC failure modes. Proceedings, ANTEC 2009, Society of Plastics Engineers, Chicago, IL, June 2009. Best Paper Award in Failure Analysis & Prevention.

Kurtz SM, Ebert M, Siskey R, Ciccarelli L, Reitman M, Harper ML, Chan FW. Natural and accelerated aging of polyurethanes in the Bryan cervical disc. Poster No. P158. Transactions of Spineweek 2008, Geneva, Switzerland, May 26–31, 2008.

Reitman M, Ledwith P, Hoffman M, Moalli J, Xu T. Environmentally driven changes in nylon. Proceedings, ANTEC 2008, Milwaukee, WI, Society of Plastics Engineers, May 2008.

Hoffman JM, Reitman M, Ledwith P. Characterization of manufacturing defects in medical balloons. Proceedings, ANTEC 2008, Milwaukee, WI, Society of Plastics Engineers, May 2008.

Reitman, MTF, Moalli JE. Polymeric coatings for medical device. Medical Device and Manufacturing Technology, Touch Briefings, pp. 28–30, 2006.

Moalli JE, Moore CD, Robertson C, Reitman MTF. Failure analysis of nitrile radiant heating tubing. Proceedings, ANTEC 2006, Society of Plastic Engineers, Charlotte, NC, May 2006.

Reitman M, McPeak J. Protective coatings for implantable medical devices. Proceedings, ANTEC 2005, Society of Plastic Engineers, Boston MA, May 2005.

McPeak J, Reitman M, Moalli J. Determination of in-service exposure temperature of thermoformed PVC via TMA. Proceedings, 31st Annual North American Thermal Analysis Society Conference, Williamsburg, VA, 2004.

Reitman MTF, Moalli JE. Product development and standards organizations: Listings and certifications for plastic products. 8th Annual International Conference on Industrial Engineering Theory, Applications and Practice, Las Vegas, NV, 2003.

Potdar YK, Reitman MTF. The role of engineering consultants in failure analysis and product development. 8th Annual International Conference on Industrial Engineering Theory, Applications and Practice, Las Vegas, NV, 2003.

Ezekoye OA, Lowman CD, Hulme-Lowe AG, Fahey MT. Polymer weld strength predictions using a thermal and polymer chain diffusion analysis. Polymer Engineering and Science 1998; 38(6):976–991, June.

Fahey MT. Nonlinear and anisotropic properties of high performance fibers. MIT Thesis, 1993.

Fahey MT. Mechanical property characterization and enhancement of rigid rod polymer fibers. MIT Thesis, 1990.

Book Contributions

Reitman M, Liu D, Rehkopf J. Chapter 38. Mechanical properties of polymers. In: Handbook of Measurement in Science and Engineering. Volume 2. Kutz, M (ed), John Wiley & Sons, Hoboken NJ, 2013. ISBN- 978-1-118-38464-0.

Reitman M, Jaekel D, Siskey R, Kurtz S. Morphology and crystalline architecture of polyarylketones, pp. 49-60. In: PEEK Biomaterials Handbook. Kurtz SM (ed), Elsevier William Andrews, Kidlington, Oxford, UK, 2012. ISBN 13:978-1-4377-4463-7

Tsuji JS, Mowat FS, Donthu S, Reitman M. Application of toxicology studies in assessing the health risks of nanomaterials in consumer products, pp. 543-580. In: Nanotoxicity: From In Vivo and In Vitro Models to Health Risks. Sahu S, and Casciano D. (eds), John Wiley & Sons, Chicester, West Sussex, UK, 2009. ISBN 978-0-470-74137-5.

Reitman MTF. The Plastics Revolution. In: Research and Discovery: Landmarks and Pioneers in American Science. Lawson RM (ed), Armonk NY: Sharpe Reference 2008. ISBN 978-0-7656-8073-0.

Klein SM. Mid-century plastic jewelry. Schiffer Publishing, Atglen, PA, 2005. (Technical advisor to author).

Selected Invited Presentations

Reitman MTF. Failure analysis tools. Workshop on Future Needs for Service Life Prediction of Polymeric Materials. NIST and Underwriters Laboratories, Gaithersburg, MD, October 2012.

Hoffman J, MacLean S, Ralston B, Reitman M, Ledwith P. Fractography of unfilled thermoplastic materials experiencing common mechanical failure modes. Materials Science & Technology 2012 Conference, Pittsburgh PA, October 2012.

Hoffman J, Reitman M, Ledwith P. Microscopic characterization of CPVC failure. Materials Science & Technology 2012 Conference, Pittsburgh PA, October 2012.

Reitman MTF. Polymer material properties for next generation medical devices. Invited Speaker: MedTech Polymers, UBM Canon, Chicago, IL, September 2012.

Reitman MTF. Polymers for medical applications. Fundamentals and Fellows Forum, ANTEC 2012, Orlando FL, April 2012.

Reitman MTF. Plastic and composite product failures. Invited lecture in Failure Analysis of Emerging Technologies. Stanford University Department of Materials Science and Engineering, Menlo Park, CA October 2009.

Reitman MTF. Factors for success: Plastics in injection molded medical devices. Part of *Injection Molding Works for Medical Design*, Design News Webcast, October 2008.

Reitman MTF. Plastic and composite product failures. Keynote Speaker: Third International Conference on Engineering Failure Analysis (ICEFA III), Elsevier, Sitges Spain, July 2008.

Reitman MTF. Multiphase materials for medical device applications, an overview. Medical Device and Manufacturing (MDM), Canon Communications, various locations, January- June 2008.

Reitman MTF. Nanotechnology and plastics for medical devices. Capitalizing on Nanoplastics, Intertek PIRA San Antonio TX, February 2008.

Reitman MTF. Nano additives in composites and coatings for medical device applications. Medical Device and Manufacturing Minneapolis, Canon Communications, Minneapolis MN, October 2007.

Reitman MTF, Swanger LA. Practical tips on how to manage your technical expert in patent disputes. Ropes & Gray IP Master Class, Live Teleconference, June 2007.

Reitman MTF, Kennedy E. Root cause failure analysis and accident investigation. Lorman Educational Services, Live Teleconference, November 2007.

Reitman MTF. Plastics failure analysis: Case studies. Baltimore/ Washington Chapter of SAMPE, October 2006.

Reitman MTF. Plastics failure analysis. Baxter Global Plastics Processing Conference 2005, Schaumburg IL, 2005.

Fahey MT. Fiber mechanics, corrosion, sealants: Tales of a 3M materials scientist. Class of 1960's Scholars Program, Williams College, 1999.

Fahey MT. Adhesives and sealants for the telecommunications industry. Riverwood V Conference, St. Paul MN, 1998.

Current Professional Appointments

- Underwriter's Laboratory Standards Technical Panel STP 746 (Polymeric Materials, includes UL94, UL 746 and UL1694)
- Underwriter's Laboratory Standards Technical Panel STP 758 (Appliance Wires/ UL758)
- Medical Plastics Division Board of Directors, Society of Plastics Engineers

Committee and Review Activities

- UL Forum on Initiatives to Improve the Long Term Aging Program, LTTA Tools Working Groups, Underwriters Laboratories
- Research and Engineering Technology Award Committee, Society of Plastics Engineers
- Reviewer, Medical Plastics Technical Program Committee, Society of Plastics Engineers
- Reviewer, Failure Analysis and Prevention Technical Program Committee, Society of Plastics Engineers
- Reviewer, various book proposals and submissions related to polymer science, ASM International, Elsevier, John Wiley

Professional Affiliations

- American Association for the Advancement of Science (member)
- American Association of Textile Chemists and Colorists—AATCC (senior member)
- American Chemical Society (member)
- ASTM International (member)
- Society for the Advancement of Material and Process Engineering (member)
- Society of Plastics Engineers (senior member)

CERTIFICATE OF SERVICE

It is certified that a copy of this PATENT OWNER'S APPELLANT'S REBUTTAL BRIEF has been served, by first class mail, postage prepaid, on May 27, 2014, in its entirety on the third party requester as provided in 37 CFR § 1.903 and 37 CFR § 1.248 at the address below.

DANIELLE L. HERRITT
McCARTER & ENGLISH LLP
265 FRANKLIN STREET
BOSTON, MASSACHUSETTS 02110

/Michael I. Chakansky/
Michael I. Chakansky
Registration No.: 31,600
Attorney for the Patentee/Appellant

Electronic Acknowledgement Receipt

EFS ID:	19140143
Application Number:	95002170
International Application Number:	
Confirmation Number:	6418
Title of Invention:	POLYETHYLENE-OXIDE BASED FILMS AND DRUG DELIVERY SYSTEMS MADE THEREFROM
First Named Inventor/Applicant Name:	7897080
Customer Number:	23869
Filer:	Michael I. Chakansky
Filer Authorized By:	
Attorney Docket Number:	117744-00023
Receipt Date:	27-MAY-2014
Filing Date:	10-SEP-2012
Time Stamp:	21:30:57
Application Type:	inter partes reexam

Payment information:

Submitted with Payment	no

File Listing:

Document Number	Document Description	File Name	File Size(Bytes)/ Message Digest	Multi Part /.zip	Pages (if appl.)
1	Rebuttal Brief - Owner	AppellantsRebuttalBrief.pdf	1869390 e4ae8c32870e5d47e495244a7cab0f9a66313b3d	no	45

Warnings:	
Information:	

Total Files Size (in bytes):	1869390

This Acknowledgement Receipt evidences receipt on the noted date by the USPTO of the indicated documents, characterized by the applicant, and including page counts, where applicable. It serves as evidence of receipt similar to a Post Card, as described in MPEP 503.

New Applications Under 35 U.S.C. 111
If a new application is being filed and the application includes the necessary components for a filing date (see 37 CFR 1.53(b)-(d) and MPEP 506), a Filing Receipt (37 CFR 1.54) will be issued in due course and the date shown on this Acknowledgement Receipt will establish the filing date of the application.

National Stage of an International Application under 35 U.S.C. 371
If a timely submission to enter the national stage of an international application is compliant with the conditions of 35 U.S.C. 371 and other applicable requirements a Form PCT/DO/EO/903 indicating acceptance of the application as a national stage submission under 35 U.S.C. 371 will be issued in addition to the Filing Receipt, in due course.

New International Application Filed with the USPTO as a Receiving Office
If a new international application is being filed and the international application includes the necessary components for an international filing date (see PCT Article 11 and MPEP 1810), a Notification of the International Application Number and of the International Filing Date (Form PCT/RO/105) will be issued in due course, subject to prescriptions concerning national security, and the date shown on this Acknowledgement Receipt will establish the international filing date of the application.

UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
95/002,170	09/10/2012	7897080	117744-00023	6418

23869 7590 04/25/2014

Hoffmann & Baron LLP
6900 Jericho Turnpike
Syosset, NY 11791

EXAMINER	
DIAMOND, ALAN D	
ART UNIT	PAPER NUMBER
3991	
MAIL DATE	DELIVERY MODE
04/25/2014	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Transmittal of Communication to Third Party Requester *Inter Partes* Reexamination	Control No.	Patent Under Reexamination	
	95/002,170	7897080	
	Examiner	Art Unit	
	Alan Diamond	3991	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address. --

(THIRD PARTY REQUESTER'S CORRESPONDENCE ADDRESS)

Danielle L. Herritt
McCarter & English LLP
265 Franklin Street
Boston, MA 02110

Enclosed is a copy of the latest communication from the United States Patent and Trademark Office in the above-identified reexamination proceeding. 37 CFR 1.903.

Prior to the filing of a Notice of Appeal, each time the patent owner responds to this communication, the third party requester of the *inter partes* reexamination may once file written comments within a period of 30 days from the date of service of the patent owner's response. This 30-day time period is statutory (35 U.S.C. 314(b)(2)), and, as such, it cannot be extended. See also 37 CFR 1.947.

If an *ex parte* reexamination has been merged with the *inter partes* reexamination, no responsive submission by any *ex parte* third party requester is permitted.

All correspondence relating to this inter partes reexamination proceeding should be directed to the **Central Reexamination Unit** at the mail, FAX, or hand-carry addresses given at the end of the communication enclosed with this transmittal.

Inter Partes Reexamination Examiner's Answer	Application No.	Applicant(s)	
	95/002,170	7897080	
	Examiner	Art Unit	
	Alan Diamond	3991	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address. --

Incorporation by Reference of the Right of Appeal Notice
The Right of Appeal Notice (RAN) mailed on December 6, 2013, including all of the grounds of rejection, determinations of patentability, and explanations set forth in the RAN is incorporated by reference. Every ground of rejection and every determination not to make a proposed rejection set forth in the RAN are being maintained by the examiner.

This examiner's answer does not contain any new ground of rejection and any new determination not to make a proposed rejection.

Status of Amendment After Action Closing Prosecution
The amendment(s) filed on _____ has/have been entered.
The amendment(s) filed on 3 September 2013 has/have not been entered.

Period for providing a Rebuttal Brief
Appellant(s) is/are given a period of ONE MONTH from the mailing date of this examiner's answer within which to file a rebuttal brief in response to the examiner's answer. Prosecution otherwise remains closed.

The rebuttal brief of the patent owner may be directed to the examiner's answer and/or any respondent's brief. The rebuttal brief of the third party requester(s) may be directed to the examiner's answer and/or the respondent's brief of the patent owner. The rebuttal brief must (1) clearly identify each issue, and (2) point out *where* the issue was raised in the examiner's answer and/or in the respondent's brief. In addition, the rebuttal brief must be limited to issues raised in the examiner's answer or in the respondent's brief. The time for filing the rebuttal brief may not be extended. No further submission (other than the rebuttal brief(s)) will be considered, and any such submission will be treated in accordance with 37 CFR 1.939 and MPEP 2667.

☐ Attachment(s)
_____

☐ Other:
_____

All correspondence relating to this *inter partes* reexamination proceeding should be directed to the **Central Reexamination Unit** at one of the following addresses:

Please mail any communications to:
Attn: Mail Stop "Inter partes Reexam"
Central Reexamination Unit
Commissioner for Patents
P.O. Box 1450
Alexandria VA 22313-1450

Please hand-deliver any communication to:
Customer Service Window
Attn: Central Reexamination Unit
Randolph Building, Lobby Level
401 Dulany Street
Alexandria VA 22314

Please FAX any communications to: (571) 273-9900

/Alan Diamond/
Patent Reexamination Specialist
Central Reexamination Unit 3991

/Jerry D. Johnson/
Patent Reexamination Specialist
Central Reexamination Unit 3991

/Deborah D. Jones/
Supervisory Patent Examiner, Art Unit 3991

Index of Claims	Application/Control No.	Applicant(s)/Patent Under Reexamination
	95002170	7897080
	Examiner	Art Unit
	ALAN DIAMOND	3991

✓	Rejected	-	Cancelled	N	Non-Elected	A	Appeal
=	Allowed	÷	Restricted	I	Interference	O	Objected

☐ Claims renumbered in the same order as presented by applicant ☐ CPA ☐ T.D. ☐ R.1.47

CLAIM		DATE								
Final	Original	10/08/2012	07/11/2013	11/25/2013	04/23/2014					
	1	✓	✓	✓	A					
	2	✓	✓	✓	A					
	3	✓	✓	✓	A					
	4	✓	✓	✓	A					
	5	✓	✓	✓	A					
	6	✓	✓	✓	A					
	7	✓	✓	✓	A					
	8	✓	✓	✓	A					
	9	✓	✓	✓	A					
	10	✓	✓	✓	A					
	11	✓	✓	✓	A					
	12	✓	-	-	-					
	13	✓	✓	✓	A					
	14	✓	✓	✓	A					
	15	✓	✓	✓	A					
	16	✓	-	-	-					
	17	✓	✓	✓	A					
	18	✓	✓	✓	A					
	19	✓	✓	✓	A					
	20	✓	✓	✓	A					
	21	✓	✓	✓	A					
	22	✓	✓	✓	A					
	23	✓	✓	✓	A					
	24	✓	✓	✓	A					
	25	✓	✓	✓	A					
	26	✓	✓	✓	A					
	27	✓	✓	✓	A					
	28	✓	✓	✓	A					
	29	✓	✓	✓	A					
	30	✓	✓	✓	A					
	31	✓	✓	✓	A					
	32	✓	✓	✓	A					
	33	✓	✓	✓	A					
	34	✓	✓	✓	A					
	35	✓	✓	✓	A					
	36	✓	✓	✓	A					

Index of Claims	Application/Control No.	Applicant(s)/Patent Under Reexamination
	95002170	7897080
	Examiner	Art Unit
	ALAN DIAMOND	3991

✓	Rejected	-	Cancelled	N	Non-Elected	A	Appeal
=	Allowed	÷	Restricted	I	Interference	O	Objected

☐ Claims renumbered in the same order as presented by applicant ☐ CPA ☐ T.D. ☐ R.1.47

CLAIM		DATE								
Final	Original	10/08/2012	07/11/2013	11/25/2013	04/23/2014					
	37	✓	✓	✓	A					
	38	✓	✓	✓	A					
	39	✓	✓	✓	A					
	40	✓	✓	✓	A					
	41	✓	✓	✓	A					
	42	✓	✓	✓	A					
	43	✓	✓	✓	A					
	44	✓	✓	✓	A					
	45	✓	✓	✓	A					
	46	✓	✓	✓	A					
	47	✓	✓	✓	A					
	48	✓	✓	✓	A					
	49	✓	✓	✓	A					
	50	✓	✓	✓	A					
	51	✓	✓	✓	A					
	52	✓	✓	✓	A					
	53	✓	✓	✓	A					
	54	✓	✓	✓	A					
	55	✓	✓	✓	A					
	56	✓	✓	✓	A					
	57	✓	✓	✓	A					
	58	✓	✓	✓	A					
	59	✓	✓	✓	A					
	60	✓	✓	✓	A					
	61	✓	✓	✓	A					
	62	✓	✓	✓	A					
	63	✓	✓	✓	A					
	64	✓	✓	✓	A					
	65	✓	✓	✓	A					
	66	✓	✓	✓	A					
	67	✓	✓	✓	A					
	68	✓	✓	✓	A					
	69	✓	✓	✓	A					
	70	✓	✓	✓	A					
	71	✓	✓	✓	A					
	72	✓	✓	✓	A					

Index of Claims	Application/Control No.	Applicant(s)/Patent Under Reexamination
	95002170	7897080
	Examiner	Art Unit
	ALAN DIAMOND	3991

✓	Rejected	-	Cancelled	N	Non-Elected	A	Appeal
=	Allowed	÷	Restricted	I	Interference	O	Objected

☐ Claims renumbered in the same order as presented by applicant ☐ CPA ☐ T.D. ☐ R.1.47

CLAIM		DATE								
Final	Original	10/08/2012	07/11/2013	11/25/2013	04/23/2014					
	73	✓	✓	✓	A					
	74	✓	✓	✓	A					
	75	✓	✓	✓	A					
	76	✓	✓	✓	A					
	77	✓	✓	✓	A					
	78	✓	✓	✓	A					
	79	✓	✓	✓	A					
	80	✓	✓	✓	A					
	81	✓	✓	✓	A					
	82	✓	✓	✓	A					
	83	✓	✓	✓	A					
	84	✓	✓	✓	A					
	85	✓	✓	✓	A					
	86	✓	✓	✓	A					
	87	✓	✓	✓	A					
	88	✓	✓	✓	A					
	89	✓	✓	✓	A					
	90	✓	✓	✓	A					
	91	✓	-	-	-					
	92	✓	✓	✓	A					
	93	✓	✓	✓	A					
	94	✓	✓	✓	A					
	95	✓	-	-	-					
	96	✓	✓	✓	A					
	97	✓	✓	✓	A					
	98	✓	✓	✓	A					
	99	✓	✓	✓	A					
	100	✓	✓	✓	A					
	101	✓	✓	✓	A					
	102	✓	✓	✓	A					
	103	✓	✓	✓	A					
	104	✓	✓	✓	A					
	105	✓	✓	✓	A					
	106	✓	✓	✓	A					
	107	✓	✓	✓	A					
	108	✓	✓	✓	A					

Index of Claims	Application/Control No.	Applicant(s)/Patent Under Reexamination
	95002170	7897080
	Examiner	Art Unit
	ALAN DIAMOND	3991

✓	Rejected	-	Cancelled	N	Non-Elected	A	Appeal
=	Allowed	÷	Restricted	I	Interference	O	Objected

☐ Claims renumbered in the same order as presented by applicant ☐ CPA ☐ T.D. ☐ R.1.47

CLAIM		DATE								
Final	Original	10/08/2012	07/11/2013	11/25/2013	04/23/2014					
	109	✓	✓	✓	A					
	110	✓	✓	✓	A					
	111	✓	✓	✓	A					
	112	✓	✓	✓	A					
	113	✓	✓	✓	A					
	114	✓	✓	✓	A					
	115	✓	✓	✓	A					
	116	✓	✓	✓	A					
	117	✓	✓	✓	A					
	118	✓	✓	✓	A					
	119	✓	✓	✓	A					
	120	✓	✓	✓	A					
	121	✓	✓	✓	A					
	122	✓	✓	✓	A					
	123	✓	✓	✓	A					
	124	✓	✓	✓	A					
	125	✓	✓	✓	A					
	126	✓	✓	✓	A					
	127	✓	✓	✓	A					
	128	✓	✓	✓	A					
	129	✓	✓	✓	A					
	130	✓	✓	✓	A					
	131	✓	✓	✓	A					
	132	✓	✓	✓	A					
	133	✓	✓	✓	A					
	134	✓	✓	✓	A					
	135	✓	✓	✓	A					
	136	✓	✓	✓	A					
	137	✓	✓	✓	A					
	138	✓	✓	✓	A					
	139	✓	✓	✓	A					
	140	✓	✓	✓	A					
	141	✓	✓	✓	A					
	142	✓	✓	✓	A					
	143	✓	✓	✓	A					
	144	✓	✓	✓	A					

Index of Claims	Application/Control No.	Applicant(s)/Patent Under Reexamination
	95002170	7897080
	Examiner	Art Unit
	ALAN DIAMOND	3991

✓	Rejected	-	Cancelled	N	Non-Elected	A	Appeal
=	Allowed	÷	Restricted	I	Interference	O	Objected

☐ Claims renumbered in the same order as presented by applicant ☐ CPA ☐ T.D. ☐ R.1.47

CLAIM		DATE								
Final	Original	10/08/2012	07/11/2013	11/25/2013	04/23/2014					
	145	✓	✓	✓	A					
	146	✓	✓	✓	A					
	147	✓	✓	✓	A					
	148	✓	✓	✓	A					
	149	✓	✓	✓	A					
	150	✓	✓	✓	A					
	151	✓	✓	✓	A					
	152	✓	✓	✓	A					
	153	✓	✓	✓	A					
	154	✓	✓	✓	A					
	155	✓	✓	✓	A					
	156	✓	✓	✓	A					
	157	✓	✓	✓	A					
	158	✓	✓	✓	A					
	159	✓	✓	✓	A					
	160	✓	✓	✓	A					
	161	✓	✓	✓	A					
	162	✓	✓	✓	A					
	163	✓	✓	✓	A					
	164	✓	✓	✓	A					
	165	✓	✓	✓	A					
	166	✓	✓	✓	A					
	167	✓	✓	✓	A					
	168	✓	✓	✓	A					
	169	✓	✓	✓	A					
	170	✓	✓	✓	A					
	171	✓	✓	✓	A					
	172	✓	✓	✓	A					
	173	✓	-	-	-					
	174	✓	✓	✓	A					
	175	✓	✓	✓	A					
	176	✓	✓	✓	A					
	177	✓	-	-	-					
	178	✓	✓	✓	A					
	179	✓	✓	✓	A					
	180	✓	✓	✓	A					

Index of Claims	Application/Control No.	Applicant(s)/Patent Under Reexamination
	95002170	7897080
	Examiner	Art Unit
	ALAN DIAMOND	3991

✓	Rejected	-	Cancelled	N	Non-Elected	A	Appeal
=	Allowed	÷	Restricted	I	Interference	O	Objected

☐ Claims renumbered in the same order as presented by applicant ☐ CPA ☐ T.D. ☐ R.1.47

CLAIM		DATE								
Final	Original	10/08/2012	07/11/2013	11/25/2013	04/23/2014					
	181	✓	✓	✓	A					
	182	✓	✓	✓	A					
	183	✓	✓	✓	A					
	184	✓	✓	✓	A					
	185	✓	✓	✓	A					
	186	✓	✓	✓	A					
	187	✓	✓	✓	A					
	188	✓	✓	✓	A					
	189	✓	✓	✓	A					
	190	✓	✓	✓	A					
	191	✓	✓	✓	A					
	192	✓	✓	✓	A					
	193	✓	✓	✓	A					
	194	✓	✓	✓	A					
	195	✓	✓	✓	A					
	196	✓	✓	✓	A					
	197	✓	✓	✓	A					
	198	✓	✓	✓	A					
	199	✓	✓	✓	A					
	200	✓	✓	✓	A					
	201	✓	✓	✓	A					
	202	✓	✓	✓	A					
	203	✓	✓	✓	A					
	204	✓	✓	✓	A					
	205	✓	✓	✓	A					
	206	✓	✓	✓	A					
	207	✓	✓	✓	A					
	208	✓	✓	✓	A					
	209	✓	✓	✓	A					
	210	✓	✓	✓	A					
	211	✓	✓	✓	A					
	212	✓	✓	✓	A					
	213	✓	✓	✓	A					
	214	✓	✓	✓	A					
	215	✓	✓	✓	A					
	216	✓	✓	✓	A					

Index of Claims	Application/Control No.	Applicant(s)/Patent Under Reexamination
	95002170	7897080
	Examiner	Art Unit
	ALAN DIAMOND	3991

✓	Rejected	-	Cancelled	N	Non-Elected	A	Appeal
=	Allowed	÷	Restricted	I	Interference	O	Objected

☐ Claims renumbered in the same order as presented by applicant ☐ CPA ☐ T.D. ☐ R.1.47

CLAIM		DATE								
Final	Original	10/08/2012	07/11/2013	11/25/2013	04/23/2014					
	217	✓	✓	✓	A					
	218	✓	✓	✓	A					
	219	✓	✓	✓	A					
	220	✓	✓	✓	A					
	221	✓	✓	✓	A					
	222	✓	✓	✓	A					
	223	✓	✓	✓	A					
	224	✓	✓	✓	A					
	225	✓	✓	✓	A					
	226	✓	✓	✓	A					
	227	✓	✓	✓	A					
	228	✓	✓	✓	A					
	229	✓	✓	✓	A					
	230	✓	✓	✓	A					
	231	✓	✓	✓	A					
	232	✓	✓	✓	A					
	233	✓	✓	✓	A					
	234	✓	✓	✓	A					
	235	✓	✓	✓	A					
	236	✓	✓	✓	A					
	237	✓	✓	✓	A					
	238	✓	✓	✓	A					
	239	✓	✓	✓	A					
	240	✓	✓	✓	A					
	241	✓	✓	✓	A					
	242	✓	✓	✓	A					
	243	✓	✓	✓	A					
	244	✓	✓	✓	A					
	245	✓	✓	✓	A					
	246	✓	✓	✓	A					
	247	✓	✓	✓	A					
	248	✓	✓	✓	A					
	249	✓	✓	✓	A					
	250	✓	✓	✓	A					
	251	✓	✓	✓	A					
	252	✓	✓	✓	A					

Index of Claims	Application/Control No.	Applicant(s)/Patent Under Reexamination
	95002170	7897080
	Examiner	Art Unit
	ALAN DIAMOND	3991

✓	Rejected	-	Cancelled	N	Non-Elected	A	Appeal
=	Allowed	÷	Restricted	I	Interference	O	Objected

☐ Claims renumbered in the same order as presented by applicant ☐ CPA ☐ T.D. ☐ R.1.47

CLAIM		DATE								
Final	Original	10/08/2012	07/11/2013	11/25/2013	04/23/2014					
	253	✓	✓	✓	A					
	254	✓	-	-	-					
	255	✓	-	-	-					
	256	✓	✓	✓	A					
	257	✓	-	-	-					
	258	✓	✓	✓	A					
	259	✓	✓	✓	A					
	260	✓	✓	✓	A					
	261	✓	✓	✓	A					
	262	✓	✓	✓	A					
	263	✓	✓	✓	A					
	264	✓	✓	✓	A					
	265	✓	✓	✓	A					
	266	✓	✓	✓	A					
	267	✓	✓	✓	A					
	268	✓	✓	✓	A					
	269	✓	✓	✓	A					
	270	✓	✓	✓	A					
	271	✓	✓	✓	A					
	272	✓	-	-	-					
	273	✓	-	-	-					
	274	✓	✓	✓	A					
	275	✓	-	-	-					
	276	✓	✓	✓	✓					
	277	✓	✓	✓	✓					
	278	✓	✓	✓	✓					
	279	✓	✓	✓	✓					
	280	✓	✓	✓	✓					
	281	✓	✓	✓	✓					
	282	✓	✓	✓	✓					
	283	✓	✓	✓	✓					
	284	✓	✓	✓	✓					
	285	✓	✓	✓	✓					
	286	✓	✓	✓	✓					
	287	✓	✓	✓	✓					
	288	✓	✓	✓	✓					

Index of Claims	Application/Control No.	Applicant(s)/Patent Under Reexamination
	95002170	7897080
	Examiner	Art Unit
	ALAN DIAMOND	3991

✓	Rejected	-	Cancelled	N	Non-Elected	A	Appeal
=	Allowed	÷	Restricted	I	Interference	O	Objected

☐ Claims renumbered in the same order as presented by applicant ☐ CPA ☐ T.D. ☐ R.1.47

CLAIM		DATE								
Final	Original	10/08/2012	07/11/2013	11/25/2013	04/23/2014					
	289	✓	✓	✓	✓					
	290	✓	-	-	-					
	291	✓	-	-	-					
	292	✓	✓	✓	A					
	293	✓	-	-	-					
	294	✓	✓	✓	A					
	295	✓	✓	✓	A					
	296	✓	✓	✓	A					
	297	✓	✓	✓	A					
	298	✓	✓	✓	A					
	299	✓	✓	✓	A					
	300		✓	✓	A					
	301		✓	✓	A					
	302		✓	✓	A					
	303		✓	✓	A					
	304		✓	✓	A					
	305		✓	✓	A					
	306		✓	✓	A					
	307		✓	✓	A					
	308		✓	✓	A					
	309		✓	✓	A					
	310		✓	✓	A					
	311		✓	✓	A					
	312		✓	✓	A					
	313		✓	✓	A					
	314		✓	✓	A					
	315		✓	✓	A					
	316		✓	✓	A					
	317		✓	✓	A					
	318		✓	✓	A					

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re *Inter Partes* Reexamination of:	)	
	)	
US Patent No. 7,897,080	)	Confirmation No.: 6418
	)	
Named Inventor: Robert K. Yang *et al.*	)	Group Art Unit: 3991
	)	
Control No.: 95/002,170	)	Examiner: Alan D. Diamond
	)	
Request Filed: September 10, 2012	)	M&E Docket: 117744-00023
	)	
Title: POLYETHYLENE OXIDE-BASED FILMS AND DRUG DELIVERY SYSTEMS MADE THEREFROM	)	H&B Docket: 1199-26 RCE/CON/REX

Mail Stop *Inter Partes* Reexam
Attn: Central Reexamination Unit
Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

TRANSMITTAL OF PAYMENT OF RESPONDENT BRIEF FEE (37 C.F.R. § 41.20(b)(2)(ii))

Requester hereby submits payment of the fee for filing the respondent brief in support of the appeal of the above-identified *inter partes* reexamination on April 10, 2014. If additional fees are believed to be due, please charge our Deposit Account No. 50-4876, under Order No. 117744-00023 from which the undersigned is authorized to draw.

Respectfully submitted,
McCarter & English LLP

Dated: April 18, 2014

By: /Danielle L. Herritt/
Danielle L. Herritt Reg. 43,670
Kia Freeman Reg. 47,577
Direct Dial: 617-449-6513
Attorneys for Requester, BioDelivery Sciences International, Inc.

CERTIFICATE OF SERVICE

The undersigned hereby certifies that a copy of the foregoing Transmittal of Payment of Respondent Brief Fee was served on April 18, 2014, by first class mail, directed to the patent owner at the correspondence address of record for the subject patent at the following address:

Daniel A. Scola, Jr.

HOFFMANN & BARON, LLP

6900 JERICHO TURNPIKE

SYOSSET, NY 11791,

By: /Danielle L. Herritt/
Danielle L. Herritt
Registration No. 43,670
Attorney for Requester

Electronic Patent Application Fee Transmittal

Application Number:	95002170
Filing Date:	10-Sep-2012
Title of Invention:	POLYETHYLENE-OXIDE BASED FILMS AND DRUG DELIVERY SYSTEMS MADE THEREFROM
First Named Inventor/Applicant Name:	7897080
Filer:	Danielle L. Herritt/Maureen Tierney
Attorney Docket Number:	117744-00023

Filed as Large Entity

inter partes reexam Filing Fees

Description	Fee Code	Quantity	Amount	Sub-Total in USD($)
Basic Filing:				
Pages:				
Claims:				
Miscellaneous-Filing:				
Petition:				
Patent-Appeals-and-Interference:				
Filing Appeal Brief Inter Partes Reexam	1404	1	2000	2000
Post-Allowance-and-Post-Issuance:				
Extension of Time:				

Description	Fee Code	Quantity	Amount	Sub-Total in USD($)
Miscellaneous:				
			Total in USD ($)	**2000**

Electronic Acknowledgement Receipt

EFS ID:	18801479
Application Number:	95002170
International Application Number:	
Confirmation Number:	6418
Title of Invention:	POLYETHYLENE-OXIDE BASED FILMS AND DRUG DELIVERY SYSTEMS MADE THEREFROM
First Named Inventor/Applicant Name:	7897080
Customer Number:	23869
Filer:	Danielle L. Herritt/kia freeman
Filer Authorized By:	Danielle L. Herritt
Attorney Docket Number:	117744-00023
Receipt Date:	18-APR-2014
Filing Date:	10-SEP-2012
Time Stamp:	19:44:58
Application Type:	inter partes reexam

Payment information:

Submitted with Payment	yes
Payment Type	Deposit Account
Payment was successfully received in RAM	$2000
RAM confirmation Number	4077
Deposit Account	504876
Authorized User	

File Listing:

Document Number	Document Description	File Name	File Size(Bytes)/ Message Digest	Multi Part / .zip	Pages (if appl.)

1	Reexam Miscellaneous Incoming Letter	080BDSIRespondentIBriefFeeTransmittal.PDF	8779 37cde13ded906c1333c7949b9c18a0f3380f8a63	no	2
Warnings:					
Information:					
2	Fee Worksheet (SB06)	fee-info.pdf	30024 2087d8f1b02504f73f893ab67bb421f70f6af985	no	2
Warnings:					
Information:					
			Total Files Size (in bytes):	38803	

This Acknowledgement Receipt evidences receipt on the noted date by the USPTO of the indicated documents, characterized by the applicant, and including page counts, where applicable. It serves as evidence of receipt similar to a Post Card, as described in MPEP 503.

New Applications Under 35 U.S.C. 111
If a new application is being filed and the application includes the necessary components for a filing date (see 37 CFR 1.53(b)-(d) and MPEP 506), a Filing Receipt (37 CFR 1.54) will be issued in due course and the date shown on this Acknowledgement Receipt will establish the filing date of the application.

National Stage of an International Application under 35 U.S.C. 371
If a timely submission to enter the national stage of an international application is compliant with the conditions of 35 U.S.C. 371 and other applicable requirements a Form PCT/DO/EO/903 indicating acceptance of the application as a national stage submission under 35 U.S.C. 371 will be issued in addition to the Filing Receipt, in due course.

New International Application Filed with the USPTO as a Receiving Office
If a new international application is being filed and the international application includes the necessary components for an international filing date (see PCT Article 11 and MPEP 1810), a Notification of the International Application Number and of the International Filing Date (Form PCT/RO/105) will be issued in due course, subject to prescriptions concerning national security, and the date shown on this Acknowledgement Receipt will establish the international filing date of the application.

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re *Inter Partes* Reexamination of:	)	
	)	
US Patent No. 7,897,080	)	Confirmation No.: 6418
	)	
Named Inventor: Robert K. Yang *et al.*	)	Group Art Unit: 3991
	)	
Control No.: 95/002,170	)	Examiner: Alan D. Diamond
	)	
Request Filed: September 10, 2012	)	M&E Docket: 117744-00023
	)	
Title: POLYETHYLENE OXIDE-BASED FILMS AND DRUG DELIVERY SYSTEMS MADE THEREFROM	)	H&B Docket: 1199-26 RCE/CON/REX
	)	
Mailing Date: April 10, 2014	)	

Mail Stop *Inter Partes* Reexam
Attn: Central Reexamination Unit
Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

BDSI'S RESPONDENT BRIEF IN *INTER PARTES* REEXAMINATION

BioDelivery Sciences International, Inc. ("BDSI") respectfully submits this Respondent's Brief pursuant to 37 CFR 41.66 and 41.68.

Certificate Regarding Word Count Pursuant to 37 CFR 1.943(c)

I hereby certify that, pursuant to 37 CFR 1.943(c), based on the Word version word count of 6,878 words, Respondent's Brief does not exceed 7,000 words in length.

Signed: Danielle L. Herritt /Danielle L. Herritt/ Reg. No. 43,670 Dated: April 10, 2014

Table of Contents

Table of Contents
(continued)

Page

Table of Contents
(continued)

Page

Table of Contents
(continued)

Page

I. REAL PARTY IN INTEREST

BioDelivery Sciences International, Inc., the Requestor in the underlying *inter partes* reexamination, is the real party in interest for this brief.

II. RELATED APPEALS, INTERFERENCES, AND TRIALS

BDSI agrees with Patent Owner MonoSol's March 10, 2014 Appeal Brief (hereinafter "AB") except as follows.

- Neither US Patent No. 7,357,891 nor US Patent No. 7,425,292 successfully exited reexamination. No original or substantially identical claims were confirmed in either of the *ex parte* reexamination certificates.
- Requestor properly petitioned for *Inter Partes* Review of the new claims of '891C1 Patent and the substantially amended claims of the '292C1 Patent.
- BDSI presumes that MonoSol's reference to "the '150 Patent" is a reference to MonoSol's US Patent No. 8,017,150. In any event, to be clear, BDSI is not involved in any patent infringement action involving "the '150 Patent."

III. STATUS OF CLAIMS

BDSI agrees.

IV. STATUS OF AMENDMENTS

BDSI agrees.

V. SUMMARY OF CLAIMED SUBJECT MATTER

BDSI disagrees with the support cited by MonoSol for its newly added recitations and to any alleged distinction between the claimed methods and the prior art, whether based on uniformity, locking-in/preventing migration, performing analytical chemical testing, or any other claim element.

BDSI disputes, for example, that the invention is directed to methods "(i) where the degree of uniformity of content of active throughout a particular lot of resulting films, as well as (ii) where the degree of uniformity of content of active in dosage units taken from different lots of resulting films can also be strictly maintained through the claimed processes." AB at 5. None of the claims recite these alleged points of novelty, either "lot of resulting films" or "different lots of resulting films."

BDSI also disputes that "[p]rocesses for such control of content uniformity are not present in the prior art." AB at 5. None of MonoSol's claims recite "controlling content uniformity," nor do they provide any novel or non-obvious methods for controlling anything.

VI. ISSUES TO BE REVIEWED ON APPEAL

A. Whether the panel erred in rejecting the claims of the '080 patent when it relied upon substantial evidence and where MonoSol failed to dispute the findings underlying the panel's *prima facie* case.

B. Whether the panel erred in rejecting MonoSol's rebuttal arguments, where (i) no nexus has been established between the rebuttal evidence and the claimed invention, (ii) the rebuttal evidence is not commensurate with the scope of the claims, and (iii) MonoSol has not rebutted the substantial evidence that the newly-recited properties already existed in the prior art films.

VII. ARGUMENT

Preliminary Statement

The underlying issue of this reexamination is that if MonoSol has an inventive process, it has failed to claim it. MonoSol is unable to point to any claimed operative step or condition that is not taught or suggested by the prior art. And, despite several opportunities to do so, MonoSol is unable to explain why the prior art methods would not necessarily achieve the claimed desired results. The panel's *prima facie* case is also supported by extensive factual findings and substantial evidence. *See*, *e.g.*, RAN at 30-44 (*Chen*), 52-62 (*Staab*), 63-71 (*Le Person*); Reitman Declaration; Cohen Declaration.

And MonoSol has failed to rebut the panel's *prima facie* case. Instead, MonoSol argues that recitations of characteristics inherent to the prior art processes and/or recitations of well-known post-manufacturing steps render the claims novel and non-obvious. "However, arguments of counsel cannot take the place of factually supported objective evidence." MPEP 2145, *citing In re Huang*, 100 F.3d 135, 139-40 (Fed. Cir. 1996). With respect to all of its rebuttal evidence, *e.g.*, there is no nexus between the rebuttal evidence and the claimed invention. Many of MonoSol's arguments are presented without any discernible allegation of

error by the panel. Where no error has been alleged, MonoSol's arguments do not present proper issues for appeal. MonoSol is not entitled to *de novo* review.

A. Whether the panel erred in rejecting the claims of the '080 patent when it relied upon substantial evidence and where MonoSol failed to dispute the findings underlying the panel's *prima facie* case.

MonoSol's claims recite a process. As the panel has repeatedly found, MonoSol's process claims do not recite any process step or condition that can distinguish the methods disclosed in the prior art from the claimed methods. RAN at 74 (*Chen*), 82 (*Staab*). MonoSol is unable to point out any claimed operative step or condition that is not taught or suggested by the prior art. RAN at 82. Instead, MonoSol argues that two types of new recitations render the claims novel and non-obvious: (i) recitations of uniformity (which are inherent to the prior art processes) and (ii) recitations of a post-manufacturing testing step (which was well-known in the prior art).

"Where the claimed and prior art products are identical or substantially identical in structure or composition, or are produced by identical or substantially identical processes, a *prima facie* case of either anticipation or obviousness has been established." MPEP 2112.01(I), *citing In re Best*, 562 F.2d 1252, 1255 (CCPA 1977). The panel has met this burden.

In addition, the panel's findings are supported by substantial evidence, including: (i) the claimed uniformity disclosed in the *Chen* films (*Chen* at 17:15-16, and Table 4); (ii) the evidence in the Reitman Declaration reproducing Example 7 in *Chen* and confirming uniformity in the *Chen* films (Reitman Decl. ¶¶ 5-7); (iii) the evidence in the Cohen Declaration confirming the ability of one of ordinary skill to make uniform films when starting with a homogeneous polymer matrix or solution (Cohen Decl. ¶ 10); and (iv) the evidence in the Reitman Declaration demonstrating that MonoSol's newly-recited scientific theories are inherent in *Chen* (Reitman Decl. ¶ 8). Despite several opportunities to do so, MonoSol has been unable to respond to the panel's findings (RAN at 82-83) that the prior art methods would not necessarily achieve the claimed desired results or provide rebuttal evidence.

Finally, substantial evidence supports the panel's findings that the recited post-manufacturing steps were known in the prior art. MonoSol admits the worldwide regulatory requirement for consistent pharmaceutical dosages was known ('080 patent 2:38-45), and the panel correctly found motivation for the step of performing uniformity testing existed at the time the invention was made. RAN at 38-39. MonoSol also admits that the step of performing analytical chemical

testing for content uniformity was known in the prior art. '080 patent; *see also* 29:35-39 ("[a]ny conventional means for…testing…for example…use of analytical equipment,"); *see also* AB at 56 ("Le Person went on to support Patentee's position that the only way to actually determine uniformity of content in the amount of active is through assaying (analytical chemical testing)" (*citing Le Person* at 257, col. 2). The panel's finding of the same (RAN at 38-39) was not disputed in MonoSol's Appeal Brief.

B. Whether the panel erred in rejecting MonoSol's rebuttal arguments, where (i) no nexus has been established between the rebuttal evidence and the claimed invention, (ii) the rebuttal evidence is not commensurate with the scope of the claims, and (iii) MonoSol has not rebutted the substantial evidence that the newly-recited properties already existed in the prior art films.

Once the panel made its proper *prima facie* case, the burden of proof shifted to MonoSol to present rebuttal evidence and arguments. MPEP 2145, *citing In re Dillon*, 919 F.2d 688, 692 (Fed. Cir. 1990). Attorney argument cannot take the place of "factually supported objective evidence." MPEP 2145, *citing In re Huang*, 100 F.3d 135, 139-40 (Fed. Cir. 1996); MPEP 2145. "[T]o be entitled to substantial weight, the applicant should establish a nexus between the rebuttal

evidence and the claimed invention, *i.e.,* objective evidence of nonobviousness must be attributable to the claimed invention." MPEP 2145.

1. Bogue and Uniformity: there is no nexus between Bogue's lots and the claimed invention.

MonoSol argues that the panel did not give sufficient weight to the declarations of MonoSol's expert, Dr. Bogue, regarding the uniformity of "lots" of Suboxone® films. AB at 18 n.2. However, the panel fully considered and weighed Dr. Bogue's March 13, 2013 Declaration ("Bogue I") and September 3, 2013 Declaration ("Bogue II"), and found that MonoSol failed to establish a nexus between the process described in the Declarations and any of the claimed processes:

> Bogue Declaration I lacks specific details about the film production. For example, it is not clear in Bogue Declaration I which materials, e.g., the specific polymers and solvent, are used; it is not clear if other materials are present when preparing the films; it is not clear exactly what is done to form the flowable polymer matrix or how and on what it is casted, or, in particular, exactly how the controlled drying is performed and for what exact amount of time the drying is done, etc.

RAN at 74 (Bogue I); *see also* RAN at 78-80 (Bogue II). The Bogue Declarations merely recite general process steps and assert—without support—that the films

were made according to the '080 patent. Bogue I, ¶ 4; Bogue II, ¶ 4. Such statements do not establish a nexus. *See* RAN at 78-80, *citing* MPEP 716 and MPEP 716.03; *see also Ex Parte Standish*, 10 USPQ2d 1454, 1458 (BPAI 1988) (nexus is not established by generic statements regarding construction of products or process from declarants).

Thus, MonoSol failed to establish that Suboxone® is manufactured "in accordance with the '080 Patent" (AB at 33) or its claims; and the panel properly found that MonoSol had not established a nexus between the rebuttal evidence and the claimed invention. RAN at 78-79; MPEP 2145, *citing In re Huang*, 100 F.3d 135, 139-40 (Fed. Cir. 1996).

2. Bogue and Uniformity: Bogue's lots are not commensurate with the claim scope.

Even if Bogue established that the lots were made in accordance with even one claim—which it did not—it is unclear how a single product containing one polymer combination and one active can be commensurate in scope with claims covering hundreds of thousands of polymer combinations and actives.

3. Bogue Commercial Success: there is no nexus between the sales of Suboxone® and the claimed invention.

For the same reasons discussed above with respect to Bogue and uniformity, MonoSol failed to establish a nexus between the process described in its Declarations and any of the claimed processes. In its lengthy arguments relating to commercial success, MonoSol does not dispute the panel's findings that MonoSol failed to show a nexus between the evidence and the claimed methods and that the evidence is not commensurate in scope with claims (RAN at 80; AB at 18-25, 31-33).

Indeed, as stated in the RAN, the evidenced commercial success appears to be the result of product conversion, not the claimed invention. RAN at 79. The evidence of commercial success must be deemed to derive from the invention and not from an unrelated business event. RAN at 79, *citing* MPEP 716.03(b)(I). As explained in MonoSol's own exhibit, the tablet form of Suboxone® was recently discontinued. RAN at 79 (reproducing Exhibit 5 of the Response to ACP). As a result, existing users of the tablet form who were treating their opiate dependence and wanted to continue with the same branded drug were left with no option but to

convert to the Suboxone® film. *Id.* MonoSol did not dispute this in its brief or allege any error in the findings of the panel.

4. Bogue Commercial Success: one product is not commensurate with the claim scope.

The evidence of commercial success is not commensurate with the scope of the claims. As the panel found, "evidence of sales of Suboxone® film is not commensurate in scope with claims that are not limited to Suboxone®." RAN at 80. MonoSol does not dispute this finding.

5. The facts in *Leo* are the direct opposite of the facts in the instant appeal.

MonoSol relies heavily on *Leo Pharmaceutical Products, Ltd. v. Rea*, 726 F.3d 1346 (Fed. Cir. 2013) in constructing its rebuttal argument, contending that a person of ordinary skill would not have been able to optimize the necessary parameters recited in the claims of the '080 patent to arrive at the claimed invention. AB at 30-31.

First, even if MonoSol were to overcome the panel's conclusions regarding optimization (RAN at 37), it is unclear how that would advance MonoSol's

appeal. MonoSol failed to address the panel's primary conclusions that the claimed uniformity was explicitly or inherently disclosed. RAN at 36-37.

Second, the fact pattern in *Leo* is completely different from the facts in the present case. Some of the many differences between the facts in *Leo* and the present case are below:

Facts in *Leo* Relied upon by the Federal Circuit	**Facts in Present Case**
The prior art explicitly taught away from the claimed invention. *Leo*, 726 F.3d at 1353-54.	In contrast, the panel found that the prior art explicitly teaches the claimed invention. *See, e.g.*, RAN at 74 ("the prior art either explicitly, inherently and/or obviously performs the claimed generic manufacturing steps using the claimed generic ingredients"), 82 ("Despite multiple opportunities during these proceedings, *MonoSol has not explained what step or condition is claimed but not taught in the prior art*.")
The problem solved by the claimed invention was not recognized in the prior art. *Leo*, 726 F.3d at 1353.	MonoSol admits that the "problem" of content uniformity was recognized by the prior art, *i.e.*, *Le Person*. AB at 30. Further, the panel found that the solution was already provided by the prior art. RAN at 37; *see also* Cohen Decl., ¶ 10 ("When working with a homogeneous or completely dissolved coating mixtures as in

	Chen, it would be difficult for a person of ordinary skill in the film art ***not*** to obtain a film that has uniform content of active.") (emphasis added).
The elapsed time between the prior art and the patent's filing date was very long: 14 and 22 years. *Leo,* 726 F.3d at 1356.	The elapsed time between the prior art and the earliest priority date was a little more than one year. (*Chen, e.g.*, published July 27, 2000 and the first priority date of the '080 patent is October 12, 2001.)
The patent owner presented experimental evidence that the formulations disclosed in the prior art did not achieve the desired results. *Leo*, 726 F.3d at 1354.	In contrast, MonoSol presents no evidence that the methods of the prior art do not achieve its recited desired result. And MonoSol does not dispute the Reitman Declaration, which demonstrates that *Chen* achieved the desired results. (Reitman Decl., ¶¶ 5-7).

As such, the facts in *Leo* are the direct opposite of the facts in the instant appeal.

Even if the facts in *Leo* were not the direct opposite of the facts in the instant appeal, the Board has noted that *Leo* is only applicable in limited circumstances:

> [T]he Federal Circuit limited *Leo Pharm. Prods., Ltd.* to a situation where the applied prior art did not provide any apparent reason for one of ordinary skill in the art to arrive at the claimed subject matter not only due to the failure of the applied prior art to recognize and address

> the problem found by Appellants, but also due to the divergent teachings and express disclaimer in the applied prior art that would have precluded one of ordinary skill in the art from arriving at such combination.

Ex Parte Deorkar, 2013 WL 6217838, *2 (PTAB Nov. 27, 2013).

6. Example M has no nexus with the claimed invention, is not commensurate with the claimed invention, and, in any event, there is evidence that the prior art already teaches both uniformity and performing analytical testing.

MonoSol cites Example M of the '080 patent as evidence of the non-obviousness of the recited analytical chemical testing step to the claimed invention, relying on the proposition that there is no legal requirement that a patent disclose examples for each embodiment. AB at 27. In doing so, MonoSol admits that Example M is not covered by the claims and—therefore—there is no nexus and this example is not commensurate in scope with the claimed subject matter. It is not relevant whether or not Example M is an example of either "unexpected" uniformity or an analytical chemical test in both are in the prior art. MonoSol's argument does not address or rebut the panel's factual findings that the prior art disclosed the recited uniformity (RAN at 36-38 (discussing *Chen* at 17:15-16 and

Table 4); RAN at 56-57 (discussing *Staab* at cols. 1-13)) and that analytical chemical testing was well-known (RAN at 38-39, and 84).

For example, it is unclear how the disclosure of "degrees of uniformity … approaching 4%" (AB at 26) supports patentability when the prior art shows variation of 0% using the same criteria and to the same degree as the '080 patent. RAN at 36 (*Chen*) and 57 (*Staab*).

And, MonoSol cannot rely on recitation of the analytical claimed testing step itself to support non-obviousness of the claimed methods for making films. AB at 17 ("[o]nly by analytical chemical testing is it possible to determine the actual amount of active present ...[t]his is the essence of the '080 patent claims."). Even if Example M measured a pharmaceutical active—which it does not—the claimed testing step, by whatever method, is a known, post-manufacturing step. RAN at 38-39. With or without the performance of analytical chemical testing, the resulting film product made according to the claimed methods would be the same.

C. Claim Rejections Based on Sections 102 and/or 103

1. The panel did not err in rejecting claims 1-11, 13-15, 17-71, 82-90, 92-94, 96-150, 161-172, 174-176, 178-232, 243-253, 256, 258-271, 274, 276-289, 292, and 294-318 under 35 USC 103(a) over *Chen*.

a) *MonoSol's preliminary argument.*

According to MonoSol, "the Examiner has not even considered all of the elements of step (d) of Claim 1 or step (c) of Claims 82, 161 and 315-318." AB at 35. MonoSol asserts that the panel ignores that the claims require not only creation of viscoelastic film, but that it does so such that the active is "locked-in." AB at 36-37. But the panel did not ignore this requirement. The panel carefully considered this step and correctly and without error established its *prima facie* case with respect to "locked-in," by relying on *Chen*'s teaching of the same ingredients, homogeneously mixed, and the same process as the claimed invention. RAN at 36; 82-83. MonoSol has not explained why performing all of the claimed steps with the claimed materials, as the prior art does, would not dry a film such that active is "locked-in." RAN at 82. If there is a unique step for MonoSol's process, or if "locking-in" is meant to indicate a physical step or process condition, such step or condition has not yet been indentified and claimed. RAN at 82.

In addition, the Reitman Declaration reproduced *Chen* and provides evidence that "[w]ithin about 4 minutes after initiation of drying, the film was self-supporting, non-tacky, flexible, and viscoelastic." Reitman Decl. at ¶ 8. Therefore, Reitman demonstrates that the active in *Chen*'s films are locked-in within about 4 minutes after initation of drying and achieves the recited desired degrees of uniformity. Reitman at ¶ 5-8. MonoSol does not dispute Reitman.

b) Chen's *Figure 5 is not evidence of non-uniform films.*

Regarding Figure 5 in *Chen*, MonoSol fails to allege any panel error. Without addressing the findings of the panel, MonoSol merely repeats its old argument that Figure 5 in *Chen* discloses:

> in six instances the amount of pharmaceutical active released from Chen's unit dose films is greater than 110% *of the expected/desired amount of pharmaceutical active* for that drug and thus outside the '080 Patent's claim limitations.

AB at 39 (emphasis added).

As a preliminary matter, this argument is at best relevant only to independent claims 82 and 315, the only claims containing the limitation "varies by no more than 10% *from the desired amount of active*."

MonoSol's argument is entitled to little or no weight for several reasons.

First, MonoSol's own expert, Dr. Lin, stated "[t]hese data [in Figure 5] indicate that the test method used in the analysis is not reproducible ***and/or*** there is a lack of active agent content uniformity between individual dosage units." Lin Declaration ¶ 22 (emphasis added). That is, MonoSol's expert admits that the error bars in Figure 5 could indicate uncertainty in the testing measurement, rather than a variation regarding release. *Id.* "Reduced to its logical components, Lin's conclusion (X demonstrates B) does not follow from Lin's own premise (X indicates A and/or B). In other words, Lin's conclusion is logically invalid based on Lin's own stated premise." RAN at 92. In its brief, MonoSol does not mention, much less explain, its own expert's uncertainty.

Second, not only does the data in Figure 5 not support Lin's conclusion, it in fact supports the opposite conclusion, *i.e.*, that the error bars indicate uncertainty in the test measurement. The total release of hydromorphone decreases between 4 and 5 minutes, and again between 8 and 10 minutes and the total release of oxybutynin decreases between 6 and 8 minutes. But the total amount of active that has been released cannot decrease over time—no matter how irregular the film samples might be the drug cannot be "unreleased." If anything, these decreases in

total release over time support uncertainty in the test measurement. This point was made in the RAN (92-94), and MonoSol failed to rebut the panel's finding.

Third, Figure 5 is not relevant to the recited uniformity per dosage unit. Uniformity per dosage unit is not what is shown in Figure 5. Figure 5 shows cumulative active released over time, and it is not even clear that at 10 minutes the films are fully dissolved.

Finally, to the extent that MonoSol is claiming that "locking-in" uniform distribution and/or prevention of migration within the first 4 minutes is demonstrated by uniformity (AB at 40), *Chen* demonstrates it. MonoSol does not dispute that *Chen* discloses 0% variation using the same criteria and to the same degree as disclosed in the '080 patent in Table 4; 17:15-16 and that the Reitman Declaration confirms it (Reitman Decl. ¶¶ 5-6).

In view of the above, the rejection was proper and should be affirmed.

c) *MonoSol's optimization argument is based on* Leo*, a case that has no discernible relationship to the facts in the instant case.*

See detailed argument above with respect to the *Leo* case (Section VII(B)(5)).

2. The panel did not err in rejecting claims 2, 3, 32, 55, 72-81, 111, 134, 151-160, 193, 216 and 233-242 under 35 USC 103(a) over *Chen* in view of *Staab*.

MonoSol presents no arguments specific to the panel's findings of obviousness over *Chen* in view of *Staab*, other than to incorporate remarks from other sections relating to *Chen* and *Staab* separately. AB at 43. BDSI addresses these remarks above and below. *See* Sections (B) (rebuttal arguments), (C)(1) (*Chen*), and (C)(5) (*Staab*). MonoSol alleged no further panel error and did not challenge the motivation to combine *Chen* with *Staab*.

In view of the above, the rejection was proper and should be affirmed.

3. The panel did not err in rejecting claims 317 and 318 under 35 USC 103 over *Chen* in view of *Arter*

MonoSol incorporated its previous remarks relating to *Chen*, including "locking in," and alleging a lack of proof of uniformity of *Chen*'s films, and a lack of description of what happens to *Chen*'s films during the drying process. AB at 43-44. BDSI addresses these remarks above. *See* Section (C)(1) (*Chen*).

a) *The panel did not err in combining* Chen *with* Arter.

MonoSol argues that it is improper to combine *Arter* with *Chen* because "[*Arter*'s] process and apparatus is not at all transferrable to drying methods for

pharmaceutical films, and particularly pharmaceutical films which are aqueous-based and self-supporting." AB at 44-45. However, MonoSol failed to substantively address or point out any error in the RAN rejection, including the findings of the relevance and pertinence of *Arter*. *See* RAN at 103-06.

As noted in the RAN, it is not necessary to consider whether drying methods for organic solvent solutions are transferrable to aqueous solutions, because *Arter* plainly states the method of the invention can be useful in drying layers formed from "aqueous solutions of hydrophilic colloids." RAN at 105, *quoting Arter* at 9:8; *see also Arter* at 5:57-68 (including "cellulosic" polymers (*i.e.*, HPMC) and "aqueous composition").

Regarding "transferrable," *Arter*'s drying methods are "in no way limited to use in the manufacture of photographic materials, and can be advantageously employed in any process, used in the manufacture of any product, in which a gaseous drying medium is utilized in the drying of a coated layer…." *Arter* at 5:37-42. *Strobush,* which the Board has found to be pertinent art to the '080 patent family (*see* Section (C)(4)), cites and discusses *Arter*. *Strobush* at 2:60-3:9. Regarding "self-supporting," neither of the methods in claims 317 and 318 recite "self-supporting." Even if the claims did recite this limitation, MonoSol has not

disputed that *Chen* discloses a pharmaceutical "stand alone and self-supporting" film. *Chen* at 15; RAN at 3.

b) *MonoSol does not dispute* Arter's *teachings.*

In all of MonoSol's arguments, it did not dispute what the panel relies on *Arter* to teach. RAN at 48-50. For example, the panel found that "*Arter* teaches 'using air currents, which have forces below a yield value of the polymer matrix during drying, to evaporate at least a portion of said solvent'." RAN at 49.

The remaining arguments are irrelevant or immaterial. For example, in view of the explicit teachings above, whether or not "mottle" is the same as, related to, or different from MonoSol's so-called problem (AB at 45) is immaterial. *Chen* recognized and solved the content uniformity "problem," if there was one, so *Arter* need not do so. RAN at 105. Contrary to MonoSol's arguments (AB at 45), the panel did not rely on *Arter* to demonstrate either quantitative content uniformity, or a teaching of analytical chemical testing. RAN at 48-50.

In view of the above, the panel did not err in combining *Arter* and *Chen*. The rejection should be affirmed.

4. The panel did not err in rejecting claims 317 and 318 under 35 USC 103(a) over *Chen* in view of *Strobush.*

MonoSol presents previously-made arguments with respect to *Chen* regarding these rejections. AB at 46. BDSI addresses these remarks above. *See* Section (C)(1).

a) *The panel did not err in combining* Chen *with* Strobush.

In response to the panel's rejection of claims 317 and 318 over *Chen* in view of *Strobush,* MonoSol again argues that it is improper to combine *Strobush* with *Chen* because the films of *Strobush* are "photographic" and the films of '080 patent are pharmaceutical. AB at 46; MonoSol Response to ACP at 85. However, MonoSol fails to point out any specific error in the panel's findings and conclusion that it was proper to combine them. RAN at 109-11. For example, in rejecting similar arguments by MonoSol in an appeal of a related application, the Board found that "Strobush may…reasonably be considered to be within the field of Appellant's endeavor (as stated under the 'Field of the Invention' on page 1 of the Specification)." RAN at 110, *citing* Board Decision regarding U.S. Application No. 10/074,272 (which resulted in U.S. Patent No. 7,425,292, over which the '080 patent is terminally disclaimed), February 21, 2008, at 13:21-24. The fields of invention of the '080 patent and of the related '292 patent are "remarkably

similar," both relating to drying aqueous systems to achieve more uniformity, including uniform distribution of components. *See* RAN at 110. MonoSol did not appeal the Board Decision in the parent case and therefore has waived its right to reprise its arguments 6 years later in this appeal.

b) *The panel correctly relied upon* Strobush *for teachings of controlled and rapid drying with air currents so as not to exceed a yield value of the polymer matrix.*

MonoSol persists in misreading *Strobush*, repeating mischaracterizations that were refuted point-by-point in the RAN, without identifying any panel error. AB at 46-47; RAN at 107-111.

For example, contrary to MonoSol's argument (AB at 46-47), the panel has made a factual finding that *Strobush* teaches controlling the force of the air so as not to exceed a yield value of the polymer matrix. RAN at 108. And the panel has also found that *Strobush* further teaches that, without differential top airflow, there is no shearing force acting on the top of the wet coating, and thus the inherent viscosity of the wet film is not overcome. RAN at 110; *Strobush* at 16:18-22.

The panel has found that *Strobush* provides a drying oven with bottom-only drying (Fig. 12); and a drying oven with top and bottom air vents to permit controlled drying (RAN at 50-51, 107-08), for example "drying apparatus 10 can

be used such that no gas is supplied by the air bars 34 when top-side gas is not needed or desired." *Strobush* at 11:15-37, 16:14-22.

Contrary to MonoSol's argument (AB at 46), *Strobush* does not teach slow evaporation or low heat transfer rates. Actually, *Strobush* teaches how to maximize heat transfer rate and dry films rapidly. *See, e.g.*, RAN at 109; *Strobush* at 14:30-36 ("Figs. 21-22 show that by increasing the heat transfer rate to correspond to the increasing maximum allowable heat transfer rate, the rate of drying can be increased even more rapidly…").

MonoSol fails to point out any error in the panel's findings relating to *Strobush* and its conclusory arguments lack factual and evidentiary support.

c) *MonoSol's other arguments are irrelevant.*

MonoSol presents arguments that are irrelevant because the limitation is not found in the subject claims, for example, *Strobush*'s films "are not self-supporting." AB at 47. The limitation "self-supporting" does not appear in any of the claims under this rejection, although it is explicitly taught by *Chen* at 15. MonoSol also argues alleged deficiencies of the prior art that are irrelevant because the panel did not rely on the cited art for that particular teaching or suggestion of a limitation, for example, "Strobush does not and cannot inherently form or make

obvious visco-elastic film…which locks in uniformity." *Compare* AB at 47 *with* RAN at 50-52. In view of the above, the rejection was proper and should be affirmed.

5. The panel did not err in rejecting claims 1-5, 10, 13-15, 21, 24, 25, 32, 44-46, 54, 55, 59, 63-70, 72-75, 78-84, 89, 92-94, 100, 103, 104, 111, 123-125, 133, 134, 138, 142-149, 151-154, 157-166, 171, 174-176, 182, 185, 186, 193, 205-207, 215, 216, 220, 224-231, 233-236, 239-242, 249-252, 258-260, 267-270, 276-278, 285-288, and 294-318 under 35 USC 102(b)/103(a) in view of *Staab*.

MonoSol repeats its previous arguments concerning *Leo* and optimization, analytical chemical testing, and the locking-in recitation. AB at 48-49, 52-53. BDSI addresses these remarks above. *See* Sections (B)(5) (*Leo*) and (C)(1) (*Chen*).

a) *The panel did not err in finding support for active uniformity in the examples of* Staab*, because MonoSol has misread* Staab.

MonoSol presents a new argument (never presented to the panel) regarding *Staab*'s film-making example at column 11, based on a misreading of *Staab* that takes the language out of context. AB at 50-52. MonoSol's argument is based on an allegedly 100% variation from a "desired" amount. AB at 50. Importantly, MonoSol does not dispute that the variation among films in *Staab* is 0%. *See id.* at

50-52. With two exceptions, none of the independent claims recite the limitation of a variation from a desired amount. At best, this argument pertains only to independent claims 82 and 315 (and claims depending therefrom).

The panel misread one line in *Staab*, the third line in the table on column 11 ("Benzalkonium chloride (50% aqueous) … 10%") and stated that the "water content [of *Staab*'s film] before drying is 5%." RAN at 55. Based on this misreading, MonoSol argues that *Staab* intended the films to contain 5% active, *i.e.*, 9.5 mg. AB at 49-52. But the sentence above the table cited by MonoSol—the first sentence of the example—explicitly states the intended amount, *i.e.*, "film containing 19 mg of [active]." *Staab*, at 11:24-25. The following paragraph, describing the example, confirms that the amount intended was obtained, "this procedure was utilized to produce 2 inch square films, each containing 19 mg [active] and about 190 mg in weight" (*Staab* 11:49-51), *i.e.*, film dosages each containing 10% active.

MonoSol attempts to manufacture an intended amount in *Staab*, which does not exist—*i.e.*, that *Staab* intended the films to contain 9.5 mg—but then obtained

twice that amount, or 19 mg films. Read in context, it is clear that, not only did *Staab* obtain 19 mg films, it intended to do so.

Again, MonoSol does not dispute the panel's finding that *Staab* shows 0% variation. RAN at 56.

b) *To the extent the panel erred, the error is harmless and does not affect any rejection.*

To the extent the panel erred in its misreading, any error is harmless. Again, the panel interpreted 10% active (50% aqueous solution) as 5% active and 5% water. RAN at 55. The panel reasoned that, because "the water content before drying is 5%," the dried film met the claim limitation of a water content of 10% or less. RAN at 55. As correctly read—the water content before drying is 10%—*Staab's* films still have a water content of 10% or less. RAN at 55. Thus, the panel's original rejection is still proper and any error harmless because under either interpretation, the claim recitation is anticipated.

In short, the panel was correct in relying on *Staab's* "19 mg" example to demonstrate the claimed degree of uniformity of content, and with respect to the water content of *Staab's* films, the panel did not err and should be affirmed.

6. The panel did not err in rejecting claims 8, 9, 76, 77, 87, 88, 155, 156, 169, 170, 237, and 238 under 35 USC 103(a) in view of *Staab*.

MonoSol referred to previous arguments without presenting any new arguments relating to *Staab*, without pointing out any error, and without arguing any claim separately. AB at 54. BDSI addresses these arguments above. *See* Section (C)(5) (*Staab*).

In view of the above, the rejection was proper and should be affirmed.

7. The panel did not err in rejecting claims 82, 89, 90, 92, 161, 171, 172, 174, 274, 292, 304-311, and 313-318 under 35 USC 103(a) in view of *Le Person*.

a) *MonoSol is not entitled to* de novo *review of the rejection.*

MonoSol asserts "[t]here is no **teaching in Le Person**, as to **how to make films** with the required degree of uniformity of content in the amount of active." AB at 56 (emphases in original). Without specifying any panel error, or substantiating its conclusion in any way, MonoSol then changes the topic in the next sentence.

In veiw of this, MonoSol fails to present a proper issue to be reviewed on appeal. MonoSol submits no discernible arguments or evidence, and does not

challenge even one finding in the detailed RAN rejection. *See* RAN at 64-71. It is unclear what aspect of the rejection MonoSol disputes.

b) *The facts in* Leo *are the direct opposite of the facts in the instant appeal.*

Without specifying any panel error, MonoSol makes the same arguments about variations and potential combinations and undue experimentation, *citing Leo*. AB at 54-55. BDSI addresses these remarks above. *See* Section (B)(5) (distinguishing *Leo*).

c) *Contrary to MonoSol's argument,* Le Person *does not teach the difficulty in making the claimed films.*

Presumably in an attempt to find prior art that "teaches away" (as in *Leo*), MonoSol argues that *Le Person* recognizes the "difficulties involved" (AB at 55) and quotes a passage from *Le Person*, but this passage mentions nothing about difficulty. *Id.*, first block quotation. Next, MonoSol quotes *Le Person*'s comment that diffusion in a system with two immiscible solvents "cannot be tracked by text book equations." AB at 55-56, *quoting Le Person* at 257. However, none of MonoSol's claims recite either two immiscible solvents or the cross-diffusivities caused by them. In any case, a person of ordinary skill is not limited to the knowledge of "text book equations."

d) *MonoSol points out how* Le Person *supports obviousness of the claimed invention.*

As explained above, contrary to MonoSol's argument, MonoSol itself admitted that *Le Person* recognized the problem of uniformity of content as recited in the claims. *See* Section (A)*; Le Person* at 257; *compare* AB at 55-56 *with* AB at 17.

Also, MonoSol reads *Le Person* as "support[ing] Patentee's position that the only way to actually determine uniformity of content in the amount of active is through assaying (analytical chemical testing)." AB at 56. Whether or not this is a correct characterization of *Le Person*, MonoSol's reading contradicts its argument in favor of non-obviousness based on analytical chemical testing. Elsewhere in the Brief, MonoSol argues that analytical chemical testing is "the essence" of the claims:

> Only by analytical chemical testing is it possible to determine the actual amount of active present and hence whether uniformity of active content has been maintained during processing. This is the essence of the '080 Patent claims.

AB at 17.

If this is the essence of the '080 invention, MonoSol appears to admit that the essence is in the prior art.

In view of the above, the rejection was proper and should be affirmed.

D. Claim Rejections Based on Section 112

MonoSol proposes, without any explanation, that the panel erred in not entering the proposed amendment to claim 318 filed September 3, 2013. AB at 34-35. But MonoSol failed to petition under 37 CFR § 1.182 for entry of that proposed amendment, which is the proper procedure for reconsideration of non-entry. Moreover, MonoSol could not, and has not, presented the required showing of good and sufficient reasons why the proposed amendment was necessary and was not presented earlier. *See* 37 CFR § 1.116(b)(3). MonoSol suggests that the amendments were necessitated by the introduction of "new" references and states that the amendments advance prosecution. Response to ACP at 44. Neither is true. First, the "new" references, *Strobush* and *Arter*—which was discussed in *Strobush*—were well-known to MonoSol. *See, e.g.*, Board Decision regarding U.S. Application No. 10/074,272 (which resulted in U.S. Patent No. 7,425,292, over which the '080 patent is terminally disclaimed), February 21, 2008, at 13:12-24 (finding *Strobush* to be within the field of endeavor).

Second, as pointed out in the RAN, the amendment would not advance prosecution or simplify issues for appeal. RAN at 3. Among the amendments

proposed, for example, MonoSol also attempted to add "self-supporting" to every independent claim. MonoSol acknowledged in its March 13, 2013 Remarks (at 75-76) that this limitation is disclosed in *Chen*. *Chen* specifically describes its films as "stand alone and self-supporting." *See* RAN at 3, *citing Chen* at 15, lines 30-31. Because this amendment regarding "self-supporting" would not have addressed any prior art rejection of record, nor simplified the issues on appeal, and because the amendments must be either entered or not entered as a whole, the panel did not err in refusing to enter the amendment relating to claim 318. RAN at 3.

1. The panel did not err in rejecting claim 318 under 35 USC 112 (pre-AIA) first paragraph.

MonoSol failed to identify any alleged error in the 112 rejection, and therefore waived its appeal of that rejection. *See* 37 CFR 41.67(c)(1)(vii). ("Any arguments…not included in the brief…will be refused consideration by the Board unless good cause is shown.")

Instead, MonoSol proposes, without any explanation or specificity, that the panel erred in not entering the proposed amendment to claim 318 filed September 3, 2013. AB at 34-35.

As discussed above, not only is this an inappropriate forum for reconsideration of non-entry of amendments, but also MonoSol has failed to dispute the panel's grounds for non-entry.

2. The panel did not err in rejecting claim 318 under 35 USC 112 (pre-AIA) second paragraph.

MonoSol failed to identify any alleged error in the 112 rejection, and therefore waived its appeal of that rejection. *See* 37 CFR 41.67(c)(1)(vii). ("Any arguments…not included in the brief…will be refused consideration by the Board unless good cause is shown.")

Instead, MonoSol proposes, without any explanation or specificity, that the panel erred in not entering the proposed amendment to claim 318 filed September 3, 2013. AB at 34-35.

As discussed above, not only is this an inappropriate forum for reconsideration of non-entry of amendments, but also MonoSol has failed to dispute the panel's grounds for non-entry.

Conclusion

MonoSol identified no error by the panel that would make any of the existing final rejections improper. Therefore, BDSI respectfully requests affirmation of all of the rejections.

Respectfully submitted,
McCarter & English LLP

Dated: April 10, 2014

By: /Danielle L. Herritt/

Danielle L. Herritt	Reg. 43,670
Evelyn D. Shen	Reg. 39,834
Kia Freeman	Reg. 47,577

Direct Dial: 617-449-6513

Attorneys for Requester, BioDelivery Sciences International, Inc.

VIII. EVIDENCE APPENDIX

DECLARATION BY MAUREEN REITMAN, SC.D. UNDER 37 CFR § 1.132

This Declaration by Maureen Reitman, Sc.D. under 37 CFR. § 1.132, dated February 28, 2013 (Reitman Decl.), was submitted by BDSI/Third Party Requester in connection with its April 12, 2013 "Inter Partes Reexamination Comments Under 37 CFR § 1.947" to the Reply mailed on March 13, 2013. The Reitman Decl. was admitted in the record, and referred to in the Action Closing Prosecution, mailed July 31, 2013.

Pursuant to 37 CFR § 41.71, Third Party Requester is using this declaration which was admitted.

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re *Inter Partes* Reexamination of:	)
US Patent No. 7,897,080	)
Issued: March 1, 2011	) Confirmation No.: 6418
Named Inventor: Robert K. Yang *et al.*	) Group Art Unit: 3991
Control No.: 95/002,170	) Examiner: Diamond, Alan D.
Filed: September 10, 2012	) M&E Docket: 117744-00023
Title: POLYETHYLENE-OXIDE BASED FILMS AND DRUG DELIVERY SYSTEMS MADE THEREFROM	) H&B Docket: 1199-26 RCE/CON/REX

Mail Stop *Inter Partes* Reexam
Attn: Central Reexamination Unit
Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

DECLARATION BY MAUREEN REITMAN, SC.D.
UNDER 37 CFR § 1.132

Sir/Madam:

I, Maureen Reitman, do hereby make the following declaration:

I. Technical Background

1. I am a Principal and the Director of the Polymer Science and Materials Chemistry Practice at Exponent. I hold two academic degrees: (1) a Bachelor of Science in Materials Science and Engineering from the Massachusetts Institute of Technology (MIT), and (2) a Doctor of Science in Materials Science and Engineering, with a thesis in the field of polymers, from MIT. I have been practicing in the field of polymer science and engineering for more than 20 years as a researcher at MIT, in a variety of technical roles at the 3M Company, and as a consultant with Exponent. I provide consulting engineering services in all aspects of polymer science and engineering including, but not limited to material selection, product design and development, mechanical and chemical testing, failure analysis, polymer chemistry, polymer

physics, and polymer processing. My specialties include formulation, processing and performance evaluation of polymeric materials, including films, coatings, adhesives and transdermal drug delivery systems. I have been directly involved in product development, product line extensions, transfer of new products to manufacturing, qualification of alternative materials and manufacturing equipment, evaluating field performance, and assessing intellectual property. I am a past chairman and continue to serve as a member of the board of directors of the Medical Plastics Division of the Society of Plastics Engineers. My *curriculum vitae* is provided in Appendix A.

2. While Exponent is being paid for my time, I am not an employee of, nor do I have any financial interest in, BioDelivery Sciences International, Inc.

3. I have been asked to carefully review International Publication No. WO 00/42992 ("*Chen*"), and manufacture a film as described in *Chen*. I carefully reviewed *Chen*. Under my direction, my team manufactured a film in accordance with Example 7 of *Chen*. I have also been asked to take samples and perform various analytical tests to confirm the uniform distribution of the pharmaceutical active in substantially equal sized individual dosage units of the film, which we did.

4. Manufacturing Example 7 of *Chen*

Chen states: "According to Examples 1-8, the hydrocolloid [Methocel E5(HPMC)] was dissolved in water under agitated mixing to form a uniform and viscous solution." Chen 17:7-8.

- Methocel E5(HPMC) was dissolved in water under agitated mixing to form a uniform and viscous solution, by my team.

Chen states: "Additional ingredients were then added sequentially to the viscous solution such as peppermint, aspartame, propyl[ene] glycol, benzoic acid and citric acid under agitated mixing until they were uniformly dispersed or dissolved in the hydrocolloid." Chen 17:8-11.

- Additional ingredients were then added sequentially to the viscous solution including peppermint oil, aspartame, propylene glycol, benzoic acid and citric acid under agitated mixing until they were uniformly dispersed or dissolved in the hydrocolloid, by my team.

- Kolliphor EL was also added to the viscous solution.

Chen states: "Therapeutic agents were added to the homogeneous mixture (coating solution) prior to forming the film." *Chen* 20:19-20.

- Oxybutynin chloride (the therapeutic agent of Example 7) was added to the homogeneous mixture (coating solution) prior to forming the film, by my team.

Chen's Table 5 specifies the composition for Example 7.

- We used the ingredients in the amounts identified in *Chen*'s Table 5. *See* Table 1.

Table 1			
Formulation, Ex. 7, Table 5, *Chen*	% Weight	Formulation, Prepared by Maureen Reitman Team	% Weight
Oxybutynin	3.71	Oxybutynin chloride	3.71
Methocel E5 (HPMC)	21.06	Methocel E5 Premium LV	21.06
Water	70.72	Water, distilled	70.72
Cremophor EL40	1	Kolliphor EL[1]	1
Propylene glycol	1	Propylene glycol	1
Peppermint	1	Peppermint oil	1
Aspartame	0.8	Aspartame	0.8
Benzoic acid	0.013	Benzoic acid	0.013
Citric acid	0.7	Citric acid, monohydrate	0.7

Chen states: "The resultant mixture was degassed in a vacuum chamber until trapped air bubbles were removed." Chen 17:11-12.

- The resultant mixture was degassed in a vacuum chamber until trapped air bubbles were removed, by my team.

Chen states: "The formulation was then coated on the non-siliconized side of a polyester film at a wet thickness of 10 mil and dried in a hot air circulating oven at 50°C for 9 minutes." Chen 17:13-15.

- The formulation was then coated on a non-siliconized side of a polyester film at a wet thickness of 10 mil and dried in a hot air circulating oven at 50°C for up to 9 minutes, on commercial manufacturing equipment by my team.

Chen states: "Methods for manufacturing the dosage unit include the solvent casting methods as shown in Figure 2." Chen 15:13-14. "The manufacturing process for forming the dosage unit is illustrated in Figure 2. The dry film formed by this process is a glossy, stand alone, self supporting, non-tacky and flexible film (12)." Chen 15:29-31.

- A solvent casting manufacturing process for forming the dosage unit as illustrated in Figure 2 was used[2], by my team.

[1] The Cremophor line of products now owned by BASF and renamed Kolliphor. Based on the naming convention of the Cremophor/ Kolliphor products, EL40 is Polyoxyl 40 Castor Oil and EL is Polyoxyl 35 Castor Oil (*i.e.*, they are based on a 1:40 and 1:35 ratio, respectively, of castor oil:ethylene oxide). They are different materials. However, one of skill in the art would recognize Kolliphor EL as an appropriate substitute, as Cremophor EL40 is no longer available.

- The film was manufactured using a controlled drying process.
- As illustrated in Figure 2, the drying oven featured aeration controller with 3 zones set such that in each successive zone air impingement on the surface of the film increased.
- The dry film formed by the process is a glossy, stand alone, self-supporting, non-tacky and flexible film.

Chen states: "A glossy, substantially transparent, stand alone, self-supporting, non-tacky and flexible film was obtained after drying." Chen 17:15-16.

- A glossy, substantially transparent, stand alone, self-supporting, non-tacky and flexible film was obtained after drying, by my team.

5. Verification of Content Uniformity – Visual Inspection

- By examination with the naked eye, uniformity was verified by my team.

6. Verification of Content Uniformity – Unit Dose Weight

- By weighing individual dosage units of substantially identical size, uniformity was verified by my team. *See* Table 2.

Table 2

Sample	Weight of 5 cm^2 dosage unit (grams)
1	0.034
2	0.034
3	0.034
4	0.034
5	0.034
6	0.034
7	0.034

7. Verification of Content Uniformity – Dissolution Test (HPLC)

- By dissolution of individual dosage units of substantially identical size and analysis by High Performance Liquid Chromatography (HPLC) active content uniformity was verified by my team. *See* Table 3.

[2] Our backing was not looped and we did not die cut in line, but the solvent casting and drying under aeration is matched.

Table 3	
Sample	Oxybutynin weight (mg)
A	4.4
B	4.4
C	4.3
D	4.4
E	4.1

- As can be seen in Table 3, the active varies by less than 10%.

8. Additional Observations

   - The components of the formulation, including the active component, were uniformly distributed in the viscous solution, which was used to cast the film, as was verified by my team.

   - The viscous solution, which was used to cast the film, exhibited the flow properties of honey (around 10,000 cps), as observed by my team.

   - Water content of the film was less than 10%, as verified by my team.

   - Within about 4 minutes after initiation of drying, the film was self-supporting, non-tacky, flexible and viscoelastic, as verified by my team.

9. I hereby declare that all statements made herein of my own knowledge are true and that all statements made on information and belief are believed to be true; and further that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine, or imprisonment, or both, under section 1001 of Title 18 of the United States Code, and that such willful statements may jeopardize the validity of the application or any patents issued thereon.

Dated: February 28, 2013

Maureen Reitman, Sc.D.

Appendix A

Exponent
Failure Analysis Associates

Exponent
[illegible]
[illegible]
[illegible]

[illegible]
[illegible]
[illegible]

Maureen T. F. Reitman, Sc.D.
Principal and Practice Director

Professional Profile

Dr. Maureen Reitman is a Principal and the Director of Exponent's Polymer Science and Material Chemistry practice. Her expertise includes polymer and composite technology, mechanics of materials, adhesion science, fiber mechanics, history and technology of plastics, and material failure analysis. She is skilled in the development and use of testing tools and methods and has applied them to plastic, rubber, textile, metal, glass, ceramic, and composite materials and systems. She is experienced in major aspects of product development, including materials selection, formulation, scale-up, end-use testing, failure analysis, certification procedures and issues related to intellectual property.

Dr. Reitman has conducted research in the areas of packaging and barrier materials; paints and coatings; plastic pipes; transdermal drug delivery; adhesives, sealants, and encapsulants; molding compounds; high temperature resins; nanoparticles; fibers and textiles; protective coatings and finishes; polymer chemical resistance; plastic insulation; connectors and splices; plastic packaging; medical devices; environmental effects on durability; and product aging. She has used her expertise to solve a broad range of problems related to coatings, fibers, films, and extruded and molded products, and their use in the telecom, electronics, electrical, transportation, construction, fire protection, medical, and consumer products markets.

Dr. Reitman is a member of the Board of Directors of the Medical Plastics Division of the Society of Plastics Engineers and an active member of two Underwriters Laboratories Standard Technical Panels, addressing Polymeric Materials (UL 94, UL 746, UL 1694) and Appliance Wiring (UL758).

Prior to joining Exponent, Dr. Reitman worked for the 3M Company in both research and management roles. Her activities included technology identification, materials selection and qualification, product development, customer support, program management, acquisition integration, intellectual property analysis, and patent litigation support.

Academic Credentials and Professional Honors

Sc.D., Materials Science and Engineering/ Program in Polymer Science and Technology, Massachusetts Institute of Technology, 1993
B.S., Materials Science and Engineering, Massachusetts Institute of Technology, 1990

National Academy of Engineering Frontiers of Engineering, 2009; Tau Beta Pi; Sigma Xi
John Wulff Award; Carl Loeb Fellowship; NCAA Postgraduate Scholarship;
Malcolm G. Kispert Award; GTE Academic All-American

02/13

Patents

Patent 6,311,524: Accelerated Method for Increasing the Photosensitivity of a Glassy Material, issued November 6, 2001.

European Patent EP0830428: Tackified Polydiorganosiloxane Polyurea Segmented Copolymers and a Process for Making Same, published March 25, 1998.

Patent 5,371,051: Fiber Optic Fusion Splice Protector Sleeve, issued March 24, 1998.

Publications

Kurtz S, Siskey R, Reitman M. Accelerated aging, natural aging, and small punch testing of gamma-air sterilized polycarbonate urethane acetabular components. Journal of Biomedical Materials Research Part B: Applied Biomaterials 2010 May; 93B(2):422–447.

Hoffman JM, Reitman M, Donthu S, Ledwith P. Complimentary failure analysis methods and their application to CPVC pipe. Proceedings, ANTEC 2010, Society of Plastics Engineers, Orlando, FL, May 2010.

Hoffman JM, Reitman M, Donthu S, Ledwith P, Wills D. Microscopic characterization of CPVC failure modes. Proceedings, ANTEC 2009, Society of Plastics Engineers, Chicago, IL, June 2009. Best Paper Award in Failure Analysis & Prevention.

Kurtz SM, Ebert M, Siskey R, Ciccarelli L, Reitman M, Harper ML, Chan FW. Natural and accelerated aging of polyurethanes in the Bryan cervical disc. Poster No. P158. Transactions of Spineweek 2008, Geneva, Switzerland, May 26–31, 2008.

Reitman M, Ledwith P, Hoffman M, Moalli J, Xu T. Environmentally driven changes in nylon. Proceedings, ANTEC 2008, Milwaukee, WI, Society of Plastics Engineers, May 2008.

Hoffman JM, Reitman M, Ledwith P. Characterization of manufacturing defects in medical balloons. Proceedings, ANTEC 2008, Milwaukee, WI, Society of Plastics Engineers, May 2008.

Reitman, MTF, Moalli JE. Polymeric coatings for medical device. Medical Device and Manufacturing Technology, Touch Briefings, pp. 28–30, 2006.

Moalli JE, Moore CD, Robertson C, Reitman MTF. Failure analysis of nitrile radiant heating tubing. Proceedings, ANTEC 2006, Society of Plastic Engineers, Charlotte, NC, May 2006.

Reitman M, McPeak J. Protective coatings for implantable medical devices. Proceedings, ANTEC 2005, Society of Plastic Engineers, Boston MA, May 2005.

McPeak J, Reitman M, Moalli J. Determination of in-service exposure temperature of thermoformed PVC via TMA. Proceedings, 31st Annual North American Thermal Analysis Society Conference, Williamsburg, VA, 2004.

Reitman MTF, Moalli JE. Product development and standards organizations: Listings and certifications for plastic products. 8th Annual International Conference on Industrial Engineering Theory, Applications and Practice, Las Vegas, NV, 2003.

Potdar YK, Reitman MTF. The role of engineering consultants in failure analysis and product development. 8th Annual International Conference on Industrial Engineering Theory, Applications and Practice, Las Vegas, NV, 2003.

Ezekoye OA, Lowman CD, Hulme-Lowe AG, Fahey MT. Polymer weld strength predictions using a thermal and polymer chain diffusion analysis. Polymer Engineering and Science 1998; 38(6):976–991, June.

Fahey MT. Nonlinear and anisotropic properties of high performance fibers. MIT Thesis, 1993.

Fahey MT. Mechanical property characterization and enhancement of rigid rod polymer fibers. MIT Thesis, 1990.

Book Contributions

Reitman M, Liu D, Rehkopf J. Chapter 38. Mechanical properties of polymers. In: Handbook of Measurement in Science and Engineering. Volume 2. Kutz, M (ed), John Wiley & Sons, Hoboken NJ, 2013. ISBN- 978-1-118-38464-0.

Reitman M, Jaekel D, Siskey R, Kurtz S. Morphology and crystalline architecture of polyarylketones, pp. 49-60. In: PEEK Biomaterials Handbook. Kurtz SM (ed), Elsevier William Andrews, Kidlington, Oxford, UK, 2012. ISBN 13:978-1-4377-4463-7

Tsuji JS, Mowat FS, Donthu S, Reitman M. Application of toxicology studies in assessing the health risks of nanomaterials in consumer products, pp. 543-580. In: Nanotoxicity: From In Vivo and In Vitro Models to Health Risks. Sahu S, and Casciano D. (eds), John Wiley & Sons, Chicester, West Sussex, UK, 2009. ISBN 978-0-470-74137-5.

Reitman MTF. The Plastics Revolution. In: Research and Discovery: Landmarks and Pioneers in American Science. Lawson RM (ed), Armonk NY: Sharpe Reference 2008. ISBN 978-0-7656-8073-0.

Klein SM. Mid-century plastic jewelry. Schiffer Publishing, Atglen, PA, 2005. (Technical advisor to author).

Selected Invited Presentations

Reitman MTF. Failure analysis tools. Workshop on Future Needs for Service Life Prediction of Polymeric Materials. NIST and Underwriters Laboratories, Gaithersburg, MD, October 2012.

Hoffman J, MacLean S, Ralston B, Reitman M, Ledwith P. Fractography of unfilled thermoplastic materials experiencing common mechanical failure modes. Materials Science & Technology 2012 Conference, Pittsburgh PA, October 2012.

Hoffman J, Reitman M, Ledwith P. Microscopic characterization of CPVC failure. Materials Science & Technology 2012 Conference, Pittsburgh PA, October 2012.

Reitman MTF. Polymer material properties for next generation medical devices. Invited Speaker: MedTech Polymers, UBM Canon, Chicago, IL, September 2012.

Reitman MTF. Polymers for medical applications. Fundamentals and Fellows Forum, ANTEC 2012, Orlando FL, April 2012.

Reitman MTF. Plastic and composite product failures. Invited lecture in Failure Analysis of Emerging Technologies. Stanford University Department of Materials Science and Engineering, Menlo Park, CA October 2009.

Reitman MTF. Factors for success: Plastics in injection molded medical devices. Part of *Injection Molding Works for Medical Design*, Design News Webcast, October 2008.

Reitman MTF. Plastic and composite product failures. Keynote Speaker: Third International Conference on Engineering Failure Analysis (ICEFA III), Elsevier, Sitges Spain, July 2008.

Reitman MTF. Multiphase materials for medical device applications, an overview. Medical Device and Manufacturing (MDM), Canon Communications, various locations, January- June 2008.

Reitman MTF. Nanotechnology and plastics for medical devices. Capitalizing on Nanoplastics, Intertek PIRA San Antonio TX, February 2008.

Reitman MTF. Nano additives in composites and coatings for medical device applications. Medical Device and Manufacturing Minneapolis, Canon Communications, Minneapolis MN, October 2007.

Reitman MTF, Swanger LA. Practical tips on how to manage your technical expert in patent disputes. Ropes & Gray IP Master Class, Live Teleconference, June 2007.

Reitman MTF, Kennedy E. Root cause failure analysis and accident investigation. Lorman Educational Services, Live Teleconference, November 2007.

Reitman MTF. Plastics failure analysis: Case studies. Baltimore/ Washington Chapter of SAMPE, October 2006.

Reitman MTF. Plastics failure analysis. Baxter Global Plastics Processing Conference 2005, Schaumburg IL, 2005.

Fahey MT. Fiber mechanics, corrosion, sealants: Tales of a 3M materials scientist. Class of 1960's Scholars Program, Williams College, 1999.

Fahey MT. Adhesives and sealants for the telecommunications industry. Riverwood V Conference, St. Paul MN, 1998.

Current Professional Appointments

- Underwriter's Laboratory Standards Technical Panel STP 746 (Polymeric Materials, includes UL94, UL 746 and UL1694)
- Underwriter's Laboratory Standards Technical Panel STP 758 (Appliance Wires/ UL758)
- Medical Plastics Division Board of Directors, Society of Plastics Engineers

Committee and Review Activities

- UL Forum on Initiatives to Improve the Long Term Aging Program, LTTA Tools Working Groups, Underwriters Laboratories
- Research and Engineering Technology Award Committee, Society of Plastics Engineers
- Reviewer, Medical Plastics Technical Program Committee, Society of Plastics Engineers
- Reviewer, Failure Analysis and Prevention Technical Program Committee, Society of Plastics Engineers
- Reviewer, various book proposals and submissions related to polymer science, ASM International, Elsevier, John Wiley

Professional Affiliations

- American Association for the Advancement of Science (member)
- American Association of Textile Chemists and Colorists—AATCC (senior member)
- American Chemical Society (member)
- ASTM International (member)
- Society for the Advancement of Material and Process Engineering (member)
- Society of Plastics Engineers (senior member)

DECLARATION BY EDWARD D. COHEN, PH.D. UNDER 37 CFR § 1.132

This Declaration by Edward D. Cohen, Ph.D. under 37 CFR. § 1.132, dated September 6, 2012 (Cohen Decl.), was submitted by BDSI/Third Party Requester in connection with its September 10, 2012 "Request for Inter Partes Reexamination". The Cohen Decl. was admitted in the record, and referred to in the Action Closing Prosecution, mailed July 31, 2013.

Pursuant to 37 CFR § 41.71, Third Party Requester is using this declaration which was admitted.

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re *Inter Partes* Reexamination of:	)	
	)	
US Patent No. 7,897,080	)	
	)	
Issued: March 1, 2011	)	
	)	
Named Inventor: Robert K. Yang *et al.*	)	Group Art Unit: To Be Assigned
	)	
Control No.: To Be Assigned	)	Examiner: To Be Assigned
	)	
Filed: September 10, 2012	)	
	)	
Title: Polyethylene-oxide based films and drug delivery systems made therefrom	)	

Mail Stop *Inter Partes* Reexam
Attn: Central Reexamination Unit
Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

DECLARATION BY EDWARD D. COHEN, PH.D. UNDER 37 C.F.R. § 1.132

Sir/Madam:

I, Edward D. Cohen, Ph.D., do hereby make the following declaration:

I. Technical Background

1. I have worked for over 45 years in the field of coating and drying, in research, manufacturing, and more recently in industry consulting. I have a B.S. in Chemical Engineering from Tufts University and a Ph.D. in Physical Chemistry from the University of Delaware.

2. I have technical experience in thin film coating and drying process development, formulating coatings, coating machine design, new product process development, and troubleshooting manufacturing process problems. My experience includes more than 30 years at E.I. DuPont de Nemours and Co., from which I retired as a DuPont Fellow.

3. I have published extensively in the field of coating and converting, including several books and industry publications (see Appendix A for a shortened list of publications). I am a contributing editor for Converting Quarterly, a peer-reviewed journal. Converting is the field of coating and drying a substrate, and cutting the resulting product. I have chaired committees and symposia in both the American Institute of Chemical Engineers and the American Chemical Society. I was founding president of the International Society of Coating Science and Technology ("ISCST").

4. I have taught professional continuing education courses in the coating fields for more than 22 years, for the Association of Metallizers, Coaters, and Laminators ("AIMCAL); University of Minnesota; American Institute of Chemical Engineers; and the International Society of Coating Science and Technology.

5. My honors include the John Tallmadge Award for Contributions to Coating Technology; the AIMCAL President's Award in recognition of Meritorious Service to AIMCAL and the Converting Industry, and the ISCST Founders Award.

6. I am currently an independent consultant for the coating and converting industries and a Technical Consultant for AIMCAL. I was retained by BDSI as a consultant in 2011, for which I am paid on an hourly basis. I have been hired as a consultant by McCarter & English, LLP, to provide an expert analysis of certain issues in connection with the reexamination of U.S. Patent No. 7,897,080 ("'080 patent"). While I am being paid for my time, I am not an employee of BioDelivery Sciences, Inc., nor do I have any financial interest in BioDelivery Sciences, Inc.

7. I have read the '080 patent, and Chen *et al.* (PCT Publication No. WO2000/42992, or "Chen").

8. Chen provides coating mixtures containing active that are described as "homogeneous", "completely dissolved", or "completely dispersed". Drying such hydrocolloid coating mixtures would be expected to yield films with substantially uniform content of active per unit of film, where the unit of film is a typical dosage unit or per sheet of uncut film. It is my opinion that Chen teaches films with substantially uniform content of active per unit of film, where the unit of film is, for example, a dosage unit or an uncut sheet of film.

9. In general, as a homogeneous or completely dispersed coating mixture is dried, the solvent is removed, the viscosity increases and the active would be more firmly fixed in place. When working with a homogeneous or completely dissolved coating mixture, for example, it would be difficult for a person of

ordinary skill in the thin film art not to obtain a film that has uniform content of active.

10. It is my opinion that drying the film coating mixtures of Chen according to the drying methods of Chen would yield films with uniform content of active per unit dosage. When working with a homogeneous or completely dissolved or completely dispersed coating mixture, it is my opinion that the drying methods disclosed in Chen would not be expected to create any agglomeration, aggregation, or otherwise non-uniform content of active. There would have been a variety of drying processes or apparatus known in the art at the time the '080 Patent was filed, including bottom drying, that would have been able to provide a film with uniform content of active.

11. I hereby declare that all statements made herein of my own knowledge are true and that all statements made on information and belief are believed to be true; and further that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine, or imprisonment, or both, under section 1001 of Title 18 of the United States Code, and that such willful statements may jeopardize the validity of the application or any patents issued thereon.

Dated this 6 day of September, 2012. Edward D Cohen

Edward D. Cohen, Ph.D.

Appendix A

Publications List Condensed

Books

Cohen, E. and Lightfoot, E. J., 2011. Coating Processes, Kirk-Othmer Encyclopedia of Chemical Technology. 1-68.

Cohen, E. D. & Gutoff E. B., *Water and Solvent Based Coating Technology*, in J. R, Wagner, Jr., Multilayer Flexible Packaging, Elsevier, First edition, 2010.

Cohen, E. D. & Gutoff E. B., *Coating and Drying Defects Troubleshooting Operating Problems*, second edition, John Wiley and Sons, New York, 2006.

Cohen, E. D. & Gutoff E. B., *Coating and Drying Defects Troubleshooting Operating Problems*, John Wiley and Sons, New York, 1995.

Cohen, E. D. & Gutoff E. B., *Modern Coating & Drying Technology*, VCH Publishers, New York, April 1992.

Journal Articles

E. D. Cohen, *Web Coating Defects: Controlling Dryer Defects, Part2*, Converting Quarterly, 2011 Quarter 4.

E. D. Cohen, *What is the Impregnation-coating Process and Why is it Used?* Converting Quarterly, 2011 Quarter 3.

E. D. Cohen, *Why is Pre-metered Slot-die Coating Increasing in Popularity?* Converting Quarterly, 2011 Quarter 1.

E. D. Cohen, *Web Coating Defects: Streaks And How To Eliminate Them,* Converting Quarterly, 2011 Quarter 1.

E. D. Cohen, *Technology Trends,* Paper Film & Foil Converter, May 2010.

E. D. Cohen & D. Bemi, *Conserve Energy*, Paper Film & Foil Converter, February, 2009.

E. D. Cohen, *Older methods: Still effective for web coating*, Converting Magazine, June 2007.

E. D. Cohen & E. B. Gutoff, *Coating Process Survey*, Kirk Othmer Concise Encyclopedia of Chemical Technology, 4th Ed., John Wiley & Sons, Inc. NY (1999).

E. Cohen, E. J. Lightfoot, K. N. Christodoulou, *Important Issues in Drying of Thin Films: An Industrial Engineers Perspective*, Part 2 Models. Industrial Coating Research, Vol. 4, pp.47-72 (1998).

E. B. Gutoff & E. D. Cohen, R&*D Needs in the Drying of Coatings*, Drying Technology, 14(6), 1315-1328 (1996).

E. Cohen, E. J. Lightfoot, K. N. Christodoulou, *Important Issues in Drying of Thin Films: An Industrial Engineers Perspective*, Industrial Coating Research, Vol. 3, pp.45-68 (1995).

IX. RELATED PROCEEDINGS APPENDIX

None.

X. CERTIFICATE OF SERVICE

CERTIFICATE OF SERVICE

The undersigned hereby certifies that a copy of the instant brief was served on April 10, 2014, by first class mail, directed to the patent owner at the correspondence address of record for the subject patent at the following address:

Daniel A. Scola, Jr.

HOFFMANN & BARON, LLP

6900 JERICHO TURNPIKE

SYOSSET, NY 11791,

By: /Danielle L. Herritt/
Danielle L. Herritt
Registration No. 43,670
Attorney for Respondent

Electronic Acknowledgement Receipt

EFS ID:	18732595
Application Number:	95002170
International Application Number:	
Confirmation Number:	6418
Title of Invention:	POLYETHYLENE-OXIDE BASED FILMS AND DRUG DELIVERY SYSTEMS MADE THEREFROM
First Named Inventor/Applicant Name:	7897080
Customer Number:	23869
Filer:	Danielle L. Herritt/Maureen Tierney
Filer Authorized By:	Danielle L. Herritt
Attorney Docket Number:	117744-00023
Receipt Date:	10-APR-2014
Filing Date:	10-SEP-2012
Time Stamp:	17:37:11
Application Type:	inter partes reexam

Payment information:

Submitted with Payment	no

File Listing:

Document Number	Document Description	File Name	File Size(Bytes)/ Message Digest	Multi Part /.zip	Pages (if appl.)
1	Respondent Brief - Requester	117744_00023_080_Respondent_Brief_FINAL_2014APR10.PDF	1102636 cd63f3422ee43816f6cc817c18e2987a5d99cf26	no	62

Warnings:

The page size in the PDF is too large. The pages should be 8.5 x 11 or A4. If this PDF is submitted, the pages will be resized upon entry into the Image File Wrapper and may affect subsequent processing	
Information:	
Total Files Size (in bytes):	1102636

This Acknowledgement Receipt evidences receipt on the noted date by the USPTO of the indicated documents, characterized by the applicant, and including page counts, where applicable. It serves as evidence of receipt similar to a Post Card, as described in MPEP 503.

New Applications Under 35 U.S.C. 111

If a new application is being filed and the application includes the necessary components for a filing date (see 37 CFR 1.53(b)-(d) and MPEP 506), a Filing Receipt (37 CFR 1.54) will be issued in due course and the date shown on this Acknowledgement Receipt will establish the filing date of the application.

National Stage of an International Application under 35 U.S.C. 371

If a timely submission to enter the national stage of an international application is compliant with the conditions of 35 U.S.C. 371 and other applicable requirements a Form PCT/DO/EO/903 indicating acceptance of the application as a national stage submission under 35 U.S.C. 371 will be issued in addition to the Filing Receipt, in due course.

New International Application Filed with the USPTO as a Receiving Office

If a new international application is being filed and the international application includes the necessary components for an international filing date (see PCT Article 11 and MPEP 1810), a Notification of the International Application Number and of the International Filing Date (Form PCT/RO/105) will be issued in due course, subject to prescriptions concerning national security, and the date shown on this Acknowledgement Receipt will establish the international filing date of the application.

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Inter Partes Reexamination of Yang et al.	Examiner: Alan D. Diamond
U.S. Patent No. 7,897,080	Group Art Unit: 3991
Reexamination Control No. 95/002,170	Confirmation No. 6418
Filed: September 10, 2012	H&B Docket: 1199-26 RCE/CON/REX M&E Docket: 117744-00023

For: POLYETHYLENE-OXIDE BASED FILMS AND DRUG DELIVERY SYSTEMS MADE THEREFROM

PATENT OWNER'S CROSS-RESPONDENT'S BRIEF

Mail Stop *Inter Partes* Reexam
Central Reexamination Unit
Commissioner for Patents
U.S. Patent and Trademark Office
P.O. Box 1450
Alexandria, VA 22313-1450

Certificate of EFS-Web Transmission
I hereby certify that this correspondence is being transmitted via the U.S. Patent and Trademark Office electronic filing system (EFS-Web) to the USPTO on April 10, 2014.

Signed: Michael I. Chakansky /Michael I Chakansky/Reg. No. 31,600

I hereby certify that, pursuant to 37 CFR § 1.943(c), based on the WordPerfect word count of 6,981 words, Patent Owner's Cross-Respondent's Brief, counting the words on those pages beginning at page 1 (entitled Patent Owner's Cross-Respondent's Brief) and continuing through and including all words of the signature page (entitled Conclusion), does not exceed 7,000 words in length.

Signed: Michael I. Chakansky /Michael I Chakansky/Reg. No. 31,600

Dear Madame:

On March 10, 2014, Third Party Requester BioDelivery Sciences International, Inc. ("BDSI" or "Third Party Requester" or "Cross-Appellant") filed its cross Appeal Brief in *Inter Partes* Reexamination ("BDSI's Brief") regarding certain claims rejections not adopted by the Examiner in the RAN. This Patent Owner's Cross-Respondent's Brief, filed April 10, 2014

("MonoSol's Brief") is timely.

MonoSol submits this brief in opposition to BDSI's Cross-Appeal, and authorizes the Commissioner to charge all fees associated therewith, including, without limitation, the $2,000.00 fee for filing this respondent's brief in an *inter partes* reexamination proceeding, pursuant to 37 C.F.R. § 41.20(b)(2), to Deposit Account No. 08-2461.

TABLE OF CONTENTS

TABLE OF AUTHORITIES

CASES

STATUTES

PTAB DECISIONS

PATENT OWNER'S CROSS-RESPONDENT'S BRIEF

I. Real Party in Interest

MonoSol Rx, LLC ("MonoSol"), owner of U.S. Patent No. 7,897,080 (the " '080 Patent"), is the real party in interest.

II. Related Appeals and Interferences

MonoSol commenced a patent infringement action asserting U.S. 7,824,588 (the " '588 Patent"), U.S. 7,357,891 (the " '891 Patent") and U.S. 7,425,292 (the " '292 Patent") against BDSI, *inter alia*, in the District of New Jersey, *MonoSol Rx, LLC v. BioDelivery Sciences International, Inc., MEDA Pharmaceuticals, Inc. and Aveva Drug Delivery Systems, Inc.*, 10-cv-5695 ("the Litigation"). Then, BDSI requested *inter partes* reexamination of the '588 Patent (95/001,753) and then *ex parte* reexamination of the '891 Patent (90/012,098) and the '292 Patent (90/012,097). The Court stayed the Litigation. The '891 Patent and the '292 Patent successfully exited reexamination with reexamination certificates, leaving the '588 Patent *inter partes* reexamination pending and currently on appeal to the PTAB. BDSI also requested *inter partes* reexamination of two additional patents of MonoSol, namely, the '080 Patent, herein, and US 7,666,337 (the " '337 Patent") (95/002,171). The '337 Patent reexamination is currently on appeal to the PTAB.

Several actions have been recently commenced for patent infringement arising from the

submission of ANDAs regarding U.S. 8,017,150 (" '150 Patent"), *inter alia*, in the U.S. District Court for the District of Delaware. The actions are 1:13-cv-014611; 1:13-cv-01674; and 1:13-cv-02003. The '150 Patent is a divisional of the application for the '337 Patent, of which the '080 Patent is a continuation.

III. Status of Claims

MonoSol accepts BDSI's statement that the following claims are pending and currently stand rejected: claims: 1-11, 13-15, 17-90, 92-94, 96-172, 174-176, 178-253, 256, 258-271, 274, 276-289, 292 and 294-318. Moreover, MonoSol is appealing all claims rejected and all the grounds therefor.

IV. Status of Amendments

MonoSol accepts BDSI's statement, except notes that the reply and amendment dated January 29, 2013 are not part of the record.

V. Summary of Claimed Subject Matter

MonoSol disputes BDSI's summary. MonoSol's invention is directed to novel and non-obvious processes for manufacturing pharmaceutical and bioactive (hereinafter, collectively "pharmaceutical") active-containing films suitable for commercialization and FDA approval. Suitability for commercialization and FDA approval in the context of the present invention is clearly directed to maintaining the uniformity of the pharmaceutical active from start to finish in the process of manufacturing pharmaceutical resulting film. Moreover, commercialization inherently requires the ability to mass produce the films at scale and that resulting film products from different manufacturing runs meet the requisite degree of uniformity in amount of drug.

The '080 Patent process steps require, *inter alia*, that the degree of uniformity be demonstrated by chemical testing using analytical equipment, that is, by analytical chemical testing. Although physical observations and testing are very useful to suggest **non-uniformity** of pharmaceutical active content (*see, e.g.*, '080 Patent, col. 29, ll. 20 through 47), only analytical chemical testing can determine the actual degree of **uniformity**[1] of pharmaceutical active content as required by the FDA. Importantly, the FDA requirements talk about both types of testing, but always require analytical chemical testing of samples to ensure the amount of pharmaceutical active.

[1] Of course, analytical chemical testing can be used determine non-uniformity as well.

BDSI correctly states that there are seven independent claims pending on appeal, *i.e.*, claims 1, 82, 161, 315, 316, 317 and 318. The independent claim language appears below.

A process for **manufacturing resulting films suitable for commercialization and regulatory approval,** said regulatory approval including analytical chemical testing which meets the **standards of the U.S. Food and Drug Administration relating to variation of an active in individual dosage units**, said films having **a substantially uniform distribution of components comprising a substantially uniform distribution of [a desired amount of] said active in individual dosage units of said resulting films**, comprising the steps of:

[Preamble - Claims 82 and 315 included bracketed limitation; claim 161 adds "film capable of being administered to a body surface".]

(a) **forming a flowable polymer matrix** comprising a water-soluble polymer, a solvent and said active, said active selected from the group consisting **of bioactive actives, pharmaceutical actives and combinations thereof**, said matrix having a substantially uniform distribution of said active;

[(a) - Claim 1 does step (a) in 2 steps (a) and (b), generally by adding active last.]

(b) **casting said flowable polymer matrix**, said flowable polymer matrix having a **viscosity from about 400 to about 100,000 cps;**

[(b) - Claim 1's version is denoted step (c).]

(c) **controlling drying through a process comprising conveying said flowable polymer matrix through a drying apparatus** [at a temperature of about **60 °C** and **using air currents,** which have **forces below a yield value of the polymer matrix during drying**,] to evaporate at least a portion of said solvent to form a visco-elastic film, having said active substantially uniformly distributed throughout, **within about the first 4 minutes by rapidly increasing the viscosity of said flowable polymer matrix upon initiation of drying** to **maintain said substantially uniform distribution** of said active **by locking-in** or substantially preventing migration of said active within said visco-elastic film[[, such that uniformity of content in the amount of said active in substantially equal sized individual dosage units, sampled from different locations of said visco-elastic film, **varies by less than 5%,**]] and wherein during said drying said flowable **polymer matrix temperature is 100 °C or less**;

[(c) - Claim 1 does not have the bracketed limitations and it is denoted as step (d); in claims 82 and 161 the double bracketed percent is 10%; only claim 318 has single bracketed limitation of 60 °C .]

(d) **forming said resulting film from said visco-elastic film by further controlling drying** by continuing evaporation to a **water content of said resulting film of 10% or less** and wherein said **substantially uniform distribution of active by said locking-in** or substantially preventing migration of said active **is maintained**[, such that **uniformity of content** in the amount of said active in substantially equal sized individual dosage

units, sampled from different locations of said resulting film**, varies by no more than 10%**];

[(d) - Claim 1 denotes this as step (e); claims 1, 82 and 161 do not have bracketed limitation; claim 318 replaces bracketed "varies by no more than 10%" with "varies by less than 5%".]

(e) **performing analytical chemical tests for uniformity of content of said active** in said substantially equal sized individual dosage units of said sampled resulting film, said tests indicating that uniformity of content in the amount of said **active varies by no more than 10%** and said **resulting film is suitable for commercial and regulatory approval**, wherein said regulatory approval is provided by the U.S. Food and Drug Administration.

[(e) - Claim 1 denotes this as step (f); claim 318 replaces "varies by no more than 10%" with "varies by less than 5%".]

(f) **repeating steps (a) through (e)** to form additional resulting films, such that **uniformity of content** in the amount of said active in said resulting film and said additional resulting films **varies no more than 10%** from **the desired amount** of said active as indicated by said analytical chemical tests.

[(f) - only claims 82 and 315 have this step.]

(f) **administering said resulting film to a body surface**.

[(f) - only claim 161 has this step.]

BDSI alleges that there is no support for some of the above claim elements. MonoSol disagrees. Support for the claims may be found throughout the '080 Patent, for example:

***Preamble and Step (e); step (f) for claim 1*:** col. 3, ll. 58-60.

***Step (a); steps (a) and (b) for claim 1*:** col. 19, l. 30 through col. 21, l. 31.

***Steps (b) and (c); steps (c) and (d) for claim 1*:** col. 6, ll. 49-52; Figures 6, 7, 8, 35 and 36 and col. 14, ll. 20-25; col. 11, ll. 17-19; col. 11, ll. 21-23; col. 12, ll. 20-36, col. 13, ll. 37-38; col. 29, ll. 11-13; col. 33, l. 10 through col. 34, l. 24; col. 44, 11. 9-13; col. 6, ll. 52-60; col. 7, lines 5 through 16; col. 27, ll. 53-55; col. 41, ll. 49-50; col. 13, ll. 23-36; col. 16, l. 62 through col. 17, l. 3.

Step (e); step (f) for claim 1: col. 28, l. 66 through col. 29, l. 6; col. 29, ll. 20 through 47 ; col. 32, ll. 34-41; col. 33, l. 10 through col. 34, l. 24; col. 15, ll. 28-43.

***Step (f), only claims 82 and 315*:** col. 2, ll. 27-46.

***Step (f), only claim 161*:** col. 29, l. 64 to col. 30, l. 2.

VI. Issues to be Reviewed on Appeal

MonoSol disputes certain of the characterizations of the non-adoption of BDSI's proposed 35 U.S.C. § 112 rejections which form the sole basis for its Cross-Appeal. For example, BDSI in its appeal issue C proposes that the specified issue C recitation has no written description. Yet, BDSI did not propose, nor did the Examiner find, a lack of written description with respect to this recitation. RAN, pp. 17-20. Thus, it cannot be part of BDSI's Cross-Appeal. This is one example of the dispute. These are addressed and corrected by the counter statement *infra*.

Finally, many of the arguments made in BDSI's Brief are improper, self-serving arguments about the RAN's rejection of '080 Patent claims based on §§ 102 and 103. Such arguments exceed the scope of BDSI's Cross-Appeal, and should not be considered.

Issues to be Reviewed on Appeal

A. The Examiner did not err in finding that the recitation of "suitable for commercialization and regulatory approval, said regulatory approval including analytical chemical testing which meets the standards of the U.S. Food and Drug Administration relating to variation of an active in individual dosage units" is enabled, definite and has written description (RAN, pp. 12-15).

B. The Examiner did not err in finding that the recitation of "chemical analytical tests" is clear and has written description (RAN pp. 15-16).

C. The Examiner did not err in finding that the recitation of "individual dosage units vary by no more than 10%, 5%, 2%, 1% or 0.5%" is clear and enabled (RAN, pp. 17 -20).

D. The Examiner did not err in finding that the recitation of the term "varies by no more than 10% from desired amount of active" is clear, enabled and has written description (RAN, pp. 20-22).

E. The Examiner did not err in finding that the recitation of the term "rapidly increasing the viscosity of said flowable polymer matrix" is clear (RAN, p. 22).

F. The Examiner did not err in finding that the recitation of "during said drying said flowable polymer matrix temperature is 100 °C or less" is clear (RAN, p. 23).

G. There is no section in the RAN regarding the non-adoption of BDSI's proposed § 112 rejections labeled "G".

H. The Examiner did not err in finding that the various recitations of the entered claim amendments requiring various degrees of uniformity are clear, enabled and have written description (RAN, pp. 24-27).

VII. ARGUMENT

Preliminary Statement

Due to space limitations and, *inter alia*, the overlapping nature of BDSI's arguments, each of the arguments made by MonoSol herein are hereby explicitly incorporated into all of the argument sections.

A. The Examiner did not err in finding that the recitation of "suitable for commercialization and regulatory approval, said regulatory approval including analytical chemical testing which meets the standards of the U.S. Food and Drug Administration relating to variation of an active in individual dosage units" is enabled, definite and has written description (RAN, pp. 12-15; BDSI's Brief, pp. 14-21).

BDSI complains that the Examiner erred by not adopting BDSI's interpretation of "suitable for commercialization and regulatory approval...", and for not rejecting the recitation as lacking written description and enablement under that interpretation, and further for not rejecting the recitation for being susceptible to two interpretations -- the PTO's and MonoSol's. However, there is only one interpretation set forth by both the Examiner and MonoSol and that interpretation is supported by the specification, *see supra* and *infra*.

BDSI's interpretation, an interpretation that BDSI tries to attribute to MonoSol, is absurd. BDSI's argument that the recitation requires compliance with each and every FDA requirement for a drug to be accepted for use in humans, from determining the chemistry, through the manufacturing process, including requirements for packaging and presumably the labeling as well, is unfounded and unsupported. As the Examiner recognized, the '080 Patent and this recitation address maintaining the uniformity of content of the active in dosage units on a commercial scale so as to provide a drug-containing film suitable for FDA approval in that it can meet the FDA's uniformity of content requirements -- not how the dosage units are packaged! The recitation is definite.

Again, suitability for commercialization and FDA approval in the context of the present invention is clearly directed to maintaining the uniformity of content of the pharmaceutical active

from start to finish in the manufacture of the pharmaceutical resulting film. Moreover, commercialization inherently requires the ability to mass produce the films at scale and that film products from different manufacturing runs will fall within the FDA uniformity requirements. BDSI's attempt to create a strawman by morphing Dr. Lin's declaration into support for its wishful desire that the '080 Patent claims require a process meeting all the requirements of a "FDA CMC submission" (BDSI's Brief, p. 20) is just that -- wishful thinking. The term "FDA CMC" does not appear in the '080 Patent or its claims. It only appears in Dr. Lin's declaration in the paragraphs concerning his background experience and responsibilities. Lin Declaration, ¶¶ 4 & 5.

Although MonoSol's Dr. Lin discusses in the background section (Lin Declaration, p. 3) his experience with many of the U.S. regulatory requirements for a drug to be approved for marketing and distribution, his focus is clearly directed to meeting the requirement of maintaining the "uniformity of content of the drug active" so as to be suitable for FDA approval. This can be clearly seen by Dr. Lin's statements.

> "**the manufacture of films with uniformity of content (strength) of drug active required for FDA approval**." Lin Declaration ¶ 17 (emphasis supplied).

> "**the determination of the actual amount of drug (active) in individual dosage units**." Lin Declaration ¶ 18 (emphasis supplied).

> "As required for FDA approval . . . would not **ensure that films containing drug could be manufactured to meet specifications that ensure consistent strength [uniformity of content]**." Lin Declaration ¶ 19 (emphasis supplied).
>
> "the disclosure necessary **to provide for the manufacture of drug-containing films with the uniformity of content in amount of drug (active) in individual dosage units to make FDA approvable film products**." Lin Declaration ¶ 21 (emphasis supplied).

BDSI's argument that the recitation requires satisfaction of the full panoply of FDA requirements is illogical on its face. Taken to its illogical conclusion, BDSI is arguing that the recitation includes ensuring fulfillment of the FDA requirements regarding drug labeling! BDSI is just wrong. BDSI cites to MonoSol's Reply to the Non-Final Office Action, filed on March 13, 2013 ("MonoSol's Reply to OA" or "Reply-2"), as supporting its position. However, a more complete look at the sections cited by BDSI does not support BDSI's position, but rather supports MonoSol's and the Examiner's position. For example, the complete first two sentences provide:

> "As explained throughout the '080 Patent and as summarized above, the present invention is based upon the discovery that certain process parameters, such as, viscosity and controlled drying methods to **avoid non-uniformity of content in the amount of active must be employed to provide a commercially and FDA viable film product.** . . . See Lin Declaration, ¶¶ 17-22."
>
> MonoSol's Reply to OA (Reply-2), p. 78, ll. 4-8 (emphasis supplied).

BDSI's reliance on Dr. Clevenger's declaration (BDSI's Brief, p. 21) is also misplaced. It is clear from the portion of the declaration cited by BDSI that Dr. Clevenger is not discussing suitability for FDA approval and commercialization in connection with maintaining the uniformity of content in the amount of active but, instead, is discussing something he describes as the "route to regulatory approval". Clevenger Declaration, ¶ 4.

BDSI's strawman has been shown to be without substance, or clothes for that matter and, for that reason alone, must fall.

For all of the above reasons, there was no error in the Examiner's refusal to apply BDSI's constructions to the recitation. The Examiner's finding that the recitation is enabled, definite and has written description must be affirmed.

B. The Examiner did not err in finding that the recitation of "chemical analytical tests" is clear and has written description (RAN pp. 15-16; BDSI's Brief, pp. 21-25).

BDSI complains that the Examiner erred in declining to adopt BDSI's proposed rejections for the term "analytical chemical tests" because, according to BDSI, the term is not used, not described, not defined, and not exemplified in the '080 patent. BDSI is wrong.

The '080 Patent expressly provides:

> "It may be **desirable to test the films of the present invention for chemical and physical uniformity during the film manufacturing process**. . . . Uniform films are desired, **particularly for films containing pharmaceutical active** components for safety and efficacy reasons."
>
> '080 Patent, col. 28, l. 66 through col. 29, l. 6 (emphasis supplied).
>
> "After the end pieces, or sampling sections, are removed from **the film portion(s), they may be tested for uniformity in the content of components between samples**. Any conventional means for examining and testing the film pieces may be employed, such as, for example, visual inspection, **use of analytical equipment**, and any other suitable means known to those skilled in the art"
>
> '080 Patent, col. 29, ll. 33-38 (emphasis supplied).

> "An alternative method of determining the uniformity of the active is to cut the film into individual doses. **The individual doses may then be dissolved and tested for the amount of active in films of particular size. This demonstrates that films of substantially similar size cut from different locations on the same film contain substantially the same amount of active**."
>
> '080 Patent, col. 32, ll. 34-41 (emphasis supplied).

MonoSol agrees with the Examiner's reasoning and findings. As the Examiner stated:

> "This proposed rejection is not adopted for the following reasons. As noted above in the Scope of Claims section, which cites to the '080 patent specification for support, the term "analytical chemical tests" means analytical tests for determining the amount of active content in the recited sample. **The distinguishing point between analytical chemical tests as here claimed and physical testing (analytical or nonanalytical)** is whether there is **direct testing for the amount of active**. Accordingly, the term "analytical chemical tests" is clear and has written description."
>
> RAN, p.16 (emphasis supplied).

In the Scope of the Claims section referred to *supra*, the Examiner stated:

> "It is clear that when the '080 patent refers to 'physical' uniformity it is referring to, for example, uniformity based on the appearance of the film or the weight of individual doses cut from the film. **Likewise, it is clear that when the '080 patent refers to 'chemical' uniformity, it is referring to uniformity with respect to the actual amount of active, *i.e.*, chemical, present in the sample. Accordingly, the term 'analytical chemical tests' when read in light of the '080 patent**

> **specification means analytical tests for determining the amount of active content in the recited sample.**"
>
> RAN, p. 8 (emphasis supplied).

The section of the RAN at pp. 86-87 that BDSI relies on to support its argument that the '080 Patent lacks written description for "analytical chemical tests" actually demonstrates written description for the above recitation. In particular, the following language quoted directly from BDSI's Comments filed 10/03/13, in which **BDSI relied on the '080 Patent disclosure**, clearly demonstrates written description for the above recitation for "chemical analytical tests". Thus, as quoted by the Examiner, BDSI in its Comments stated:

> "**Indeed, analytical chemical tests were among many known ways to measure the amount of active in each dosage form.** Reply at 64-66; **'080 patent, cols. 31-32.** Thus, the ACP does not and need not rely on Example M for the rejection of claims including the step of performing analytical chemical testing. Even in the interpretation most favorable to MonoSol--which may or may not be correct--Example M only confirms what is already admittedly known regarding this post-manufacturing step. **That is, measuring active content in samples from pharmaceutical commercial runs is obvious**. ACP at 37-38."
>
> RAN, p. 87, quoting BDSI's Comments (emphasis supplied).

Certainly, using BDSI's own argument above, BDSI admits that Example M from the '080 Patent provides an actual example of using a chemical analytical test to determine directly the amount of active in films made by the '080 Patent processes. '080 Patent, col. 33, l. 10 through col. 34, l. 24. The uniformity of content was measured using a spectrophotometer (analytical chemical testing) which measures light absorption and is directly related to the amount of active present. Example M used percent difference of active concentration as measured by light absorption found in equally sized samples. Highest minus lowest = 1.774 – 1.700 = .074; Average of 8 samples = 1.725; 0.074 divided by 1.725 = 0.043; = **4.3%** degree of uniformity.

For all of the above reasons, there is no error in the Examiner's refusal to apply BDSI's constructions to the recitation. The Examiner's finding that the recitation is definite and has written description must be affirmed.

C. The Examiner did not err in finding that the recitation of "individual dosage units vary by no more than 10%, 5%, 2%, 1% or 0.5%" is clear and enabled (RAN, pp. 17 -20; BDSI's Brief, pp. 25-32).

BDSI complains that the Examiner erred in declining to adopt BDSI's proposed rejections for the step of performing analytical tests to verify specific levels of uniformity because, in BDSI's words, this step is not used, not described, not defined, and not exemplified in the '080 patent. BDSI is wrong. Moreover, BDSI proposes in its issues on appeal, that the

recitation has no written description. Yet, BDSI never proposed a lack of written description with respect to this recitation and the Examiner never found it lacking. RAN, pp. 17-20. Thus, this ground should not be part of the Cross-Appeal. Additionally, BDSI once again improperly addresses §§ 102 and 103 matters outside the scope of its Cross-Appeal. These arguments should not be considered.

BDSI relies on Chen (as interpreted by Reitman) and Staab in its attempts to establish that the prior art provided examples of the recited claimed degrees of content uniformity, which it did not. Indeed, when relying just on physical measurements, Reitman's declaration demonstrates that samples taken from Chen's Example 7, and samples taken from Reitman's exact copying of Chen's Example 7 process, differed in weight by 30% from the desired weight and thus exhibited a 30% non-uniformity in weight of pharmaceutical active from the desired amount as well. Moreover, Staab's supposed 0% variation on uniformity of active turns out to be a variation in uniformity of content in weight of active of between 90 and 100% from the desired amount. See discussion below.

1. Respondent's Reitman Declaration (EA-4) demonstrates that Chen's processes produce films which are 30% from the desired dosage weight.

BDSI and the Examiner have both relied on the false assumption that uniformity of weight of equally sized film samples is, by itself, sufficient to demonstrate that the amount of active present in prior art references meets the '080 Patent claimed uniformity of active. *See. e.g.*, RAN, pp. 77, 97. However, using this "assumption," BDSI's Reitman Declaration (EA-4)

instead clearly demonstrates the inability of Chen to provide film dosage units meeting the '337 Patent's claimed substantial uniformity across different manufactured resulting films (lots).

BDSI's Reitman declares that she and her team "**manufactured a film in accordance with Example 7 of *Chen***", *i.e.*, Chen Example 7 film (Reitman Declaration, EA-4, p. 2, ¶ 3, emphasis supplied).

Reitman further declares that her 5 cm^2 dosage samples of **Reitman's Chen Example 7 film all weighed exactly 34 mg.** *See* Reitman Declaration, EA-4, Table 2, page 4, ¶ 6.

Chen provides enough information to calculate the weight of the 5 cm^2 dosage unit sample of Chen Example 7 film. Indeed, **Chen's 5 cm^2 dosage unit sample of Example 7 film weighed 48.8 mg**.[2]

Taking Chen's 5 cm^2 Example 7 film weight as the expected or desired dosage unit weight of Chen's Example 7 samples, **the weight difference between Chen's** Example 7 dosage units and **Reitman's** Chen Example 7 dosage units amounts to a 30% difference in weight.

Hence, in accordance with BDSI's and the Examiner's assumption that purely physical characteristics, *e.g.,* weight, can determine uniformity of content in the amount of active, as there is a **30% weight difference between Chen's Example 7 samples and Reitman's Chen's**

---

[2] Chen provides the following information regarding its film formed in Chen Example 7 (Chen, p. 22, Table 6, and p. 16, l. 5): Thickness = 3.2 mil = 0.008128 cm; Size = 5 cm^2; and Density = 1.2 gm/cm^3. From this information the weight of the dosage sample can be calculated. Area x Thickness x Density = Weight of Film Sample. 5 cm^2 x 0.008128 cm x 1.2 gm/cm^3 = 0.0488 gm =48.8 mg. Thus, the weight of Chen's 5 cm^2 Example 7 sample is expected (desired) to be **48.8 mg.**

Example 7 samples, the assumption requires there to be a 30% difference in the weight (amount) of active between Chen's and Reitman's samples.[3] Thus, **Chen's Example 7 and Reitman's Chen's Example 7 demonstrates a lack of uniformity of content in the amount of active of 30% between their separately manufactured films.**

[3] Chen's Example 7 Weight of Samples was 48.8 mg. Reitman's Example 7 Weight of Samples was 34 mg. ((48.8 mg - 34 mg)/(48.8 mg)) = (14.8 mg)/(48.8 mg) = 30%.

2. Staab's example demonstrates a 100% - 90% difference in unformity

Staab states (Staab, col. 11, l. 22 to col. 12, l. 3) that when he incorporated 10% of a 50% by weight benzalkonium chloride aqueous solution into a film-forming mixture, he obtained, after drying, a film product having exactly 19 mg benzalkonium chloride ("active") in all 190 mg film samples. According to BDSI and the Examiner, as all the film samples had 19 mg of active, this demonstrated a 0% variation in uniformity of content in the active, and the Examiner relied on this 0% in his rejections. **0% is wrong! Staab's lack of degree of uniformity of active content is 100% from the desired amount**.

The following is based on Staab, col.11, lines 22- 51, and assumes no water is driven off. Staab starts with 10% by weight of benzalkonium chloride (50% aqueous). Thus, Staab's starts with **5%** by weight of benzalkonium chloride active. Staab and any reader would expect the resulting film would maintain the 5% by weight of benzalkonium chloride active.[4] Staab cut out 190 mg samples from his resulting film. If Staab maintained the 5% by weight of active, the expected or desired amount of active in a 190 mg sample would be 9.5 mg of benzalkonium chloride active.

[4] This is assuming that everything else stays the same, except perhaps for the water content. In the extreme example where all of the water is removed, the expected, desired amount of active becomes 5.26% (.0526) by weight of benzalkonium chloride.

190 mg x 5% = **9.5 mg**[5] **= Staab's desired amount of active**.

Instead Staab's 190 mg samples each contained 19 mg of benzalkonium chloride active.

19 mg is Staab's actual amount of active.

The variation in uniformity of distribution of benzalkonium chloride active in Staab's resulting films **was 100% from the desired amount**.

$$\frac{\text{19.0 mg (actual amount of active) - 9.5 mg (desired amount of active)}}{\text{9.5 mg (desired amount of active)}}$$

$$= (9.5)/(9.5) = \mathbf{100\%}!$$

[5] **So far we have assumed that no water was driven off because Staab says nothing about the water content of his films. But even if we assume that all the water is driven off, then the difference is still too much at 90%.** If all the water was driven off, then 10.0 mg of active would be the desired amount of active (190 mg x .0526 = 9.994 mg) and Staab's 19 mg of active results in a 90% difference from the 10 mg desired amount. A 90% difference would not meet the FDA requirements either.

3. Example M from the '080 Patent - Degree of Uniformity 4.3%

Example M of the '080 Patent exemplifies the use of analytical chemical testing demonstrating that active-containing films manufactured in accordance with the invention obtain **degrees of uniformity of content in the amount of active of 4.3%**. '080 Patent, col. 33, l. 10 through col. 34, l. 24. *See* discussion, *supra*.

MonoSol obtains even better degrees of uniformity of content with its commercial manufacturing production runs. As the Examiner stated in the RAN, pp. 19-20.

> **As seen in Appendices A and C of Bogue Declaration I [EA-1], a variation as low as 2% was obtained. The variation was calculated by taking the maximum active content of a lot minus the minimum active content of that lot, divided by the average active content of that lot (see ¶ 9).** While the red dye of the '080 Patent's Example M is not a pharmaceutical active or bioactive active, a similar calculation is made in Example M at col. 34, lines 18-20 based on absorbance measurements, which are directly related to concentration of the red dye (see also col. 33, lines 49-51). Further, ¶¶ 10-11 of Bogue Declaration I, citing Appendix B, allege that "the amount of active across different lots of resulting film varies no more than 10% from the desired amount of the active."

RAN, pp. 19-20 (emphasis supplied).

Finally, BDSI alleges that because MonoSol's Bogue declaration only provided "results" and not the underlying "data" it must be given little weight. BDSI Brief, pp. 29-30. Bogue provided the way the results were calculated. Bogue Declaration I, ¶¶ 9-11. Bogue also attested

that he "compiled individual dosage unit assay data for individual Lots 1 - 73, **all of which were disclosed in MonoSol's 2012 Annual Product Review to the FDA**." Bogue Declaration I, EA-1, ¶ 6 (emphasis supplied). The fact that MonoSol, in the ordinary course of business, disclosed the same data to the FDA to meet compliance regulations supports **the great weight that should be given to the Bogue declarations**.

For all of the above reasons, there is no error in the Examiner's refusal to apply BDSI's constructions to the recitation, and the Examiner's finding that the recitation is definite and enabled must be affirmed. The PTAB should also find that there is written description.

D. The Examiner did not err in finding that the recitation of the term "varies by no more than 10% from desired amount of active" is clear, enabled and has written description (RAN, pp. 20-22; BDSI's Brief, pp. 32-35).

BDSI complains that the Examiner erred in declining to adopt BDSI's proposed rejections based on its arguments that somehow requiring manufactured films to comply with the varies by no more than 10% from desired amount of active is not described, not defined, and not exemplified in the '080 patent. BDSI is wrong.

The '080 Patent expressly provides that:

> "Currently, as required by various world regulatory authorities, dosage forms may not vary more than 10% in the amount of active present. When applied to dosage units based on films, this virtually mandates that uniformity in the film be present."

'080 Patent, col. 2, ll. 42-46.

That being said, BDSI's argument as to the "repeating steps" is also without basis. BDSI argues that "[l]ogically, repeating a set of steps should produce more of the same film, but not change the quality of the film." BDSI Brief, p. 33. However, as demonstrated *supra*, using only physical characteristics, Reitman's repeat of Chen Example 7 steps produced film samples which were not uniform, when compared to Chen's Example 7 steps film samples. The difference in uniformity between the two separate productions of film was **30%**.

Moreover, the pending claims do enable by addressing the problem of maintaining uniformity. For example, claim 1 recites, *inter alia*, casting a flowable polymer matrix having a

viscosity from about 400 to about 100,000 cps and controlling drying by conveying said flowable polymer matrix through a drying apparatus and evaporating at least a portion of said solvent from said flowable polymer matrix to form a visco-elastic film within about the first 4 minutes by rapidly increasing the viscosity of said flowable polymer matrix upon initiation of drying to maintain said substantially uniform distribution of said active by locking-in or substantially preventing migration of said active within said visco-elastic film, wherein during said drying said flowable polymer matrix temperature is 100 °C or less. No more is required.

Finally, as set forth *supra*, dosage units must not vary by more than 10% in the amount of pharmaceutical active prescribed by the FDA. The amount of pharmaceutical active prescribed is the amount desired to be delivered to the patient. The '080 Patent discloses that the amount of active is permitted to vary no more than 10% from the desired amount. In effect, although this can result in about a 20% range in amount of active between dosage units, there still is only a 10% difference in amount of active from the desired amount. Because the '080 Patent discloses processes which are suitable for commercialization, including scaling up and reproducibility, it is inherent that the process provides that same degree of uniformity in amount of active in dosage units produced from one manufacture of a resulting film to another manufacture of a resulting film and that the resulting films would be tested and should fall within the stated degree of uniformity.

For all of the above reasons, there is no error in the Examiner's refusal to apply BDSI's constructions to the recitation, and the Examiner's finding that the recitation is enabled, definite and has written description must be affirmed.

E. The Examiner did not err in finding that the recitation of the term "rapidly increasing the viscosity of said flowable polymer matrix" is clear (RAN, p. 22; BDSI's Brief, pp. 35-37).

BDSI complains that the Examiner erred in declining to adopt BDSI's conclusion that the scope of the claims cannot be determined because the newly-added "rapidly increasing the viscosity of said flowable polymer matrix" includes terms of degree both lacking a reference point and standards for comparison. BDSI is wrong.

MonoSol believes that the Examiner put it best when not adopting this proposed conclusion and rejection.

> "This proposed rejection is not adopted for the following reasons. The rapid increase in viscosity takes place during the step of evaporating the solvent from the flowable polymer matrix, and each of the independent claims sets forth the time period during evaporation in which the rapid increase takes place, *i.e.*, within the first 4 minutes. Thus, the rapid increase occurs within this time frame. The claims also set forth the reason for such an evaporation time, *i.e.,* 'to maintain said substantially uniform distribution of said active by locking-in or substantially preventing migration of said active within said visco-elastic film.' Accordingly, it is unnecessary to set forth a degree of viscosity increase for 'rapidly increasing the viscosity'."
>
> RAN, p. 22.

Cases cited by BDSI are inapposite. MonoSol's "rapidly" is not comparable to the "low level current" of *Sony Corporation, et al. v. Network-l Security Solutions, Inc.*, IPR2013-00092,

Paper 21, p. 8 (PTAB May 24,2013). It is closer to *Playtex Prods., Inc. v. Procter & Gamble, Co.*, 400 F.3d 901 (Fed. Cir. 2010) (*Playtex*) cited by *Sony*. "As 'substantially flattened surface' has unambiguous meaning in view of the intrinsic record, the district court erred in relying upon extrinsic evidence that directly contradicted that meaning. . . . The disputed claim term is clearly a comparative term. Comparison requires a reference point. Therefore, to flatten something, one must flatten it with respect to either itself or some other object. . . . " *Playtex* at 908. In the instant claim recitation, **rapidly's reference point is "within about the first 4 minutes" of the start of evaporation of the solvent**, and is therefore definite.

For all of the above reasons, there is no error in the Examiner's refusal to apply BDSI's constructions to the recitation, and the Examiner's finding that the recitation is definite must be affirmed.

F. The Examiner did not err in finding that the recitation of "during said drying said flowable polymer matrix temperature is 100 °C or less" is clear (RAN, p. 23; BDSI's Brief, pp. 37-38).

BDSI complains that the Examiner erred in determining that the "100 °C or less" in the "controlling drying" step clearly applies throughout the step. The Examiner did not err.

MonoSol believes that the Examiner again put it best when not adopting this proposed rejection.

> "This proposed rejection is not adopted for the following reasons. The recitation states 'during drying' the flowable polymer matrix temperature is 100°C or less. The claims specify that the flowable polymer matrix has a viscosity of about 400 to about 100,000 cps. As long as the polymer matrix has this viscosity during drying, it is a flowable polymer matrix and its temperature must be 100°C or less."
>
> RAN, p.23.

Importantly, the Examiner did not define visco-elasticity in terms of viscosity, but merely stated that, in accordance with the claims, during the time that the polymer matrix has a viscosity of about 400 to about 100,000 cps it is considered, for purposes of the claim, to be a flowable polymer matrix such that it is required to be at a temperature of 100°C or less. The following claim language makes this clear:

> "casting said flowable polymer matrix, said flowable polymer matrix having a viscosity from about 400 to about 100,000 cps;

> controlling drying through a process comprising conveying said flowable polymer matrix through a drying apparatus . . . evaporating at least a portion of said solvent from said flowable polymer matrix to form a visco-elastic film, having said active substantially uniformly distributed throughout, within about the first 4 minutes by rapidly increasing the viscosity of said flowable polymer matrix upon initiation of drying . . ., wherein during said drying said flowable polymer matrix temperature is 100 °C or less...".

For all of the above reasons, there is no error in the Examiner's refusal to apply BDSI's constructions to the recitation. The Examiner's finding that the recitation is definite must be affirmed.

G. None, see issues *supra*.

H. The Examiner did not err in finding that the various recitations of the entered claim amendments requiring various degrees of uniformity are clear, enabled and have written description (RAN, pp. 24-27; BDSI's Brief, pp. 38-44).

BDSI complains that the Examiner erred in declining to adopt BDSI's proposed § 112 rejections for the uniformity requirements required in different steps and combinations of steps even though these requirements according to BDSI are not described, not defined, and not exemplified in the '080 patent. BDSI could not be more wrong. As to BDSI's inappropriate §§ 102 and 103 based argument, they are beyond the scope of BDSI's Cross-Appeal and should not be considered, see discussions *supra*.

The '080 Patent expressly recognizes the need to test for uniformity by any and all means at various steps during the manufacturing process, *see* discussion *supra*. One of the reasons given is to be able to stop the run early and attempt to correct any problems. Indeed, the '080 Patent spends almost an entire column on this issue ('080 Patent, col. 29, ll. 6-52). A small excerpt is quoted below.

> "**Moreover, it may be desirable to repeat the steps of sampling and testing throughout the manufacturing process. Testing at multiple intervals may ensure that uniform film dosages are continuously produced. Alterations to the process can be implemented at any stage to minimize non-uniformity between samples.**"

'080 Patent, col 29, ll. 47-52 (emphasis supplied).

BDSI appears loath to admit that, depending on whether or not the quantity being measured is known or desired, when scientists compare the amounts of a substance in different samples, there are two ways to compare the amounts and both are correct depending upon the circumstance. The methods differ depending upon what is desired to be measured. One method is when trying to compare the amount in a sample relative to a pre-determined desired amount, as is the case in pharmaceutical drug dosage units. The other method is where there is no predetermined desired amount, in which case the percent difference between amount of active in each sample is used. Both differences relate to the uniformity of content in the amount of active in the film from which the samples are cut. Hence we get the two 10% differences, one from the desired amount and one measuring the percent difference in amount. The '080 Patent processes can also achieve higher degrees of uniformity, hence the other percent differences.

MonoSol was not required to provide examples of tests for all these different degrees of uniformity, though it did for some. See Example M discussion, *supra*. However, whereas the '080 Patent specification and all the claims require the maintenance of the substantially uniform distribution of active by locking-in or substantially preventing migration of the active, testing for the same at various steps is an obvious step to add, for example, to ensure early on in the manufacturing process that the degree of uniformity is being maintained.

For all of the above reasons, there is no error in the Examiner's refusal to apply BDSI's constructions to the recitation. The Examiner's finding that the recitation is enabled, definite and has written description must be affirmed.

VIII. CONCLUSION

MonoSol respectfully submits that no error has been identified by BDSI or made by the Examiner in the RAN with respect BDSI's issues on Cross-Appeal and the Cross-Appeal should be dismissed and the Examiner affirmed on these issues.

Dated: April 10, 2014

Respectfully submitted,

/Daniel A. Scola, Jr./
Daniel A. Scola, Jr.
Registration No. 29,855

Michael I. Chakansky
Registration No. 31,600

HOFFMANN & BARON, LLP
6900 Jericho Turnpike
Syosset, New York 11791
(973) 331-1700

Attorneys for the MonoSol

EVIDENCE APPENDIX

1 MonoSol's/Cross-Respondent's Declaration of B. Arlie Bogue, Ph.D. Under 37 C.F.R. § 1.132, executed March 13, 2013, filed March 13, 2013 ("Bogue Declaration I")

2 MonoSol's/Cross-Respondent's Declaration of B. Arlie Bogue, Ph.D. Under 37 C.F.R. § 1.132, executed August 29, 2013, filed September 3, 2013 ("Bogue Declaration II")

3 MonoSol's/Cross-Respondent's Declaration of David T. Lin, Ph.D. Under 37 C.F.R. § 1.132, executed March 13, 2013, filed March 13, 2013 ("Lin Declaration")

The above declarations included below were submitted by MonoSol/ Respondent, they were admitted in the record, and referred to in the Examiner's Right of Appeal Notice, mailed December 6, 2013, *see*, *inter alia*, pp. 2, 68-69, 71-72, 83-84, 87-88. Pursuant to 37 C.F.R. § 41.71, MonoSol is using these declarations which ***were*** admitted.

The below Reitman declaration was submitted by Third-Party Requester/Cross-Appellant, it was admitted in the record, and referred to in the Examiner's Right of Appeal Notice, mailed December 6, 2013, *see*, *inter alia*, pp. 2, 14, 75,77,87-92, 94, 97, 100, 105.

4 BDSI's/Cross-Appellant's Declaration by Maureen Reitman, Sc.D. Under 37 C.F.R. § 1.132, dated February 28, 2013, filed April 12, 2013 ("Reitman Declaration")

MonoSol's/Cross-Respondent's Declaration of B. Arlie Bogue, Ph.D. Under 37 C.F.R. § 1.132, dated March 13, 2013 ("Bogue Declaration I")

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Patentee:	Yang et al.	Examiner:	Diamond, Alan D.
Patent No.:	U.S. 7,897,080	Group Art Unit:	3991
Reexamination Control No.:	95/002,170	Confirmation No.	6418
Filed:	September 10, 2012	H&B Docket:	1199-26 RCE/CON/REX
Dated:	March 13, 2013	M&E Docket:	117744-00023

Mail Stop Inter Partes Reexam
Central Reexamination Unit
Commissioner for Patents
U.S. Patent and Trademark Office
P.O. Box 1450
Alexandria, VA 22313-1450

Certificate of EFS-Web Transmission
I hereby certify that this correspondence is being transmitted via the U.S. Patent and Trademark Office electronic filing system (EFS-Web) to the USPTO on
March 13, 2013.
Signed: Michael I. Chakansky /Michael I Chakansky/

DECLARATION OF B. ARLIE BOGUE, PH.D. UNDER 37 C.F.R. § 1.132

Madame:

I, B. Arlie Bogue, Ph.D., do hereby make the following declaration:

I. Technical Background

1. I have worked in the field of pharmaceutical development, and particularly oral dosage form development, for 22 years. I am employed by MonoSol Rx, LLC. ("Patentee" and/or "MonoSol"), the assignee of issued patent U.S. 7,897,080 ("the '080 Patent"), as Senior Director for Manufacturing Strategy and Innovation.

2. I have a BS in Physical Chemistry from Colorado State University and a Ph.D. in Chemical and BioEngineering from Arizona State University. I have participated in postdoctoral studies in Biochemical Engineering at the University of Virginia. During my career, I have been named as an inventor on over 23 U.S. patents and numerous foreign patents directed to the formulation,

processing and/or packaging of pharmaceutical oral disintegrating unit doses (tablets and film strips). I have direct experience with the commercial scale processing of pharmaceutical film systems as well as an understanding of the uniformity of content of active and methods for testing the same.

3. I have read the '080 Patent and the Office Action issued on November 29, 2012 in the reexamination of the '080 Patent ("Office Action") and the references cited therein, and I have also reviewed the amendment as to the independent claims set forth in Patentee's Reply to the Office Action concurrently filed herewith.

II. Producing resulting films in accordance with the '080 Patent

4. Each of the 73 lots of resulting films (Lots 1-73) containing approximately 2,000,000 individual dosage units per lot discussed herein were manufactured: (i) for commercial use and regulatory approval; (ii) in compliance with U.S Food and Drug Administration ("FDA") standards and regulations, including those relating to analytical chemical testing for variation in active in individual dosage units; and (iii) in accordance with the invention disclosed in the '080 Patent, and as claimed by the '080 Patent both as issued and as amended in the Patentee's Reply to the Office Action; by:

(a) forming a flowable polymer matrix comprising a water-soluble polymer, a solvent and a pharmaceutical active, said matrix having a substantially uniform distribution of said active;

(b) casting said flowable polymer matrix, said flowable polymer matrix having a viscosity from about 400 to about 100,000 cps;

(c) controlling drying through a process comprising conveying said polymer matrix through a drying apparatus and evaporating at least a portion of said solvent to form a visco-elastic film, having said active substantially uniformly distributed throughout, within about the first 4 minutes by rapidly increasing the viscosity of said polymer matrix upon initiation of drying to maintain said substantially uniform distribution of said active by locking-in or substantially preventing migration of said active within said visco-elastic film wherein the polymer matrix temperature is 100 °C or less;

(d) forming the resulting pharmaceutical film from said visco-elastic film, wherein said resulting pharmaceutical film has a water content of 10% or less and said substantially uniform distribution of active by said locking-in or substantially preventing migration of said active is maintained, such that uniformity of content in the amount of the active in substantially equal sized individual dosage units, sampled from different locations of said resulting pharmaceutical film, varies by no more than 10%; and

(e) performing analytical chemical tests for uniformity of content of said active in substantially equal sized individual dosage units of said sampled resulting pharmaceutical film, said tests indicating that uniformity of content in the amount of the active varies by no more than 10%, [see Appendix A] said resulting pharmaceutical film suitable for commercial and regulatory approval, wherein said regulatory approval is provided by the U.S. Food and Drug Administration.

5. Additionally, the uniformity of content in the amount of active as sampled from the 73 lots of resulting film varies no more than 10% from the desired amount of the active as indicated by said analytical chemical tests from 4(e) above. [See Appendix B]

III. Analytical Chemical Testing for Uniformity of Content of Patentee's Resulting Films

6. To demonstrate the uniformity of individual dosage unit films, I compiled individual dosage unit assay data for individual Lots 1- 73, all of which were disclosed in MonoSol's 2012 Annual Product Review to the FDA.

7. Ten (10) individual dosage units all having the same dimensions were cut out from different locations of each of the 73 lots of resulting films using a commercial packaging machine, thus providing 730 randomly sampled individual dosage units, ten each from the 73 separate lots. All samples were analyzed by a validated method, in compliance with FDA guidelines and regulations regarding same, using analytical chemical testing, in which the pharmaceutical active

was extracted and analyzed by High Performance Liquid Chromatography (HPLC) against an external standard to quantify the amount of active present in each individual dosage unit.

8. According to the inventive process set forth and claimed in the '080 Patent, and in accordance with FDA nomenclature, I have prepared tables shown as Appendices A, B and C, reflecting the uniformity of content of active of individual dosage units within particular lots and across different lots.

9. First, the uniformity of content of active in a lot is determined through establishing the amount of active ($A_{N(i)}$) actually present in each sampled individual dosage unit from the same lot (N) as determined by taking the difference between the amount of active in the sample with the most active ($Max_{LOT(N)}$) minus the amount of active in the sample with the least amount of active ($Min_{LOT(N)}$) and dividing the difference by the average amount of active in the lot samples ($Lot_{(N)}$ Sample Average). That is: $(Max_{LOT(N} - Min_{LOT(N)}) / ((A_{N(1)} + A_{N(2)} + + + A_{N(10)})/10)$. The results are shown in Appendix A.

10. Second, the uniformity of content across different lots is determined through establishing the amount of active actually present in each sampled individual dosage unit from all 73 lots and comparing that amount of active with a "target" or "desired" amount of active contained therein. The target amount of active, when it is a pharmaceutical, is referred to as the "Label Claim", thus identifying the amount of pharmaceutical active in the film to a user. The desired amount is 100% of the target amount. Each individual dosage unit film cut from any individual lot must have the desired content of pharmaceutical active, varying no more that 10% from the target or desired amount. See Appendix B.

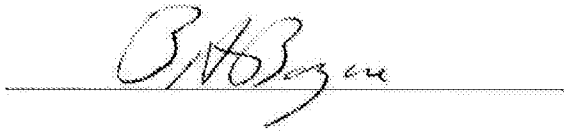
IV. '080 Patent Process Produces Films With Required Uniformity of Content of Active

11. The results shown in the appendices establish that the resulting films produced by the inventive method of the '080 Patent as disclosed and claimed have the required uniformity of content based on analytical chemical testing. First, the amount of active varies by no more than 10% between individual dosage units sampled from a particular lot of resulting film. See Appendix A.

Second, the amount of active across different lots of resulting film varies no more than 10% from the desired amount of the active. See Appendix B. Finally, the uniformity of content of the 73 lots of resulting film meets even more stringent standards, for example, the data shows: (i) 46 lots of resulting film wherein the uniformity of content of active is shown with the amount of active varying by less than 5%; (ii) 15 lots of resulting film wherein the uniformity of content of active is shown with the amount of active varying by less than 4%; 4 lots of resulting film wherein the uniformity of content of active is shown with the amount of active varying by less than 3%; and 1 lot of resulting film wherein the uniformity of content of active is shown with the amount of active varying by only 2%. See Appendix C.

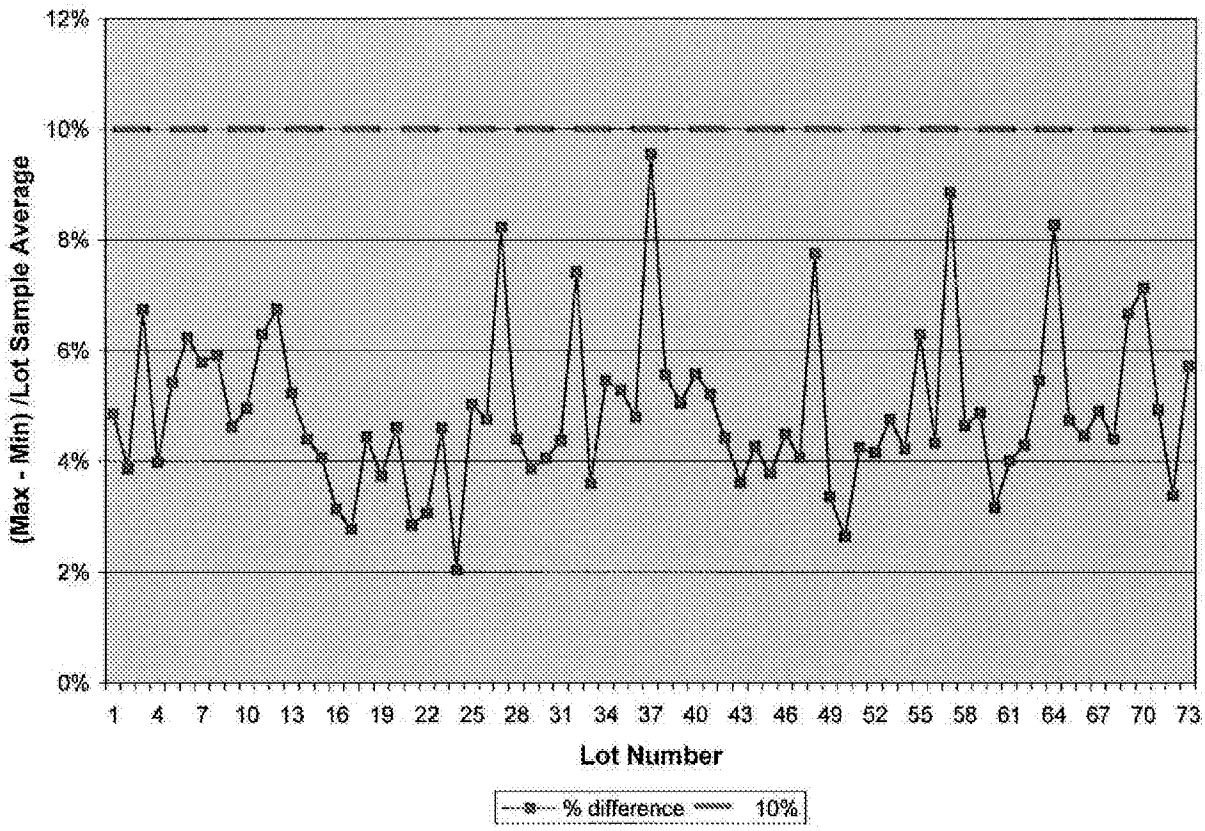
I hereby declare that all statements made herein of my own knowledge are true and that all statements made on information and belief are believed to be true; and further that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United States Code, and. that such statements may jeopardize the validity of the application or any patents issued thereon.

Dated this 13th day of March, 2013

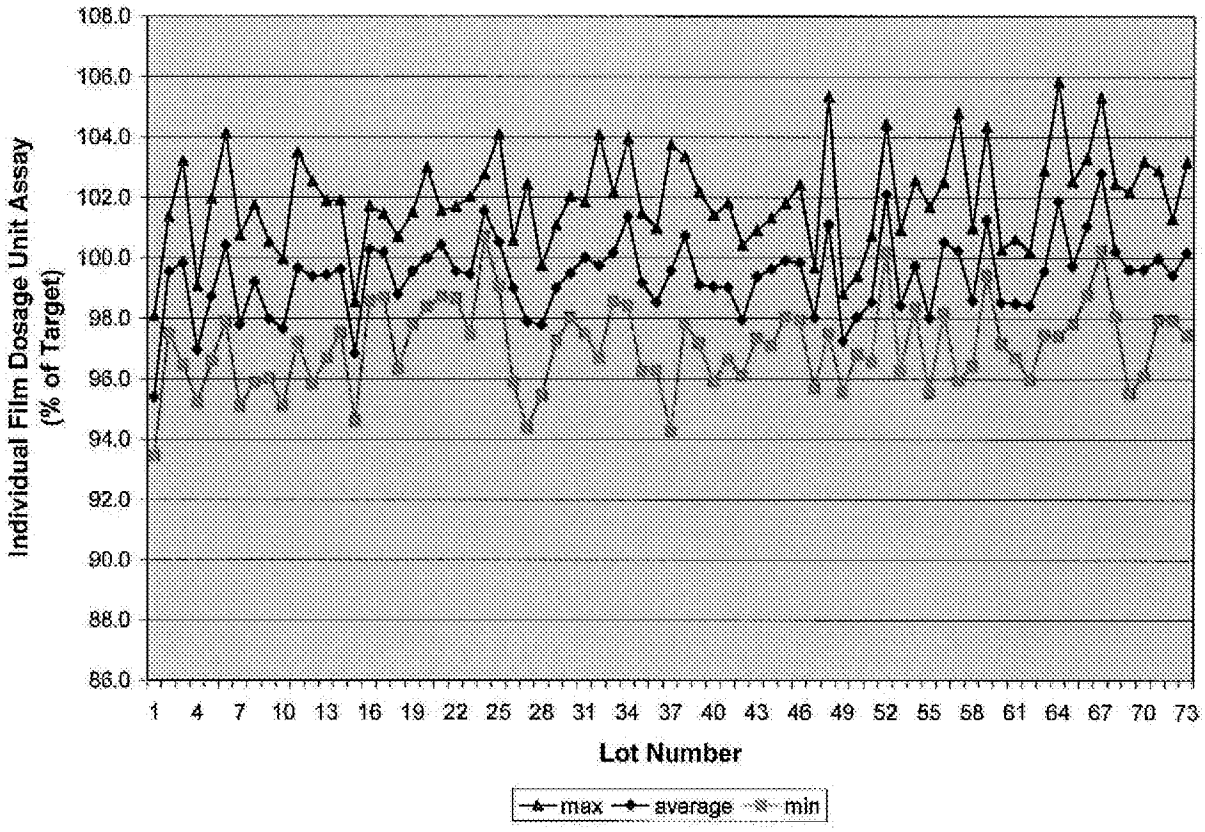


B. Arlie Bogue

APPENDIX A



APPENDIX B



APPENDIX C

Lots less than 5%			lots 5% to 10%	
Lot #	% Difference		Lot #	% Difference
24	2.0%		10	5.0%
45	2.6%		25	5.0%
17	2.8%		39	5.0%
21	2.8%		41	5.2%
22	3.1%		13	5.2%
16	3.1%		35	5.3%
60	3.2%		5	5.4%
50	3.4%		63	5.5%
72	3.4%		34	5.5%
33	3.6%		38	5.6%
43	3.6%		40	5.6%
19	3.7%		73	5.7%
46	3.8%		7	5.8%
29	3.9%		8	5.9%
2	3.9%		6	6.2%
4	4.0%		11	6.3%
61	4.0%		55	6.3%
30	4.0%		69	6.7%
48	4.1%		3	6.7%
15	4.1%		12	6.7%
52	4.2%		70	7.1%
54	4.2%		32	7.4%
51	4.2%		49	7.8%
44	4.3%		27	8.2%
62	4.3%		64	8.3%
56	4.3%		57	8.9%
31	4.4%		37	9.5%
28	4.4%			
14	4.4%			
68	4.4%			
42	4.4%			
18	4.4%			
66	4.5%			
47	4.5%			
23	4.6%			
20	4.6%			
9	4.6%			
58	4.6%			
65	4.7%			
26	4.8%			
53	4.8%			
36	4.8%			
1	4.9%			
59	4.9%			
67	4.9%			
71	4.9%			
total	46		total	27

MonoSol's/Cross-Respondent's Declaration of B. Arlie Bogue, Ph.D. Under 37 C.F.R. § 1.132, executed August 29, 2013 ("Bogue Declaration II")

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Patentee:	Yang et al.	Examiner:	Diamond, Alan D.
Patent No.:	U.S. 7,897,080	Group Art Unit:	3991
Reexamination Control No.:	95/002,170	Confirmation No.	6418
Filed:	September 10, 2012	H&B Docket:	1199-26 RCE/CON/REX
Dated:	September 3, 2013	M&E Docket:	117744-00023

Mail Stop Inter Partes Reexam
Central Reexamination Unit
Commissioner for Patents
U.S. Patent and Trademark Office
P.O. Box 1450
Alexandria, VA 22313-1450

Certificate of EFS-Web Transmission
I hereby certify that this correspondence is being transmitted via the U.S. Patent and Trademark Office electronic filing system (EFS-Web) to the USPTO on September 3, 2013.
Signed: Michael I. Chakansky /Michael I Chakansky/

DECLARATION OF B. ARLIE BOGUE, PH.D. UNDER 37 C.F.R. § 1.132

Madame:

I, B. Arlie Bogue, Ph.D., do hereby make the following declaration:

I. Technical Background

1. I have worked in the field of pharmaceutical development, and particularly oral dosage form development, for 22 years. I am employed by MonoSol Rx, LLC. ("Patentee" and/or "MonoSol"), the assignee of issued patent U.S. 7,897,080 ("the '080 Patent"), as Senior Director for Manufacturing Strategy and Innovation.

2. I have a BS in Physical Chemistry from Colorado State University and a Ph.D. in Chemical and BioEngineering from Arizona State University. I have participated in postdoctoral studies in Biochemical Engineering at the University of Virginia. During my career, I have been named as an inventor on over 23 U.S. patents and numerous foreign patents directed to the formulation, processing and/or packaging of pharmaceutical oral disintegrating unit doses (tablets and film

strips). I have direct experience with the commercial scale processing of pharmaceutical film systems as well as an understanding of the uniformity of content of active and methods for testing the same.

3. My declaration dated March 13, 2013 was submitted in support of Patentee's response to the Office Action issued on November 29, 2012 in the reexamination of the '080 Patent ("Bogue Declaration I").

4. In Bogue Declaration I, I disclosed Patentee's method of producing resulting films in accordance with the '080 Patent and analytical chemical testing for uniformity of content thereof.

5. I hereby identify the resulting films in Bogue Declaration I as Suboxone® sublingual unit dose film products, and further declare that the Suboxone® sublingual unit dose film products were manufactured for Reckitt Benckiser Pharmaceuticals Inc. by Patentee, MonoSol.

6. Patentee is the exclusive source of Suboxone® sublingual unit dose film products for Reckitt Benckiser.

7. Suboxone® sublingual unit dose film products are FDA approved drug products.

8. In Patentee's production of unit dose film products, described in the '080 Patent, including its production of Suboxone® sublingual unit dose film products, the wet film thicknesses, from which the dry resulting products such as Suboxone® sublingual unit dose film products are produced, are always significantly greater in thickness than the dry resulting unit dose film products.

9. The Suboxone® sublingual unit dose film products made by MonoSol, and described in Bogue Declaration I, have dry thicknesses ranging from approximately 110 to approximately 175 microns, depending on the particular Suboxone® sublingual unit dose film product. Hence, the wet films from which these products are made have wet film thicknesses significantly greater than approximately 110 to approximately 175 microns.

10. I have reviewed the documents attached as Exhibits 7 and 8 to the Response by Patentee to the Action Closing Prosecution and referred to as Chapter <905> Uniformity of Dosage Units (2011) (Ex. 7) and Chapter <905> Uniformity of Dosage Units (2007) (Ex. 8).

11. Chapter <905> Uniformity of Dosage Units (2007), Ex. 8, specifies at p.1 that: "Content Uniformity is the default test and may be applied in all cases. The test for Weight Variation is applicable for dosage forms specified as W1, W2, W3, and W4.

12. Patentee's unit dose film products manufactured in accordance with the '080 Patent, including its Suboxone® sublingual unit dose film products are **not** dosage forms W1, W2, W3 or W4 as disclosed in the box on page 1, first column, in Chapter <905> Uniformity of Dosage Units (2011), Ex. 7.

13. Patentee's unit dose film products manufactured in accordance with the '080 Patent, including its Suboxone® sublingual unit dose film products are considered an "Others" dosage form for which CU or Content Uniformity with assaying is required. See, Table 1, second column, Chapter <905> Uniformity of Dosage Units (2011), Ex. 7.

14. Patentee's unit dose film products manufactured in accordance with the '080 Patent, including its Suboxone® sublingual unit dose film products, are **not** the "Tablets-Coated-with-a-Film" dosage forms in Table 1, Chapter <905> Uniformity of Dosage Units (2011), Ex. 7, second column.

15. **Weight Variation always requires that the relevant party "[c]arry out an assay for the drug substance(s) on a representative sample of the batch using an appropriate analytical method."** *See* Chapter <905> Uniformity of Dosage Units (2011), Ex. 7, p. 3, first column.

Dated this 29th day of August, 2013

B. Arlie Bogue

MonoSol's/Cross-Respondent's Declaration of David T. Lin, Ph.D. Under 37 C.F.R. § 1.132, executed March 13, 2013, filed March 13, 2013 ("Lin Declaration")

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Patentee:	Yang et al.	Examiner:	Diamond, Alan D.
Patent No.:	U.S. 7,897,080	Group Art Unit:	3991
Reexamination Control No.:	95/002,170	Confirmation No.	6418
Filed:	September 10, 2012	H&B Docket:	1199-26 RCE/CON/REX
Dated:	March 13, 2013	M&E Docket:	117744-00023

Mail Stop Inter Partes Reexam
Central Reexamination Unit
Commissioner for Patents
U.S. Patent and Trademark Office
P.O. Box 1450
Alexandria, VA 22313-1450

Certificate of EFS-Web Transmission
I hereby certify that this correspondence is being transmitted via the U.S. Patent and Trademark Office electronic filing system (EFS-Web) to the USPTO on
March 13, 2013.
Signed: Michael I. Chakansky /Michael I Chakansky/

DECLARATION OF DAVID T. LIN, PH.D. UNDER 37 C.F.R. § 1.132

Madame:

I, David T. Lin, Ph.D. do hereby make the following declaration:

I. SUMMARY OF CREDENTIALS AND EXPERIENCE

1. Since January 2005, I have served as a Senior Consultant to Biologics Consulting Group, Inc. ("BCG"), a team of consultants who provide national and international regulatory and product development advice on the development and commercial production of small molecular weight synthetic drug, biotechnological and biological products.

2. While BCG is being paid for my time, I am not an employee of, nor do I have any financial interest in, MonoSol Rx, LLC ("Patentee" and/or "MonoSol").

3. Before joining BCG, I held various positions with the United States Food and Drug Administration ("FDA"). From 1997-2001, I was a Chemistry Reviewer in the Division of Reproductive and Urologic Drug Products, Center for Drug Evaluation and Research ("CDER"). In 2001, I became the Team Leader in the same Division and served in that role until 2003 when I was promoted to the position of acting Deputy Division Director in the Division of New Drug Chemistry III, Office of New Drug Chemistry (currently referred to as Office of New Drug Quality Assessment). In 2004, I was promoted to the position of acting Division Director.

4. As a Chemistry Reviewer at CDER, I was responsible for the comprehensive review of Chemistry, Manufacturing and Controls ("CMC") data for drugs being investigated during Phase 1, 2, and 3 clinical studies. I was also responsible for the review of CMC data in New Drug Applications and provided regulatory input to CMC reviewers responsible for review of Abbreviated New Drug Applications. This included providing scientific and regulatory guidance during development of small molecular weight drugs and biotechnological/biological drugs across a wide variety of dosage forms. I have reviewed CMC data submitted with respect to over 100 Investigational New Drug Applications and New Drug Applications (original and supplemental) as a chemistry reviewer, contributed to decisions regarding the approval of drugs, made presentations before scientific and regulatory conferences and participated in a variety of special FDA projects and committees, including serving as the co-Chair of the CMC Good Review Practices Committee.

5. As Team Leader, acting Deputy Division Director and acting Division Director in the Office of New Drug Chemistry, I was actively involved in directing the content of FDA guidances that pertained to CMC topics. As acting Deputy Division Director and Division Director, I was directly involved in discussions, regarding the content of the 2003 FDA draft guidance on Drug Product-Chemistry, Manufacturing, and Controls Information, with the committee responsible for writing this guidance. I had signatory authority for this draft guidance prior to public issuance by FDA. As acting Deputy Division Director and Division Director, I was involved in regular meetings with the supervisory staff in the Office of Generic Drugs to discuss regulatory and review policy issues that are common to both New Drug Applications and Abbreviated New Drug Applications.

6. I consider myself an expert in the fields of FDA practice and procedure as applicable to the testing requirements for drugs and review of Investigational New Drug Applications (INDs) and New Drug Applications (NDAs).

7. I received my B.A. in Biochemistry from the University of Pennsylvania in 1984, my Ph.D. in Organic Chemistry from the University of Maryland in 1989 and my M.B.A. from the University of Maryland's RH Smith School of Business in 2002. Attached hereto as Exhibit A is my curriculum vitae, including a list of my publications for the past ten years.

8. I have carefully reviewed Chen (WO 00/42992) ("Chen").

II. U.S. STATUTORY AND REGULATORY BACKGROUND FOR TESTING DRUGS FOR POTENCY AND DOSAGE UNITS FOR UNIFORMITY

9. From a US regulatory perspective, for a drug to be approved for commercial marketing and distribution, specifications necessary to ensure the identity, strength, quality, purity, potency, and bioavailability of the drug product must be provided in a New Drug Application.[1] In addition, reference to the current U.S. Pharmacopeia (USP) may satisfy these requirements.

10. Section 501(b) of the Food, Drug, and Cosmetic Act (the Act) deems an official drug (i.e., a drug represented as a drug which is recognized in the U.S. Pharmacopeia) to be adulterated if it fails to conform to compendial standards of quality, strength or purity. Compendial tests or assay methods are used when determining such conformance under 501(b); the standards are stated in individual monographs as well as portions of the General Notices section of the USP/NF. Standards and test methods have been established for such characteristics as potency and content uniformity.

11. Section 501(c) of the Act deems a drug that is not recognized in the USP to be adulterated if it fails to meet the strength, purity or quality which it is represented to possess.

[1] 21 CFR 314.50(d)(1)(ii)(a)

The applicable quality standards for a drug not recognized in the USP can be determined from such sources as the labeling of the drug (or drug product), the manufacturer's written specifications, and new drug applications.

12. The current good manufacturing practice (cGMP) regulations include the minimum requirements for the preparation of drug product for administration to humans. One of the requirements is that the strength[2] of the drug (active ingredient) in the drug product must be determined for each batch of drug product manufactured for commercial distribution.[3] Strength is taken to mean content or assay of the drug.

13. Batch uniformity of the drug products is ensured with procedures that describe the in-process controls, and tests, or examinations to be conducted on appropriate samples of in-process materials of each batch.[4] FDA also describes in guidance that it is expected the sampling plan for drug product is representative of the batch.[5]

14. Controls include the establishment of scientifically sound and appropriate specifications, standards, sampling plans, and test procedures designed to assure that the drug product conform to appropriate standards of identity, strength, quality, and purity.[6]

15. Regulatory specifications must be established to ensure that the dosage form will meet acceptable therapeutic and physicochemical standards throughout the shelf-life of the marketed product.[5] These specifications include tests for strength (content or assay) and uniformity of dosage units.

---

[2] 21 CFR 210.3(b)(16)

[3] 21 CFR 211.165(a)

[4] 21 CFR 211.110(a)

[5] FDA Guideline for Submitting Documentation for the Manufacture and Controls for Drug Products, February 1987

[6] 21 CFR 211.160(b)

16. Testing to establish uniformity of dosage units is defined in the USP under the USP general chapter <905>.[7]

III. CHEN'S DISCLOSURE IS INSUFFICIENT

17. I have been asked to review Chen and render an opinion as to whether there is sufficient information contained within to allow regulatory FDA approval and commercialization of a drug product that is manufactured as described. After review of the patent in light of FDA practice and procedure, it is my opinion that there is insufficient disclosure to allow FDA to determine that a drug product as described can be manufactured for commercial distribution, manufactured in a consistent manner and meet specifications that will ensure the identity, strength, quality, purity, and potency of the drug product. In particular, Chen lacks any disclosure which would necessarily lead to the manufacture of films with uniformity of content (strength) of drug active required for FDA approval.

18. As would be required for FDA approval Chen does not disclose sufficient information that films containing drug can be produced consistently with respect to uniformity of content of the drug. No information was disclosed that demonstrated uniformity of content in the amounts of drug in individual dosage units. Chen discloses no specific test methods, and hence no test results, that could allow for the determination of the actual amount of drug (active) in individual dosage units.

19. As required for FDA approval, Chen's patent did not disclose sufficient information regarding the manufacturing process and process controls. The information disclosed by Chen would not ensure that films containing drug could be manufactured to meet specifications that ensure consistent strength.

20. Even if the information disclosed in Chen could be utilized to develop a manufacturing process for films containing drug, there is no information regarding the test methods that are necessary to determine the amount of drug in individual dosage units.

---

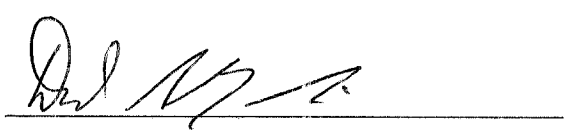
[7] USP General Chapter <905> Uniformity of Dosage Units

21. Therefore, Chen's disclosure is lacking, both explicitly and inherently, the disclosure necessary to provide for the manufacture of drug-containing films with the uniformity of content in amount of drug (active) in individual dosage units to make FDA approvable film products. It is my understanding that an inherent disclosure may not be established by probabilities or possibilities and that the mere fact that a certain thing may result from a given set of circumstances is not sufficient and that to be inherent requires that the missing disclosure is necessarily present.

22. Finally, Chen's patent discloses the release profiles of four active agents from films. See Chen, Figure 5. The release profile data presented in Figure 5 show a high degree of variability at each data point. For example, the release profile for nicotine containing film product show that the amount of nicotine released at the 5 minute and 8 minute time point can be as high as approximately 115-120%. This level of active agent is greater than the 110% level (from an expected amount of 100%) that is considered acceptable to FDA for regulatory approval of a product that purports to be manufactured consistently with acceptable content uniformity. These data indicate that the test method used in the analysis is not reproducible and/or there is a lack of active agent content uniformity between individual dosage units. These deficiencies demonstrate the lack of manufacturing consistency and lack of active agent content uniformity in the film.

23. I hereby declare that all statements made herein of my own knowledge are true and that all statements made on information and belief are believed to be true; and further that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United States Code, and. that such statements may jeopardize the validity of the application or any patents issued thereon.

Dated this 13th day of March, 2013



David T. Lin

EXHIBIT A

DAVID TSOCHUNG LIN

9121 Fall River Lane, Potomac, MD 20854 (301) 299-2853 dlin@bcg-usa.com

EXPERTISE

- 18+ years pharmaceutical regulatory experience.
  - 7+ years regulatory chemistry, manufacturing and controls (CMC) experience at CDER/FDA on small molecular-weight drugs, botanical drugs, peptide drugs, and protein drugs formulated in a broad range of sterile and non-sterile dosage forms.
  - 3+ years research experience at CBER/FDA.
  - 8+ years experience as regulatory CMC consultant.
- Unique combination of biologic/biotechnological and small molecular-weight drug regulatory experience, including device/drug and device/biologics combination products.
- Understanding of FDA regulatory requirements and expectations for drug development and marketing approval.
- Performed primary CMC review and assessment of drug products for treatment of reproductive and urologic disorders and diseases.
- Supervised CMC review activities in 7 CDER medical reviewing divisions including Reproductive/Urologic, Anti-viral, Dermatologic/Dental, Anti-inflammatory/ Analgesic/Ophthalmologic, Anti-infective, Special Pathogen/Immunologic, and Over-the-Counter drug products.
- Understanding of drug substance and drug product analytical method development and validation.
- Understanding of drug substance and drug product stability protocol development and stability data analysis.
- Understanding of current Good Manufacturing Practices (cGMPs)
- Experienced in chemical synthesis, small-scale and pilot-scale fermentation, biologics/ biotechnology, and protein chemistry.
- Experienced working in cross-functional teams (i.e., Pharmacology/toxicology, Clinical, Biostatistics, Biopharmaceutics, and Analytical).
- Ph.D. in Organic Chemistry; M.B.A. degree and training for managers.

EXPERIENCE

BIOLOGICS CONSULTING GROUP, INC. Alexandria, VA
January 2005 – Present
Senior Consultant

- Evaluate and provide advice on client CMC scientific and regulatory strategies for a wide range of therapeutic drug products (biologic and non-biologic) in dosage forms that include tablets, topicals, injectables, transdermals, implants, sprays, and inhalation, at all stages of product development, from pre-IND through post-NDA/BLA approval.
- Review and provide advice on IND and NDA/BLA submissions for suitability relative to FDA expectations for CMC data.
- Perform gap analysis audits for deficiencies relative to FDA expectations.
- Conduct regulatory and scientific due diligence audits for business acquisitions and licensing partnerships. Provide assessment of strengths and deficiencies.
- Represent clients in interactions with FDA.
- Prepare and write submissions to FDA, with focus on CMC sections.
- Represent client as FDA regulatory expert in legal proceedings.
- Advise clients on manufacturing contractor and vendor evaluation and selection.
- Provide management and technical oversight of contract manufacturing organizations (CMOs).
- Involved in business development to increase client base.
- Provide scientific and regulatory training and presentations at pharmaceutical/biopharmaceutical conferences.

FOOD & DRUG ADMINISTRATION, CENTER FOR DRUG EVALUATION AND RESEARCH, OFFICE OF NEW DRUG CHEMISTRY, DIVISION OF NEW DRUG CHEMISTRY III. Rockville, MD
July 2003 – December 2004
Division Director (acting) *March 2004 – December 2004*
Deputy Division Director (acting) *July 2003 – March 2004*

- Supervised 34 employees in 9 therapeutic product classes, includes 6 Team Leaders, review chemists and administrative staff. Responsible for employee work performance review and career development.
- Planned and set long-range plans and schedules for Division work. Directed and coordinated workload, and assured implementation of Division policies, goals and objectives.
- Evaluated budget and fiscal controls to manage Division functions.
- Made critical decisions and provided expert advice concerning regulatory, scientific and compliance approaches and options consistent with Office policies and objectives.
- Represented FDA in dealing and negotiating with the regulated industry, and professional and industry organizations.
- Participated as invited speaker at regulatory and scientific conferences on behalf of FDA.
- Served as the Chair of the Stability Guidance Technical Committee, Co-chair of the Conjugated Estrogens Working Group and Co-chair of the Good Review Practices Working Group.

FOOD & DRUG ADMINISTRATION, CENTER FOR DRUG EVALUATION AND RESEARCH, DIVISION OF REPRODUCTIVE AND UROLOGIC DRUG PRODUCTS. Rockville, MD
October 2001-July 2003
Lead Chemist (Team Leader)

- Managed a team of 4 review chemists in 2 therapeutic product classes.
- Responsible for secondary review, consistency of CMC reviews and adherence to FDA/ONDC policies and guidances.
- Coordinated reviewers' workload of IND and NDA submissions to ensure that reviews were conducted in timely manner.
- Interacted extensively with the regulated industry to provide regulatory direction during IND drug development and NDA post-approval activities.
- Active in the development of FDA guidances for industry and internal good review practices. Served as the Chair of the Stability Guidance Technical Committee, Co-chair of the Conjugated Estrogens Working Group and Co-chair of the Good Review Practices Working Group.

FOOD & DRUG ADMINISTRATION, CENTER FOR DRUG EVALUATION AND RESEARCH, DIVISION OF REPRODUCTIVE AND UROLOGIC DRUG PRODUCTS. Rockville, MD
April 1997-October 2001
Chemistry Reviewer

- Evaluated the quality of new drug products submitted to the FDA for approval.
- Integral part of a cross-functional review team responsible for evaluating the quality and effectiveness of reproductive and urologic drug products being investigated in clinical studies.
- Major contributor to committees responsible for establishing drug product quality standards and publishing guidances for pharmaceutical companies.
- Provided regulatory guidance to pharmaceutical company representatives during drug development.
- Mentored new reviewers.
- Served as computer focal point to facilitate and troubleshoot computer issues.

FOOD & DRUG ADMINISTRATION, CENTER FOR BIOLOGICS EVALUATION AND RESEARCH, LABORATORY OF PARASITIC BIOLOGY AND BIOCHEMISTRY. Bethesda, MD
February 1994-April 1997
National Research Council Fellow

- Investigated the biological role of specific proteins in the sexual differentiation of the malaria parasite. Published three research papers in peer-reviewed journals.
- Presented research data at three separate scientific conferences.
- Supervised the research projects of college students.
- Responsible for the coordination of instrument repairs and the ordering of laboratory supplies.

GENERAL ELECTRIC CO., CORPORATE RESEARCH & DEVELOPMENT, BIOLOGICAL SCIENCES LABORATORY. Schenectady, NY
July 1989-January 1994
Staff Scientist

- Developed recombinant biphenyl-metabolizing microorganisms capable of degrading environmental contaminants. Marketed this technology to the GE business units and government agencies responsible for environmental clean-up.
- Investigated the factors affecting aerobic biodegradation of indigenous PCBs in Hudson River sediment by various bacterial strains.
- Isolated and conducted mechanistic studies of the dioxygenase enzymes involved in biodegradation.
- Investigated the scientific and economic feasibility of biologically synthesizing aromatic monomers for use as a feedstock to produce biodegradable polymers.
- Supervised research projects of summer interns.
- Published research in peer-reviewed journals.
- Recruited at major East Coast universities. Interviewed and screened graduating science Ph.D. students for second round interviews at the Research Center.

UNIVERSITY OF MARYLAND, Dept. of Chemistry/Biochemistry. College Park, MD
May 1985-May 1989
Research Assistant

- Investigated mechanism of action of two bacterial enzymes, mandelate racemase and D-amino acid oxidase.
- Synthesized and tested novel halogenated aromatic hydroxy- and amino- acid analogs as potential irreversible inhibitors.
- Published research in peer-reviewed journals and co-authored one chapter in a biotechnology book. In addition, the research data was presented at two national scientific conferences.
- Served as the computer expert for the laboratory group.

EDUCATION

ROBERT H. SMITH SCHOOL OF BUSINESS. College Park, MD
University of Maryland
Master of Business Administration (MBA), *2002*
Concentration: Finance

UNIVERSITY OF MARYLAND. College Park, MD
Department of Chemistry and Biochemistry
Ph. D. -- Organic Chemistry, *1989*
Research Advisor -- Dr. John W. Kozarich

UNIVERSITY OF PENNSYLVANIA. Philadelphia, PA
Bachelor of Arts with Honors – Biochemistry, *1984*
Dean's List, Phi Lambda Upsilon Chemical Honor Society

TRAINING

- Facilitation Skills, CDER/FDA (Fall 2002)
- Six Sigma Strategy and Methods, Univ. of MD (Summer 2002)
- Group Decision-Making Techniques, CDER/FDA (Feb. 2002)
- Managing Written Communications for Team Leaders, CDER/FDA (Spring 2002)
- Organizational Behavior and Human Resources, Univ. of MD (Fall 1999)
- Management of Human Resources, Univ. of MD (Fall 1999)
- Introduction to Drug Law and Regulation, CDER/FDA (Nov. 1998)
- Basic Statistical Methods, CDER/FDA (Fall 1998)

HONORS/AWARDS

- CDER's Team Excellence Award (Nov 2004)
- FDA's Group Recognition Award (May 2004)
- CDER's Special Recognition Award (Nov 2002)
- CDER's Team Excellence Award (Nov 2002)
- OPS/ONDC Special Recognition Award (Dec 2001)
- CDER's Team Excellence Award (Nov 2000)
- OPS/ONDC Special Recognition Award (Jun 2000)
- CDER's Excellence in Mentoring Award (Nov 1999)

PRESENTATIONS

- Conducting Effective & Compliant Stability Programs for Pharmaceuticals & Biologics, "Stability Studies During Development", "Stability of Biopharmaceuticals", "Development of Specifications for Biopharmaceuticals", and "Extractables, Leachables, and Particulates – Safety Concern for Biotechnology Products", Dubai, UAE (Sep 2012).
- 4th DIA China Annual Meeting, "ICH Guidelines Q1D, Bracketing and Matrixing Designs for Stability Testing of New Drug Substances and Products", and "Q1E, Evaluation of Stability Data", Shanghai, China (May 2012).
- IPA's Current Trends and Practices in Stability Testing, "Stability Testing Requirements for Biopharmaceutical Products", Montreal, Canada (Oct 2011)
- IPA's Current Trends and Practices in Stability Testing, "Stability Program for Combination Products", Montreal, Canada (Oct 2011)
- 3rd DIA China Annual Meeting, "Thinking About Comparability for Biosimilar Proteins", Beijing, China (May 2011).
- IPA's Current Trends and Practices in Stability Testing, "Stability Challenges for Combination Products", Boston, MA (May 2011).
- IPA's Current Trends and Practices in Stability Testing, "Country Specific Stability Requirements", Boston, MA (May 2011).
- Stability Programs Forum, "Stability Testing for Biotechnology/Biologic Products", Philadelphia, PA (Dec 2010).
- 11th Annual EuroTIDES/EuroPEPTIDES Conference, "Stability Considerations and Testing for Peptide-and Oligo-Based Therapeutics", Barcelona, Spain (Nov 2010).
- International Summit of China Pharmaceutical Industry, "FDA Requirements for Peptide Product Development: Considerations from Small Molecule and Biological Products", Hangzhou, China (Oct 2010).

- 7th Annual Method Validation Conference, "Ensure Method Validation Compliance through a Review of FDA Warning Letters", San Francisco, CA (Jul 2010).
- 6th Annual BioProcess International European Conference, "Extractables, Leachables and Particulates – Safety Concern for Biotechnology Products," Vienna, Austria (May 2010)
- ISPE-CSAC Meeting, "Biotechnological Drug Development and Interactions with CDER," Raleigh, NC (Oct 2009).
- Seminar on China International Bio-medicine Outsourcing Service, "Product Quality Issues with GLPs and GCPs," Hangzhou, China (Sep 2009).
- Informa Stability Testing for Biologics Conference, "Understanding Product Expiry and Shelf-Life," Prague, Czech Republic (Sep 2009).
- Informa Stability Testing for Biologics Conference Workshop, "Stability Testing Performed Over a Product Lifecycle," Prague, Czech Republic (Sep 2009).
- IVT Lab Compliance Conference, "Implement a Comprehensive and Compliant Stability Program," Philadelphia, PA (Aug 2009).
- OKBio ACCELERATE Workshop, "Product Development – Regulatory CMC Considerations," Oklahoma City, OK (Jun 2009).
- IVT Method Validation Conference, "Challenges in Understanding Impurities and Degradants for Biological/Biotechnological Products," San Francisco, CA (Oct 2008).
- IVT Method Validation Conference, "Strategies for Setting Biological Product Specifications," San Francisco, CA (Oct 2008).
- CBI 3rd Annual Stability Programs Conference, "Complex Stability Programs for Biologics," Philadelphia, PA (Jun 2008).
- IVT Lab Compliance Conference, "Stability Testing Fundamentals and Considerations in the Current Regulatory Environment," Baltimore, MD (Apr 2008).
- R&D Direction's 5th Annual Drug Development Summit, "Looking Forward in 2008: Regulatory Priorities and Considerations," Amelia Island, FL (Feb 2008).
- 2007 AAPS Annual Meeting, "Critical Stability Evaluation of Biopharmaceuticals During Clinical Development Stages," San Diego, CA (Nov 2007).
- 2007 DIA Annual Meeting, "The Impact of FDA's Quality by Design Initiative on Biologics Development," Atlanta, GA (Jun 2007).
- Institute for International Research: Formulation and Forced Degradation Strategies for Biomolecules, "Regulatory Requirements for Successful Product Development," San Diego, CA (Mar 2007).
- International Pharmaceutical Academy: Effective Management of Stability Programs, "Stability Design Considerations for Global Regulatory Filings," Toronto, Canada (Feb 2007).
- Cambridge Healthtech Institute's PepTalk: Optimizing Protein and Antibody Therapeutics, "Regulatory Considerations for the Development of Protein Therapeutic Products," San Diego, CA (Jan 2007).
- 2006 AAPS Annual Meeting, "The Impact of FDA Initiatives on the Development of Biological Products," San Antonio, TX (Nov 2006).
- SWE Enterprises: Stability Testing for the FDA Regulated Industry, "In-Use Testing of Biotechnological and Biologic Products," Boston, MA (Oct 2006).
- SWE Enterprises: Stability Testing for the FDA Regulated Industry, "Cost Efficient Design of Stability Studies," Boston, MA (Oct 2006).
- Institute for International Research: Chemistry Manufacturing & Controls, "Clarifying and Understanding ICH Guidance to Help Meet International Requirements for Submissions," Philadelphia, PA (July 2006).
- IVT Stability Testing: Implementing Effective Processes for Stability Program Development, "Cost Efficient Design of Stability Studies," San Diego, CA (June 2006).
- IVT Stability Testing: Implementing Effective Processes for Stability Program Development, "Stability Requirements for Global Regulatory Filings," San Diego, CA (June 2006).

- CBI Stability Programs: New Approaches to Test, Analyze and Document Data for Improved Program Design and Global Compliance, "In Use Testing of Biotechnological and Biological Products," Princeton, NJ (June 2006).
- IBC/TIDES: Oligonucleotide and Peptide Technology and Product Development, "Stability Considerations and Testing for Oligo- and Peptide-Based Therapeutics," Carlsbad, CA (May 2006).
- IBC Biopharm Manufacturing and Distribution Summit: Logistics for Biopharmaceutics, "Stability Studies to Support the Chain of Custody of Biotechnology Products," Reston, VA (Dec 2005).
- 2005 AAPS Annual Meeting: AAPS Short Course on Degradation and Stability in Small Molecule Active Pharmaceutical Ingredients/Stability Testing for Global Filings, "Stability Requirements for Global Regulatory Filings," Nashville, TN (Nov 2005).
- Therapeutic Strategies Against Neurodegenerative Conditions, "The Regulatory Product Development Process," Burlington, MA (Oct 2005).
- International Pharmaceutical Federation (FIP) Workshop: Harmonizing Clinical Trial GMP and Quality Requirements Across the EU and Beyond, "The US Investigational New Drug (IND) System," Noordwijk Zee, The Netherlands (Mar 2005).
- 2004 AAPS Annual Meeting, "Phase 2 and 3 IND CMC Guidance: FDA Perspective," Baltimore, MD (Nov 2004).
- 64th Annual World FIP Congress, "Clinical Trial Application Process – CMC: US FDA Perspective," New Orleans, LA (Sep 2004).
- AAPS Pharmaceutical Technologies 3rd Summer Conference: Optimizing the Global Clinical Trial Process, "IND Applications – FDA Perspective," Cherry Hill, NJ (Aug 2004).
- 2004 DIA Annual Meeting, "FDA Stability Guidance Update," Washington, DC (Jun 2004).
- DIA Meeting on CM&C/Regulatory and Technical Strategies, "Challenges and Opportunities in CMC Requirements for Phase 2-3," Bethesda, MD (Mar 2004).
- 2003 PDA Annual Meeting, "Draft FDA Stability Guidance," Atlanta, GA (Nov 2003).
- 2003 DIA Annual Meeting, "Product Quality of Non-clinical and Clinical Trial Materials," San Antonio, TX (Jun 2003).
- PARCS Meeting, "Managing CMC Requirements during IND," Irvine, CA (Apr 2003).
- PARCS Meeting, "Use of SUPAC Guidances during IND Development," Irvine, CA (Apr 2003).
- DIA Meeting on Global Chemistry, Manufacturing and Controls: Pre IND/CTX and IND/CTX Development Challenges, "FDA Perspective on Stability Testing during IND Development," Philadelphia, PA (Feb 2003).

PUBLICATIONS

- C. Syin, D. Parzy, F. Traincard, I. Boccaccio, M.G. Joshi, D.T. Lin, X.-M. Yang, K. Assemat, C. Doerig, and G. Langeley, "The H89 cAMP-dependent protein kinase inhibitor blocks *Plasmodium falciparum* development in infected erythrocytes," *Eur. J. Biochem. 268*, 4842 (2001).
- J.P. McDaniel, C. Syin, D.T. Lin, M.B. Joshi, S. Li, and N.D. Goldman, "Expression and characterization of a *Plasmodium falciparum* protein containing domains homologous to sarcalumenin and a tyrosine kinase substrate, eps15," *Int. J. Parasitol. 29*, 723 (1999).
- D.T. Lin, N.D. Goldman, and C. Syin, "Stage specific expression of a *Plasmodium falciparum* protein related to the eukaryotic mitogen-activated protein kinase," *Mol. Biochem. Parasitol. 78*, 67 (1995).
- M.R. Harkness, J.B. McDermott, D.A. Abramowicz, J.J. Salvo, W.P. Flanagan, M.L. Stephens, F.J. Mondello, R.J. May, J.H. Lobos, K.M. Carroll, M.J.Brennan, A.A. Bracco, K.M. Fish, G.L. Warner, P.R. Wilson, D.K. Dietrich, D.T. Lin, C.B. Morgan, and W.L. Gately, "*In situ* stimulation of aerobic PCB biodegradation in Hudson River sediments," *Science 259*, 503 (1993).
- D.T. Lin, V.M. Powers, L.J. Reynolds, C.P. Whitman, G.L. Kenyon and J.W. Kozarich, "Evidence for the generation of α-carboxy-α-hydroxy-*p*-xylylene from *p*-(bromomethyl)mandelate by mandelate racemase," *J. Am. Chem. Soc. 110*, 323 (1988).

- M.S. Lakshmikumaran, E. D'Ambrosio, L.A. Laimins, D.T. Lin and A.V. Furano, "Long interspersed repeat DNA(LINE) causes polymorphism at the rat insulin 1 locus," *Mol. Cell. Biol. 5*, 2197 (1985).

BOOK CHAPTER

- N.R. Schmuff and D.T. Lin, "Contents of Module 3 for an Electronic Common Technical Document Investigational New Drug Application," in Preparation and Maintenance of the IND Application in eCTD Format, W.K. Sietsema (ed.), FDAnews, Falls Church, VA, 117-134 (2008).
- N.R. Schmuff and D.T. Lin, "Chemistry, Manufacturing and Controls (CMC)," in Wiley Encyclopedia of Clinical Trials, (2008).
- J.A. Gerlt, G.L. Kenyon, J.W. Kozarich, D.T. Lin, D.C. Neidhart, G.A. Petsko, V.M. Powers, S.C. Ransom and A.Y. Tsou, "Structure-function relationships in mandelate racemase and muconate lactonizing enzyme," in Chemical Aspects of Enzyme Biotechnology, T.O. Baldwin, F.M. Raushel and A.I. Scott (eds.), Plenum, New York, NY, 9-21 (1990).

PROCEEDINGS OF MEETINGS

- D.T. Lin, N.D. Goldman, and C. Syin, "*Plasmodium falciparum* mitogen-activated protein kinase homologue contains an unusually large carboxyl terminal domain which is highly charged and homologous to merozoite surface antigens," Molecular Parasitology Meeting, Woods Hole, MA (1995).
- C. Syin, D. Lin, B. Krzyzanowska, and N.D. Goldman, "*Plasmodium* cGMP-dependent protein kinase," FDA Science Forum on Regulatory Sciences, Washington, D.C. (1994).
- J. H. Lobos, M. J. Brennan, J. T. Jackman and D. T. Lin, "*In situ* stimulation of PCB biodegradation in Hudson River sediment: III. enumeration and characterization of aerobic bacteria," ASM Meeting, New Orleans (1992).
- G.L. Kenyon, D.T. Lin, V.M. Powers, L.J. Reynolds, C.P. Whitman and J.W. Kozarich, "Generation of α-carboxy-α-hydroxy-*p*-xylylene from *p*-bromomethyl-mandelate by mandelate racemase-- further evidence for a carbanion mechanism," *FASEB J. 2*, 1329 (1988).
- D.T. Lin, V.M. Powers, L.J. Reynolds, C.P. Whitman, G.L. Kenyon and J.W. Kozarich, "Formation of *p*-xylylene species in the mandelate racemase catalyzed reaction of *p*-(bromomethyl)mandelate," *Fed. Proc. 46*, 2042 (1987)

BDSI's/Cross-Appellant's Declaration by Maureen Reitman, Sc.D. Under 37 C.F.R. § 1.132, dated February 28, 2013, filed April 12, 2013 ("Reitman Declaration")

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re *Inter Partes* Reexamination of:	)
US Patent No. 7,897,080	)
Issued: March 1, 2011	) Confirmation No.: 6418
Named Inventor: Robert K. Yang *et al.*	) Group Art Unit: 3991
Control No.: 95/002,170	) Examiner: Diamond, Alan D.
Filed: September 10, 2012	) M&E Docket: 117744-00023
Title: POLYETHYLENE-OXIDE BASED FILMS AND DRUG DELIVERY SYSTEMS MADE THEREFROM	) H&B Docket: 1199-26 RCE/CON/REX

Mail Stop *Inter Partes* Reexam
Attn: Central Reexamination Unit
Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

DECLARATION BY MAUREEN REITMAN, SC.D.
UNDER 37 CFR § 1.132

Sir/Madam:

I, Maureen Reitman, do hereby make the following declaration:

I. Technical Background

1. I am a Principal and the Director of the Polymer Science and Materials Chemistry Practice at Exponent. I hold two academic degrees: (1) a Bachelor of Science in Materials Science and Engineering from the Massachusetts Institute of Technology (MIT), and (2) a Doctor of Science in Materials Science and Engineering, with a thesis in the field of polymers, from MIT. I have been practicing in the field of polymer science and engineering for more than 20 years as a researcher at MIT, in a variety of technical roles at the 3M Company, and as a consultant with Exponent. I provide consulting engineering services in all aspects of polymer science and engineering including, but not limited to material selection, product design and development, mechanical and chemical testing, failure analysis, polymer chemistry, polymer

physics, and polymer processing. My specialties include formulation, processing and performance evaluation of polymeric materials, including films, coatings, adhesives and transdermal drug delivery systems. I have been directly involved in product development, product line extensions, transfer of new products to manufacturing, qualification of alternative materials and manufacturing equipment, evaluating field performance, and assessing intellectual property. I am a past chairman and continue to serve as a member of the board of directors of the Medical Plastics Division of the Society of Plastics Engineers. My *curriculum vitae* is provided in Appendix A.

2. While Exponent is being paid for my time, I am not an employee of, nor do I have any financial interest in, BioDelivery Sciences International, Inc.

3. I have been asked to carefully review International Publication No. WO 00/42992 ("*Chen*"), and manufacture a film as described in *Chen*. I carefully reviewed *Chen*. Under my direction, my team manufactured a film in accordance with Example 7 of *Chen*. I have also been asked to take samples and perform various analytical tests to confirm the uniform distribution of the pharmaceutical active in substantially equal sized individual dosage units of the film, which we did.

4. Manufacturing Example 7 of *Chen*

Chen states: "According to Examples 1-8, the hydrocolloid [Methocel E5(HPMC)] was dissolved in water under agitated mixing to form a uniform and viscous solution." Chen 17:7-8.

- Methocel E5(HPMC) was dissolved in water under agitated mixing to form a uniform and viscous solution, by my team.

Chen states: "Additional ingredients were then added sequentially to the viscous solution such as peppermint, aspartame, propyl[ene] glycol, benzoic acid and citric acid under agitated mixing until they were uniformly dispersed or dissolved in the hydrocolloid." Chen 17:8-11.

- Additional ingredients were then added sequentially to the viscous solution including peppermint oil, aspartame, propylene glycol, benzoic acid and citric acid under agitated mixing until they were uniformly dispersed or dissolved in the hydrocolloid, by my team.

- Kolliphor EL was also added to the viscous solution.

Chen states: "Therapeutic agents were added to the homogeneous mixture (coating solution) prior to forming the film." *Chen* 20:19-20.

- Oxybutynin chloride (the therapeutic agent of Example 7) was added to the homogeneous mixture (coating solution) prior to forming the film, by my team.

Chen's Table 5 specifies the composition for Example 7.

- We used the ingredients in the amounts identified in *Chen*'s Table 5. *See* Table 1.

Table 1			
Formulation, Ex. 7, Table 5, *Chen*	% Weight	Formulation, Prepared by Maureen Reitman Team	% Weight
Oxybutynin	3.71	Oxybutynin chloride	3.71
Methocel E5 (HPMC)	21.06	Methocel E5 Premium LV	21.06
Water	70.72	Water, distilled	70.72
Cremophor EL40	1	Kolliphor EL[1]	1
Propylene glycol	1	Propylene glycol	1
Peppermint	1	Peppermint oil	1
Aspartame	0.8	Aspartame	0.8
Benzoic acid	0.013	Benzoic acid	0.013
Citric acid	0.7	Citric acid, monohydrate	0.7

Chen states: "The resultant mixture was degassed in a vacuum chamber until trapped air bubbles were removed." Chen 17:11-12.

- The resultant mixture was degassed in a vacuum chamber until trapped air bubbles were removed, by my team.

Chen states: "The formulation was then coated on the non-siliconized side of a polyester film at a wet thickness of 10 mil and dried in a hot air circulating oven at 50°C for 9 minutes." Chen 17:13-15.

- The formulation was then coated on a non-siliconized side of a polyester film at a wet thickness of 10 mil and dried in a hot air circulating oven at 50°C for up to 9 minutes, on commercial manufacturing equipment by my team.

Chen states: "Methods for manufacturing the dosage unit include the solvent casting methods as shown in Figure 2." Chen 15:13-14. "The manufacturing process for forming the dosage unit is illustrated in Figure 2. The dry film formed by this process is a glossy, stand alone, self supporting, non-tacky and flexible film (12)." Chen 15:29-31.

- A solvent casting manufacturing process for forming the dosage unit as illustrated in Figure 2 was used[2], by my team.

[1] The Cremophor line of products now owned by BASF and renamed Kolliphor. Based on the naming convention of the Cremophor/ Kolliphor products, EL40 is Polyoxyl 40 Castor Oil and EL is Polyoxyl 35 Castor Oil (*i.e.*, they are based on a 1:40 and 1:35 ratio, respectively, of castor oil:ethylene oxide). They are different materials. However, one of skill in the art would recognize Kolliphor EL as an appropriate substitute, as Cremophor EL40 is no longer available.

- The film was manufactured using a controlled drying process.
- As illustrated in Figure 2, the drying oven featured aeration controller with 3 zones set such that in each successive zone air impingement on the surface of the film increased.
- The dry film formed by the process is a glossy, stand alone, self-supporting, non-tacky and flexible film.

Chen states: "A glossy, substantially transparent, stand alone, self-supporting, non-tacky and flexible film was obtained after drying." Chen 17:15-16.

- A glossy, substantially transparent, stand alone, self-supporting, non-tacky and flexible film was obtained after drying, by my team.

5. Verification of Content Uniformity – Visual Inspection

- By examination with the naked eye, uniformity was verified by my team.

6. Verification of Content Uniformity – Unit Dose Weight

- By weighing individual dosage units of substantially identical size, uniformity was verified by my team. *See* Table 2.

Table 2	
Sample	Weight of 5 cm^2 dosage unit (grams)
1	0.034
2	0.034
3	0.034
4	0.034
5	0.034
6	0.034
7	0.034

7. Verification of Content Uniformity – Dissolution Test (HPLC)

- By dissolution of individual dosage units of substantially identical size and analysis by High Performance Liquid Chromatography (HPLC) active content uniformity was verified by my team. *See* Table 3.

[2] Our backing was not looped and we did not die cut in line, but the solvent casting and drying under aeration is matched.

Table 3	
Sample	Oxybutynin weight (mg)
A	4.4
B	4.4
C	4.3
D	4.4
E	4.1

- As can be seen in Table 3, the active varies by less than 10%.

8. Additional Observations

   - The components of the formulation, including the active component, were uniformly distributed in the viscous solution, which was used to cast the film, as was verified by my team.

   - The viscous solution, which was used to cast the film, exhibited the flow properties of honey (around 10,000 cps), as observed by my team.

   - Water content of the film was less than 10%, as verified by my team.

   - Within about 4 minutes after initiation of drying, the film was self-supporting, non-tacky, flexible and viscoelastic, as verified by my team.

9. I hereby declare that all statements made herein of my own knowledge are true and that all statements made on information and belief are believed to be true; and further that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine, or imprisonment, or both, under section 1001 of Title 18 of the United States Code, and that such willful statements may jeopardize the validity of the application or any patents issued thereon.

Dated: February 28, 2013

Maureen Reitman, Sc.D.

Appendix A

Exponent
Failure Analysis Associates

Exponent
[illegible]
Suite 700
Rockville, Maryland 20850

Telephone [illegible]
Facsimile [illegible]
www.exponent.com

Maureen T. F. Reitman, Sc.D.
Principal and Practice Director

Professional Profile

Dr. Maureen Reitman is a Principal and the Director of Exponent's Polymer Science and Material Chemistry practice. Her expertise includes polymer and composite technology, mechanics of materials, adhesion science, fiber mechanics, history and technology of plastics, and material failure analysis. She is skilled in the development and use of testing tools and methods and has applied them to plastic, rubber, textile, metal, glass, ceramic, and composite materials and systems. She is experienced in major aspects of product development, including materials selection, formulation, scale-up, end-use testing, failure analysis, certification procedures and issues related to intellectual property.

Dr. Reitman has conducted research in the areas of packaging and barrier materials; paints and coatings; plastic pipes; transdermal drug delivery; adhesives, sealants, and encapsulants; molding compounds; high temperature resins; nanoparticles; fibers and textiles; protective coatings and finishes; polymer chemical resistance; plastic insulation; connectors and splices; plastic packaging; medical devices; environmental effects on durability; and product aging. She has used her expertise to solve a broad range of problems related to coatings, fibers, films, and extruded and molded products, and their use in the telecom, electronics, electrical, transportation, construction, fire protection, medical, and consumer products markets.

Dr. Reitman is a member of the Board of Directors of the Medical Plastics Division of the Society of Plastics Engineers and an active member of two Underwriters Laboratories Standard Technical Panels, addressing Polymeric Materials (UL 94, UL 746, UL 1694) and Appliance Wiring (UL758).

Prior to joining Exponent, Dr. Reitman worked for the 3M Company in both research and management roles. Her activities included technology identification, materials selection and qualification, product development, customer support, program management, acquisition integration, intellectual property analysis, and patent litigation support.

Academic Credentials and Professional Honors

Sc.D., Materials Science and Engineering/ Program in Polymer Science and Technology, Massachusetts Institute of Technology, 1993
B.S., Materials Science and Engineering, Massachusetts Institute of Technology, 1990

National Academy of Engineering Frontiers of Engineering, 2009; Tau Beta Pi; Sigma Xi
John Wulff Award; Carl Loeb Fellowship; NCAA Postgraduate Scholarship;
Malcolm G. Kispert Award; GTE Academic All-American

02/13

Patents

Patent 6,311,524: Accelerated Method for Increasing the Photosensitivity of a Glassy Material, issued November 6, 2001.

European Patent EP0830428: Tackified Polydiorganosiloxane Polyurea Segmented Copolymers and a Process for Making Same, published March 25, 1998.

Patent 5,371,051: Fiber Optic Fusion Splice Protector Sleeve, issued March 24, 1998.

Publications

Kurtz S, Siskey R, Reitman M. Accelerated aging, natural aging, and small punch testing of gamma-air sterilized polycarbonate urethane acetabular components. Journal of Biomedical Materials Research Part B: Applied Biomaterials 2010 May; 93B(2):422–447.

Hoffman JM, Reitman M, Donthu S, Ledwith P. Complimentary failure analysis methods and their application to CPVC pipe. Proceedings, ANTEC 2010, Society of Plastics Engineers, Orlando, FL, May 2010.

Hoffman JM, Reitman M, Donthu S, Ledwith P, Wills D. Microscopic characterization of CPVC failure modes. Proceedings, ANTEC 2009, Society of Plastics Engineers, Chicago, IL, June 2009. Best Paper Award in Failure Analysis & Prevention.

Kurtz SM, Ebert M, Siskey R, Ciccarelli L, Reitman M, Harper ML, Chan FW. Natural and accelerated aging of polyurethanes in the Bryan cervical disc. Poster No. P158. Transactions of Spineweek 2008, Geneva, Switzerland, May 26–31, 2008.

Reitman M, Ledwith P, Hoffman M, Moalli J, Xu T. Environmentally driven changes in nylon. Proceedings, ANTEC 2008, Milwaukee, WI, Society of Plastics Engineers, May 2008.

Hoffman JM, Reitman M, Ledwith P. Characterization of manufacturing defects in medical balloons. Proceedings, ANTEC 2008, Milwaukee, WI, Society of Plastics Engineers, May 2008.

Reitman, MTF, Moalli JE. Polymeric coatings for medical device. Medical Device and Manufacturing Technology, Touch Briefings, pp. 28–30, 2006.

Moalli JE, Moore CD, Robertson C, Reitman MTF. Failure analysis of nitrile radiant heating tubing. Proceedings, ANTEC 2006, Society of Plastic Engineers, Charlotte, NC, May 2006.

Reitman M, McPeak J. Protective coatings for implantable medical devices. Proceedings, ANTEC 2005, Society of Plastic Engineers, Boston MA, May 2005.

McPeak J, Reitman M, Moalli J. Determination of in-service exposure temperature of thermoformed PVC via TMA. Proceedings, 31st Annual North American Thermal Analysis Society Conference, Williamsburg, VA, 2004.

Reitman MTF, Moalli JE. Product development and standards organizations: Listings and certifications for plastic products. 8th Annual International Conference on Industrial Engineering Theory, Applications and Practice, Las Vegas, NV, 2003.

Potdar YK, Reitman MTF. The role of engineering consultants in failure analysis and product development. 8th Annual International Conference on Industrial Engineering Theory, Applications and Practice, Las Vegas, NV, 2003.

Ezekoye OA, Lowman CD, Hulme-Lowe AG, Fahey MT. Polymer weld strength predictions using a thermal and polymer chain diffusion analysis. Polymer Engineering and Science 1998; 38(6):976–991, June.

Fahey MT. Nonlinear and anisotropic properties of high performance fibers. MIT Thesis, 1993.

Fahey MT. Mechanical property characterization and enhancement of rigid rod polymer fibers. MIT Thesis, 1990.

Book Contributions

Reitman M, Liu D, Rehkopf J. Chapter 38. Mechanical properties of polymers. In: Handbook of Measurement in Science and Engineering. Volume 2. Kutz, M (ed), John Wiley & Sons, Hoboken NJ, 2013. ISBN- 978-1-118-38464-0.

Reitman M, Jaekel D, Siskey R, Kurtz S. Morphology and crystalline architecture of polyarylketones, pp. 49-60. In: PEEK Biomaterials Handbook. Kurtz SM (ed), Elsevier William Andrews, Kidlington, Oxford, UK, 2012. ISBN 13:978-1-4377-4463-7

Tsuji JS, Mowat FS, Donthu S, Reitman M. Application of toxicology studies in assessing the health risks of nanomaterials in consumer products, pp. 543-580. In: Nanotoxicity: From In Vivo and In Vitro Models to Health Risks. Sahu S, and Casciano D. (eds), John Wiley & Sons, Chicester, West Sussex, UK, 2009. ISBN 978-0-470-74137-5.

Reitman MTF. The Plastics Revolution. In: Research and Discovery: Landmarks and Pioneers in American Science. Lawson RM (ed), Armonk NY: Sharpe Reference 2008. ISBN 978-0-7656-8073-0.

Klein SM. Mid-century plastic jewelry. Schiffer Publishing, Atglen, PA, 2005. (Technical advisor to author).

Selected Invited Presentations

Reitman MTF. Failure analysis tools. Workshop on Future Needs for Service Life Prediction of Polymeric Materials. NIST and Underwriters Laboratories, Gaithersburg, MD, October 2012.

Hoffman J, MacLean S, Ralston B, Reitman M, Ledwith P. Fractography of unfilled thermoplastic materials experiencing common mechanical failure modes. Materials Science & Technology 2012 Conference, Pittsburgh PA, October 2012.

Hoffman J, Reitman M, Ledwith P. Microscopic characterization of CPVC failure. Materials Science & Technology 2012 Conference, Pittsburgh PA, October 2012.

Reitman MTF. Polymer material properties for next generation medical devices. Invited Speaker: MedTech Polymers, UBM Canon, Chicago, IL, September 2012.

Reitman MTF. Polymers for medical applications. Fundamentals and Fellows Forum, ANTEC 2012, Orlando FL, April 2012.

Reitman MTF. Plastic and composite product failures. Invited lecture in Failure Analysis of Emerging Technologies. Stanford University Department of Materials Science and Engineering, Menlo Park, CA October 2009.

Reitman MTF. Factors for success: Plastics in injection molded medical devices. Part of *Injection Molding Works for Medical Design*, Design News Webcast, October 2008.

Reitman MTF. Plastic and composite product failures. Keynote Speaker: Third International Conference on Engineering Failure Analysis (ICEFA III), Elsevier, Sitges Spain, July 2008.

Reitman MTF. Multiphase materials for medical device applications, an overview. Medical Device and Manufacturing (MDM), Canon Communications, various locations, January- June 2008.

Reitman MTF. Nanotechnology and plastics for medical devices. Capitalizing on Nanoplastics, Intertek PIRA San Antonio TX, February 2008.

Reitman MTF. Nano additives in composites and coatings for medical device applications. Medical Device and Manufacturing Minneapolis, Canon Communications, Minneapolis MN, October 2007.

Reitman MTF, Swanger LA. Practical tips on how to manage your technical expert in patent disputes. Ropes & Gray IP Master Class, Live Teleconference, June 2007.

Reitman MTF, Kennedy E. Root cause failure analysis and accident investigation. Lorman Educational Services, Live Teleconference, November 2007.

Reitman MTF. Plastics failure analysis: Case studies. Baltimore/ Washington Chapter of SAMPE, October 2006.

Reitman MTF. Plastics failure analysis. Baxter Global Plastics Processing Conference 2005, Schaumburg IL, 2005.

Fahey MT. Fiber mechanics, corrosion, sealants: Tales of a 3M materials scientist. Class of 1960's Scholars Program, Williams College, 1999.

Fahey MT. Adhesives and sealants for the telecommunications industry. Riverwood V Conference, St. Paul MN, 1998.

Current Professional Appointments

- Underwriter's Laboratory Standards Technical Panel STP 746 (Polymeric Materials, includes UL94, UL 746 and UL1694)
- Underwriter's Laboratory Standards Technical Panel STP 758 (Appliance Wires/ UL758)
- Medical Plastics Division Board of Directors, Society of Plastics Engineers

Committee and Review Activities

- UL Forum on Initiatives to Improve the Long Term Aging Program, LTTA Tools Working Groups, Underwriters Laboratories
- Research and Engineering Technology Award Committee, Society of Plastics Engineers
- Reviewer, Medical Plastics Technical Program Committee, Society of Plastics Engineers
- Reviewer, Failure Analysis and Prevention Technical Program Committee, Society of Plastics Engineers
- Reviewer, various book proposals and submissions related to polymer science, ASM International, Elsevier, John Wiley

Professional Affiliations

- American Association for the Advancement of Science (member)
- American Association of Textile Chemists and Colorists—AATCC (senior member)
- American Chemical Society (member)
- ASTM International (member)
- Society for the Advancement of Material and Process Engineering (member)
- Society of Plastics Engineers (senior member)

RELATED PROCEEDINGS APPENDIX

NONE.

CERTIFICATE OF SERVICE

It is certified that a copy of this **PATENT OWNER'S CROSS-RESPONDENT'S BRIEF** has been served, by first class mail, postage prepaid, on April 10, 2014, in its entirety on the third party requester as provided in 37 CFR § 1.903 and 37 CFR § 1.248 at the address below.

DANIELLE L. HERRITT
McCARTER & ENGLISH LLP
265 FRANKLIN STREET
BOSTON, MASSACHUSETTS 02110

/Michael I. Chakansky/
Michael I. Chakansky
Registration No.: 31,600
Attorney for the Patentee/MonoSol

Electronic Patent Application Fee Transmittal

Application Number:	95002170
Filing Date:	10-Sep-2012
Title of Invention:	POLYETHYLENE-OXIDE BASED FILMS AND DRUG DELIVERY SYSTEMS MADE THEREFROM
First Named Inventor/Applicant Name:	7897080
Filer:	Michael I. Chakansky
Attorney Docket Number:	117744-00023

Filed as Large Entity

inter partes reexam Filing Fees

Description	Fee Code	Quantity	Amount	Sub-Total in USD($)
Basic Filing:				
Pages:				
Claims:				
Miscellaneous-Filing:				
Petition:				
Patent-Appeals-and-Interference:				
Filing Appeal Brief Inter Partes Reexam	1404	1	2000	2000
Post-Allowance-and-Post-Issuance:				
Extension of Time:				

Description	Fee Code	Quantity	Amount	Sub-Total in USD($)
Miscellaneous:				
			Total in USD ($)	**2000**

Electronic Acknowledgement Receipt

EFS ID:	18734581
Application Number:	95002170
International Application Number:	
Confirmation Number:	6418
Title of Invention:	POLYETHYLENE-OXIDE BASED FILMS AND DRUG DELIVERY SYSTEMS MADE THEREFROM
First Named Inventor/Applicant Name:	7897080
Customer Number:	23869
Filer:	Michael I. Chakansky
Filer Authorized By:	
Attorney Docket Number:	117744-00023
Receipt Date:	10-APR-2014
Filing Date:	10-SEP-2012
Time Stamp:	21:13:47
Application Type:	inter partes reexam

Payment information:

Submitted with Payment	yes
Payment Type	Credit Card
Payment was successfully received in RAM	$2000
RAM confirmation Number	7010
Deposit Account	
Authorized User	

File Listing:

Document Number	Document Description	File Name	File Size(Bytes)/ Message Digest	Multi Part / Zip	Pages (if appl.)

1	Respondent Brief - Owner	PORESPONDENTBRIEF.pdf	2715868 d3588755f1e73187176f64eaaac2e1c877714b2b	no	86
Warnings:					
Information:					
2	Fee Worksheet (SB06)	fee-info.pdf	30166 c70c3d4add45ac64e9931aae07c6b480ee291de7	no	2
Warnings:					
Information:					
			Total Files Size (in bytes):	2746034	

This Acknowledgement Receipt evidences receipt on the noted date by the USPTO of the indicated documents, characterized by the applicant, and including page counts, where applicable. It serves as evidence of receipt similar to a Post Card, as described in MPEP 503.

New Applications Under 35 U.S.C. 111
If a new application is being filed and the application includes the necessary components for a filing date (see 37 CFR 1.53(b)-(d) and MPEP 506), a Filing Receipt (37 CFR 1.54) will be issued in due course and the date shown on this Acknowledgement Receipt will establish the filing date of the application.

National Stage of an International Application under 35 U.S.C. 371
If a timely submission to enter the national stage of an international application is compliant with the conditions of 35 U.S.C. 371 and other applicable requirements a Form PCT/DO/EO/903 indicating acceptance of the application as a national stage submission under 35 U.S.C. 371 will be issued in addition to the Filing Receipt, in due course.

New International Application Filed with the USPTO as a Receiving Office
If a new international application is being filed and the international application includes the necessary components for an international filing date (see PCT Article 11 and MPEP 1810), a Notification of the International Application Number and of the International Filing Date (Form PCT/RO/105) will be issued in due course, subject to prescriptions concerning national security, and the date shown on this Acknowledgement Receipt will establish the international filing date of the application.

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re *Inter Partes* Reexamination of:	)	
	)	
US Patent No. 7,897,080	)	Confirmation No.: 6418
	)	
Named Inventor: Robert K. Yang *et al.*	)	Group Art Unit: 3991
	)	
Control No.: 95/002,170	)	Examiner: Alan D. Diamond
	)	
Request Filed: September 10, 2012	)	M&E Docket: 117744-00023
	)	
Title: POLYETHYLENE OXIDE-BASED FILMS AND DRUG DELIVERY SYSTEMS MADE THEREFROM	)	H&B Docket: 1199-26 RCE/CON/REX

Mail Stop *Inter Partes* Reexam
Attn: Central Reexamination Unit
Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

TRANSMITTAL OF PAYMENT OF APPEAL BRIEF FEE (37 C.F.R. § 41.20(b)(2)(ii))

Requester hereby submits payment of the fee for filing the brief in support of the appeal of the above-identified *inter partes* reexamination on March 10, 2014. If additional fees are believed to be due, please charge our Deposit Account No. 50-4876, under Order No. 117744-00023 from which the undersigned is authorized to draw.

Respectfully submitted,
McCarter & English LLP

Dated: April 1, 2014

By: /Danielle L. Herritt/
Danielle L. Herritt Reg. 43,670
Kia Freeman Reg. 47,577
Direct Dial: 617-449-6513
Attorneys for Requester, BioDelivery Sciences International, Inc.

Electronic Patent Application Fee Transmittal

Application Number:	95002170
Filing Date:	10-Sep-2012
Title of Invention:	POLYETHYLENE-OXIDE BASED FILMS AND DRUG DELIVERY SYSTEMS MADE THEREFROM
First Named Inventor/Applicant Name:	7897080
Filer:	Danielle L. Herritt/Maureen Tierney
Attorney Docket Number:	117744-00023

Filed as Large Entity

inter partes reexam Filing Fees

Description	Fee Code	Quantity	Amount	Sub-Total in USD($)
Basic Filing:				
Pages:				
Claims:				
Miscellaneous-Filing:				
Petition:				
Patent-Appeals-and-Interference:				
Filing Appeal Brief Inter Partes Reexam	1404	1	2000	2000
Post-Allowance-and-Post-Issuance:				
Extension of Time:				

Description	Fee Code	Quantity	Amount	Sub-Total in USD($)
Miscellaneous:				
			Total in USD ($)	**2000**

Electronic Acknowledgement Receipt

EFS ID:	18639818
Application Number:	95002170
International Application Number:	
Confirmation Number:	6418
Title of Invention:	POLYETHYLENE-OXIDE BASED FILMS AND DRUG DELIVERY SYSTEMS MADE THEREFROM
First Named Inventor/Applicant Name:	7897080
Customer Number:	23869
Filer:	Danielle L. Herritt/Maureen Tierney
Filer Authorized By:	Danielle L. Herritt
Attorney Docket Number:	117744-00023
Receipt Date:	01-APR-2014
Filing Date:	10-SEP-2012
Time Stamp:	14:16:26
Application Type:	inter partes reexam

Payment information:

Submitted with Payment	yes
Payment Type	Deposit Account
Payment was successfully received in RAM	$2000
RAM confirmation Number	493
Deposit Account	504876
Authorized User	

The Director of the USPTO is hereby authorized to charge indicated fees and credit any overpayment as follows:

Charge any Additional Fees required under 37 C.F.R. Section 1.16 (National application filing, search, and examination fees)

Charge any Additional Fees required under 37 C.F.R. Section 1.17 (Patent application and reexamination processing fees)

Charge any Additional Fees required under 37 C.F.R. Section 1.19 (Document supply fees)

Charge any Additional Fees required under 37 C.F.R. Section 1.20 (Post Issuance fees)

Charge any Additional Fees required under 37 C.F.R. Section 1.21 (Miscellaneous fees and charges)

File Listing:

Document Number	Document Description	File Name	File Size(Bytes)/ Message Digest	Multi Part /.zip	Pages (if appl.)
1	Transmittal Letter	080AppealBriefFeeTransmittal2014APR01.PDF	6764 9b27ec0e471ac28d6592fe3d75ffee9457b1724a	no	1
Warnings:					
Information:					
2	Fee Worksheet (SB06)	fee-info.pdf	30023 e24dc34b74d04389b720a7f133c9593e5364be7a	no	2
Warnings:					
Information:					
		Total Files Size (in bytes):	36787		

This Acknowledgement Receipt evidences receipt on the noted date by the USPTO of the indicated documents, characterized by the applicant, and including page counts, where applicable. It serves as evidence of receipt similar to a Post Card, as described in MPEP 503.

New Applications Under 35 U.S.C. 111

If a new application is being filed and the application includes the necessary components for a filing date (see 37 CFR 1.53(b)-(d) and MPEP 506), a Filing Receipt (37 CFR 1.54) will be issued in due course and the date shown on this Acknowledgement Receipt will establish the filing date of the application.

National Stage of an International Application under 35 U.S.C. 371

If a timely submission to enter the national stage of an international application is compliant with the conditions of 35 U.S.C. 371 and other applicable requirements a Form PCT/DO/EO/903 indicating acceptance of the application as a national stage submission under 35 U.S.C. 371 will be issued in addition to the Filing Receipt, in due course.

New International Application Filed with the USPTO as a Receiving Office

If a new international application is being filed and the international application includes the necessary components for an international filing date (see PCT Article 11 and MPEP 1810), a Notification of the International Application Number and of the International Filing Date (Form PCT/RO/105) will be issued in due course, subject to prescriptions concerning national security, and the date shown on this Acknowledgement Receipt will establish the international filing date of the application.

CERTIFICATE OF SERVICE

The undersigned hereby certifies that a copy of the foregoing Transmittal of Payment of Appeal Brief Fee was served on April 1, 2014, by first class mail, directed to the patent owner at the correspondence address of record for the subject patent at the following address:

Daniel A. Scola, Jr.

HOFFMANN & BARON, LLP

6900 JERICHO TURNPIKE

SYOSSET, NY 11791,

By: /Danielle L. Herritt/
Danielle L. Herritt
Registration No. 43,670
Attorney for Requester

Electronic Acknowledgement Receipt

EFS ID:	18641248
Application Number:	95002170
International Application Number:	
Confirmation Number:	6418
Title of Invention:	POLYETHYLENE-OXIDE BASED FILMS AND DRUG DELIVERY SYSTEMS MADE THEREFROM
First Named Inventor/Applicant Name:	7897080
Customer Number:	23869
Filer:	Danielle L. Herritt/Maureen Tierney
Filer Authorized By:	Danielle L. Herritt
Attorney Docket Number:	117744-00023
Receipt Date:	01-APR-2014
Filing Date:	10-SEP-2012
Time Stamp:	15:19:17
Application Type:	inter partes reexam

Payment information:

Submitted with Payment	no

File Listing:

Document Number	Document Description	File Name	File Size(Bytes)/ Message Digest	Multi Part /.zip	Pages (if appl.)
1	Reexam Certificate of Service	080AppealBriefFeePaymentCOS.PDF	4946 770e72161972c089589f9b6f5c9f504a4970a2ca	no	1

Warnings:	
Information:	

Total Files Size (in bytes):	4946

This Acknowledgement Receipt evidences receipt on the noted date by the USPTO of the indicated documents, characterized by the applicant, and including page counts, where applicable. It serves as evidence of receipt similar to a Post Card, as described in MPEP 503.

New Applications Under 35 U.S.C. 111

If a new application is being filed and the application includes the necessary components for a filing date (see 37 CFR 1.53(b)-(d) and MPEP 506), a Filing Receipt (37 CFR 1.54) will be issued in due course and the date shown on this Acknowledgement Receipt will establish the filing date of the application.

National Stage of an International Application under 35 U.S.C. 371

If a timely submission to enter the national stage of an international application is compliant with the conditions of 35 U.S.C. 371 and other applicable requirements a Form PCT/DO/EO/903 indicating acceptance of the application as a national stage submission under 35 U.S.C. 371 will be issued in addition to the Filing Receipt, in due course.

New International Application Filed with the USPTO as a Receiving Office

If a new international application is being filed and the international application includes the necessary components for an international filing date (see PCT Article 11 and MPEP 1810), a Notification of the International Application Number and of the International Filing Date (Form PCT/RO/105) will be issued in due course, subject to prescriptions concerning national security, and the date shown on this Acknowledgement Receipt will establish the international filing date of the application.

EXHIBIT 1

US007897080B2

(12) **United States Patent**
Yang et al.

(10) **Patent No.: US 7,897,080 B2**
(45) **Date of Patent: *Mar. 1, 2011**

(54) **POLYETHYLENE-OXIDE BASED FILMS AND DRUG DELIVERY SYSTEMS MADE THEREFROM**

(75) Inventors: **Robert K. Yang**, Flushing, NY (US); **Richard C. Fuisz**, McLean, VA (US); **Gary L. Myers**, Kingsport, TN (US); **Joseph M. Fuisz**, Washington, DC (US)

(73) Assignee: **MonoSol Rx, LLC**, Portage, IN (US)

(*) Notice: Subject to any disclaimer, the term of this patent is extended or adjusted under 35 U.S.C. 154(b) by 0 days.

This patent is subject to a terminal disclaimer.

(21) Appl. No.: **12/614,928**

(22) Filed: **Nov. 9, 2009**

(65) **Prior Publication Data**

US 2010/0092545 A1 Apr. 15, 2010

Related U.S. Application Data

(63) Continuation of application No. 10/856,176, filed on May 28, 2004, now Pat. No. 7,666,337, and a continuation-in-part of application No. 10/768,809, filed on Jan. 30, 2004, now Pat. No. 7,357,891, and a continuation-in-part of application No. PCT/US02/32575, filed on Oct. 11, 2002, and a continuation-in-part of application No. PCT/US02/32594, filed on Oct. 11, 2002, and a continuation-in-part of application No. PCT/US02/32542, filed on Oct. 11, 2002.

(60) Provisional application No. 60/473,902, filed on May 28, 2003, provisional application No. 60/443,741, filed on Jan. 30, 2003, provisional application No. 60/328,868, filed on Oct. 12, 2001, provisional application No. 60/386,937, filed on Jun. 7, 2002, provisional application No. 60/414,276, filed on Sep. 27, 2002, provisional application No. 60/371,940, filed on Apr. 11, 2002.

(51) **Int. Cl.**
B29C 39/14 (2006.01)

(52) **U.S. Cl.** **264/172.19**; 264/212; 264/217; 264/211.2; 264/234; 264/319; 264/344

(58) **Field of Classification Search** ..... None
See application file for complete search history.

(56) **References Cited**

U.S. PATENT DOCUMENTS

3,007,848 A 11/1961 Stroop

(Continued)

FOREIGN PATENT DOCUMENTS

EP	0598606 B1	6/1999
GB	1510999 A	5/1978
WO	0018365 A	4/2000
WO	03030881 A	4/2003
WO	03030882 A	4/2003
WO	03030883 A	4/2003
WO	2008011194 A2	1/2008

OTHER PUBLICATIONS

Repka et al., "Influence of Vitamin E TPGS on the properties of hydrophilic films produced by hot-melt extrusion," International Journal of Pharmaceuticals 202: 63-70 (2000).

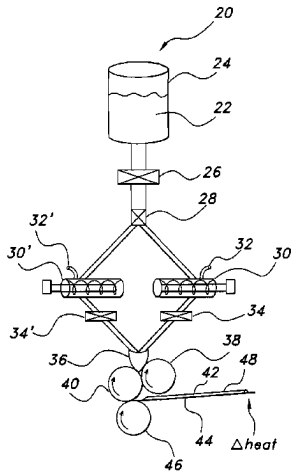
(Continued)

Primary Examiner—Edmund H. Lee
(74) *Attorney, Agent, or Firm*—Hoffmann & Baron, LLP

(57) **ABSTRACT**

The invention relates to the film products and methods of their preparation that demonstrate a non-self-aggregating uniform heterogeneity. Desirably, the films disintegrate in water and may be formed by a controlled drying process, or other process that maintains the required uniformity of the film. The films contain a polymer component, which includes polyethylene oxide optionally blended with hydrophilic cellulosic polymers. Desirably, the films also contain a pharmaceutical and/or cosmetic active agent with no more than a 10% variance of the active agent pharmaceutical and/or cosmetic active agent per unit area of the film.

299 Claims, 34 Drawing Sheets



U.S. PATENT DOCUMENTS

4,049,848	A *	9/1977	Goodale et al.	427/244
4,631,837	A	12/1986	Magoon	
4,872,270	A *	10/1989	Fronheiser et al.	34/421
4,880,416	A	11/1989	Horiuchi et al.	
5,605,696	A	2/1997	Eury et al.	
5,629,003	A *	5/1997	Horstmann et al.	424/401
5,766,525	A *	6/1998	Andersen et al.	264/40.1
5,800,832	A	9/1998	Tapolsky et al.	
5,806,284	A	9/1998	Gifford	
6,072,100	A	6/2000	Mooney et al.	
6,375,963	B1	4/2002	Repka et al.	
6,800,329	B2	10/2004	Horstmann et al.	
6,824,829	B2	11/2004	Berry et al.	
7,005,142	B2	2/2006	Leon et al.	
7,579,019	B2	8/2009	Tapolsky et al.	
2002/0127254	A1	9/2002	Fotinos et al.	
2003/0107149	A1	6/2003	Yang et al.	
2004/0096569	A1	5/2004	Barkalow et al.	
2004/0191302	A1	9/2004	Davidson	
2005/0048102	A1	3/2005	Tapolsky et al.	
2006/0210610	A1	9/2006	Davidson et al.	
2007/0087036	A1	4/2007	Durshlag et al.	
2007/0148097	A1	6/2007	Finn et al.	
2008/0254105	A1	10/2008	Tapolsky et al.	

OTHER PUBLICATIONS

Repka et al., "Bioadhesive properties of hydroxypropylcellulose topical films produced by hot-melt extrusion," Journal of Controlled Release 70: 341-351 (2001).

Lazaridou et al., "Thermophysical properties of chitosan, chitosan-starch and chitosan-pullulan films near the glass transition," Carbohydrate Polymers 48: 179-190 (2002).

* cited by examiner

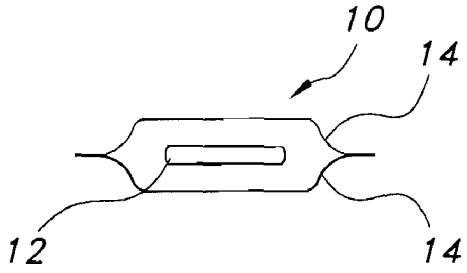


FIG. 1

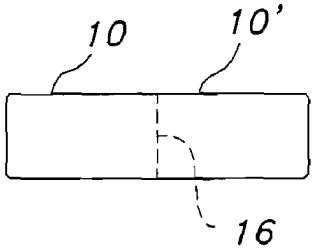


FIG. 2

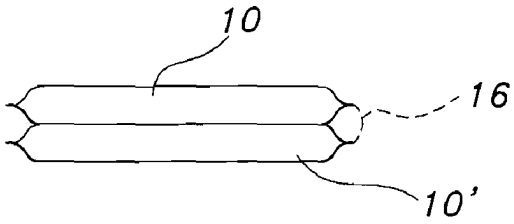


FIG. 3

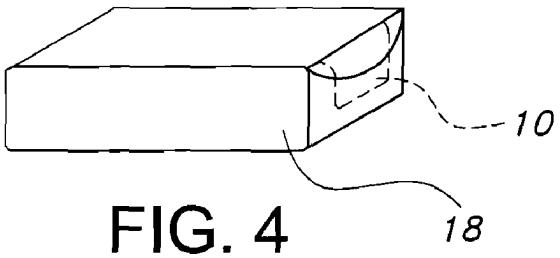


FIG. 4

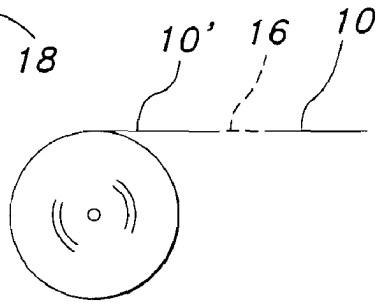


FIG. 5

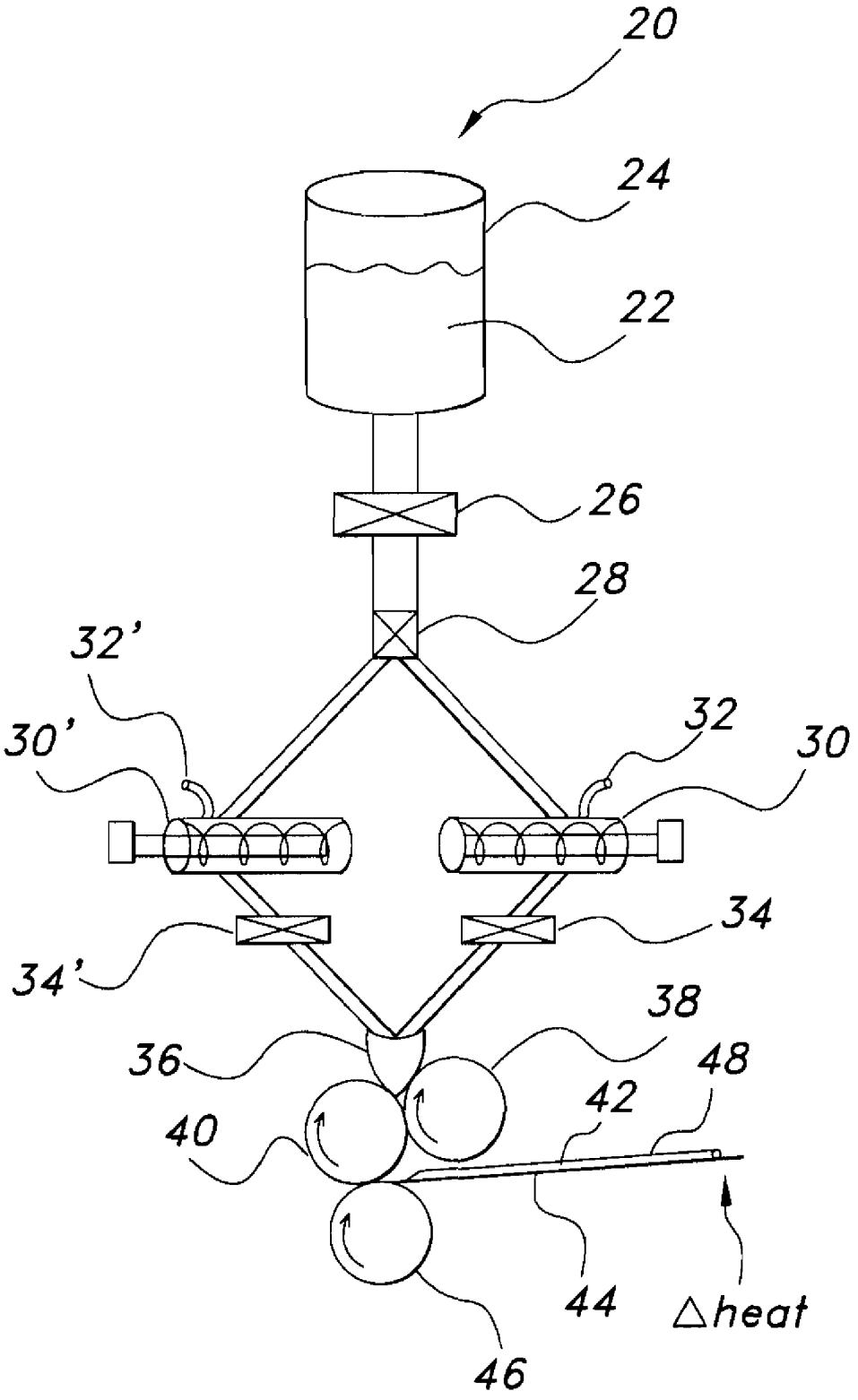


FIG. 6

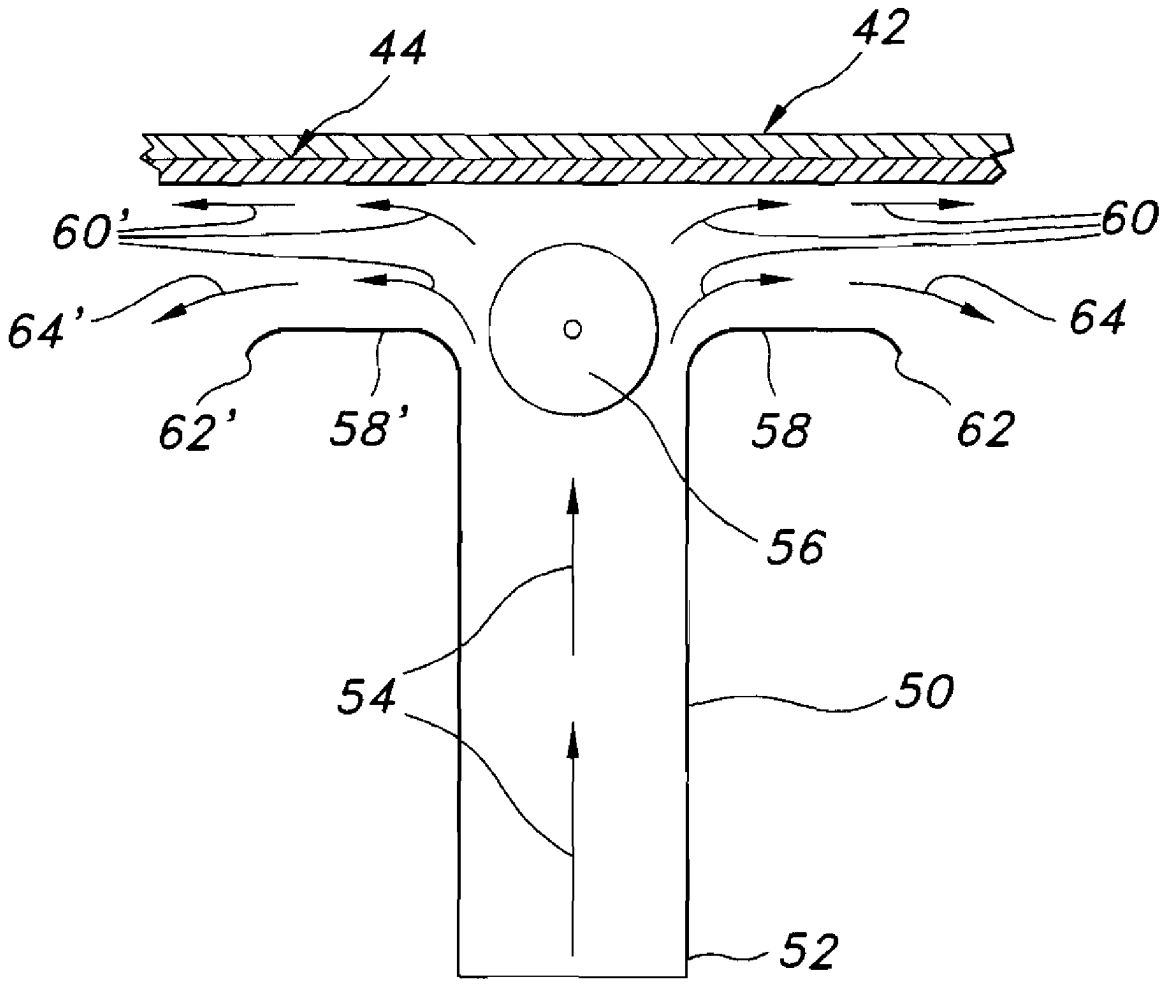


FIG. 7

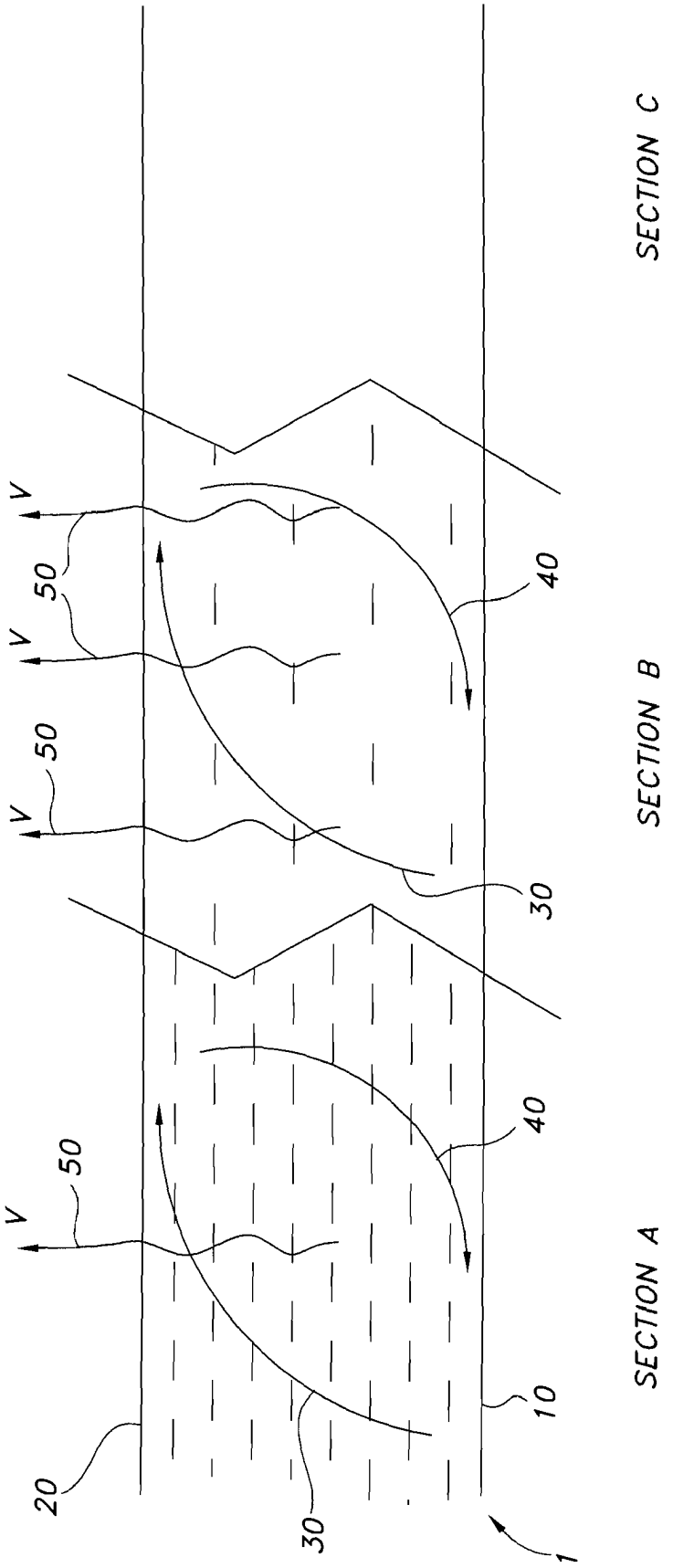


FIG. 8

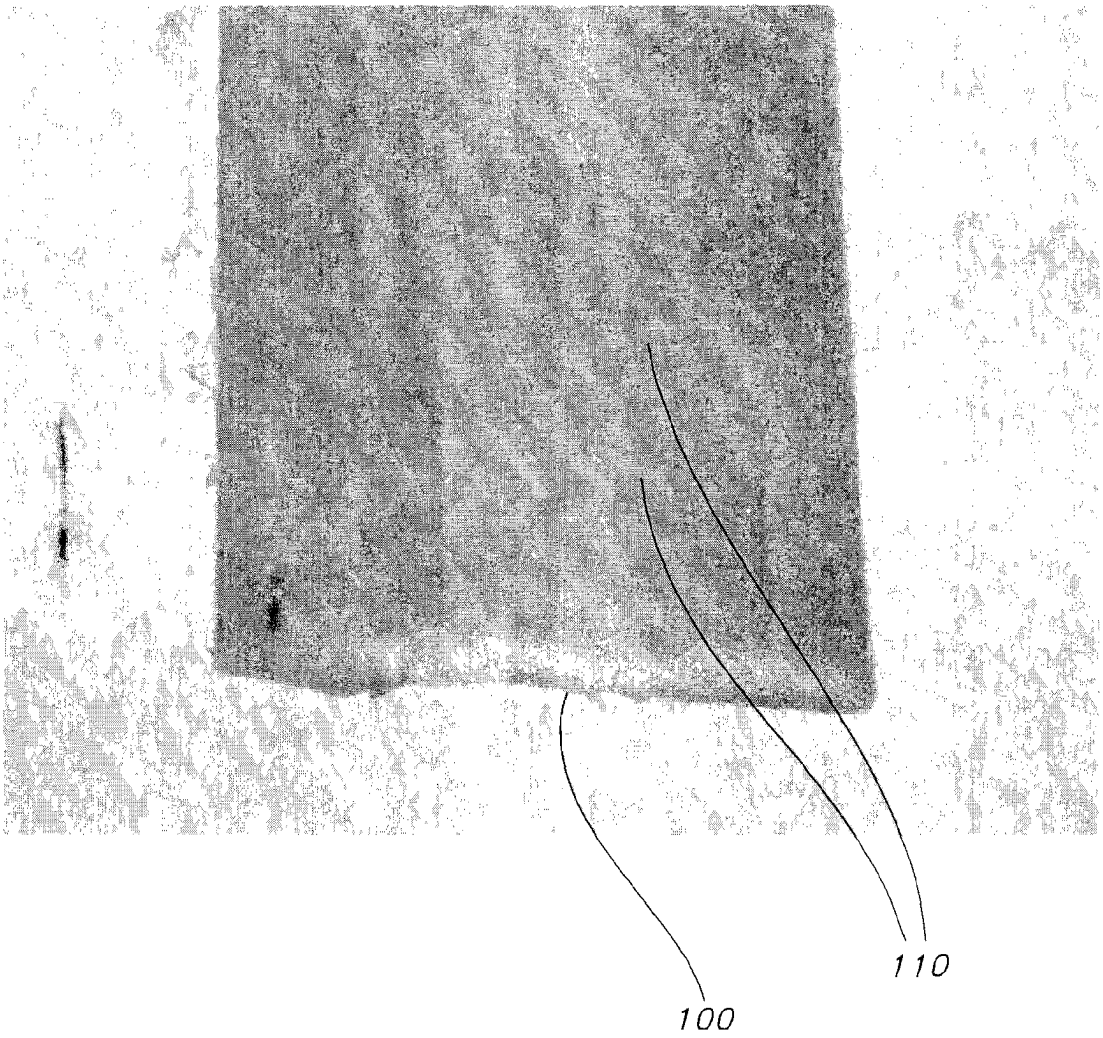


FIG. 9

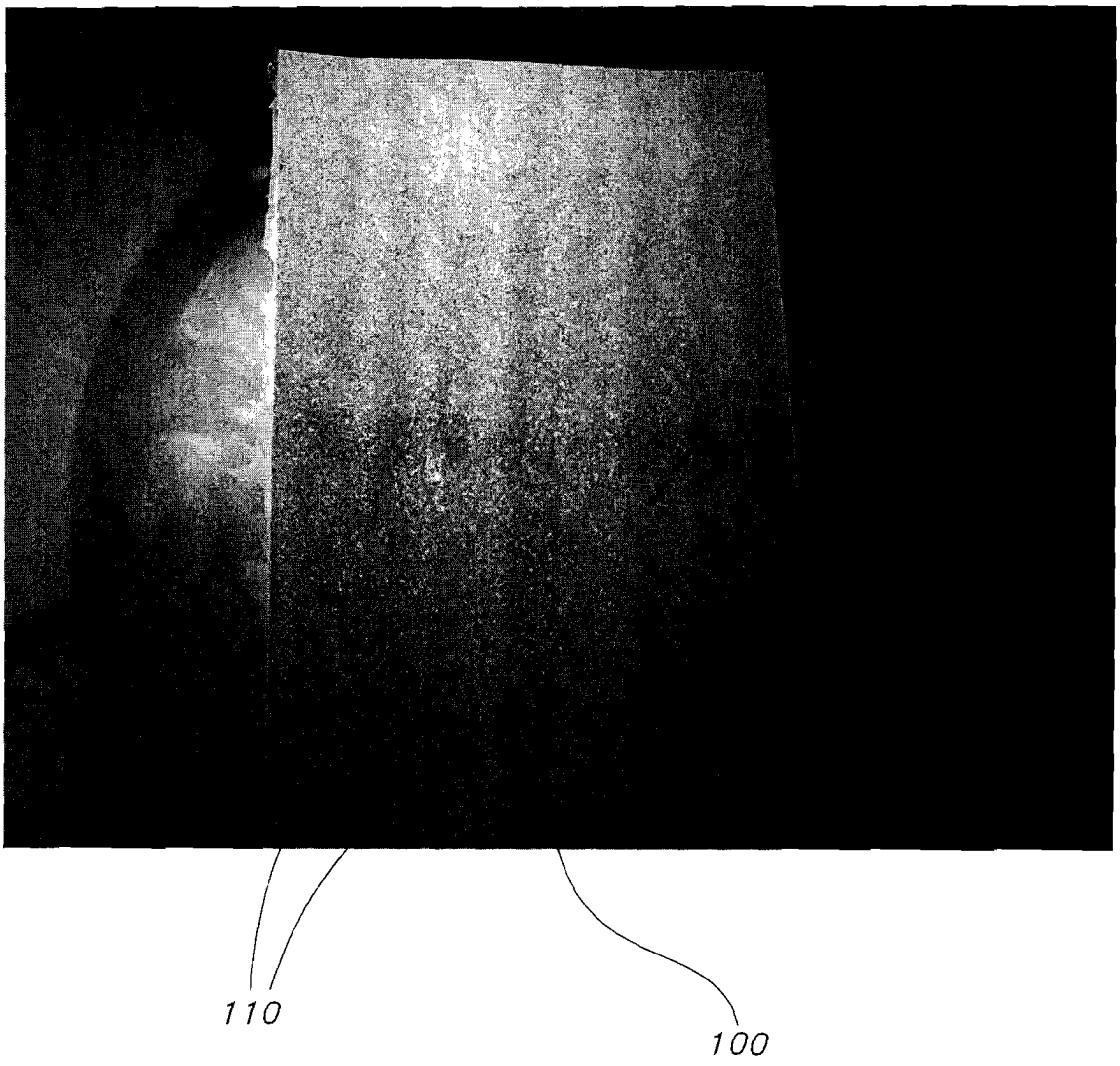


FIG. 10

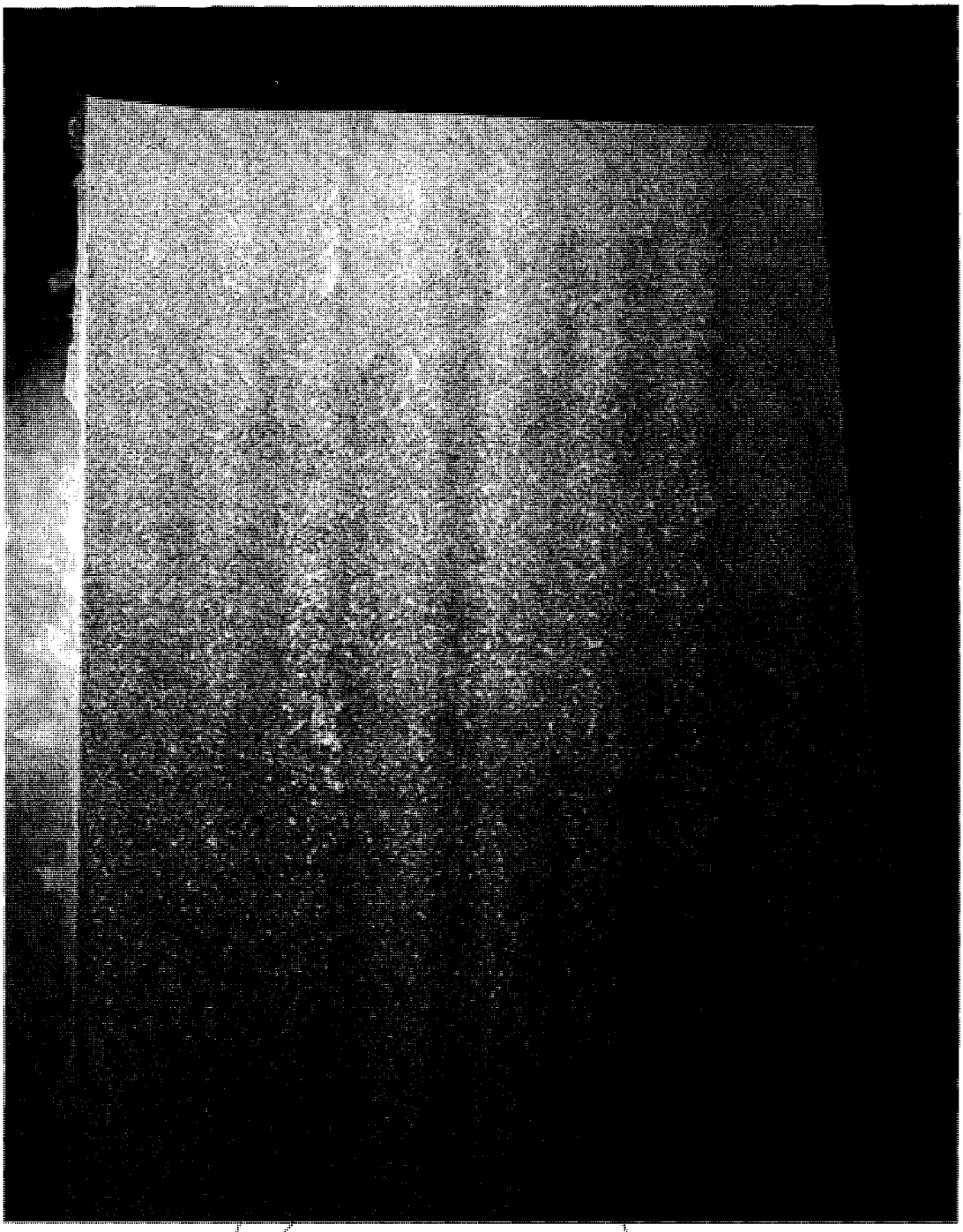


FIG. 11

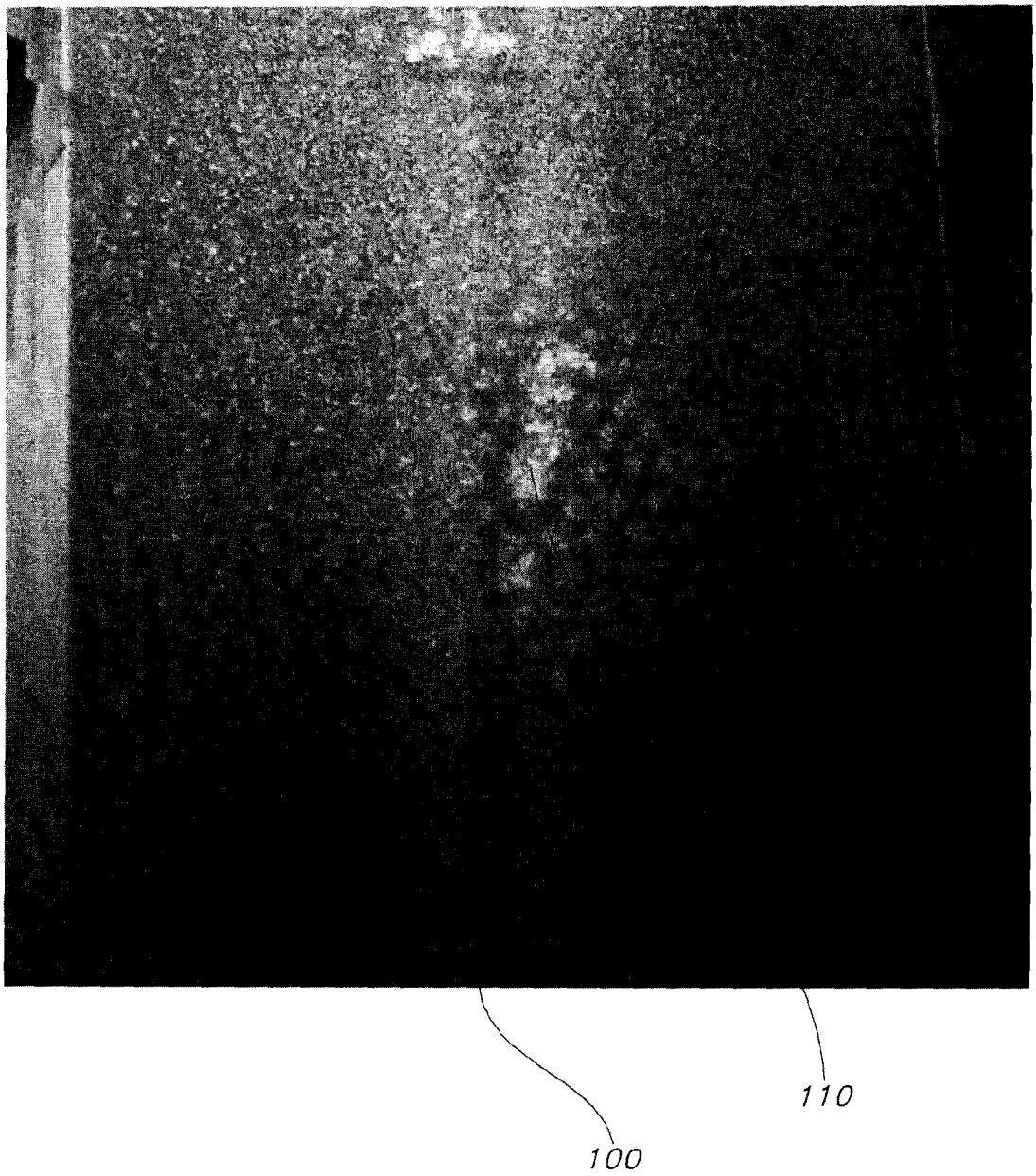


FIG. 12

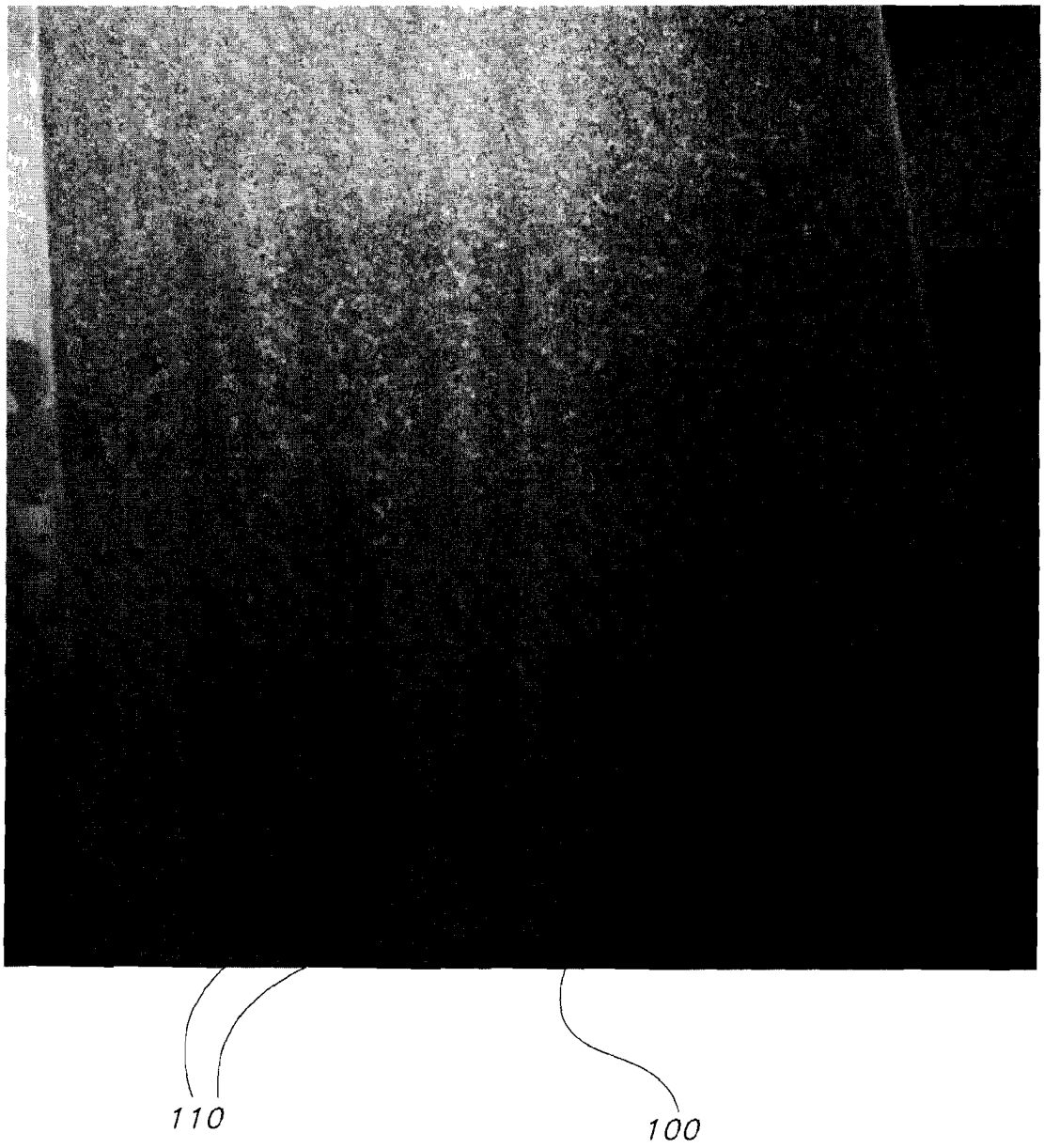


FIG. 13

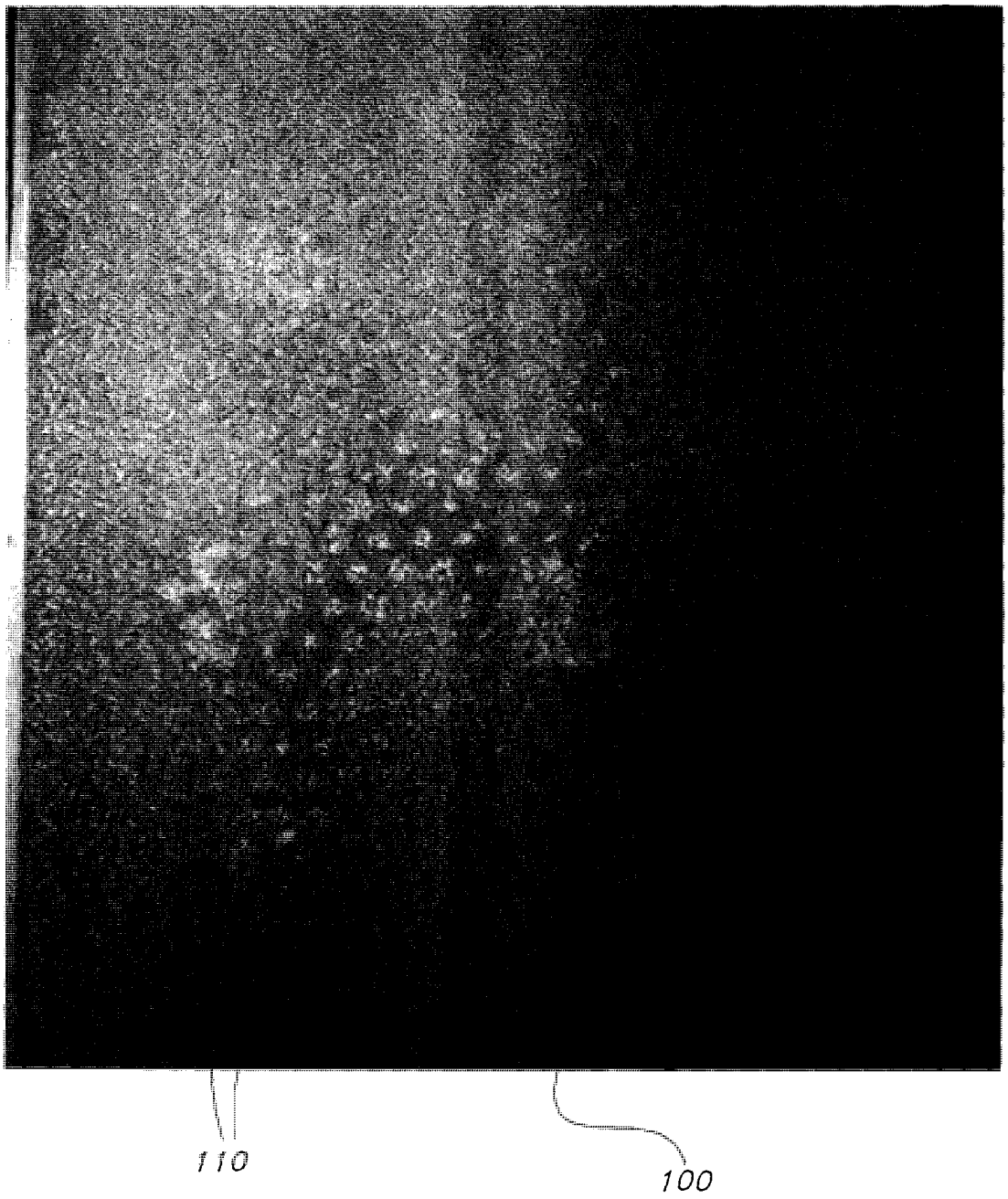


FIG. 14

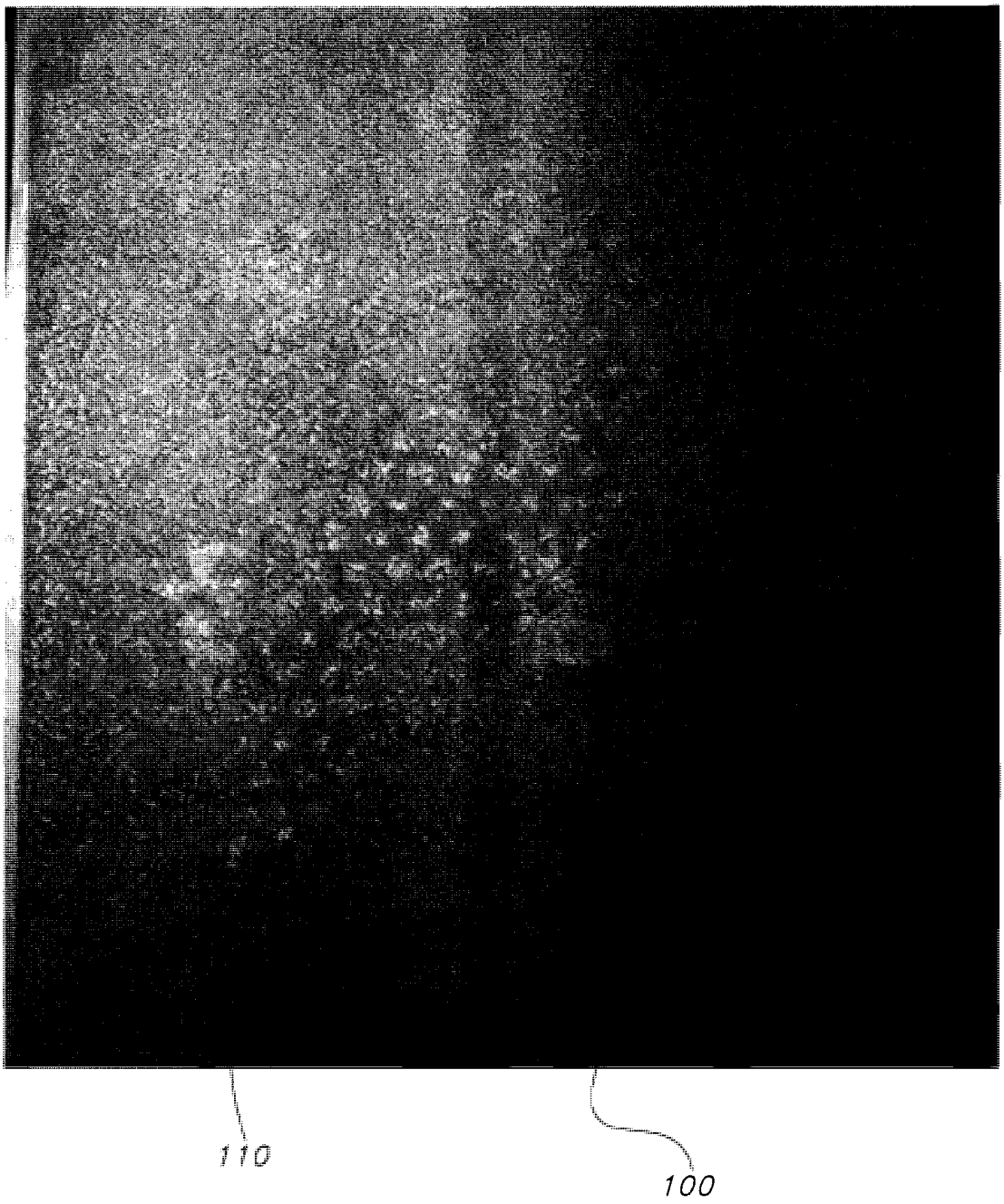


FIG. 15

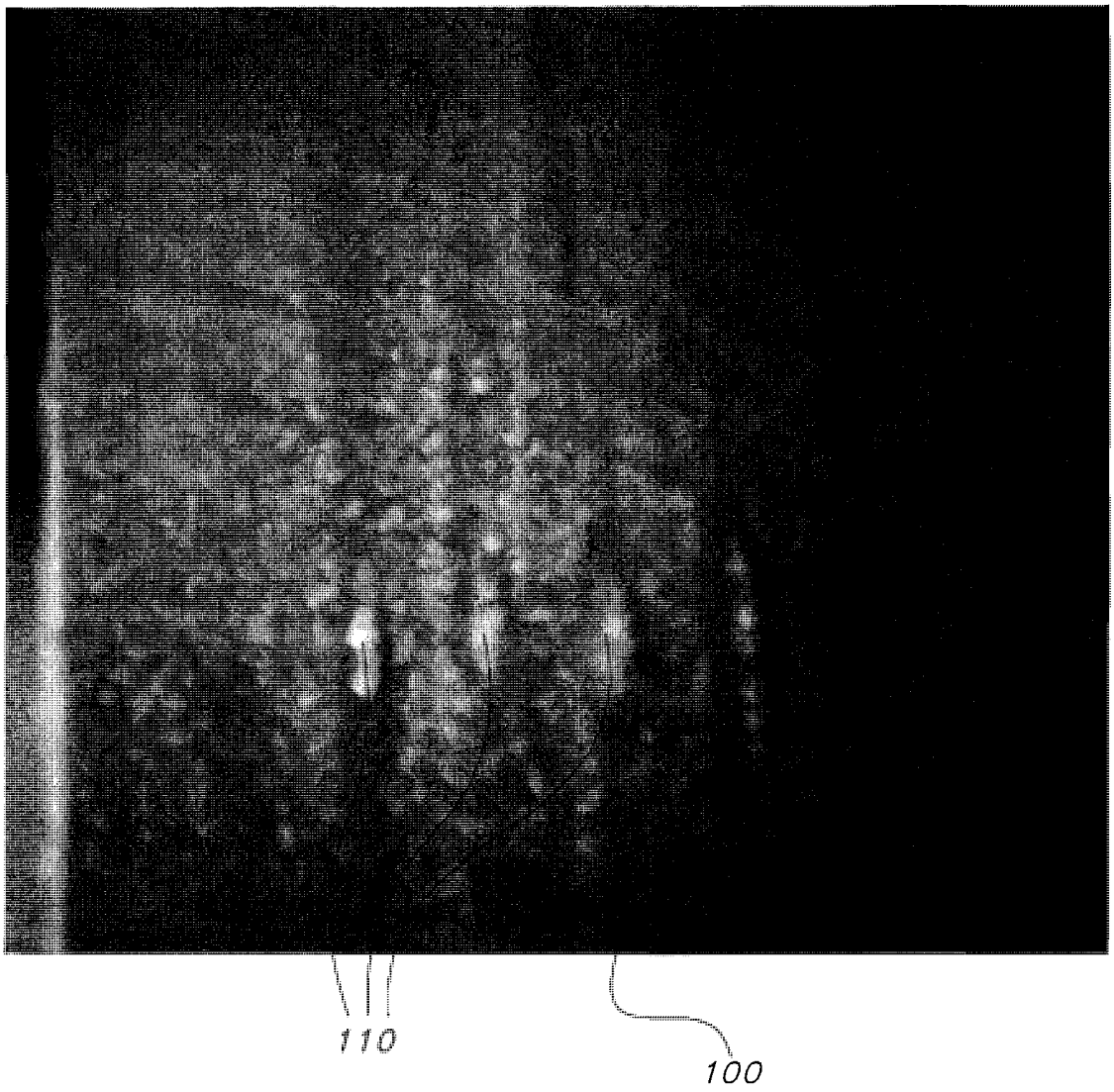


FIG. 16

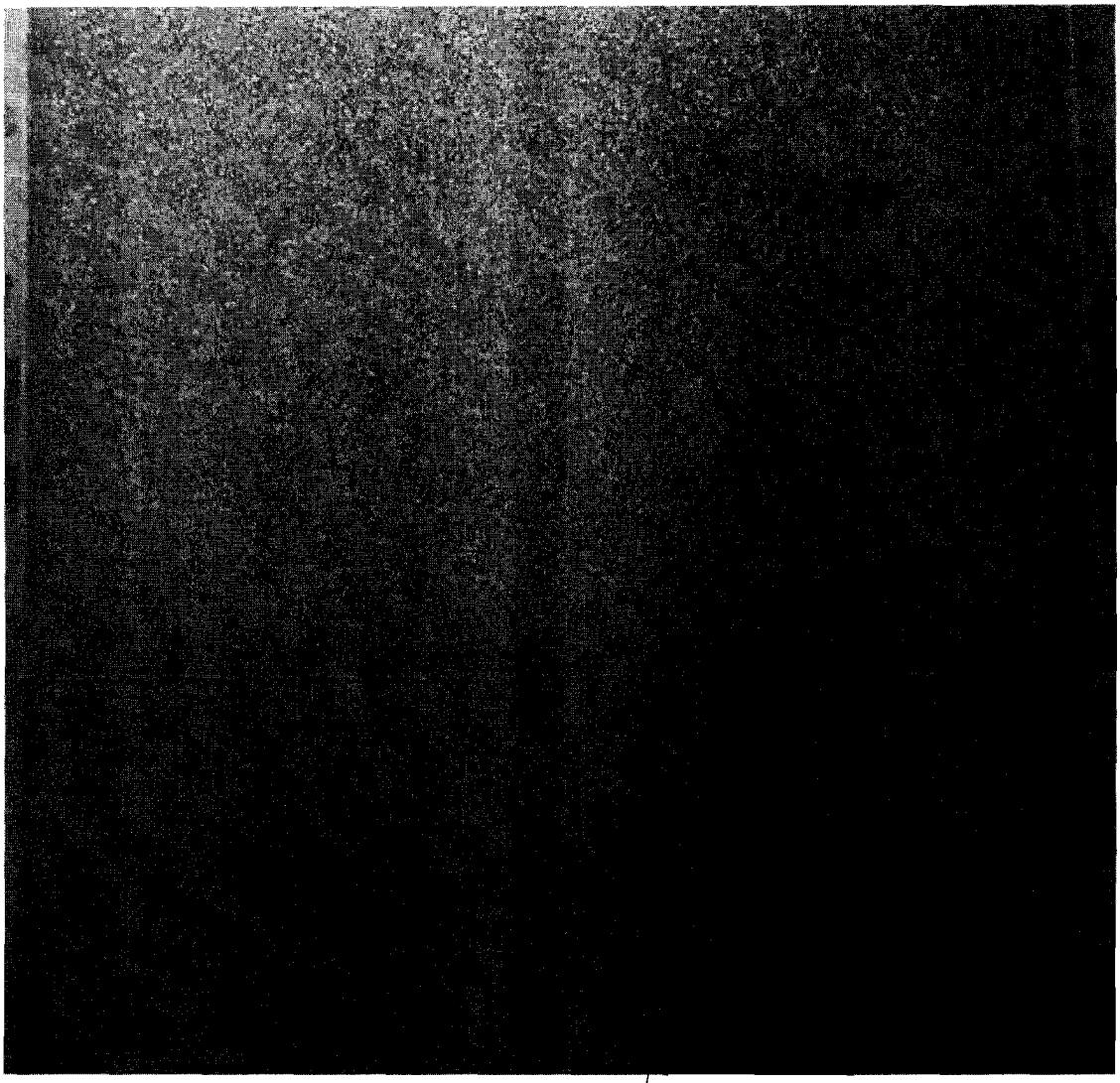


FIG. 17

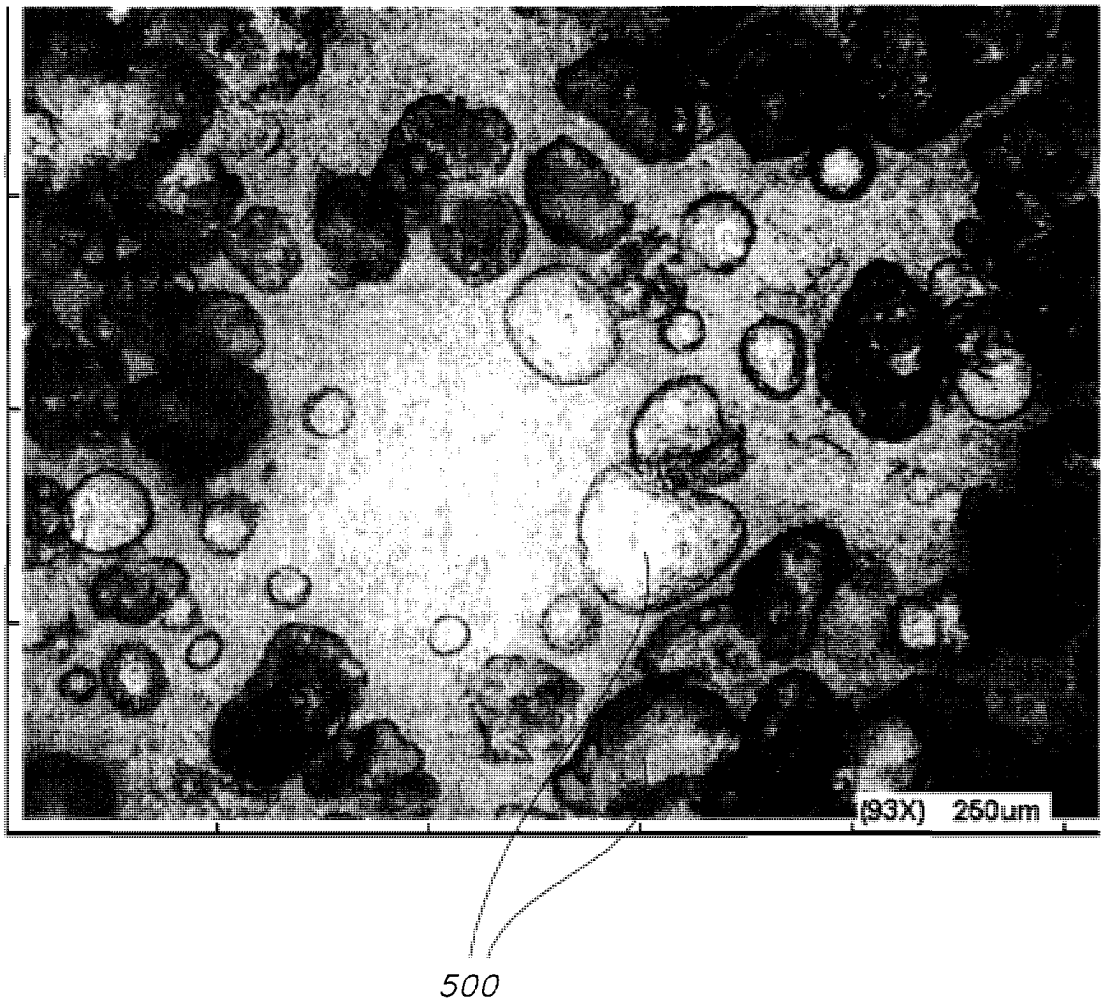


FIG. 18

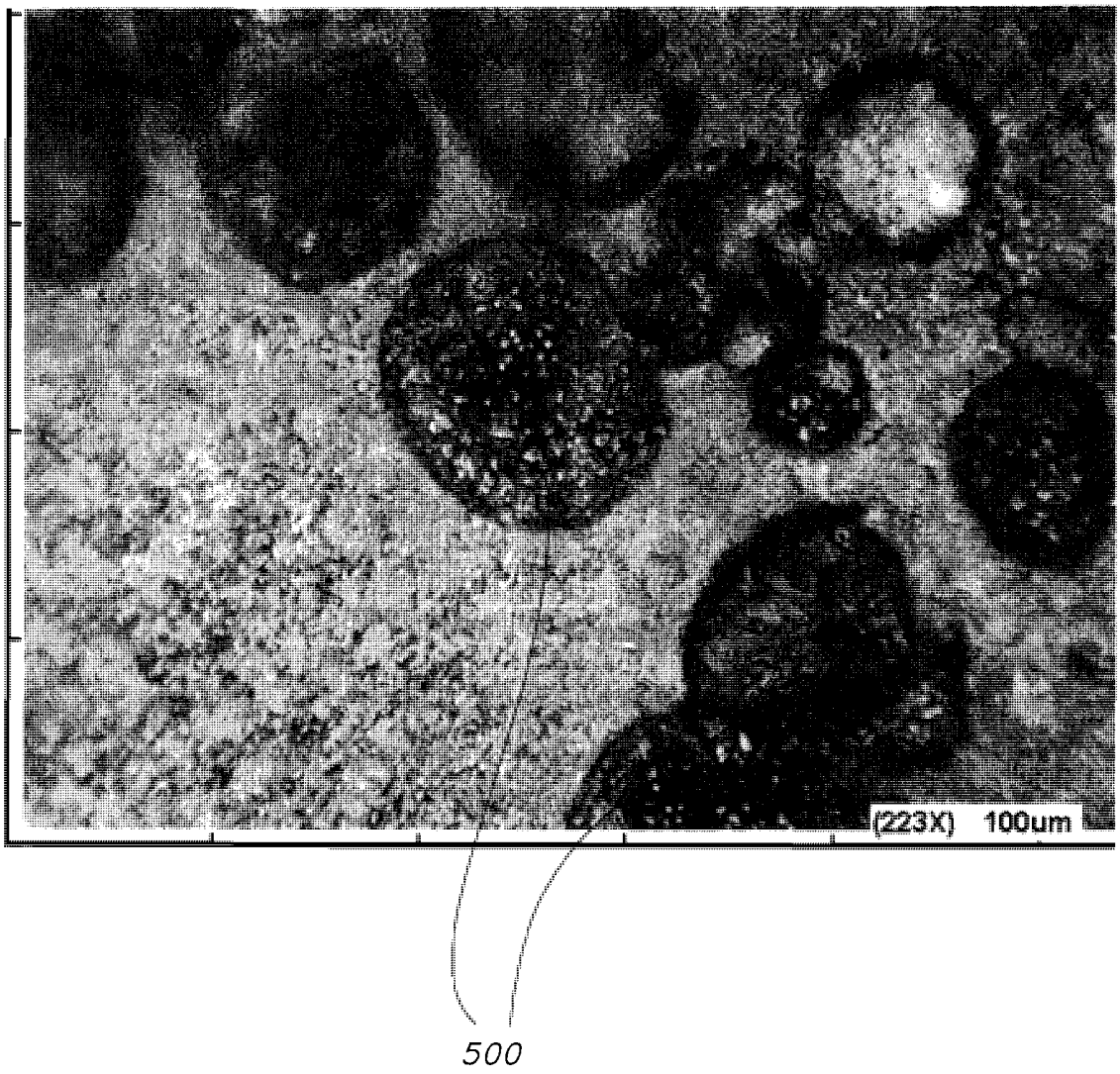


FIG. 19

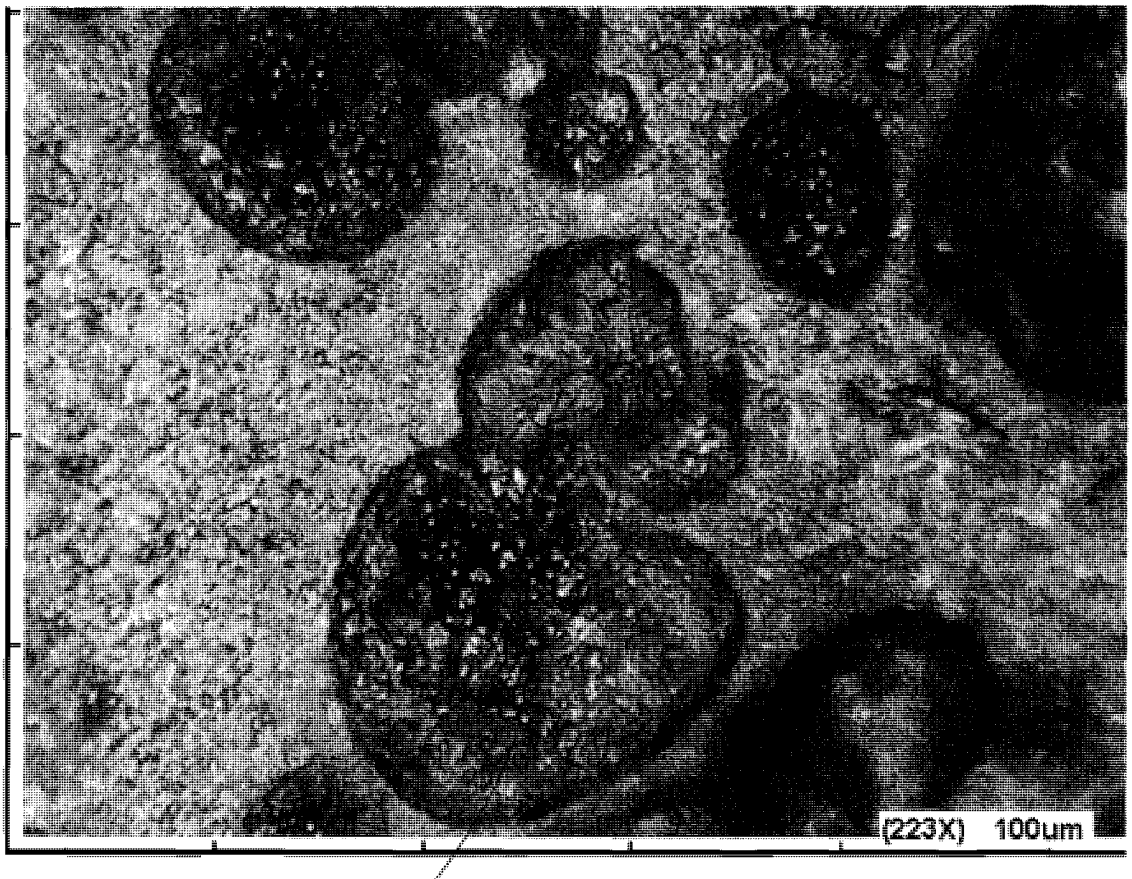


FIG. 20

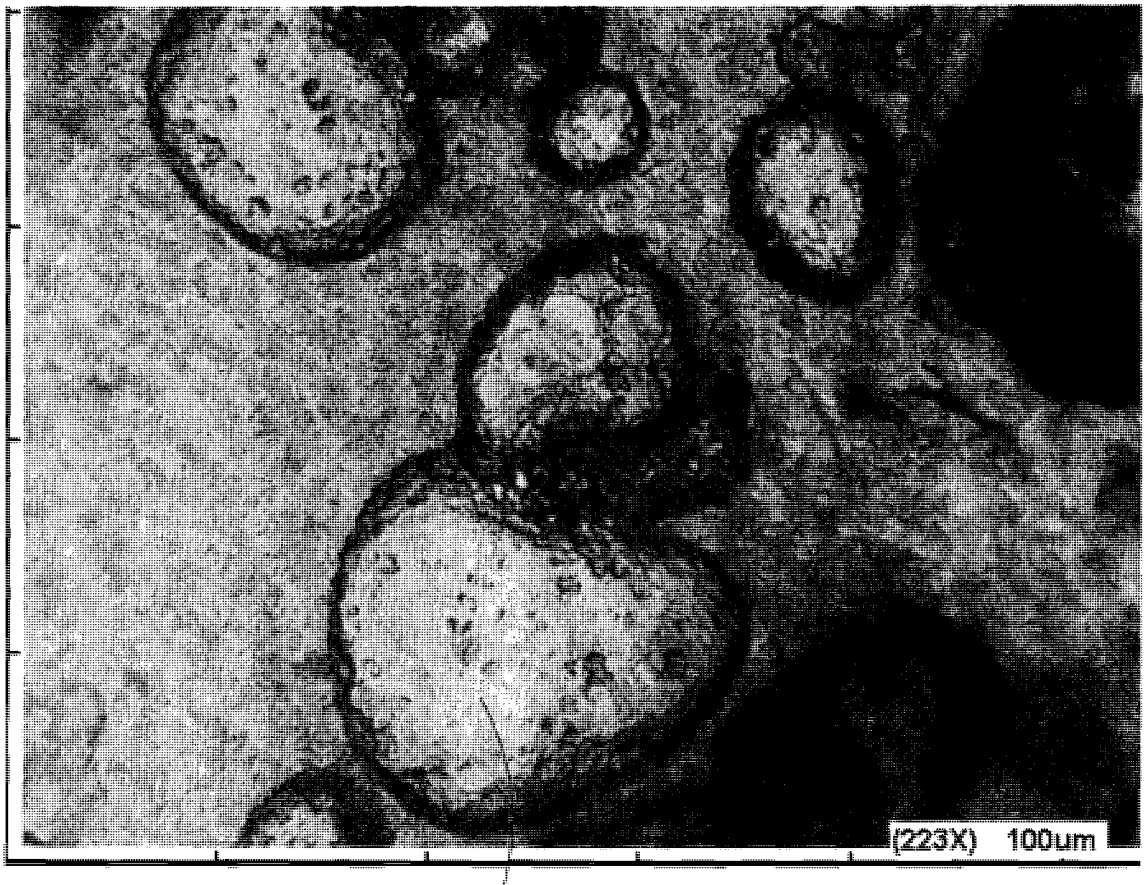


FIG. 21

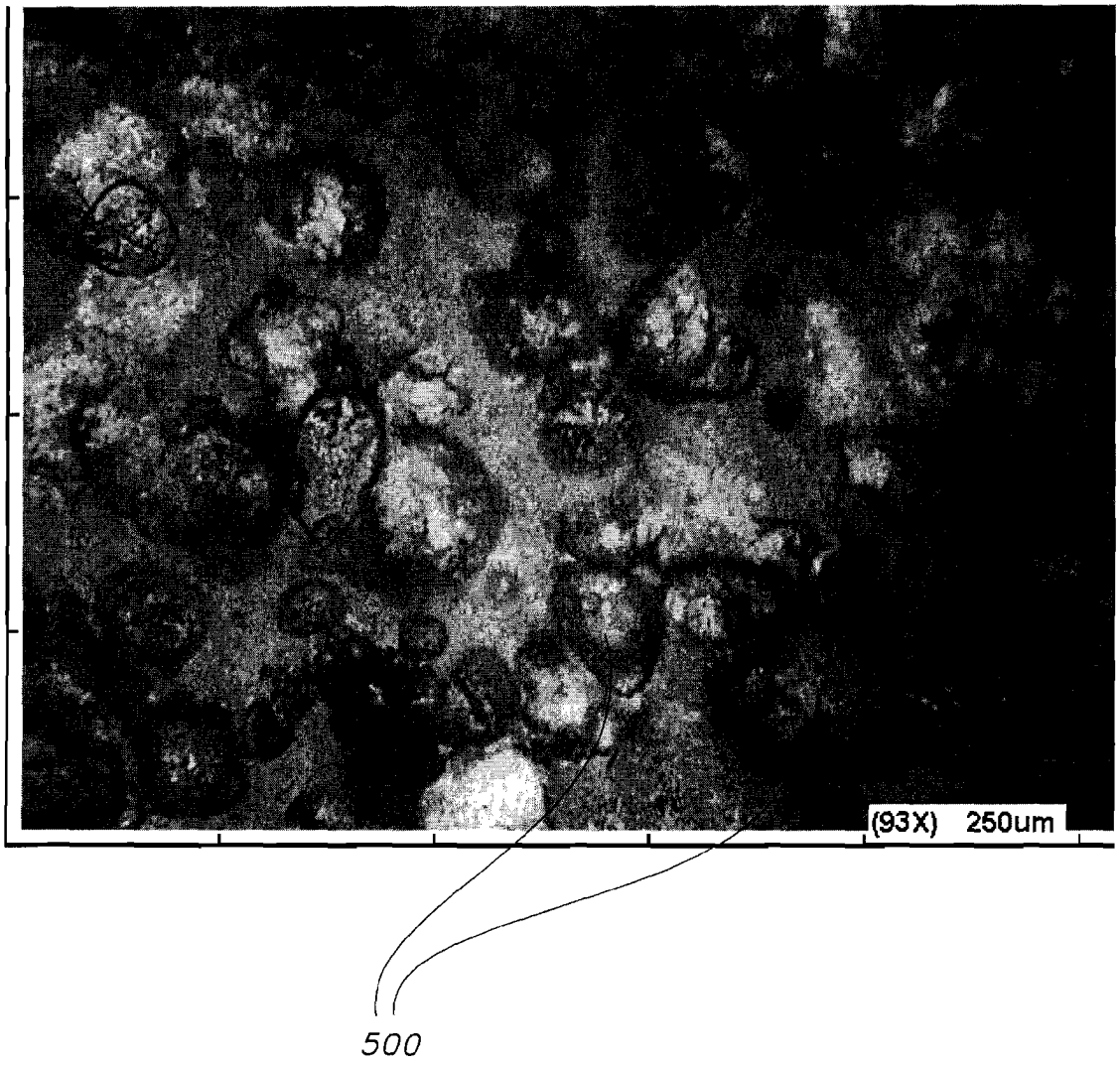


FIG. 22

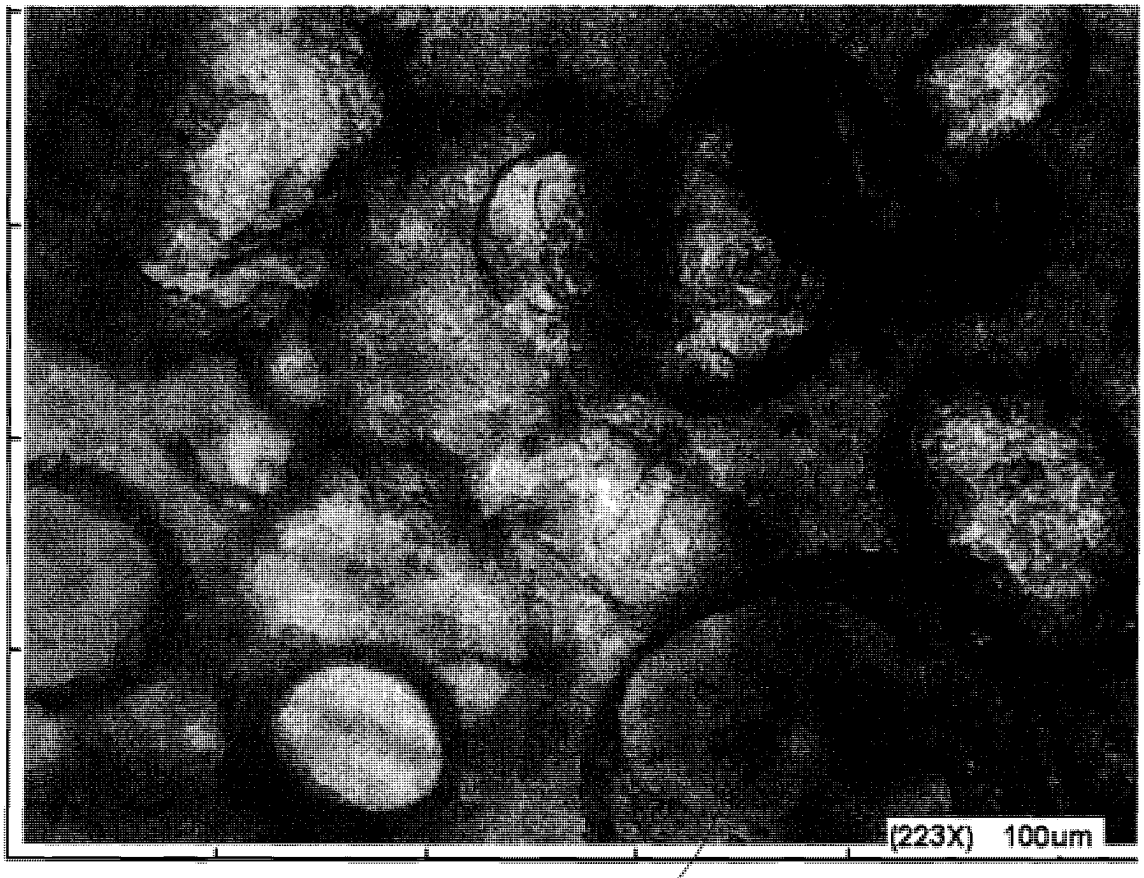


FIG. 23

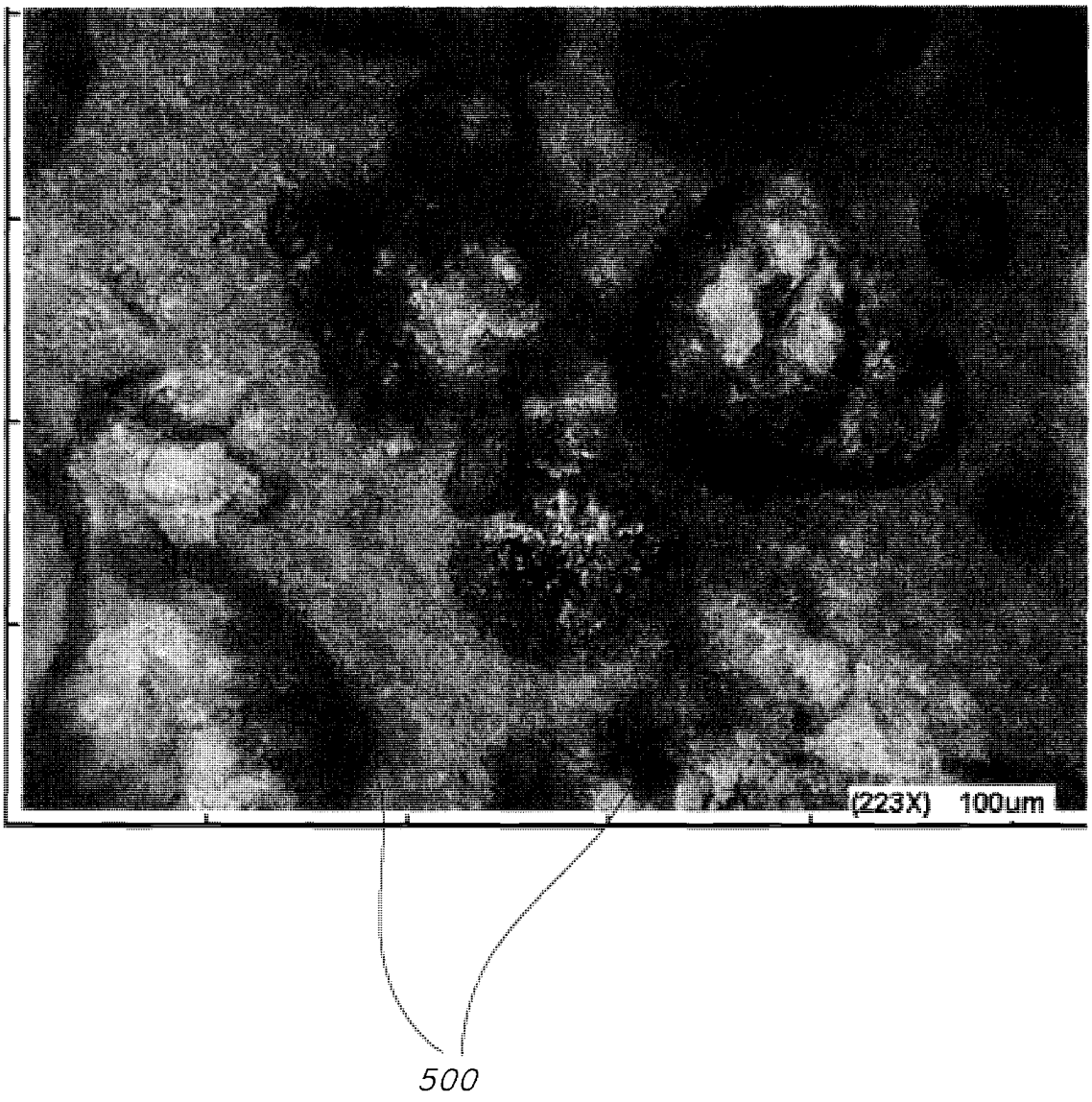


FIG. 24

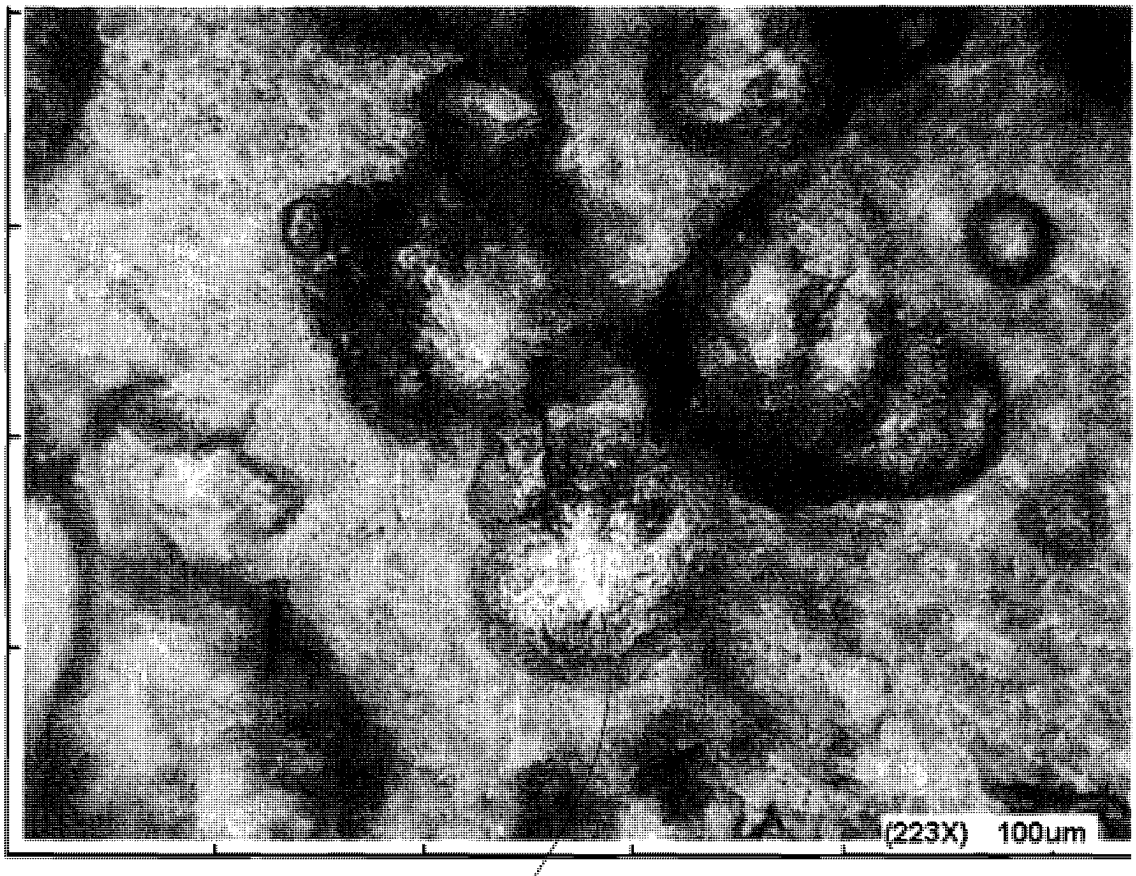


FIG. 25

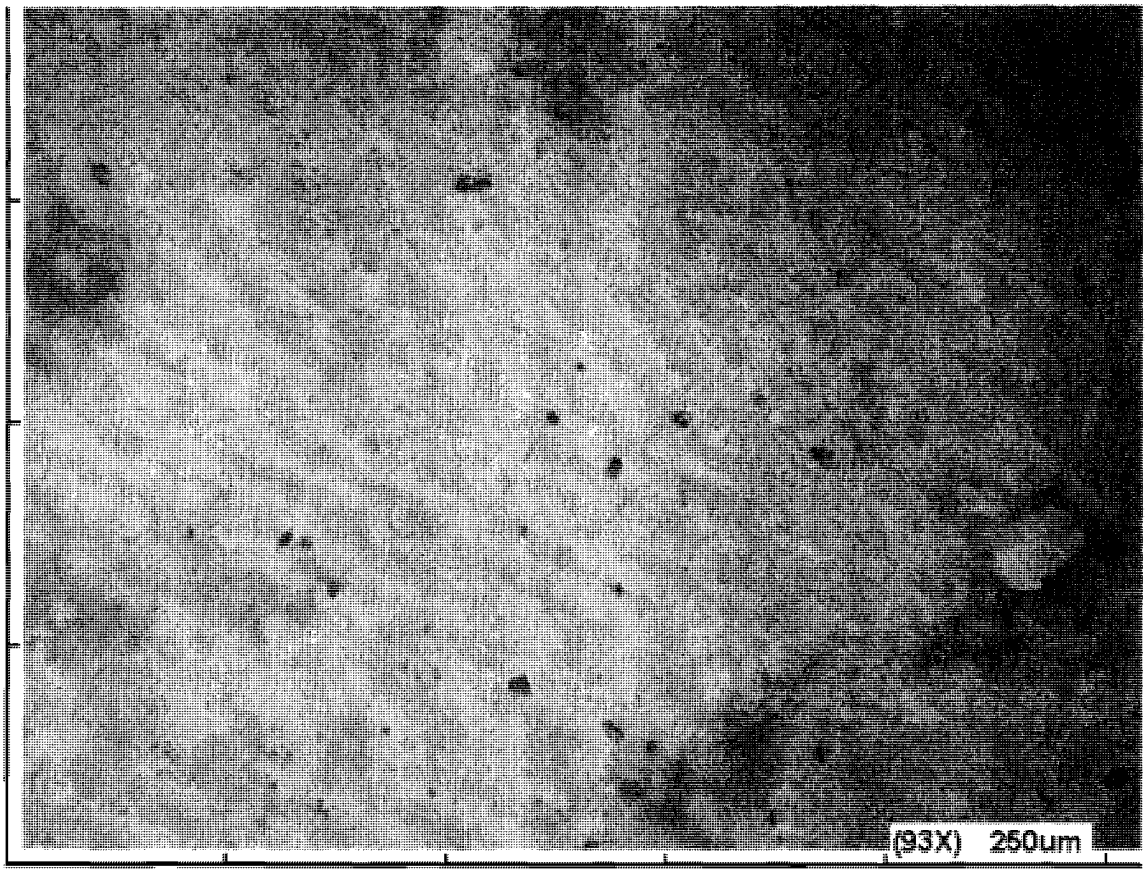


FIG. 26

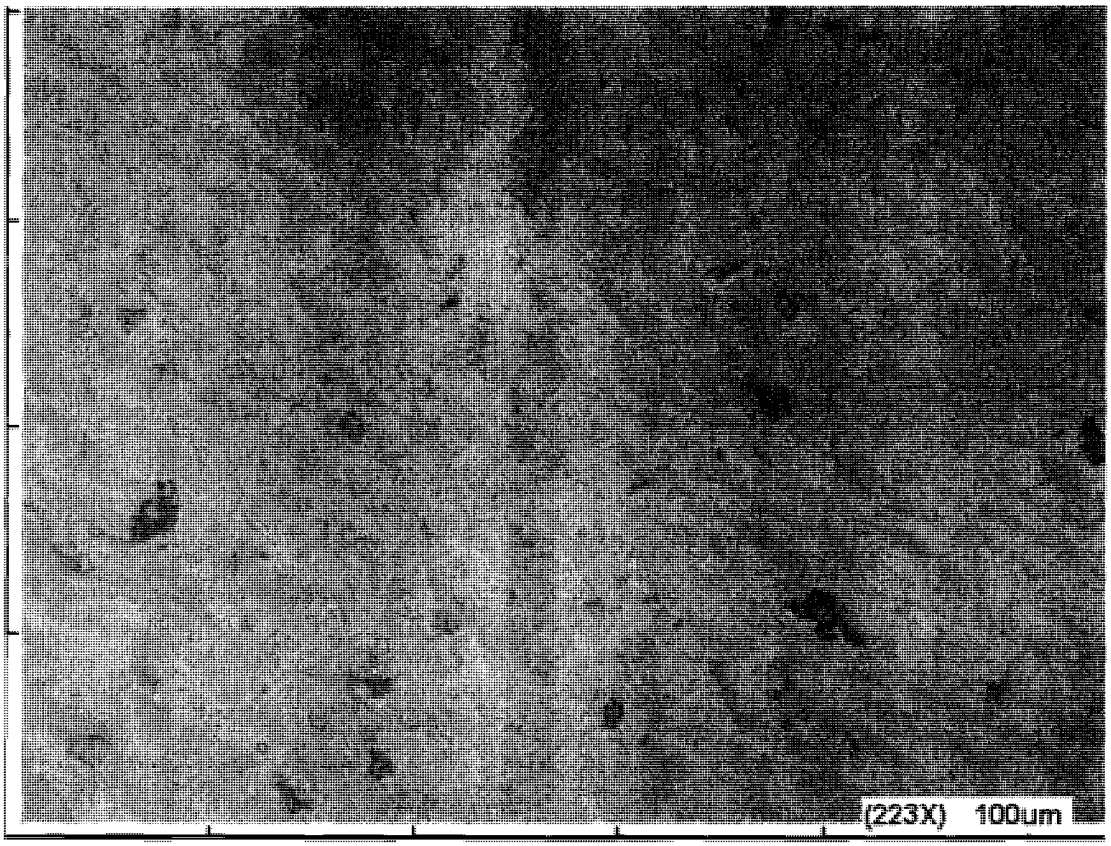


FIG. 27

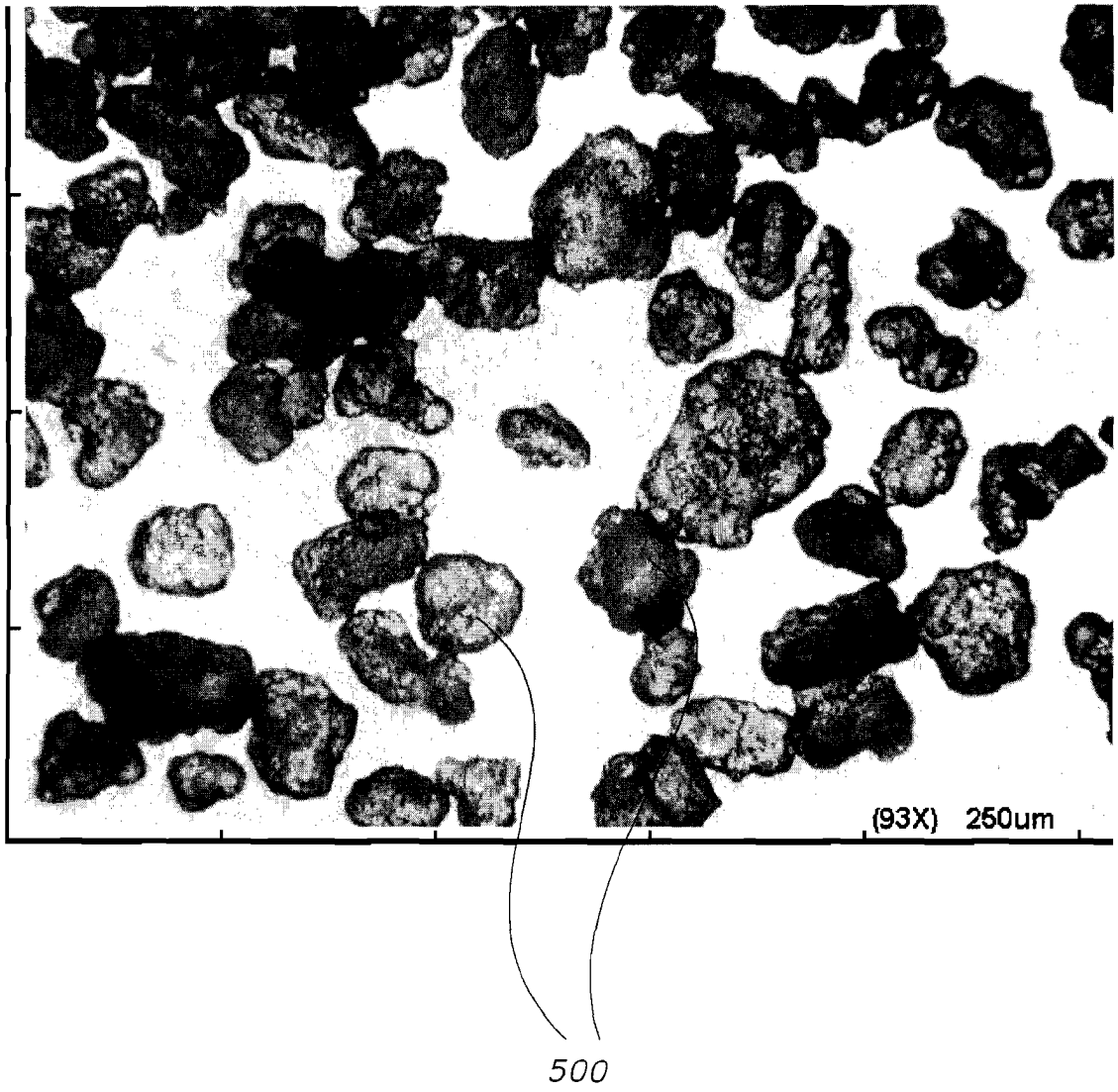


FIG. 28

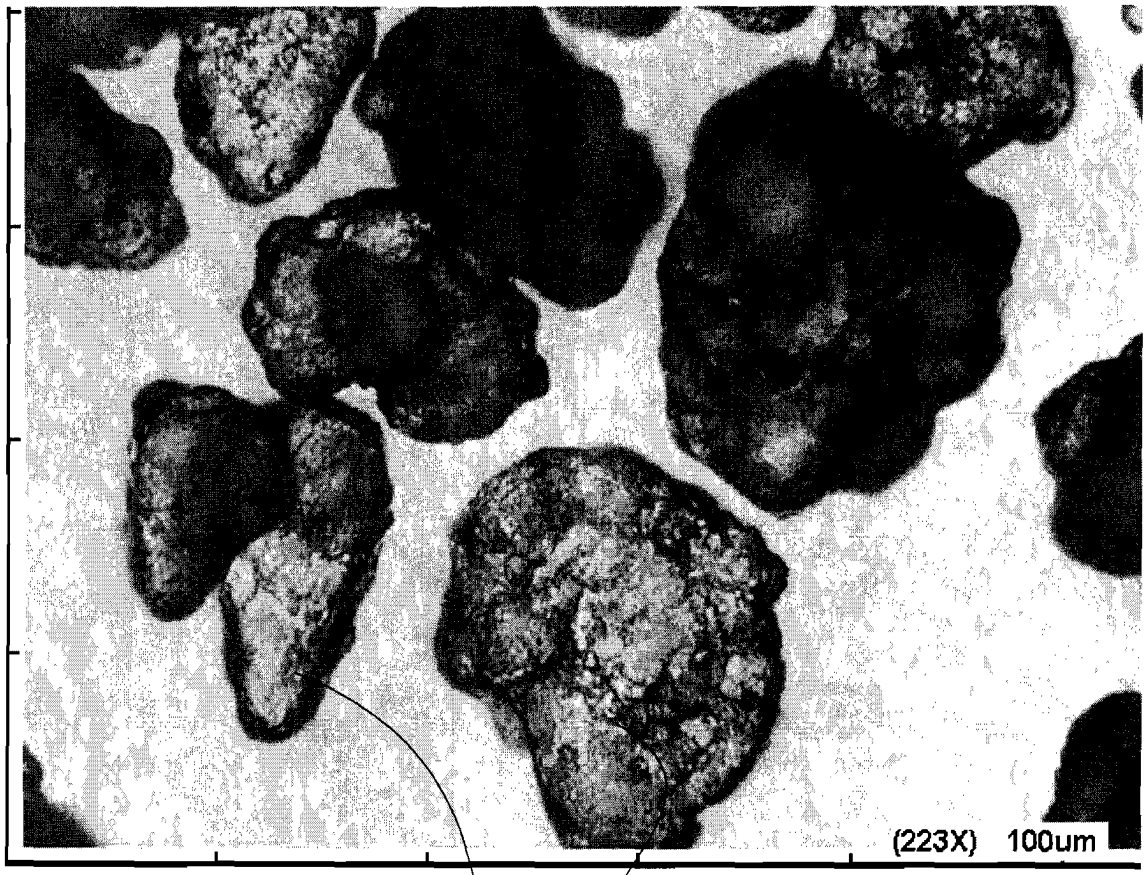


FIG. 29

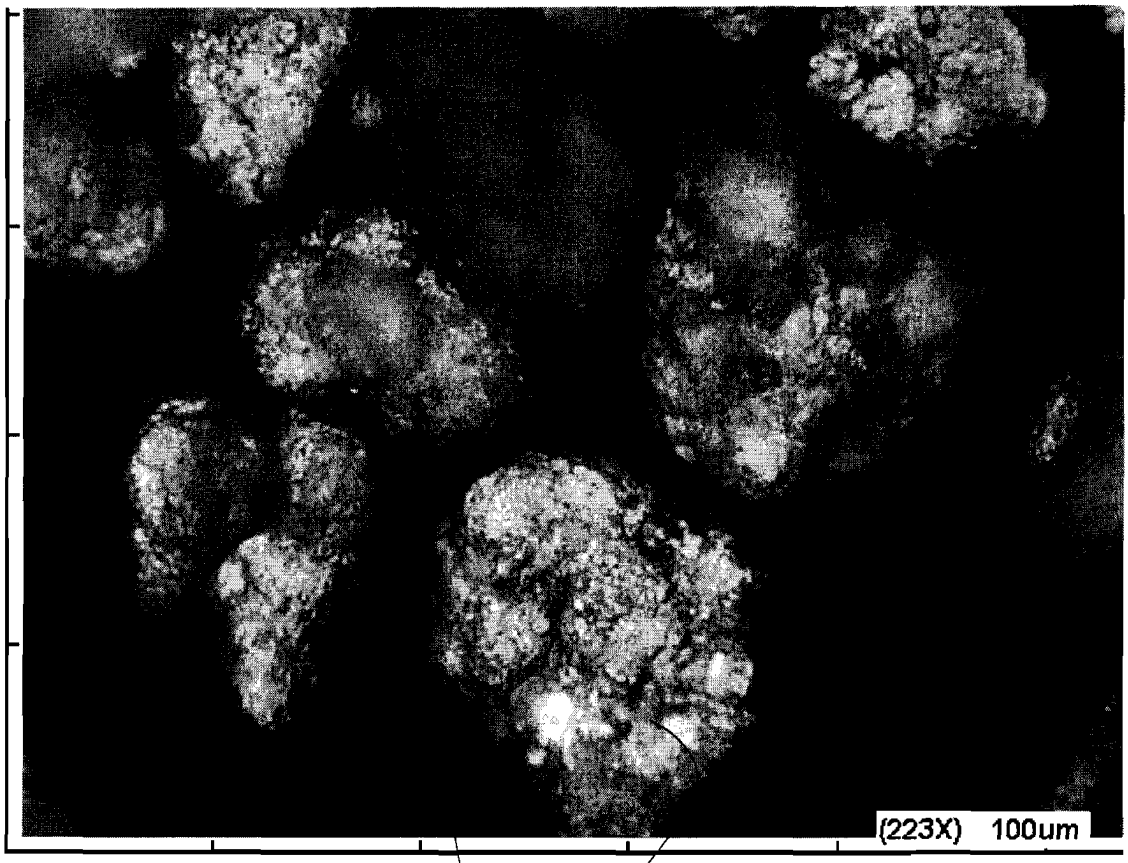


FIG. 30

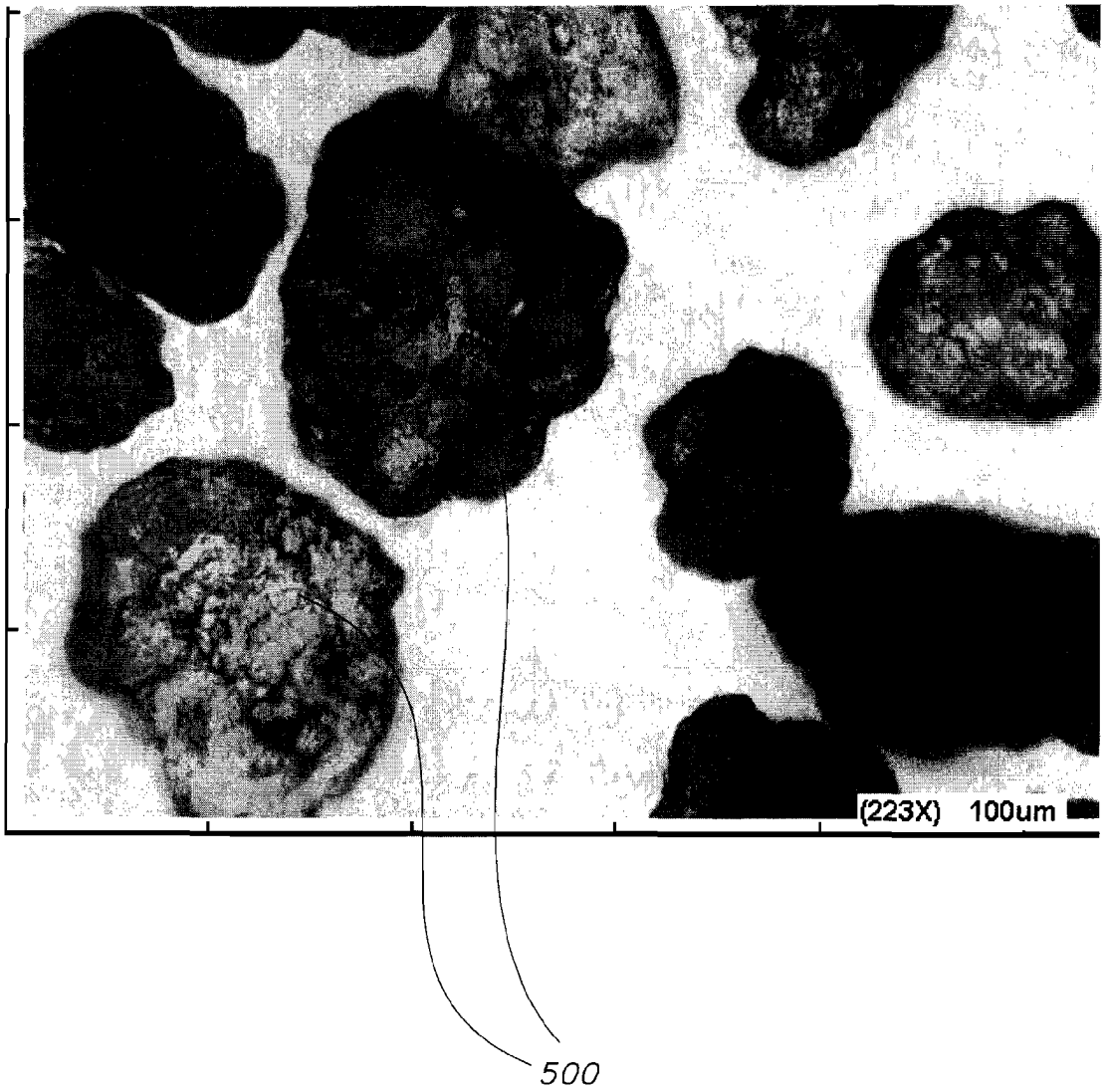
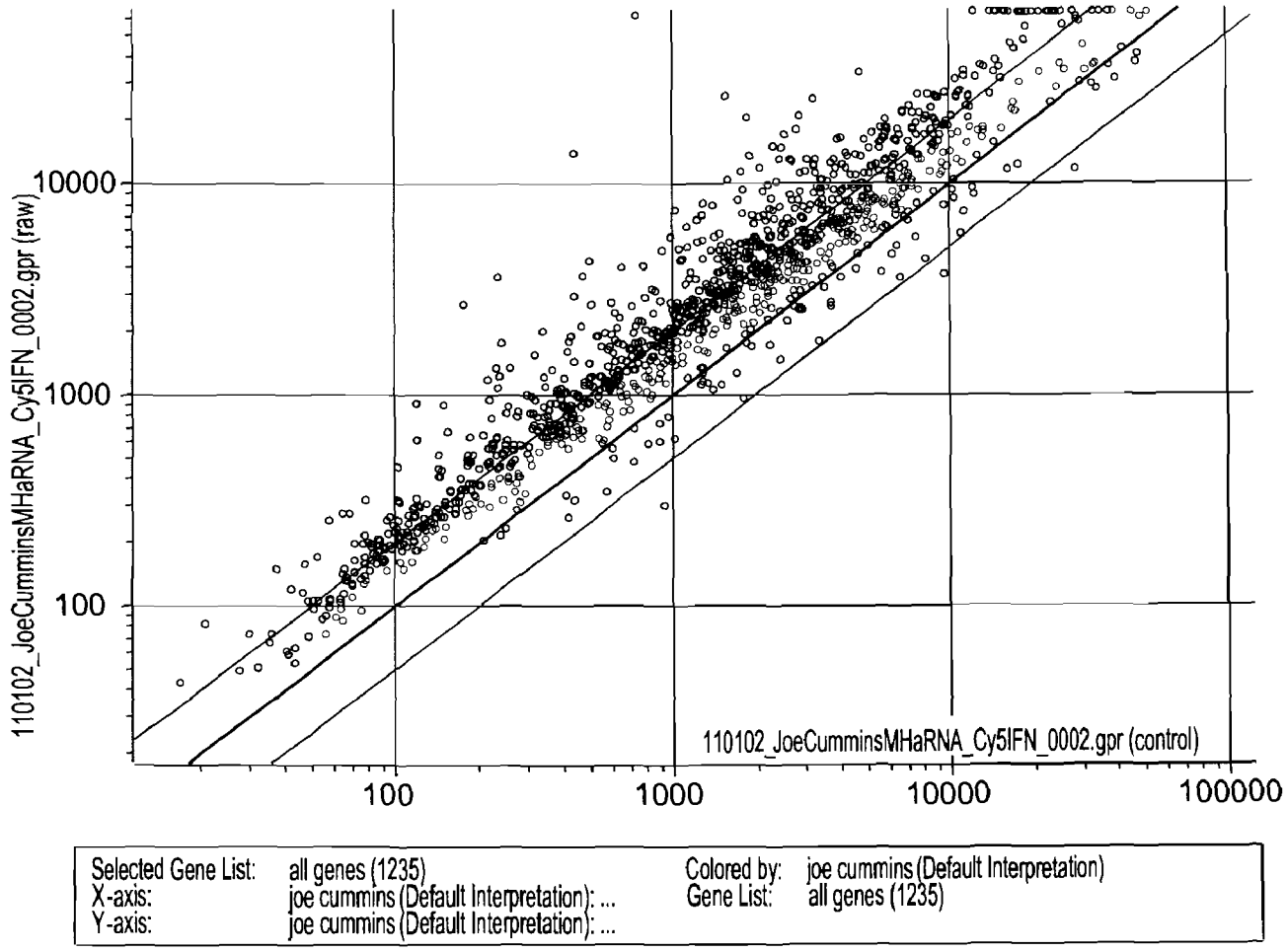


FIG. 31



Normalized to GAPDH, most of the ISGs are induced.

FIG. 32

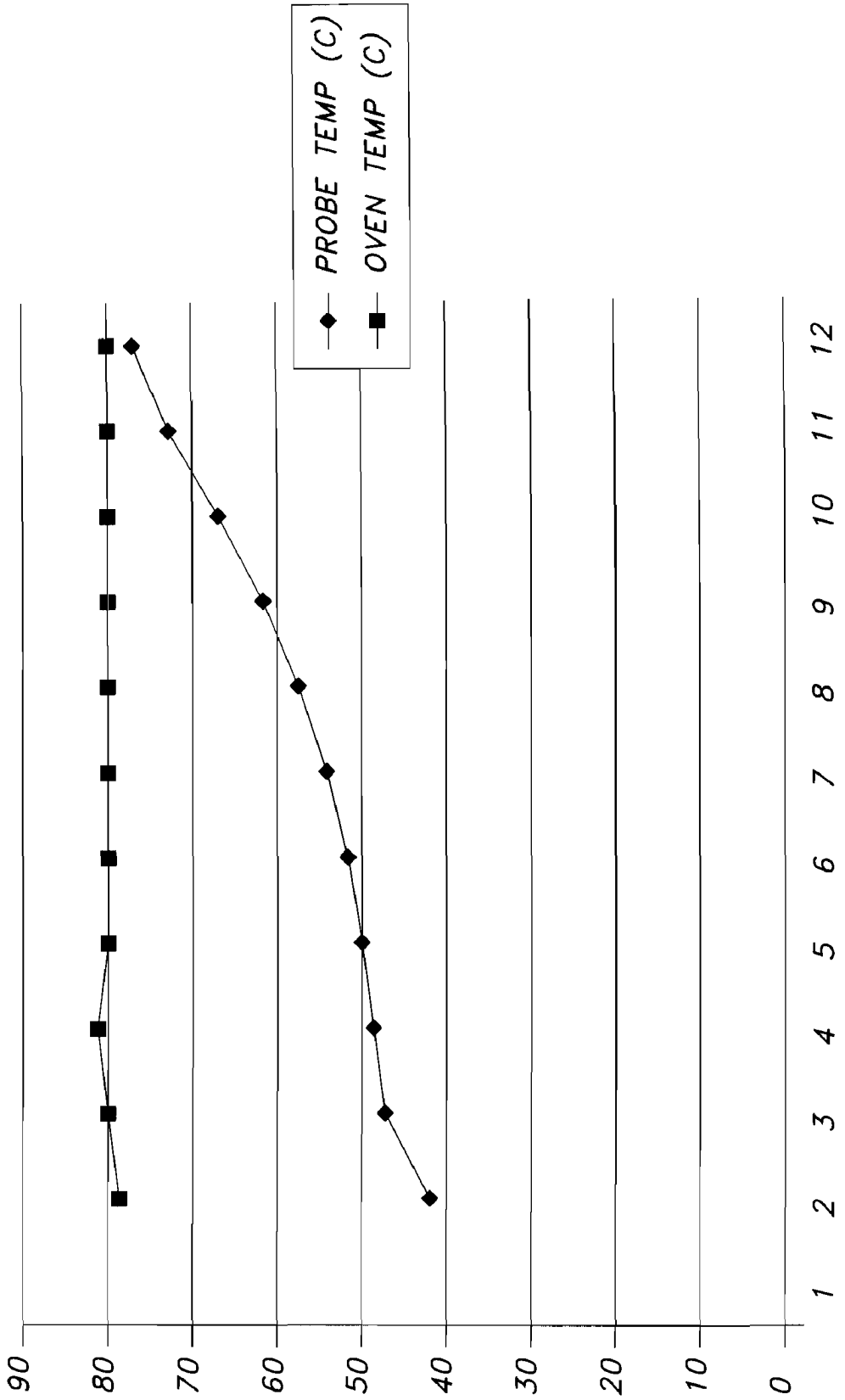


FIG. 33

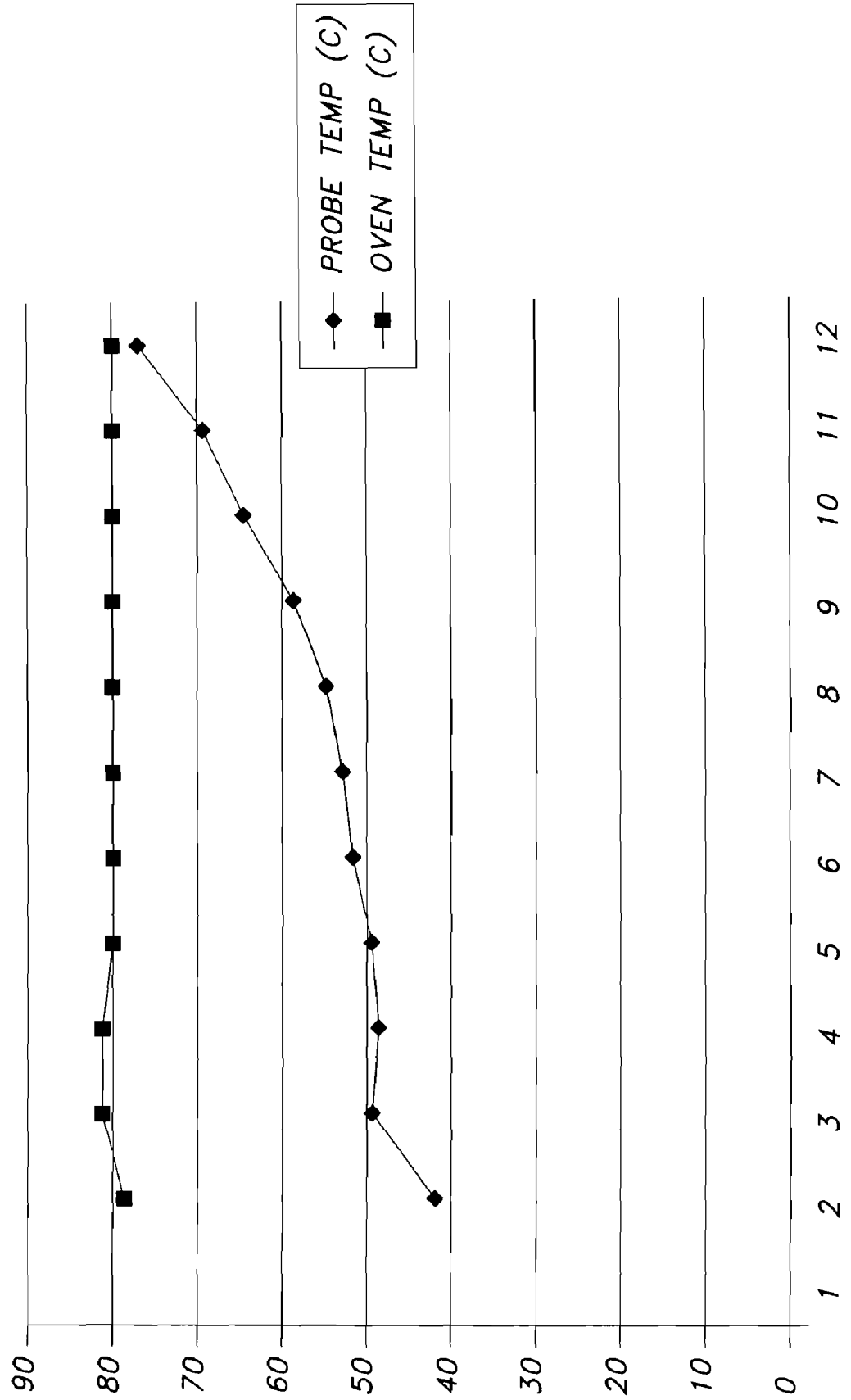


FIG. 34

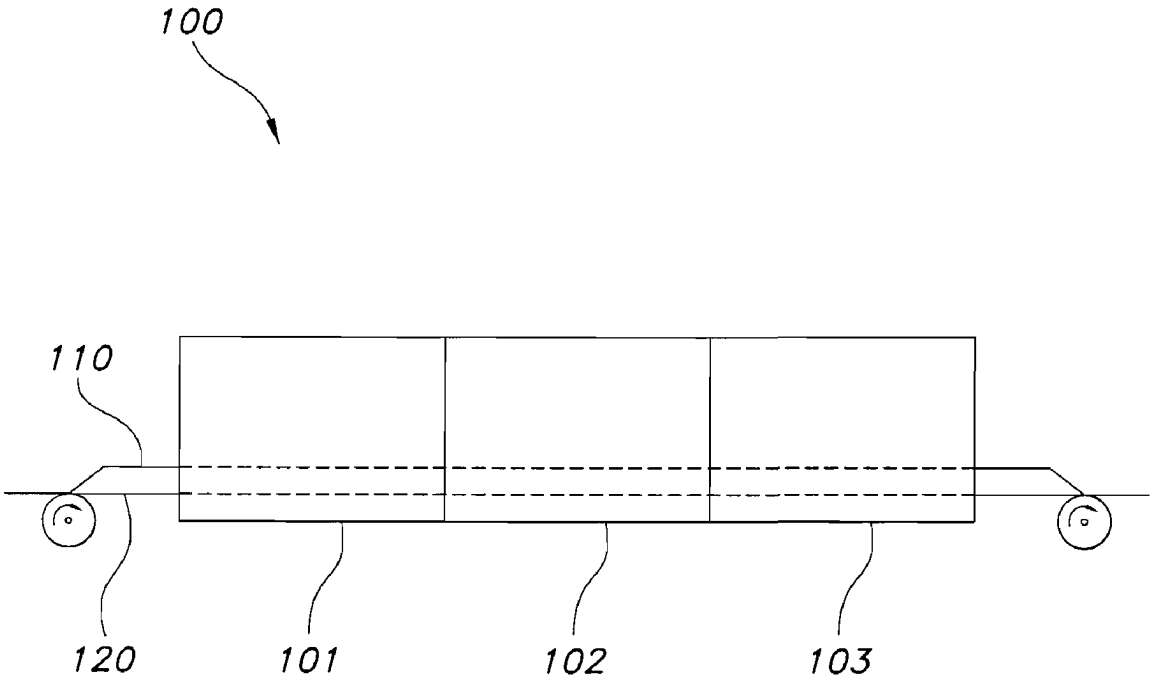


FIG. 35

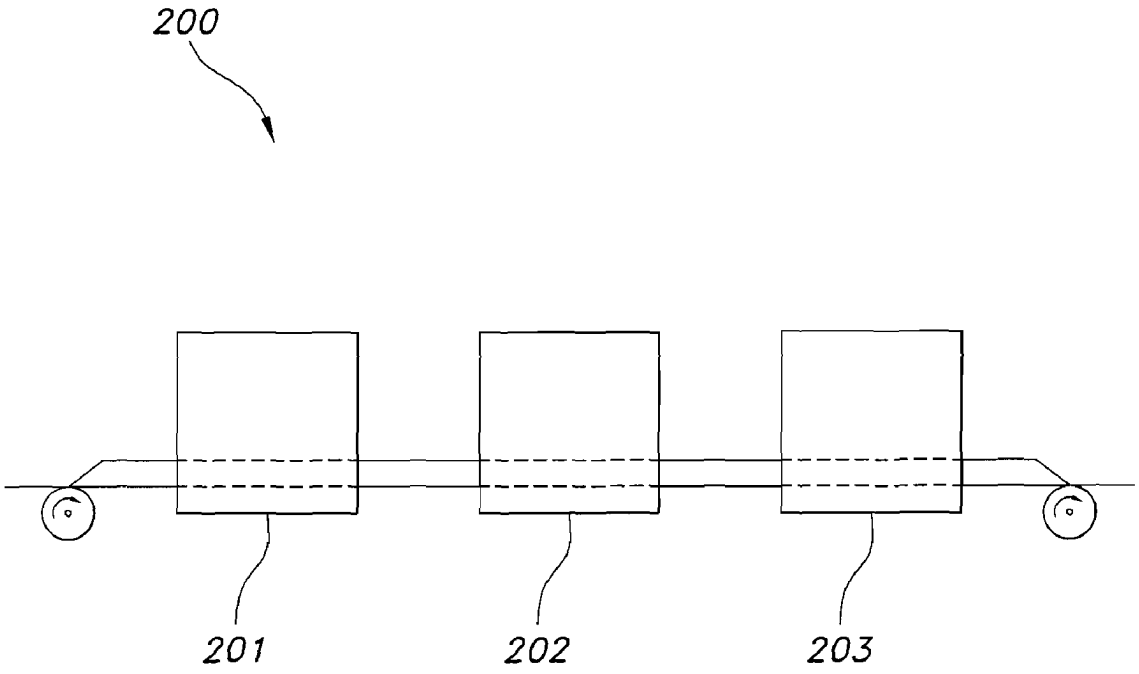


FIG. 36

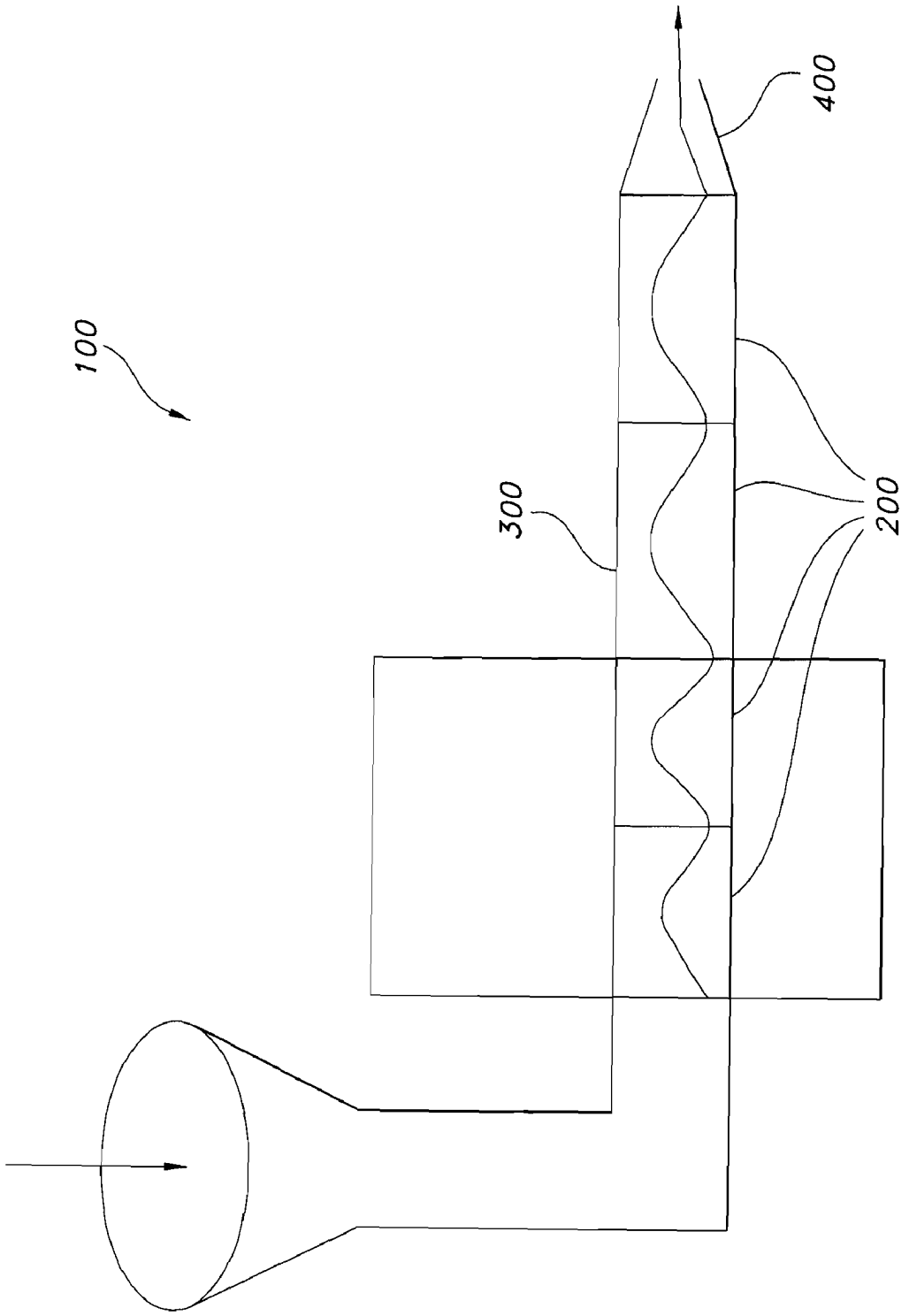


FIG. 37

FIG. 38

Ex.	Polymer Component Reference	% Solids of solution	Viscosity (cp) at 5 rpm	% moisture	Film thickness (mils)	Film strength	Tear Resistance	Tendency to go to roof of mouth	180° bend test	Film molding	Dis-solution (sec)	Rating of dissolution in mouth	Time in oven (min)
EI	PEO/PVP (60/40)	45.0	14800	2.21	3.8	Adequate	Excellent	Low	Passed	No	3	Fast to Moderate	9
EJ	PEO/PVP (40/60)	50.0	6600	2.86	4	Weak	Low to moderate	High	Passed	No	3	Fast	8
EK	PEO/Starch (80/20)	40.0	3440	2.27	4.5	Adequate to good	Excellent	High	Passed	No	3	Fast to Moderate	8
EL	PEO/CMC (80/20)	37.5	121,200	1.96	4.1	Good	Excellent	High	Passed	No	5	Slow	9
EM	PEO/CMC (60/40)	30.0	82,000	4.21	3.45	Weak	Good	High	Passed	No	3	Slow to Moderate	9
EN	PEO/CMC (40/60)	30.0	185,000	3.07	3.5	Adequate	Very low	High	Failed	No	4	Slow	9
EO	PEO/HPC (80/20)	37.5	21,200	1.65	4	Good	Excellent	High	Passed	No	4	Fast	8
EP	PEO/HPC (60/40)	37.5	17,000	2.84	3.8	Adequate	Excellent	High	Passed	No	4	Fast	9
EQ	PEO/HPC (40/60)	42.5	43,400	2.83	4.5	Poor to adequate	Poor to good	High	Passed	No	7	Fast to Moderate	7
ER	PEO/HPC (20/80)	42.5	46,400	2.33	4.4	Adequate to good	Poor	Low	Passed	No	14-15	Slow	9
ES	PEO/HPMC (80/20)	37.5	29,000	2.14	4.4	Adequate	Good	High	Passed	Yes	4	Fast to Moderate	8
ET	PEO/HPMC (60/40)	37.5	47,000	2.37	3.9	Poor to adequate	Slight	High	Passed	Yes	3	Fast to Moderate	9
EU	PEO/HPMC (40/60)	35.0	54,800	3.55	4.5	Adequate to good	Low	Low	Passed	Yes	8	Slow	8
EV	PEO/HPMC (20/80)	35.0	96,600	4.43	4.5	Good	Low	Low	Passed	No	22	Slow	10
EW	PEO/PVA (80/20)	37.5	41,600	2.92	9	Weak	Moderate	High	Passed	No	3	Moderate	10

POLYETHYLENE-OXIDE BASED FILMS AND DRUG DELIVERY SYSTEMS MADE THEREFROM

CROSS-REFERENCE TO RELATED APPLICATIONS

This application is a continuation of U.S. application Ser. No. 10/856,176, filed May 28, 2004 now U.S. Pat. No. 7,666,337, which claims the benefit of U.S. Provisional Application No. 60/473,902, filed May 28, 2003 and is a continuation-in-part of U.S. application Ser. No. 10/768,809, filed Jan. 30, 2004 now U.S. Pat. No. 7,357,891, which claims benefit to U.S. Provisional Application No. 60/443,741 filed Jan. 30, 2003 and is a continuation-in-part of:

(a) PCT/US02/32575 filed Oct. 11, 2002, which claims priority to: (1) U.S. application Ser. No. 10/074,272, filed Feb. 14, 2002 which claims benefit to U.S. Provisional Application No. 60/328,868, filed Oct. 12, 2001 and (2) U.S. Provisional Application No. 60/386,937, filed Jun. 7, 2002;

(b) PCT/US02/32594, filed Oct. 11, 2002, which claims priority to: (1) U.S. Provisional Application No. 60/414,276, filed Sep. 27, 2002, (2) U.S. application Ser. No. 10/074,272, filed Feb. 14, 2002, which claims benefit to U.S. Provisional Application No. 60/328,868, filed Oct. 12, 2001 and (3) U.S. Provisional Application No. 60/386,937, filed Jun. 7, 2002; and

(c) PCT/US02/32542, filed Oct. 11, 2002, which claims priority to: (1) U.S. Provisional Application No. 60/371,940, filed Apr. 11, 2002, (2) U.S. application Ser. No. 10/074,272, filed Feb. 14, 2002, which claims benefit to U.S. Provisional Application No. 60/328,868, filed Oct. 12, 2001 and (3) U.S. Provisional Application No. 60/386,937, filed Jun. 7, 2002.

FIELD OF THE INVENTION

The invention relates to rapidly dissolving films and methods of their preparation. The films contain a polymer component, which includes polyethylene oxide optionally blended with cellulosic polymers. The films may also contain an active ingredient that is evenly distributed throughout the film. The even or uniform distribution is achieved by controlling one or more parameters, and particularly the elimination of air pockets prior to and during film formation and the use of a drying process that reduces aggregation or conglomeration of the components in the film as it forms into a solid structure.

BACKGROUND OF THE RELATED TECHNOLOGY

Active ingredients, such as drugs or pharmaceuticals, may be prepared in a tablet form to allow for accurate and consistent dosing. However, this form of preparing and dispensing medications has many disadvantages including that a large proportion of adjuvants that must be added to obtain a size able to be handled, that a larger medication form requires additional storage space, and that dispensing includes counting the tablets which has a tendency for inaccuracy. In addition, many persons, estimated to be as much as 28% of the population, have difficulty swallowing tablets. While tablets may be broken into smaller pieces or even crushed as a means of overcoming swallowing difficulties, this is not a suitable solution for many tablet or pill forms. For example, crushing or destroying the tablet or pill form to facilitate ingestion, alone or in admixture with food, may also destroy the controlled release properties.

As an alternative to tablets and pills, films may be used to carry active ingredients such as drugs, pharmaceuticals, and the like. However, historically films and the process of making drug delivery systems therefrom have suffered from a number of unfavorable characteristics that have not allowed them to be used in practice.

Films that incorporate a pharmaceutically active ingredient are disclosed in expired U.S. Pat. No. 4,136,145 to Fuchs, et al. ("Fuchs"). These films may be formed into a sheet, dried and then cut into individual doses. The Fuchs disclosure alleges the fabrication of a uniform film, which includes the combination of water-soluble polymers, surfactants, flavors, sweeteners, plasticizers and drugs. These allegedly flexible films are disclosed as being useful for oral, topical or enteral use. Examples of specific uses disclosed by Fuchs include application of the films to mucosal membrane areas of the body, including the mouth, rectal, vaginal, nasal and ear areas.

Examination of films made in accordance with the process disclosed in Fuchs, however, reveals that such films suffer from the aggregation or conglomeration of particles, i.e., self-aggregation, making them inherently non-uniform. This result can be attributed to Fuchs' process parameters, which although not disclosed likely include the use of relatively long drying times, thereby facilitating intermolecular attractive forces, convection forces, air flow and the like to form such agglomeration.

The formation of agglomerates randomly distributes the film components and any active present as well. When large dosages are involved, a small change in the dimensions of the film would lead to a large difference in the amount of active per film. If such films were to include low dosages of active, it is possible that portions of the film may be substantially devoid of any active. Since sheets of film are usually cut into unit doses, certain doses may therefore be devoid of or contain an insufficient amount of active for the recommended treatment. Failure to achieve a high degree of accuracy with respect to the amount of active ingredient in the cut film can be harmful to the patient. For this reason, dosage forms formed by processes such as Fuchs, would not likely meet the stringent standards of governmental or regulatory agencies, such as the U.S. Federal Drug Administration ("FDA"), relating to the variation of active in dosage forms. Currently, as required by various world regulatory authorities, dosage forms may not vary more than 10% in the amount of active present. When applied to dosage units based on films, this virtually mandates that uniformity in the film be present.

The problems of self-aggregation leading to non-uniformity of a film were addressed in U.S. Pat. No. 4,849,246 to Schmidt ("Schmidt"). Schmidt specifically pointed out that the methods disclosed by Fuchs did not provide a uniform film and recognized that that the creation of a non-uniform film necessarily prevents accurate dosing, which as discussed above is especially important in the pharmaceutical area. Schmidt abandoned the idea that a mono-layer film, such as described by Fuchs, may provide an accurate dosage form and instead attempted to solve this problem by forming a multi-layered film. Moreover, his process is a multi-step process that adds expense and complexity and is not practical for commercial use.

Other U.S. patents directly addressed the problems of particle self-aggregation and non-uniformity inherent in conventional film forming techniques. In one attempt to overcome non-uniformity, U.S. Pat. No. 5,629,003 to Horstmann et al. and U.S. Pat. No. 5,948,430 to Zerbe et al. incorporated additional ingredients, i.e. gel formers and polyhydric alcohols respectively, to increase the viscosity of the film prior to drying in an effort to reduce aggregation of the components in

the film. These methods have the disadvantage of requiring additional components, which translates to additional cost and manufacturing steps. Furthermore, both methods employ the use the conventional time-consuming drying methods such as a high-temperature air-bath using a drying oven, drying tunnel, vacuum drier, or other such drying equipment. The long length of drying time aids in promoting the aggregation of the active and other adjuvant, notwithstanding the use of viscosity modifiers. Such processes also run the risk of exposing the active, i.e., a drug, or vitamin C, or other components to prolonged exposure to moisture and elevated temperatures, which may render it ineffective or even harmful.

In addition to the concerns associated with degradation of an active during extended exposure to moisture, the conventional drying methods themselves are unable to provide uniform films. The length of heat exposure during conventional processing, often referred to as the "heat history", and the manner in which such heat is applied, have a direct effect on the formation and morphology of the resultant film product. Uniformity is particularly difficult to achieve via conventional drying methods where a relatively thicker film, which is well-suited for the incorporation of a drug active, is desired. Thicker uniform films are more difficult to achieve because the surfaces of the film and the inner portions of the film do not experience the same external conditions simultaneously during drying. Thus, observation of relatively thick films made from such conventional processing shows a non-uniform structure caused by convection and intermolecular forces and requires greater than 10% moisture to remain flexible. The amount of free moisture can often interfere over time with the drug leading to potency issues and therefore inconsistency in the final product.

Conventional drying methods generally include the use of forced hot air using a drying oven, drying tunnel, and the like. The difficulty in achieving a uniform film is directly related to the rheological properties and the process of water evaporation in the film-forming composition. When the surface of an aqueous polymer solution is contacted with a high temperature air current, such as a film-forming composition passing through a hot air oven, the surface water is immediately evaporated forming a polymer film or skin on the surface. This seals the remainder of the aqueous film-forming composition beneath the surface, forming a barrier through which the remaining water must force itself as it is evaporated in order to achieve a dried film. As the temperature outside the film continues to increase, water vapor pressure builds up under the surface of the film, stretching the surface of the film, and ultimately ripping the film surface open allowing the water vapor to escape. As soon as the water vapor has escaped, the polymer film surface reforms, and this process is repeated, until the film is completely dried. The result of the repeated destruction and reformation of the film surface is observed as a "ripple effect" which produces an uneven, and therefore non-uniform film. Frequently, depending on the polymer, a surface will seal so tightly that the remaining water is difficult to remove, leading to very long drying times, higher temperatures, and higher energy costs.

Other factors, such as mixing techniques, also play a role in the manufacture of a pharmaceutical film suitable for commercialization and regulatory approval. Air can be trapped in the composition during the mixing process or later during the film making process, which can leave voids in the film product as the moisture evaporates during the drying stage. The film frequently collapse around the voids resulting in an uneven film surface and therefore, non-uniformity of the final film product. Uniformity is still affected even if the voids in the film caused by air bubbles do not collapse. This situation also provides a non-uniform film in that the spaces, which are not uniformly distributed, are occupying area that would otherwise be occupied by the film composition. None of the above-mentioned patents either addresses or proposes a solution to the problems caused by air that has been introduced to the film.

Therefore, there is a need for methods and compositions for film products, which use a minimal number of materials or components, and which provide a substantially non-self-aggregating uniform heterogeneity throughout the area of the films. Desirably, such films are produced through a selection of a polymer or combination of polymers that will provide a desired viscosity, a film-forming process such as reverse roll coating, and a controlled, and desirably rapid, drying process which serves to maintain the uniform distribution of non-self-aggregated components without the necessary addition of gel formers or polyhydric alcohols and the like which appear to be required in the products and for the processes of prior patents, such as the aforementioned Horstmann and Zerbe patents. Desirably, the films will also incorporate compositions and methods of manufacture that substantially reduce or eliminate air in the film, thereby promoting uniformity in the final film product.

SUMMARY OF THE INVENTION

The present invention is directed to rapid-dissolve film products containing at least one water-soluble polymer including polyethylene oxide alone or in combination with a hydrophilic cellulosic polymer, wherein the film product is free of added plasticizers.

Another embodiment of the rapid-dissolve film product includes at least one water-soluble polymer containing about 20% to 100% by weight polyethylene oxide, about 0% to 80% by weight hydroxypropylmethyl cellulose, and about 0% to 80% by weight hydroxypropyl cellulose; an active component; sucralose; precipitated calcium carbonate;

at least one flavoring; simethicone; water; and at least one colorant, wherein the film product is free of added plasticizers, surfactants, and polyalcohols.

Yet another embodiment of the present invention is directed to an edible water-soluble delivery system in the form of a film composition, which contains at least one water-soluble polymer comprising polyethylene oxide alone or in combination with a polymer selected from the group consisting of hydroxypropylmethyl cellulose and hydroxypropyl cellulose, wherein the edible water-soluble delivery system is essentially free of organic solvents, plasticizers, surfactants, and polyalcohols.

The present invention is also directed to processes for making a film having a substantially uniform distribution of components, including the steps of: (a) combining at least one water-soluble polymer comprising polyethylene oxide alone or in combination with a hydrophilic cellulosic polymer, a solvent, and an active component to form a matrix with a uniform distribution of the components; (b) forming a film from the matrix; and (c) drying the film, wherein the film is free of added plasticizers.

BRIEF DESCRIPTION OF THE DRAWINGS

FIG. **1** shows a side view of a package containing a unit dosage film of the present invention.

FIG. **2** shows a top view of two adjacently coupled packages containing individual unit dosage forms of the present invention, separated by a tearable perforation.

FIG. **3** shows a side view of the adjacently coupled packages of FIG. **2** arranged in a stacked configuration.

FIG. **4** shows a perspective view of a dispenser for dispensing the packaged unit dosage forms, dispenser containing the packaged unit dosage forms in a stacked configuration.

FIG. **5** is a schematic view of a roll of coupled unit dose packages of the present invention.

FIG. **6** is a schematic view of an apparatus suitable for preparation of a pre-mix, addition of an active, and subsequent formation of the film.

FIG. **7** is a schematic view of an apparatus suitable for drying the films of the present invention.

FIG. **8** is a sequential representation of the drying process of the present invention.

FIG. **9** is a photographic representation of a film dried by conventional drying processes.

FIG. **10** is a photographic representation of a film dried by conventional drying processes.

FIG. **11** is a photographic representation of a film dried by conventional drying processes.

FIG. **12** is a photographic representation of a film dried by conventional drying processes.

FIG. **13** is a photographic representation of a film dried by conventional drying processes.

FIG. **14** is a photographic representation of a film dried by conventional drying processes.

FIG. **15** is a photographic representation of a film dried by conventional drying processes.

FIG. **16** is a photographic representation of a film dried by conventional drying

FIG. **17** is a photographic representation of a film dried by the inventive drying process.

FIG. **18** is a photomicrographic representation of a film containing fat coated particles dried by the inventive drying process.

FIG. **19** is a photomicrographic representation of a film containing fat coated particles dried by the inventive drying process.

FIG. **20** is a photomicrographic representation of a film containing fat coated particles dried by the inventive drying process.

FIG. **21** is a photomicrographic representation of a film containing fat coated particles dried by the inventive drying process.

FIG. **22** is a photomicrographic representation of a film containing fat coated particles dried by the inventive drying process.

FIG. **23** is a photomicrographic representation of a film containing fat coated particles dried by the inventive drying process.

FIG. **24** is a photomicrographic representation of a film containing fat coated particles dried by the inventive drying process.

FIG. **25** is a photomicrographic representation of a film containing fat coated particles dried by the inventive drying process.

FIG. **26** is a photomicrographic representation of fat coated particles not in film, heated for 9 minutes at 80° C.

FIG. **27** is a photomicrographic representation of fat coated particles not in film, heated for 9 minutes at 80° C.

FIG. **28** is a photomicrographic representation of fat coated particles at room temperature prior to processing.

FIG. **29** is a photomicrographic representation of fat coated particles at room temperature prior to processing.

FIG. **30** is a photomicrographic representation of fat coated particles at room temperature prior to processing.

FIG. **31** is a photomicrographic representation of fat coated particles at room temperature prior to processing.

FIG. **32** is a graphical representation of a microarray on the blood of a human after ingestion by the human of a film of the present invention containing a bovine derived protein.

FIG. **33** is a graphical representation of the temperature differential between the inside and outside of a film of the present invention during drying.

FIG. **34** is a graphical representation of the temperature differential between the inside and outside of a film of the present invention during drying.

FIG. **35** is a schematic representation of a continuously-linked zone drying apparatus in accordance with the present invention.

FIG. **36** is a schematic representation of a separate zone drying apparatus in accordance with the present invention.

FIG. **37** is a schematic representation of a extrusion device for use in producing films of the present invention.

FIG. **38** provides a table of various compositions of the invention, as well as certain properties.

DETAILED DESCRIPTION OF THE INVENTION

For the purposes of the present invention the term non-self-aggregating uniform heterogeneity refers to the ability of the films of the present invention, which are formed from one or more components in addition to a polar solvent, to provide a substantially reduced occurrence of, i.e. little or no, aggregation or conglomeration of components within the film as is normally experienced when films are formed by conventional drying methods such as a high-temperature air-bath using a drying oven, drying tunnel, vacuum drier, or other such drying equipment. The term heterogeneity, as used in the present invention, includes films that will incorporate a single component, such as a polymer, as well as combinations of components, such as a polymer and an active. Uniform heterogeneity includes the substantial absence of aggregates or conglomerates as is common in conventional mixing and heat drying methods used to form films.

Furthermore, the films of the present invention have a substantially uniform thickness, which is also not provided by the use of conventional drying methods used for drying water-based polymer systems. The absence of a uniform thickness detrimentally affects uniformity of component distribution throughout the area of a given film.

The film products of the present invention are produced by a combination of a properly selected polymer and a polar solvent, optionally including an active ingredient as well as other fillers known in the art. These films provide a non-self-aggregating uniform heterogeneity of the components within them by utilizing a selected casting or deposition method and a controlled drying process. Examples of controlled drying processes include, but are not limited to, the use of the apparatus disclosed in U.S. Pat. No. 4,631,837 to Magoon ("Magoon"), herein incorporated by reference, as well as hot air impingement across the bottom substrate and bottom heating plates. Another drying technique for obtaining the films of the present invention is controlled radiation drying, in the absence of uncontrolled air currents, such as infrared and radio frequency radiation (i.e. microwaves).

The objective of the drying process is to provide a method of drying the films that avoids complications, such as the noted "rippling" effect, that are associated with conventional drying methods and which initially dry the upper surface of the film, trapping moisture inside. In conventional oven drying methods, as the moisture trapped inside subsequently evaporates, the top surface is altered by being ripped open and

then reformed. These complications are avoided by the present invention, and a uniform film is provided by drying the bottom surface of the film first or otherwise preventing the formation of polymer film formation (skin) on the top surface of the film prior to drying the depth of the film. This may be achieved by applying heat to the bottom surface of the film with substantially no top air flow, or alternatively by the introduction of controlled microwaves to evaporate the water or other polar solvent within the film, again with substantially no top air flow. Yet alternatively, drying may be achieved by using balanced fluid flow, such as balanced air flow, where the bottom and top air flows are controlled to provide a uniform film. In such a case, the air flow directed at the top of the film should not create a condition which would cause movement of particles present in the wet film, due to forces generated by the air currents. Additionally, air currents directed at the bottom of the film should desirably be controlled such that the film does not lift up due to forces from the air. Uncontrolled air currents, either above or below the film, can create non-uniformity in the final film products. The humidity level of the area surrounding the top surface may also be appropriately adjusted to prevent premature closure or skinning of the polymer surface.

This manner of drying the films provides several advantages. Among these are the faster drying times and a more uniform surface of the film, as well as uniform distribution of components for any given area in the film. In addition, the faster drying time allows viscosity to quickly build within the film, further encouraging a uniform distribution of components and decrease in aggregation of components in the final film product. Desirably, the drying of the film will occur within about ten minutes or fewer, or more desirably within about five minutes or fewer.

The present invention yields exceptionally uniform film products when attention is paid to reducing the aggregation of the compositional components. By avoiding the introduction of and eliminating excessive air in the mixing process, selecting polymers and solvents to provide a controllable viscosity and by drying the film in a rapid manner from the bottom up, such films result.

The products and processes of the present invention rely on the interaction among various steps of the production of the films in order to provide films that substantially reduce the self-aggregation of the components within the films. Specifically, these steps include the particular method used to form the film, making the composition mixture to prevent air bubble inclusions, controlling the viscosity of the film forming composition and the method of drying the film. More particularly, a greater viscosity of components in the mixture is particularly useful when the active is not soluble in the selected polar solvent in order to prevent the active from settling out. However, the viscosity must not be too great as to hinder or prevent the chosen method of casting, which desirably includes reverse roll coating due to its ability to provide a film of substantially consistent thickness.

In addition to the viscosity of the film or film-forming components or matrix, there are other considerations taken into account by the present invention for achieving desirable film uniformity. For example, stable suspensions are achieved which prevent solid (such as drug particles) sedimentation in non-colloidal applications. One approach provided by the present invention is to balance the density of the particulate (ρ_p) and the liquid phase (ρ_1) and increase the viscosity of the liquid phase (μ). For an isolated particle, Stokes law relates the terminal settling velocity (Vo) of a rigid spherical body of radius (r) in a viscous fluid, as follows:

$$V_o=(2gr^r)(\rho_p-\rho_1)/9\mu$$

At high particle concentrations, however, the local particle concentration will affect the local viscosity and density. The viscosity of the suspension is a strong function of solids volume fraction, and particle-particle and particle-liquid interactions will further hinder settling velocity.

Stokian analyses has shown that the incorporation of a third phase, dispersed air or nitrogen, for example, promotes suspension stability. Further, increasing the number of particles leads to a hindered settling effect based on the solids volume fraction. In dilute particle suspensions, the rate of sedimentation, v, can be expressed as:

$$v/V_o=1/(1+\kappa\phi)$$

where κ=a constant, and ϕ is the volume fraction of the dispersed phase. More particles suspended in the liquid phase results in decreased velocity. Particle geometry is also an important factor since the particle dimensions will affect particle-particle flow interactions.

Similarly, the viscosity of the suspension is dependent on the volume fraction of dispersed solids. For dilute suspensions of non-interaction spherical particles, an expression for the suspension viscosity can be expressed as:

$$\mu/\mu_o=1+2.5\phi$$

where μ_o is the viscosity of the continuous phase and ϕ is the solids volume fraction. At higher volume fractions, the viscosity of the dispersion can be expressed as

$$\mu/\mu_o=1+2.5\phi+C_1\phi^2+C_2\phi^3+\ldots$$

where C is a constant.

The viscosity of the liquid phase is critical and is desirably modified by customizing the liquid composition to a viscoelastic non-Newtonian fluid with low yield stress values. This is the equivalent of producing a high viscosity continuous phase at rest. Formation of a viscoelastic or a highly structured fluid phase provides additional resistive forces to particle sedimentation. Further, flocculation or aggregation can be controlled minimizing particle-particle interactions. The net effect would be the preservation of a homogeneous dispersed phase.

The addition of hydrocolloids to the aqueous phase of the suspension increases viscosity, may produce viscoelasticity and can impart stability depending on the type of hydrocolloid, its concentration and the particle composition, geometry, size, and volume fraction. The particle size distribution of the dispersed phase needs to be controlled by selecting the smallest realistic particle size in the high viscosity medium, i.e., <500 μm. The presence of a slight yield stress or elastic body at low shear rates may also induce permanent stability regardless of the apparent viscosity. The critical particle diameter can be calculated from the yield stress values. In the case of isolated spherical particles, the maximum shear stress developed in settling through a medium of given viscosity can be given as

$$\tau_{max}=3V\mu/2r$$

For pseudoplastic fluids, the viscosity in this shear stress regime may well be the zero shear rate viscosity at the Newtonian plateau.

A stable suspension is an important characteristic for the manufacture of a pre-mix composition which is to be fed into the film casting machinery film, as well as the maintenance of this stability in the wet film stage until sufficient drying has occurred to lock-in the particles and matrix into a sufficiently solid form such that uniformity is maintained. For viscoelastic fluid systems, a rheology that yields stable suspensions for

extended time period, such as 24 hours, must be balanced with the requirements of high-speed film casting operations. A desirable property for the films is shear thinning or pseudoplasticity, whereby the viscosity decreases with increasing shear rate. Time dependent shear effects such as thixotropy are also advantageous. Structural recovery and shear thinning behavior are important properties, as is the ability for the film to self-level as it is formed.

The rheology requirements for the inventive compositions and films are quite severe. This is due to the need to produce a stable suspension of particles, for example 30-60 wt %, in a viscoelastic fluid matrix with acceptable viscosity values throughout a broad shear rate range. During mixing, pumping, and film casting, shear rates in the range of $10\text{-}10^5$ sec.$^{-1}$ may be experienced and pseudoplasticity is the preferred embodiment.

In film casting or coating, rheology is also a defining factor with respect to the ability to form films with the desired uniformity. Shear viscosity, extensional viscosity, viscoelasticity, structural recovery will influence the quality of the film. As an illustrative example, the leveling of shear-thinning pseudoplastic fluids has been derived as

$$\alpha^{(n-1/n)}=\alpha_o^{(n-1/n)}-((n-1)/(2n-1))(\tau/K)^{1/n}(2\pi/\lambda)^{(3+n)/n}h^{(2n+1)/n}t$$

where α is the surface wave amplitude, α_o is the initial amplitude, λ is the wavelength of the surface roughness, and both "n" and "K" are viscosity power law indices. In this example, leveling behavior is related to viscosity, increasing as n decreases, and decreasing with increasing K.

Desirably, the films or film-forming compositions of the present invention have a very rapid structural recovery, i.e. as the film is formed during processing, it doesn't fall apart or become discontinuous in its structure and compositional uniformity. Such very rapid structural recovery retards particle settling and sedimentation. Moreover, the films or film-forming compositions of the present invention are desirably shear-thinning pseudoplastic fluids. Such fluids with consideration of properties, such as viscosity and elasticity, promote thin film formation and uniformity.

Thus, uniformity in the mixture of components depends upon numerous variables. As described herein, viscosity of the components, the mixing techniques and the rheological properties of the resultant mixed composition and wet casted film are important aspects of the present invention. Additionally, control of particle size and particle shape are further considerations. Desirably, the size of the particulate a particle size of 150 microns or less, for example 100 microns or less. Moreover, such particles may be spherical, substantially spherical, or non-spherical, such as irregularly shaped particles or ellipsoidally shaped particles. Ellipsoidally shaped particles or ellipsoids are desirable because of their ability to maintain uniformity in the film forming matrix as they tend to settle to a lesser degree as compared to spherical particles.

A number of techniques may be employed in the mixing stage to prevent bubble inclusions in the final film. To provide a composition mixture with substantially no air bubble formation in the final product, anti-foaming or surface-tension reducing agents are employed. Additionally, the speed of the mixture is desirably controlled to prevent cavitation of the mixture in a manner which pulls air into the mix. Finally, air bubble reduction can further be achieved by allowing the mix to stand for a sufficient time for bubbles to escape prior to drying the film. Desirably, the inventive process first forms a masterbatch of film-forming components without active ingredients such as drug particles or volatile materials such as flavor oils. The actives are added to smaller mixes of the masterbatch just prior to casting. Thus, the masterbatch premix can be allowed to stand for a longer time without concern for instability in drug or other ingredients.

When the matrix is formed including the film-forming polymer and polar solvent in addition to any additives and the active ingredient, this may be done in a number of steps. For example, the ingredients may all be added together or a premix may be prepared. The advantage of a pre-mix is that all ingredients except for the active may be combined in advance, with the active added just prior to formation of the film. This is especially important for actives that may degrade with prolonged exposure to water, air or another polar solvent.

FIG. **6** shows an apparatus **20** suitable for the preparation of a pre-mix, addition of an active and subsequent formation of a film. The pre-mix or master batch **22**, which includes the film-forming polymer, polar solvent, and any other additives except a drug active is added to the master batch feed tank **24**. The components for pre-mix or master batch **22** are desirably formed in a mixer (not shown) prior to their addition into the master batch feed tank **24**. Then a pre-determined amount of the master batch is controllably fed via a first metering pump **26** and control valve **28** to either or both of the first and second mixers, **30**, **30'**. The present invention, however, is not limited to the use of two mixers, **30**, **30'**, and any number of mixers may suitably be used. Moreover, the present invention is not limited to any particular sequencing of the mixers **30**, **30'**, such as parallel sequencing as depicted in FIG. **6**, and other sequencing or arrangements of mixers, such as series or combination of parallel and series, may suitably be used. The required amount of the drug or other ingredient, such as a flavor, is added to the desired mixer through an opening, **32**, **32'**, in each of the mixers, **30**, **30'**. Desirably, the residence time of the pre-mix or master batch **22** is minimized in the mixers **30**, **30'**. While complete dispersion of the drug into the pre-mix or master batch **22** is desirable, excessive residence times may result in leaching or dissolving of the drug, especially in the case for a soluble drug. Thus, the mixers **30**, **30'** are often smaller, i.e. lower residence times, as compared to the primary mixers (not shown) used in forming the pre-mix or master batch **22**. After the drug has been blended with the master batch pre-mix for a sufficient time to provide a uniform matrix, a specific amount of the uniform matrix is then fed to the pan **36** through the second metering pumps, **34**, **34'**. The metering roller **38** determines the thickness of the film **42** and applies it to the application roller. The film **42** is finally formed on the substrate **44** and carried away via the support roller **46**.

While the proper viscosity uniformity in mixture and stable suspension of particles, and casting method are important in the initial steps of forming the composition and film to promote uniformity, the method of drying the wet film is also important. Although these parameters and properties assist uniformity initially, a controlled rapid drying process ensures that the uniformity will be maintained until the film is dry.

The wet film is then dried using controlled bottom drying or controlled microwave drying, desirably in the absence of external air currents or heat on the top (exposed) surface of the film **48** as described herein. Controlled bottom drying or controlled microwave drying advantageously allows for vapor release from the film without the disadvantages of the prior art. Conventional convection air drying from the top is not employed because it initiates drying at the top uppermost portion of the film, thereby forming a barrier against fluid flow, such as the evaporative vapors, and thermal flow, such as the thermal energy for drying. Such dried upper portions

serve as a barrier to further vapor release as the portions beneath are dried, which results in non-uniform films. As previously mentioned some top air flow can be used to aid the drying of the films of the present invention, but it must not create a condition that would cause particle movement or a rippling effect in the film, both of which would result in non-uniformity. If top air is employed, it is balanced with the bottom air drying to avoid non-uniformity and prevent film lift-up on the carrier belt. A balance top and bottom air flow may be suitable where the bottom air flow functions as the major source of drying and the top air flow is the minor source of drying. The advantage of some top air flow is to move the exiting vapors away from the film thereby aiding in the overall drying process. The use of any top air flow or top drying, however, must be balanced by a number of factors including, but not limited, to rheological properties of the composition and mechanical aspects of the processing. Any top fluid flow, such as air, also must not overcome the inherent viscosity of the film-forming composition. In other words, the top air flow cannot break, distort or otherwise physically disturb the surface of the composition. Moreover, air velocities are desirably below the yield values of the film, i.e., below any force level that can move the liquids in the film-forming compositions. For thin or low viscosity compositions, low air velocity must be used. For thick or high viscosity compositions, higher air velocities may be used. Furthermore, air velocities are desirable low so as to avoid any lifting or other movement of the film formed from the compositions.

Moreover, the films of the present invention may contain particles that are sensitive to temperature, such as flavors, which may be volatile, or drugs, proteins, or antigens, which may have a low degradation temperature. In such cases, the drying temperature may be decreased while increasing the drying time to adequately dry the uniform films of the present invention. Furthermore, bottom drying also tends to result in a lower internal film temperature as compared to top drying. In bottom drying, the evaporating vapors more readily carry heat away from the film as compared to top drying which lowers the internal film temperature. Such lower internal film temperatures often result in decreased drug degradation and decreased loss of certain volatiles, such as flavors.

During film preparation, it may be desirable to dry films at high temperatures. High heat drying produces uniform films, and leads to greater efficiencies in film production. Films containing sensitive active components, however, may face degradation problems at high temperatures. Degradation is the "decomposition of a compound . . . exhibiting well-defined intermediate products." The American Heritage Dictionary of the English Language (4^{th} ed. 2000). Degradation of an active component is typically undesirable as it may cause instability, inactivity, and/or decreased potency of the active component. For instance, if the active component is a drug or bioactive material, this may adversely affect the safety or efficacy of the final pharmaceutical product. Additionally, highly volatile materials will tend to be quickly released from this film upon exposure to conventional drying methods.

Degradation of an active component may occur through a variety of processes, such as, hydrolysis, oxidation, and light degradation, depending upon the particular active component. Moreover, temperature has a significant effect on the rate of such reactions. The rate of degradation typically doubles for every 10° C. increase in temperature. Therefore, it is commonly understood that exposing an active component to high temperatures will initiate and/or accelerate undesirable degradation reactions.

Proteins are one category of useful active ingredients that will degrade, denature, or otherwise become inactive when they are exposed to high temperatures for extended periods of time. Proteins serve a variety of functions in the body such as enzymes, structural elements, hormones and immunoglobulins. Examples of proteins include enzymes such as pancreatin, trypsin, pancrelipase, chymotrypsin, hyaluronidase, sutilains, streptokinaw, urokinase, altiplase, papain, bromelainsdiastase, structural elements such as collagen and albumin, hormones such as thyroliberin, gonadoliberin, adrenocorticottropin, corticotrophin, cosyntropin, sometrem, somatropion, prolactin, thyrotropin, somatostatin, vasopressin, felypressin, lypressin, insulin, glucagons, gastrin, pentagastrin, secretin, cholecystokinin-pancreozymin, and immunomodulators which may include polysaccharides in addition to glycoproteins including cytokines which are useful for the inhibition and prevention of malignant cell growth such as tumor growth. A suitable method for the production of some useful glycoproteins is disclosed in U.S. Pat. No. 6,281,337 to Cannon-Carlson, et al., which in incorporated herein in its entirety.

Temperatures that approach 100° C. will generally cause degradation of proteins as well as nucleic acids. For example some glycoproteins will degrade if exposed to a temperature of 70° C. for thirty minutes. Proteins from bovine extract are also known to degrade at such low temperatures. DNA also begins to denature at this temperature.

Applicants have discovered, however, that the films of the present invention may be exposed to high temperatures during the drying process without concern for degradation, loss of activity or excessive evaporation due to the inventive process for film preparation and forming. In particular, the films may be exposed to temperatures that would typically lead to degradation, denaturization, or inactivity of the active component, without causing such problems. According to the present invention, the manner of drying may be controlled to prevent deleterious levels of heat from reaching the active component.

As discussed herein, the flowable mixture is prepared to be uniform in content in accordance with the teachings of the present invention. Uniformity must be maintained as the flowable mass was formed into a film and dried. During the drying process of the present invention, several factors produce uniformity within the film while maintaining the active component at a safe temperature, i.e., below its degradation temperature. First, the films of the present invention have an extremely short heat history, usually only on the order of minutes, so that total temperature exposure is minimized to the extent possible. The films are controllably dried to prevent aggregation and migration of components, as well as preventing heat build up within. Desirably, the films are dried from the bottom. Controlled bottom drying, as described herein, prevents the formation of a polymer film, or skin, on the top surface of the film. As heat is conducted from the film bottom upward, liquid carrier, e.g., water, rises to the film surface. The absence of a surface skin permits rapid evaporation of the liquid carrier as the temperature increases, and thus, concurrent evaporative cooling of the film. Due to the short heat exposure and evaporative cooling, the film components such as drag or volatile actives remain unaffected by high temperatures. In contrast, skinning on the top surface traps liquid carrier molecules of increased energy within the film, thereby causing the temperature within the film to rise and exposing active components to high, potentially deleterious temperatures.

Second, thermal mixing occurs within the film due to bottom heating and absence of surface skinning. Thermal mixing occurs via convection currents in the film. As heat is applied to the bottom of the film, the liquid near the bottom increases

in temperature, expands, and becomes less dense. As such, this hotter liquid rises and cooler liquid takes its place. While rising, the hotter liquid mixes with the cooler liquid and shares thermal energy with it, i.e., transfers heat. As the cycle repeats, thermal energy is spread throughout the film.

Robust thermal mixing achieved by the controlled drying process of the present invention produces uniform heat diffusion throughout the film. In the absence of such thermal mixing, "hot spots" may develop. Pockets of heat in the film result in the formation of particle aggregates or danger areas within the film and subsequent non-uniformity. The formation of such aggregates or agglomerations is undesirable because it leads to non-uniform films in which the active may be randomly distributed. Such uneven distribution may lead to large differences in the amount of active per film, which is problematic from a safety and efficacy perspective.

Furthermore, thermal mixing helps to maintain a lower overall temperature inside the film. Although the film surfaces may be exposed to a temperature above that at which the active component degrades, the film interior may not reach this temperature. Due to this temperature differential, the active does not degrade.

For instance, the films of the present invention desirably are dried for 10 minutes or less. Drying the films at 80° C. for 10 minutes produces a temperature differential of about 5° C. This means that after 10 minutes of drying, the temperature of the inside of the film is 5° C. less than the outside exposure temperature. In many cases, however, drying times of less than 10 minutes are sufficient, such as 4 to 6 minutes. Drying for 4 minutes may be accompanied by a temperature differential of about 30° C., and drying for 6 minutes may be accompanied by a differential of about 25° C. Due to such large temperature differentials, the films may be dried at efficient, high temperatures without causing heat sensitive actives to degrade.

FIG. **8** is a sequential representation of the drying process of the present invention. After mechanical mixing, the film may be placed on a conveyor for continued thermal mixing during the drying process. At the outset of the drying process, depicted in Section A, the film **1** preferably is heated from the bottom **10** as it is travels via conveyor (not shown). Heat may be supplied to the film by a heating mechanism, such as, but not limited to, the dryer depicted in FIG. **7**. As the film is heated, the liquid carrier, or volatile ("V"), begins to evaporate, as shown by upward arrow **50**. Thermal mixing also initiates as hotter liquid, depicted by arrow **30**, rises and cooler liquid, depicted by arrow **40**, takes its place. Because no skin forms on the top surface **20** of the film **1**, as shown in Section B the volatile liquid continues to evaporate **50** and thermal mixing **30**/**40** continues to distribute thermal energy throughout the film. Once a sufficient amount of the volatile liquid has evaporated, thermal mixing has produced uniform heat diffusion throughout the film **1**. The resulting dried film **1** is a visco-elastic solid, as depicted in Section C. The components desirably are locked into a uniform distribution throughout the film. Although minor amounts of liquid carrier, i.e., water, may remain subsequent to formation of the visco-elastic, the film may be dried further without movement of the particles, if desired.

Furthermore, particles or particulates may be added to the film-forming composition or matrix after the composition or matrix is cast into a film. For example, particles may be added to the film **42** prior to the drying of the film **42**. Particles may be controllably metered to the film and disposed onto the film through a suitable technique, such as through the use of a doctor blade (not shown) which is a device which marginally or softly touches the surface of the film and controllably disposes the particles onto the film surface. Other suitable, but non-limiting, techniques include the use of an additional roller to place the particles on the film surface, spraying the particles onto the film surface, and the like. The particles may be placed on either or both of the opposed film surfaces, i.e., the top and/or bottom film surfaces. Desirably, the particles are securably disposed onto the film, such as being embedded into the film. Moreover, such particles are desirably not fully encased or fully embedded into the film, but remain exposed to the surface of the film, such as in the case where the particles are partially embedded or partially encased.

The particles may be any useful organoleptic agent, cosmetic agent, pharmaceutical agent, or combinations thereof. Desirably, the pharmaceutical agent is a taste-masked or a controlled-release pharmaceutical agent. Useful organoleptic agents include flavors and sweeteners. Useful cosmetic agents include breath freshening or decongestant agents, such as menthol, including menthol crystals.

Although the inventive process is not limited to any particular apparatus for the above-described desirable drying, one particular useful drying apparatus **50** is depicted in FIG. **7**. Drying apparatus **50** is a nozzle arrangement for directing hot fluid, such as but not limited to hot air, towards the bottom of the film **42** which is disposed on substrate **44**. Hot air enters the entrance end **52** of the drying apparatus and travels vertically upward, as depicted by vectors **54**, towards air deflector **56**. The air deflector **56** redirects the air movement to minimize upward force on the film **42**. As depicted in FIG. **7**, the air is tangentially directed, as indicated by vectors **60** and **60'**, as the air passes by air deflector **56** and enters and travels through chamber portions **58** and **58'** of the drying apparatus **50**. With the hot air flow being substantially tangential to the film **42**, lifting of the film as it is being dried is thereby minimized. While the air deflector **56** is depicted as a roller, other devices and geometries for deflecting air or hot fluid may suitable be used. Furthermore, the exit ends **62** and **62'** of the drying apparatus **50** are flared downwardly. Such downward flaring provides a downward force or downward velocity vector, as indicated by vectors **64** and **64'**, which tend to provide a pulling or drag effect of the film **42** to prevent lifting of the film **42**. Lifting of the film **42** may not only result in non-uniformity in the film or otherwise, but may also result in non-controlled processing of the film **42** as the film **42** and/or substrate **44** lift away from the processing equipment.

Monitoring and control of the thickness of the film also contributes to the production of a uniform film by providing a film of uniform thickness. The thickness of the film may be monitored with gauges such as Beta Gauges. A gauge may be coupled to another gauge at the end of the drying apparatus, i.e. drying oven or tunnel, to communicate through feedback loops to control and adjust the opening in the coating apparatus, resulting in control of uniform film thickness.

The film products are generally formed by combining a properly selected polymer and polar solvent, as well as any active ingredient or filler as desired. Desirably, the solvent content of the combination is at least about 30% by weight of the total combination. The matrix formed by this combination is formed into a film, desirably by roll coating, and then dried, desirably by a rapid and controlled drying process to maintain the uniformity of the film, more specifically, a non-self-aggregating uniform heterogeneity. The resulting film will desirably contain less than about 10% by weight solvent, more desirably less than about 8% by weight solvent, even more desirably less than about 6% by weight solvent and most desirably less than about 2%. The solvent may be water, a

polar organic solvent including, but not limited to, ethanol, isopropanol, acetone, methylene chloride, or any combination thereof.

In alternative embodiments, the film products of the present invention may be formed by extrusion rather than casting methods. Extrusion is particularly useful for film compositions containing polyethylene oxide-based polymer components, as discussed below. For instance, a single screw extrusion process may be employed in accordance with the present invention. According to such an extrusion process, pressure builds in the polymer melt so that it may be extruded through a die or injected into a mold.

As further explanation, a single screw extruder for use in the process of the present invention may include a barrel **300** containing a number of zones **200**, as shown in the extruder **100** depicted in FIG. **37**. These zones **200** may have varying temperatures and pressures. For instance, it may be desirable for the zones to increase in temperature as the composition proceeds through the barrel **300** to the extrusion die **400**. Any number of zones may be included in accordance with the present invention. In addition, the speed of extrusion may be controlled to produce desired film properties. For example, the extrusion composition may be held for an extended time period in the screw mixing chamber. Although this discussion is directed to single screw extrusion, other forms of extrusion are known to those skilled in the art and are considered well within the scope of the present invention.

Consideration of the above discussed parameters, such as but not limited to rheology properties, viscosity, mixing method, casting method and drying method, also impact material selection for the different components of the present invention. Furthermore, such consideration with proper material selection provides the compositions of the present invention, including a pharmaceutical and/or cosmetic dosage form or film product having no more than a 10% variance of a pharmaceutical and/or cosmetic active per unit area. In other words, the uniformity of the present invention is determined by the presence of no more than a 10% by weight of pharmaceutical and/or cosmetic variance throughout the matrix. Desirably, the variance is less than 5% by weight, less than 2% by weight, less than 1% by weight, or less than 0.5% by weight.

Film-Forming Polymers

The polymer may be water soluble, water swellable, water insoluble, or a combination of one or more either water soluble, water swellable or water insoluble polymers. The polymer may include cellulose or a cellulose derivative. Specific examples of useful water soluble polymers include, but are not limited to, polyethylene oxide (PEO), pullulan, hydroxypropylmethyl cellulose (HPMC), hydroxyethyl cellulose (HPC), hydroxypropyl cellulose, polyvinyl pyrrolidone, carboxymethyl cellulose, polyvinyl alcohol, sodium aginate, polyethylene glycol, xanthan gum, tragacanth gum, guar gum, acacia gum, arabic gum, polyacrylic acid, methylmethacrylate copolymer, carboxyvinyl copolymers, starch, gelatin, and combinations thereof. Specific examples of useful water insoluble polymers include, but are not limited to, ethyl cellulose, hydroxypropyl ethyl cellulose, cellulose acetate phthalate, hydroxypropyl methyl cellulose phthalate and combinations thereof.

As used herein the phrase "water soluble polymer" and variants thereof refer to a polymer that is at least partially soluble in water, and desirably fully or predominantly soluble in water, or absorbs water. Polymers that absorb water are often referred to as being water swellable polymers. The materials useful with the present invention may be water soluble or water swellable at room temperature and other temperatures, such as temperatures exceeding room temperature. Moreover, the materials may be water soluble or water swellable at pressures less than atmospheric pressure. Desirably, the water soluble polymers are water soluble or water swellable having at least 20 percent by weight water uptake. Water swellable polymers having a 25 or greater percent by weight water uptake are also useful. Films or dosage forms of the present invention formed from such water soluble polymers are desirably sufficiently water soluble to be dissolvable upon contact with bodily fluids.

Other polymers useful for incorporation into the films of the present invention include biodegradable polymers, copolymers, block polymers and combinations thereof. Among the known useful polymers or polymer classes which meet the above criteria are: poly(glycolic acid) (PGA), poly (lactic acid) (PLA), polydioxanones, polyoxalates, poly(α-esters), polyanhydrides, polyacetates, polycaprolactones, poly(orthoesters), polyamino acids, polyaminocarbonates, polyurethanes, polycarbonates, polyamides, poly(alkyl cyanoacrylates), and mixtures and copolymers thereof. Additional useful polymers include, stereopolymers of L- and D-lactic acid, copolymers of bis(p-carboxyphenoxy) propane acid and sebacic acid, sebacic acid copolymers, copolymers of caprolactone, poly(lactic acid)/poly(glycolic acid)/polyethyleneglycol copolymers, copolymers of polyurethane and (poly(lactic acid), copolymers of polyurethane and poly(lactic acid), copolymers of α-amino acids, copolymers of α-amino acids and caproic acid, copolymers of α-benzyl glutamate and polyethylene glycol, copolymers of succinate and poly(glycols), polyphosphazene, polyhydroxy-alkanoates and mixtures thereof. Binary and ternary systems are contemplated.

Other specific polymers useful include those marketed under the Medisorb and Biodel trademarks. The Medisorb materials are marketed by the Dupont Company of Wilmington, Del. and are generically identified as a "lactide/glycolide co-polymer" containing "propanoic acid, 2-hydroxy-polymer with hydroxy-polymer with hydroxyacetic acid." Four such polymers include lactide/glycolide 100 L, believed to be 100% lactide having a melting point within the range of 338°-347° F. (170°-175° C.); lactide/glycolide 100 L, believed to be 100% glycolide having a melting point within the range of 437°-455° F. (225°-235° C.); lactide/glycolide 85/15, believed to be 85% lactide and 15% glycolide with a melting point within the range of 338°-347° F. (170°-175° C.); and lactide/glycolide 50/50, believed to be a copolymer of 50% lactide and 50% glycolide with a melting point within the range of 338°-347° F. (170°-175° C.).

The Biodel materials represent a family of various polyanhydrides which differ chemically.

Although a variety of different polymers may be used, it is desired to select polymers to provide a desired viscosity of the mixture prior to drying. For example, if the active or other components are not soluble in the selected solvent, a polymer that will provide a greater viscosity is desired to assist in maintaining uniformity. On the other hand, if the components are soluble in the solvent, a polymer that provides a lower viscosity may be preferred.

The polymer plays an important role in affecting the viscosity of the film. Viscosity is one property of a liquid that controls the stability of the active in an emulsion, a colloid or a suspension. Generally the viscosity of the matrix will vary from about 400 cps to about 100,000 cps, preferably from about 800 cps to about 60,000 cps, and most preferably from

about 1,000 cps to about 40,000 cps. Desirably, the viscosity of the film-forming matrix will rapidly increase upon initiation of the drying process.

The viscosity may be adjusted based on the selected active depending on the other components within the matrix. For example, if the component is not soluble within the selected solvent, a proper viscosity may be selected to prevent the component from settling which would adversely affect the uniformity of the resulting film. The viscosity may be adjusted in different ways. To increase viscosity of the film matrix, the polymer may be chosen of a higher molecular weight or crosslinkers may be added, such as salts of calcium, sodium and potassium. The viscosity may also be adjusted by adjusting the temperature or by adding a viscosity increasing component. Components that will increase the viscosity or stabilize the emulsion/suspension include higher molecular weight polymers and polysaccharides and gums, which include without limitation, alginate, carrageenan, hydroxypropyl methyl cellulose, locust bean gum, guar gum, xanthan gum, dextran, gum arabic, gellan gum and combinations thereof.

It has also been observed that certain polymers which when used alone would ordinarily require a plasticizer to achieve a flexible film, can be combined without a plasticizer and yet achieve flexible films. For example, HPMC and HPC when used in combination provide a flexible, strong film with the appropriate plasticity and elasticity for manufacturing and storage. No additional plasticizer or polyalcohol is needed for flexibility.

Additionally, polyethylene oxide (PEO), when used alone or in combination with a hydrophilic cellulosic polymer, achieves flexible, strong films. Additional plasticizers or polyalcohols are not needed for flexibility. Non-limiting examples of suitable cellulosic polymers for combination with PEO include HPC and HPMC. PEO and HPC have essentially no gelation temperature, while HPMC has a gelation temperature of 58-64° C. (Methocel EF available from Dow Chemical Co.). Moreover, these films are sufficiently flexible even when substantially free of organic solvents, which may be removed without compromising film properties. As such, if there is no solvent present, then there is no plasticizer in the films. PEO based films also exhibit good resistance to tearing, little or no curling, and fast dissolution rates when the polymer component contains appropriate levels of PEO.

To achieve the desired film properties, the level and/or molecular weight of PEO in the polymer component may be varied. Modifying the PEO content affects properties such as tear resistance, dissolution rate, and adhesion tendencies. Thus, one method for controlling film properties is to modify the PEO content. For instance, in some embodiments rapid dissolving films are desirable. By modifying the content of the polymer component, the desired dissolution characteristics can be achieved.

In accordance with the present invention, PEO desirably ranges from about 20% to 100% by weight in the polymer component. In some embodiments, the amount of PEO desirably ranges from about 1 mg to about 200 mg. The hydrophilic cellulosic polymer ranges from about 0% to about 80% by weight, or in a ratio of up to about 4:1 with the PEO, and desirably in a ratio of about 1:1.

In some embodiments, it may be desirable to vary the PEO levels to promote certain film properties. To obtain films with high tear resistance and fast dissolution rates, levels of about 50% or greater of PEO in the polymer component are desirable. To achieve adhesion prevention, i.e., preventing the film from adhering to the roof of the mouth, PEO levels of about 20% to 75% are desirable. In some embodiments, however, adhesion to the roof of the mouth may be desired, such as for administration to animals or children. In such cases, higher levels of PEO may be employed. More specifically, structural integrity and dissolution of the film can be controlled such that the film can adhere to mucosa and be readily removed, or adhere more firmly and be difficult to remove, depending on the intended use.

The molecular weight of the PEO may also be varied. High molecular weight PEO, such as about 4 million, may be desired to increase mucoadhesivity of the film. More desirably, the molecular weight may range from about 100,000 to 900,000, more desirably from about 100,000 to 600,000, and most desirably from about 100,000 to 300,000. In some embodiments, it may be desirable to combine high molecular weight (600,000 to 900,000) with low molecular weight (100,000 to 300,000) PEOs in the polymer component.

For instance, certain film properties, such as fast dissolution rates and high tear resistance, may be attained by combining small amounts of high molecular weight PEOs with larger amounts of lower molecular weight PEOs. Desirably, such compositions contain about 60% or greater levels of the lower molecular weight PEO in the PEO-blend polymer component.

To balance the properties of adhesion prevention, fast dissolution rate, and good tear resistance, desirable film compositions may include about 50% to 75% low molecular weight PEO, optionally combined with a small amount of a higher molecular weight PEO, with the remainder of the polymer component containing a hydrophilic cellulosic polymer (HPC or HPMC).

Controlled Release Films

The term "controlled release" is intended to mean the release of active at a pre-selected or desired rate. This rate will vary depending upon the application. Desirable rates include fast or immediate release profiles as well as delayed, sustained or sequential release. Combinations of release patterns, such as initial spiked release followed by lower levels of sustained release of active are contemplated. Pulsed drug releases are also contemplated.

The polymers that are chosen for the films of the present invention may also be chosen to allow for controlled disintegration of the active. This may be achieved by providing a substantially water insoluble film that incorporates an active that will be released from the film over time. This may be accomplished by incorporating a variety of different soluble or insoluble polymers and may also include biodegradable polymers in combination. Alternatively, coated controlled release active particles may be incorporated into a readily soluble film matrix to achieve the controlled release property of the active inside the digestive system upon consumption.

Films that provide a controlled release of the active are particularly useful for buccal, gingival, sublingual and vaginal applications. The films of the present invention are particularly useful where mucosal membranes or mucosal fluid is present due to their ability to readily wet and adhere to these areas.

The convenience of administering a single dose of a medication which releases active ingredients in a controlled fashion over an extended period of time as opposed to the administration of a number of single doses at regular intervals has long been recognized in the pharmaceutical arts. The advantage to the patient and clinician in having consistent and uniform blood levels of medication over an extended period of time are likewise recognized. The advantages of a variety of sustained release dosage forms are well known. However,

the preparation of a film that provides the controlled release of an active has advantages in addition to those well-known for controlled release tablets. For example, thin films are difficult to inadvertently aspirate and provide an increased patient compliance because they need not be swallowed like a tablet. Moreover, certain embodiments of the inventive films are designed to adhere to the buccal cavity and tongue, where they controllably dissolve. Furthermore, thin films may not be crushed in the manner of controlled release tablets which is a problem leading to abuse of drugs such as Oxycontin.

The actives employed in the present invention may be incorporated into the film compositions of the present invention in a controlled release form. For example, particles of drug may be coated with polymers such as ethyl cellulose or polymethacrylate, commercially available under brand names such as Aquacoat ECD and Eudragit E-100, respectively. Solutions of drug may also be absorbed on such polymer materials and incorporated into the inventive film compositions. Other components such as fats and waxes, as well as sweeteners and/or flavors may also be employed in such controlled release compositions.

The actives may be taste-masked prior to incorporation into the film composition, as set forth in co-pending PCT application titled, Uniform Films For Rapid Dissolve Dosage Form Incorporating Taste-Masking Compositions, (based on U.S. Provisional Application No. Express Mail Label No.: EU552991605 US of the same title, filed Sep. 27, 2003, Ser. No. 60/414,276 the entire subject matter of which is incorporated by reference herein.

Actives

When an active is introduced to the film, the amount of active per unit area is determined by the uniform distribution of the film. For example, when the films are cut into individual dosage forms, the amount of the active in the dosage form can be known with a great deal of accuracy. This is achieved because the amount of the active in a given area is substantially identical to the amount of active in an area of the same dimensions in another part of the film. The accuracy in dosage is particularly advantageous when the active is a medicament, i.e. a drug.

The active components that may be incorporated into the films of the present invention include, without limitation pharmaceutical and cosmetic actives, drugs, medicaments, proteins, antigens or allergens such as ragweed pollen, spores, microorganisms, seeds, mouthwash components, flavors, fragrances, enzymes, preservatives, sweetening agents, colorants, spices, vitamins and combinations thereof.

A wide variety of medicaments, bioactive active substances and pharmaceutical compositions may be included in the dosage forms of the present invention. Examples of useful drugs include ace-inhibitors, antianginal drugs, anti-arrhythmias, anti-asthmatics, anti-cholesterolemics, analgesics, anesthetics, anti-convulsants, anti-depressants, anti-diabetic agents, anti-diarrhea preparations, antidotes, anti-histamines, anti-hypertensive drugs, anti-inflammatory agents, anti-lipid agents, anti-manics, anti-nauseants, anti-stroke agents, anti-thyroid preparations, anti-tumor drugs, anti-viral agents, acne drugs, alkaloids, amino acid preparations, anti-tussives, anti-uricemic drugs, anti-viral drugs, anabolic preparations, systemic and non-systemic anti-infective agents, anti-neoplastics, anti-parkinsonian agents, anti-rheumatic agents, appetite stimulants, biological response modifiers, blood modifiers, bone metabolism regulators, cardiovascular agents, central nervous system stimulates, cholinesterase inhibitors, contraceptives, decongestants, dietary supplements, dopamine receptor agonists, endometriosis management agents, enzymes, erectile dysfunction therapies, fertility agents, gastrointestinal agents, homeopathic remedies, hormones, hypercalcemia and hypocalcemia management agents, immunomodulators, immunosuppressives, migraine preparations, motion sickness treatments, muscle relaxants, obesity management agents, osteoporosis preparations, oxytocics, parasympatholytics, parasympathomimetics, prostaglandins, psychotherapeutic agents, respiratory agents, sedatives, smoking cessation aids, sympatholytics, tremor preparations, urinary tract agents, vasodilators, laxatives, antacids, ion exchange resins, anti-pyretics, appetite suppressants, expectorants, anti-anxiety agents, anti-ulcer agents, anti-inflammatory substances, coronary dilators, cerebral dilators, peripheral vasodilators, psycho-tropics, stimulants, anti-hypertensive drugs, vasoconstrictors, migraine treatments, antibiotics, tranquilizers, anti-psychotics, anti-tumor drugs, anti-coagulants, anti-thrombotic drugs, hypnotics, anti-emetics, anti-nauseants, anti-convulsants, neuromuscular drugs, hyper- and hypo-glycemic agents, thyroid and anti-thyroid preparations, diuretics, anti-spasmodics, terine relaxants, anti-obesity drugs, erythropoietic drugs, anti-asthmatics, cough suppressants, mucolytics, DNA and genetic modifying drugs, and combinations thereof.

Examples of medicating active ingredients contemplated for use in the present invention include antacids, H_2-antagonists, and analgesics. For example, antacid dosages can be prepared using the ingredients calcium carbonate alone or in combination with magnesium hydroxide, and/or aluminum hydroxide. Moreover, antacids can be used in combination with H_2-antagonists.

Analgesics include opiates and opiate derivatives, such as oxycodone (available as Oxycontin®), ibuprofen, aspirin, acetaminophen, and combinations thereof that may optionally include caffeine.

Other preferred drugs for other preferred active ingredients for use in the present invention include anti-diarrheals such as immodium AD, anti-histamines, anti-tussives, decongestants, vitamins, and breath fresheners. Common drugs used alone or in combination for colds, pain, fever, cough, congestion, runny nose and allergies, such as acetaminophen, chlorpheniramine maleate, dextromethorphan, pseudoephedrine HCl and diphenhydramine may be included in the film compositions of the present invention.

Also contemplated for use herein are anxiolytics such as alprazolam (available as Xanax®); anti-psychotics such as clozopin (available as Clozaril®) and haloperidol (available as Haldol®); non-steroidal anti-inflammatories (NSAID's) such as dicyclofenacs (available as Voltaren®) and etodolac (available as Lodine®), anti-histamines such as loratadine (available as Claritin®), astemizole (available as Hismanal™), nabumetone (available as Relafen®), and Clemastine (available as Tavist®); anti-emetics such as granisetron hydrochloride (available as Kytril®) and nabilone (available as Cesamet™); bronchodilators such as Bentolin®, albuterol sulfate (available as Proventil®); anti-depressants such as fluoxetine hydrochloride (available as Prozac®), sertraline hydrochloride (available as Zoloft®), and paroxetine hydrochloride (available as Paxil®); anti-migraines such as Imigra®, ACE-inhibitors such as enelaprilat (available as Vasotec®), captopril (available as Capoten®) and lisinopril (available as Zestril®); anti-Alzheimer's agents, such as nicergoline; and Ca^H-antagonists such as nifedipine (available as Procardia® and Adalat®), and verapamil hydrochloride (available as Calan®).

Erectile dysfunction therapies include, but are not limited to, drugs for facilitating blood flow to the penis, and for effecting autonomic nervous activities, such as increasing

parasympathetic (cholinergic) and decreasing sympathetic (adrenersic) activities. Useful non-limiting drugs include sildenafils, such as Viagra®, tadalafils, such as Cialis®, vardenafils, apomorphines, such as Uprima®, yohimbine hydrochlorides such as Aphrodyne®, and alprostadils such as Caverject®.

The popular H_2-antagonists which are contemplated for use in the present invention include cimetidine, ranitidine hydrochloride, famotidine, nizatidine, ebrotidine, mifentidine, roxatidine, pisatidine and aceroxatidine.

Active antacid ingredients include, but are not limited to, the following: aluminum hydroxide, dihydroxyaluminum aminoacetate, aminoacetic acid, aluminum phosphate, dihydroxyaluminum sodium carbonate, bicarbonate, bismuth aluminate, bismuth carbonate, bismuth subcarbonate, bismuth subgallate, bismuth subnitrate, bismuth subsilysilate, calcium carbonate, calcium phosphate, citrate ion (acid or salt), amino acetic acid, hydrate magnesium aluminate sulfate, magaldrate, magnesium aluminosilicate, magnesium carbonate, magnesium glycinate, magnesium hydroxide, magnesium oxide, magnesium trisilicate, milk solids, aluminum mono- or di-basic calcium phosphate, tricalcium phosphate, potassium bicarbonate, sodium tartrate, sodium bicarbonate, magnesium aluminosilicates, tartaric acids and salts.

The pharmaceutically active agents employed in the present invention may include allergens or antigens, such as, but not limited to, plant pollens from grasses, trees, or ragweed; animal danders, which are tiny scales shed from the skin and hair of cats and other furred animals; insects, such as house dust mites, bees, and wasps; and drugs, such as penicillin.

An anti-oxidant may also be added to the film to prevent the degradation of an active, especially where the active is photosensitive.

Cosmetic active agents may include breath freshening compounds like menthol, other flavors or fragrances, especially those used for oral hygiene, as well as actives used in dental and oral cleansing such as quaternary ammonium bases. The effect of flavors may be enhanced using flavor enhancers like tartaric acid, citric acid, vanillin, or the like.

Also color additives can be used in preparing the films. Such color additives include food, drug and cosmetic colors (FD&C), drug and cosmetic colors (D&C), or external drug and cosmetic colors (Ext. D&C). These colors are dyes, their corresponding lakes, and certain natural and derived colorants. Lakes are dyes absorbed on aluminum hydroxide.

Other examples of coloring agents include known azo dyes, organic or inorganic pigments, or coloring agents of natural origin. Inorganic pigments are preferred, such as the oxides or iron or titanium, these oxides, being added in concentrations ranging from about 0.001 to about 10%, and preferably about 0.5 to about 3%, based on the weight of all the components.

Flavors may be chosen from natural and synthetic flavoring liquids. An illustrative list of such agents includes volatile oils, synthetic flavor oils, flavoring aromatics, oils, liquids, oleoresins or extracts derived from plants, leaves, flowers, fruits, stems and combinations thereof. A non-limiting representative list of examples includes mint oils, cocoa, and citrus oils such as lemon, orange, grape, lime and grapefruit and fruit essences including apple, pear, peach, grape, strawberry, raspberry, cherry, plum, pineapple, apricot or other fruit flavors.

The films containing flavorings may be added to provide a hot or cold flavored drink or soup. These flavorings include, without limitation, tea and soup flavorings such as beef and chicken.

Other useful flavorings include aldehydes and esters such as benzaldehyde (cherry, almond), citral i.e., alphacitral (lemon, lime), neral, i.e., beta-citral (lemon, lime), decanal (orange, lemon), aldehyde C-8 (citrus fruits), aldehyde C-9 (citrus fruits), aldehyde C-12 (citrus fruits), tolyl aldehyde (cherry, almond), 2,6-dimethyloctanol (green fruit), and 2-dodecenal (citrus, mandarin), combinations thereof and the like.

The sweeteners may be chosen from the following non-limiting list: glucose (corn syrup), dextrose, invert sugar, fructose, and combinations thereof saccharin and its various salts such as the sodium salt; dipeptide sweeteners such as aspartame; dihydrochalcone compounds, glycyrrhizin; Stevia Rebaudiana (Stevioside); chloro derivatives of sucrose such as sucralose; sugar alcohols such as sorbitol, mannitol, xylitol, and the like. Also contemplated are hydrogenated starch hydrolysates and the synthetic sweetener 3,6-dihydro-6-methy-1-1-1-1,2,3-oxathiazin-4-one-2,2-dioxide, particularly the potassium salt (acesulfame-K), and sodium and calcium salts thereof, and natural intensive sweeteners, such as Lo Han Kuo. Other sweeteners may also be used.

When the active is combined with the polymer in the solvent, the type of matrix that is formed depends on the solubilities of the active and the polymer. If the active and/or polymer are soluble in the selected solvent, this may form a solution. However, if the components are not soluble, the matrix may be classified as an emulsion, a colloid, or a suspension.

Dosages

The film products of the present invention are capable of accommodating a wide range of amounts of the active ingredient. The films are capable of providing an accurate dosage amount (determined by the size of the film and concentration of the active in the original polymer/water combination) regardless of whether the required dosage is high or extremely low. Therefore, depending on the type of active or pharmaceutical composition that is incorporated into the film, the active amount may be as high as about 300 mg, desirably up to about 150 mg or as low as the microgram range, or any amount therebetween.

The film products and methods of the present invention are well suited for high potency, low dosage drugs. This is accomplished through the high degree of uniformity of the films. Therefore, low dosage drugs, particularly more potent racemic mixtures of actives are desirable.

Anti-Foaming and De-Foaming Compositions

Anti-foaming and/or de-foaming components may also be used with the films of the present invention. These components aid in the removal of air, such as entrapped air, from the film-forming compositions. As described above, such entrapped air may lead to non-uniform films. Simethicone is one particularly useful anti-foaming and/or de-foaming agent. The present invention, however, is not so limited and other anti-foam and/or de-foaming agents may suitable be used.

As a related matter, simethicone and related agents may be employed for densification purposes. More specifically, such agents may facilitate the removal of voids, air, moisture, and similar undesired components, thereby providing denser, and thus more uniform films. Agents or components which perform this function can be referred to as densification or densifying agents. As described above, entrapped air or undesired components may lead to non-uniform films.

Simethicone is generally used in the medical field as a treatment for gas or colic in babies. Simethicone is a mixture of fully methylated linear siloxane polymers containing

repeating units of polydimethylsiloxane which is stabilized with trimethylsiloxy end-blocking unites, and silicon dioxide. It usually contains 90.5-99% polymethylsiloxane and 4-7% silicon dioxide. The mixture is a gray, translucent, viscous fluid which is insoluble in water.

When dispersed in water, simethicone will spread across the surface, forming a thin film of low surface tension. In this way, simethicone reduces the surface tension of bubbles air located in the solution, such as foam bubbles, causing their collapse. The function of simethicone mimics the dual action of oil and alcohol in water. For example, in an oily solution any trapped air bubbles will ascend to the surface and dissipate more quickly and easily, because an oily liquid has a lighter density compared to a water solution. On the other hand, an alcohol/water mixture is known to lower water density as well as lower the water's surface tension. So, any air bubbles trapped inside this mixture solution will also be easily dissipated. Simethicone solution provides both of these advantages. It lowers the surface energy of any air bubbles that trapped inside the aqueous solution, as well as lowering the surface tension of the aqueous solution. As the result of this unique functionality, simethicone has an excellent anti-foaming property that can be used for physiological processes (anti-gas in stomach) as well as any for external processes that require the removal of air bubbles from a product.

In order to prevent the formation of air bubbles in the films of the present invention, the mixing step can be performed under vacuum. However, as soon as the mixing step is completed, and the film solution is returned to the normal atmosphere condition, air will be re-introduced into or contacted with the mixture. In many cases, tiny air bubbles will be again trapped inside this polymeric viscous solution. The incorporation of simethicone into the film-forming composition either substantially reduces or eliminates the formation of air bubbles.

Simethicone may be added to the film-forming mixture as an anti-foaming agent in an amount from about 0.01 weight percent to about 5.0 weight percent, more desirably from about 0.05 weight percent to about 2.5 weight percent, and most desirably from about 0.1 weight percent to about 1.0 weight percent.

Optional Components

A variety of other components and fillers may also be added to the films of the present invention. These may include, without limitation, surfactants; plasticizers which assist in compatibilizing the components within the mixture; polyalcohols; anti-foaming agents, such as silicone-containing compounds, which promote a smoother film surface by releasing oxygen from the film; thermo-setting gels such as pectin, carageenan, and gelatin, which help in maintaining the dispersion of components; and inclusion compounds, such as cyclodextrins and caged molecules, which improve the solubility and/or stability of certain active components.

The variety of additives that can be incorporated into the inventive compositions may provide a variety of different functions. Examples of classes of additives include excipients, lubricants, buffering agents, stabilizers, blowing agents, pigments, coloring agents, fillers, bulking agents, sweetening agents, flavoring agents, fragrances, release modifiers, adjuvants, plasticizers, flow accelerators, mold release agents, polyols, granulating agents, diluents, binders, buffers, absorbents, glidants, adhesives, anti-adherents, acidulants, softeners, resins, demulcents, solvents, surfactants, emulsifiers, elastomers and mixtures thereof. These additives may be added with the active ingredient(s).

Useful additives include, for example, gelatin, vegetable proteins such as sunflower protein, soybean proteins, cotton seed proteins, peanut proteins, grape seed proteins, whey proteins, whey protein isolates, blood proteins, egg proteins, acrylated proteins, water-soluble polysaccharides such as alginates, carrageenans, guar gum, agar-agar, xanthan gum, gellan gum, gum arabic and related gums (gum ghatti, gum karaya, gum tragacanth), pectin, water-soluble derivatives of cellulose: alkylcelluloses hydroxyalkylcelluloses and hydroxyalkylalkylcelluloses, such as methylcellulose, hydroxymethylcellulose, hydroxyethylcellulose, hydroxypropylcellulose, hydroxyethylmethylcellulose, hydroxypropylmethylcellulose, hydroxybutylmethylcellulose, cellulose esters and hydroxyalkylcellulose esters such as cellulose acetate phthalate (CAP), hydroxypropylmethylcellulose (HPMC); carboxyalkylcelluloses, carboxyalkylalkylcelluloses, carboxyalkylcellulose esters such as carboxymethylcellulose and their alkali metal salts; water-soluble synthetic polymers such as polyacrylic acids and polyacrylic acid esters, polymethacrylic acids and polymethacrylic acid esters, polyvinylacetates, polyvinylalcohols, polyvinylacetatephthalates (PVAP), polyvinylpyrrolidone (PVP), PVY/vinyl acetate copolymer, and polycrotonic acids; also suitable are phthalated gelatin, gelatin succinate, crosslinked gelatin, shellac, water soluble chemical derivatives of starch, cationically modified acrylates and methacrylates possessing, for example, a tertiary or quaternary amino group, such as the diethylaminoethyl group, which may be quaternized if desired; and other similar polymers.

Such extenders may optionally be added in any desired amount desirably within the range of up to about 80%, desirably about 3% to 50% and more desirably within the range of 3% to 20% based on the weight of all components.

Further additives may be inorganic fillers, such as the oxides of magnesium aluminum, silicon, titanium, etc. desirably in a concentration range of about 0.02% to about 3% by weight and desirably about 0.02% to about 1% based on the weight of all components.

Further examples of additives are plasticizers which include polyalkylene oxides, such as polyethylene glycols, polypropylene glycols, polyethylene-propylene glycols, organic plasticizers with low molecular weights, such as glycerol, glycerol monoacetate, diacetate or triacetate, triacetin, polysorbate, cetyl alcohol, propylene glycol, sorbitol, sodium diethylsulfosuccinate, triethyl citrate, tributyl citrate, and the like, added in concentrations ranging from about 0.5% to about 30%, and desirably ranging from about 0.5% to about 20% based on the weight of the polymer.

There may further be added compounds to improve the flow properties of the starch material such as animal or vegetable fats, desirably in their hydrogenated form, especially those which are solid at room temperature. These fats desirably have a melting point of 50° C. or higher. Preferred are tri-glycerides with C_{12}-, C_{14}-, C_{16}-, C_{18}-, C_{20}- and C_{22}-fatty acids. These fats can be added alone without adding extenders or plasticizers and can be advantageously added alone or together with mono- and/or di-glycerides or phosphatides, especially lecithin. The mono- and di-glycerides are desirably derived from the types of fats described above, i.e. with C_{12}-, C_{14}-, C_{16}-, C_{18}-, C_{20}- and C_{22}-fatty acids.

The total amounts used of the fats, mono-, di-glycerides and/or lecithins are up to about 5% and preferably within the range of about 0.5% to about 2% by weight of the total composition

It is further useful to add silicon dioxide, calcium silicate, or titanium dioxide in a concentration of about 0.02% to about 1% by weight of the total composition. These compounds act as texturizing agents.

These additives are to be used in amounts sufficient to achieve their intended purpose. Generally, the combination of certain of these additives will alter the overall release profile of the active ingredient and can be used to modify, i.e. impede or accelerate the release.

Lecithin is one surface active agent for use in the present invention. Lecithin can be included in the feedstock in an amount of from about 0.25% to about 2.00% by weight. Other surface active agents, i.e. surfactants, include, but are not limited to, cetyl alcohol, sodium lauryl sulfate, the Spans™ and Tweens™ which are commercially available from ICI Americas, Inc. Ethoxylated oils, including ethoxylated castor oils, such as Cremophor® EL which is commercially available from BASF, are also useful. Carbowax™ is yet another modifier which is very useful in the present invention. Tweens™ or combinations of surface active agents may be used to achieve the desired hydrophilic-lipophilic balance ("HLB"). The present invention, however, does not require the use of a surfactant and films or film-forming compositions of the present invention may be essentially free of a surfactant while still providing the desirable uniformity features of the present invention.

As additional modifiers which enhance the procedure and product of the present invention are identified, Applicants intend to include all such additional modifiers within the scope of the invention claimed herein.

Other ingredients include binders which contribute to the ease of formation and general quality of the films. Non-limiting examples of binders include starches, pregelatinize starches, gelatin, polyvinylpyrrolidone, methylcellulose, sodium carboxymethylcellulose, ethylcellulose, polyacrylamides, polyvinyloxoazolidone, and polyvinylalcohols.

Further potential additives include solubility enhancing agents, such as substances that form inclusion compounds with active components. Such agents may be useful in improving the properties of very insoluble and/or unstable actives. In general, these substances are doughnut-shaped molecules with hydrophobic internal cavities and hydrophilic exteriors. Insoluble and/or instable actives may fit within the hydrophobic cavity, thereby producing an inclusion complex, which is soluble in water. Accordingly, the formation of the inclusion complex permits very insoluble and/or instable actives to be dissolved in water. A particularly desirable example of such agents are cyclodextrins, which are cyclic carbohydrates derived from starch. Other similar substances, however, are considered well within the scope of the present invention.

Forming the Film

The films of the present invention must be formed into a sheet prior to drying. After the desired components are combined to form a multi-component matrix, including the polymer, water, and an active or other components as desired, the combination is formed into a sheet or film, by any method known in the art such as extrusion, coating, spreading, casting or drawing the multi-component matrix. If a multi-layered film is desired, this may be accomplished by co-extruding more than one combination of components which may be of the same or different composition. A multi-layered film may also be achieved by coating, spreading, or casting a combination onto an already formed film layer.

Although a variety of different film-forming techniques may be used, it is desirable to select a method that will provide a flexible film, such as reverse roll coating. The flexibility of the film allows for the sheets of film to be rolled and transported for storage or prior to being cut into individual dosage forms. Desirably, the films will also be self-supporting or in other words able to maintain their integrity and structure in the absence of a separate support. Furthermore, the films of the present invention may be selected of materials that are edible or ingestible.

Coating or casting methods are particularly useful for the purpose of forming the films of the present invention. Specific examples include reverse roll coating, gravure coating, immersion or dip coating, metering rod or meyer bar coating, slot die or extrusion coating, gap or knife over roll coating, air knife coating, curtain coating, or combinations thereof, especially when a multi-layered film is desired.

Roll coating, or more specifically reverse roll coating, is particularly desired when forming films in accordance with the present invention. This procedure provides excellent control and uniformity of the resulting films, which is desired in the present invention. In this procedure, the coating material is measured onto the applicator roller by the precision setting of the gap between the upper metering roller and the application roller below it. The coating is transferred from the application roller to the substrate as it passes around the support roller adjacent to the application roller. Both three roll and four roll processes are common.

The gravure coating process relies on an engraved roller running in a coating bath, which fills the engraved dots or lines of the roller with the coating material. The excess coating on the roller is wiped off by a doctor blade and the coating is then deposited onto the substrate as it passes between the engraved roller and a pressure roller.

Offset Gravure is common, where the coating is deposited on an intermediate roller before transfer to the substrate.

In the simple process of immersion or dip coating, the substrate is dipped into a bath of the coating, which is normally of a low viscosity to enable the coating to run back into the bath as the substrate emerges.

In the metering rod coating process, an excess of the coating is deposited onto the substrate as it passes over the bath roller. The wire-wound metering rod, sometimes known as a Meyer Bar, allows the desired quantity of the coating to remain on the substrate. The quantity is determined by the diameter of the wire used on the rod.

In the slot die process, the coating is squeezed out by gravity or under pressure through a slot and onto the substrate. If the coating is 100% solids, the process is termed "Extrusion" and in this case, the line speed is frequently much faster than the speed of the extrusion. This enables coatings to be considerably thinner than the width of the slot.

It may be particularly desirable to employ extrusion methods for forming film compositions containing PEO polymer components. These compositions contain PEO or PEO blends in the polymer component, and may be essentially free of added plasticizers, and/or surfactants, and polyalcohols. The compositions may be extruded as a sheet at processing temperatures of less than about 90° C. Extrusion may proceed by squeezing the film composition through rollers or a die to obtain a uniform matrix. The extruded film composition then is cooled by any mechanism known to those of ordinary skill in the art. For example, chill rollers, air cooling beds, or water cooling beds may be employed. The cooling step is particularly desirable for these film compositions because PEO tends to hold heat.

The gap or knife over roll process relies on a coating being applied to the substrate which then passes through a "gap"

between a "knife" and a support roller. As the coating and substrate pass through, the excess is scraped off.

Air knife coating is where the coating is applied to the substrate and the excess is "blown off" by a powerful jet from the air knife. This procedure is useful for aqueous coatings.

In the curtain coating process, a bath with a slot in the base allows a continuous curtain of the coating to fall into the gap between two conveyors. The object to be coated is passed along the conveyor at a controlled speed and so receives the coating on its upper face.

Drying the Film

The drying step is also a contributing factor with regard to maintaining the uniformity of the film composition. A controlled drying process is particularly important when, in the absence of a viscosity increasing composition or a composition in which the viscosity is controlled, for example by the selection of the polymer, the components within the film may have an increased tendency to aggregate or conglomerate. An alternative method of forming a film with an accurate dosage, that would not necessitate the controlled drying process, would be to cast the films on a predetermined well. With this method, although the components may aggregate, this will not result in the migration of the active to an adjacent dosage form, since each well may define the dosage unit per se.

When a controlled or rapid drying process is desired, this may be through a variety of methods. A variety of methods may be used including those that require the application of heat. The liquid carriers are removed from the film in a manner such that the uniformity, or more specifically, the non-self-aggregating uniform heterogeneity, that is obtained in the wet film is maintained.

Desirably, the film is dried from the bottom of the film to the top of the film. Desirably, substantially no air flow is present across the top of the film during its initial setting period, during which a solid, visco-elastic structure is formed. This can take place within the first few minutes, e.g. about the first 0.5 to about 4.0 minutes of the drying process. Controlling the drying in this manner, prevents the destruction and reformation of the film's top surface, which results from conventional drying methods. This is accomplished by forming the film and placing it on the top side of a surface having top and bottom sides. Then, heat is initially applied to the bottom side of the film to provide the necessary energy to evaporate or otherwise remove the liquid carrier. The films dried in this manner dry more quickly and evenly as compared to air-dried films, or those dried by conventional drying means. In contrast to an air-dried film that dries first at the top and edges, the films dried by applying heat to the bottom dry simultaneously at the center as well as at the edges. This also prevents settling of ingredients that occurs with films dried by conventional means.

The temperature at which the films are dried is about 100° C. or less, desirably about 90° C. or less, and most desirably about 80° C. or less.

Another method of controlling the drying process, which may be used alone or in combination with other controlled methods as disclosed above includes controlling and modifying the humidity within the drying apparatus where the film is being dried. In this manner, the premature drying of the top surface of the film is avoided.

Additionally, it has also been discovered that the length of drying time can be properly controlled, i.e. balanced with the heat sensitivity and volatility of the components, and particularly the flavor oils and drugs. The amount of energy, temperature and length and speed of the conveyor can be balanced to accommodate such actives and to minimize loss, degradation or ineffectiveness in the final film.

A specific example of an appropriate drying method is that disclosed by Magoon. Magoon is specifically directed toward a method of drying fruit pulp. However, the present inventors have adapted this process toward the preparation of thin films.

The method and apparatus of Magoon are based on an interesting property of water. Although water transmits energy by conduction and convection both within and to its surroundings, water only radiates energy within and to water. Therefore, the apparatus of Magoon includes a surface onto which the fruit pulp is placed that is transparent to infrared radiation. The underside of the surface is in contact with a temperature controlled water bath. The water bath temperature is desirably controlled at a temperature slightly below the boiling temperature of water. When the wet fruit pulp is placed on the surface of the apparatus, this creates a "refractance window." This means that infrared energy is permitted to radiate through the surface only to the area on the surface occupied by the fruit pulp, and only until the fruit pulp is dry. The apparatus of Magoon provides the films of the present invention with an efficient drying time reducing the instance of aggregation of the components of the film.

Another method of controlling the drying process involves a zone drying procedure. A zone drying apparatus may include a continuous belt drying tunnel having one or more drying zones located within. The conditions of each drying zone may vary, for example, temperature and humidity may be selectively chosen. It may be desirable to sequentially order the zones to provide a stepped up drying effect.

The speed of the zone drying conveyor desirably is continuous. Alternatively, the speed may be altered at a particular stage of the drying procedure to increase or decrease exposure of the film to the conditions of the desired zone. Whether continuous or modified, the zone drying dries the film without surface skinning.

According to an embodiment of the zone drying apparatus **100**, shown in FIG. **35**, the film **110** may be fed onto the continuous belt **120**, which carries the film through the different drying zones. The first drying zone that the film travels through **101** may be a warm and humid zone. The second zone **102** may be hotter and drier, and the third zone **103** may also be hot and dry. These different zones may be continuous, or alternatively, they may be separated, as depicted by the zone drying apparatus **200** in FIG. **36**. The zone drying apparatus, in accordance with the present invention, is not limited to three drying zones. The film may travel through lesser or additional drying zones of varying heat and humidity levels, if desired, to produce the controlled drying effect of the present invention.

To further control temperature and humidity, the drying zones may include additional atmospheric conditions, such as inert gases. The zone drying apparatus further may be adapted to include additional processes during the zone drying procedure, such as, for example, spraying and laminating processes, so long as controlled drying is maintained in accordance with the invention.

The films may initially have a thickness of about 500 μm to about 1,500 μm, or about 20 mils to about 60 mils, and when dried have a thickness from about 3 μm to about 250 μm, or about 0.1 mils to about 10 mils. Desirably, the dried films will have a thickness of about 2 mils to about 8 mils, and more desirably, from about 3 mils to about 6 mils.

Testing Films for Uniformity

It may be desirable to test the films of the present invention for chemical and physical uniformity during the film manu-

facturing process. In particular, samples of the film may be removed and tested for uniformity in film components between various samples. Film thickness and over all appearance may also be checked for uniformity. Uniform films are desired, particularly for films containing pharmaceutical active components for safety and efficacy reasons.

A method for testing uniformity in accordance with the present invention includes conveying a film through a manufacturing process. This process may include subjecting the film to drying processes, dividing the film into individual dosage units, and/or packaging the dosages, among others. As the film is conveyed through the manufacturing process, for example on a conveyor belt apparatus, it is cut widthwise into at least one portion. The at least one portion has opposing ends that are separate from any other film portion. For instance, if the film is a roll, it may be cut into separate sub-rolls. Cutting the film may be accomplished by a variety of methods, such as with a knife, razor, laser, or any other suitable means for cutting a film.

The cut film then may be sampled by removing small pieces from each of the opposed ends of the portion(s), without disrupting the middle of the portion(s). Leaving the middle section intact permits the predominant portion of the film to proceed through the manufacturing process without interrupting the conformity of the film and creating sample-inducted gaps in the film. Accordingly, the concern of missing doses is alleviated as the film is further processed, e.g., packaged. Moreover, maintaining the completeness of cut portions or sub-rolls throughout the process will help to alleviate the possibility of interruptions in further film processing or packaging due to guilty control issues, for example, alarm stoppage due to notice of missing pieces.

After the end pieces, or sampling sections, are removed from the film portion(s), they may be tested for uniformity in the content of components between samples. Any conventional means for examining and testing the film pieces may be employed, such as, for example, visual inspection, use of analytical equipment, and any other suitable means known to those skilled in the art. If the testing results show non-uniformity between film samples, the manufacturing process may be altered. This can save time and expense because the process may be altered prior to completing an entire manufacturing run. For example, the drying conditions, mixing conditions, compositional components and/or film viscosity may be changed. Altering the drying conditions may involve changing the temperature, drying time, moisture level, and dryer positioning, among others.

Moreover, it may be desirable to repeat the steps of sampling and testing throughout the manufacturing process. Testing at multiple intervals may ensure that uniform film dosages are continuously produced. Alterations to the process can be implemented at any stage to minimize non-uniformity between samples.

Uses of Thin Films

The thin films of the present invention are well suited for many uses. The high degree of uniformity of the components of the film makes them particularly well suited for incorporating pharmaceuticals. Furthermore, the polymers used in construction of the films may be chosen to allow for a range of disintegration times for the films. A variation or extension in the time over which a film will disintegrate may achieve control over the rate that the active is released, which may allow for a sustained release delivery system. In addition, the films may be used for the administration of an active to any of several body surfaces, especially those including mucous membranes, such as oral, anal, vaginal, opthalmological, the surface of a wound, either on a skin surface or within a body such as during surgery, and similar surfaces.

The films may be used to orally administer an active. This is accomplished by preparing the films as described above and introducing them to the oral cavity of a mammal. This film may be prepared and adhered to a second or support layer from which it is removed prior to use, i.e. introduction to the oral cavity. An adhesive may be used to attach the film to the support or backing material which may be any of those known in the art, and is preferably not water soluble. If an adhesive is used, it will desirably be a food grade adhesive that is ingestible and does not alter the properties of the active. Mucoadhesive compositions are particularly useful. The film compositions in many cases serve as mucoadhesives themselves.

The films may be applied under or to the tongue of the mammal. When this is desired, a specific film shape, corresponding to the shape of the tongue may be preferred. Therefore the film may be cut to a shape where the side of the film corresponding to the back of the tongue will be longer than the side corresponding to the front of the tongue. Specifically, the desired shape may be that of a triangle or trapezoid. Desirably, the film will adhere to the oral cavity preventing it from being ejected from the oral cavity and permitting more of the active to be introduced to the oral cavity as the film dissolves.

Another use for the films of the present invention takes advantage of the films' tendency to dissolve quickly when introduce to a liquid. An active may be introduced to a liquid by preparing a film in accordance with the present invention, introducing it to a liquid, and allowing it to dissolve. This may be used either to prepare a liquid dosage form of an active, or to flavor a beverage.

The films of the present invention are desirably packaged in sealed, air and moisture resistant packages to protect the active from exposure oxidation, hydrolysis, volatilization and interaction with the environment. Referring to FIG. **1**, a packaged pharmaceutical dosage unit **10**, includes each film **12** individually wrapped in a pouch or between foil and/or plastic laminate sheets **14**. As depicted in FIG. **2**, the pouches **10**, **10'** can be linked together with tearable or perforated joints **16**. The pouches **10**, **10'** may be packaged in a roll as depicted in FIG. **5** or stacked as shown in FIG. **3** and sold in a dispenser **18** as shown in FIG. **4**. The dispenser may contain a full supply of the medication typically prescribed for the intended therapy, but due to the thinness of the film and package, is smaller and more convenient than traditional bottles used for tablets, capsules and liquids. Moreover, the films of the present invention dissolve instantly upon contact with saliva or mucosal membrane areas, eliminating the need to wash the dose down with water.

Desirably, a series of such unit doses are packaged together in accordance with the prescribed regimen or treatment, e.g., a 10-90 day supply, depending on the particular therapy. The individual films can be packaged on a backing and peeled off for use.

The features and advantages of the present invention are more fully shown by the following examples which are provided for purposes of illustration, and are not to be construed as limiting the invention in any way.

EXAMPLES

Examples A-I

Water soluble thin film compositions of the present invention are prepared using the amounts described in Table 1.

TABLE 1

Component	Weight (g) A	B	C	D	E	F	G	H	I
Hydroxypropylmethyl cellulose		1.76		1.63	32.00		3.67		32.00
Peppermint oil		0.90	1.0	1.05		8.0	2.67		
Sweetener	0.15	0.15	0.22	0.10		4.6	1.53	0.15	
Polyvinylpyrrolidone		0.94		1.05		7.0	2.33		
Tween 80[1]	0.5	0.5	2.0	0.65	11.80		1.35	0.5	11.80
Simethicone[2]	0.2	0.2	0.15	0.30	1.80		0.21	0.2	1.80
Listerine[3]	83.35							83.35	
Methylcellulose	6.0								
Cornstarch[4]			1.75						
Agar			1.25						
Water		42.24	93.63	39.22	768.0	280.0	88.24		768.0
Loratadine[5]					19.2				19.2
Pullulan[6]								6.0	
Ibuprofen									38.4

[1]Available from ICI Americas

[2]Available from OSI

[3]Available from Pfizer, Inc. including thymol (0.064%), eucalyptol (0.092%), methyl salicylate (0.060%), menthol (0.042%), water (up to 72.8%), alcohol (26.9%), benzoic acid, poloxamer 407, sodium benzoate, and caramel color

[4]Available from Grain Processing Corporation as Pure Cote B792

[5]Available from Schering Corporation as Claritin

[6]Available from Hayashibara Biochemical Laboratories, Inc., Japan

The ingredients of inventive compositions A-I were combined by mixing until a uniform mixture was achieved. The compositions were then formed into a film by reverse roll coating. These films were then dried on the top side of an infrared transparent surface, the bottom side of which was in contact with a heated water bath at approximately 99° C. No external thermal air currents were present above the film. The films were dried to less than about 6% by weight water in about 4 to 6 minutes. The films were flexible, self-supporting and provided a uniform distribution of the components within the film.

The uniform distribution of the components within the film was apparent by examination by either the naked eye or under slight magnification. By viewing the films it was apparent that they were substantially free of aggregation, i.e. the carrier and the actives remained substantially in place and did not move substantially from one portion of the film to another. Therefore, there was substantially no disparity among the amount of active found in any portion of the film.

Uniformity was also measured by first cutting the film into individual dosage forms. Twenty-five dosage forms of substantially identical size were cut from the film of inventive composition (E) above from random locations throughout the film. Then eight of these dosage forms were randomly selected and additively weighed. The additive weights of eight randomly selected dosage forms, are as shown in Table 2 below:

TABLE 2

Sample	Additive Weight (g) Trial 1	Trial 2
1	0.04	0.04
2	0.08	0.08
3	0.12	0.12
4	0.16	0.16
5	0.20	0.20
6	0.24	0.24
7	0.28	0.28
8	0.32	0.32

The individual dosages were consistently 0.04 gm, which shows that the distribution of the components within the film was consistent and uniform. This is based on the simple principal that each component has a unique density. Therefore, when the components of different densities are combined in a uniform manner in a film, as in the present invention, individual dosages forms from the same film of substantially equal dimensions, will contain the same mass.

An alternative method of determining the uniformity of the active is to cut the film into individual doses. The individual doses may then be dissolved and tested for the amount of active in films of particular size. This demonstrates that films of substantially similar size cut from different locations on the same film contain substantially the same amount of active.

When the films formed from inventive compositions A-H are placed on the tongue, they rapidly dissolve, releasing the active ingredient. Similarly, when they are placed in water, the films rapidly dissolve which provides a flavored drink when the active is chosen to be a flavoring.

Examples J-L

Thin films that have a controlled degradation time and include combinations of water soluble and water insoluble polymers and water soluble films that allow controlled release of an active are prepared using approximately the amounts described in Table 3.

TABLE 3

Component	Weight (g) J	K	L
Hydroxypropylmethyl cellulose		1.0	1.0
Tween 80[1]	0.7	0.7	0.7
Water			5.0
Aquacoat ECD[2]	17.0	17.0	17.5
Peppermint oil	1.0	0.4	1.1

[1]Available from ICI Americas

[2]A 30% by weight aqueous dispersion of ethyl cellulose available from FMC

The components of inventive compositions J-L were combined and formed into films using the methods for preparing

inventive compositions A-I above. These films were also flexible, self-supporting and provided a uniform distribution of active which permits accuracy in dosing.

The uniformity of the films prepared from inventive compositions J-L may also be tested by either visual means measuring the weights of individual dosage films, or by dissolving the films and testing for the amount of active as described above.

Examples M-O

An alternative method of preparing films which provides an accurate dosing may be used for any of inventive compositions A-I. The method begins with first combining the ingredients with mixing. The combination of ingredients is then divided among individual wells or molds. In such a method, aggregation of the components during drying is prevented by the individual wells.

TABLE 4

	Weight %		
Component	M	N	O
5% Methylcellulose Solution[1]	73.22	44.22	74.22
Raspberry Flavor	3.28	3.28	3.28
Sweetener Blends	1.07	1.07	1.07
Tween-80[2]	2.47	2.47	2.47
Polyvinylpyrrolidone	3.30	3.30	3.30
Ethanol 95%	8.24	8.24	8.24
Propylene Glycol	1.65	1.65	1.65
Calcium Carbonate	4.12	4.12	4.12
Cornstarch[3]	1.65	1.65	1.65
Red Dye[4]	1.00		
Corn Syrup[5]		30.00	

[1]Available from Dow Chemical Co. as Methocel K35
[2]Available from ICI Americas
[3]Available from Grain Processing Corporation as Pure Cote B792
[4]Available from McCormick
[5]Available from Bestfoods, Inc. as Karo Syrup

The ingredients in the above Table 4 were combined and formed into a film by casting the combination of ingredients onto the glass surface and applying heat to the bottom side of the glass. This provided inventive compositions M-O.

The film of composition M was examined both prior to and after drying for variations in the shading provided by the red dye. The film was examined both under sunlight and by incandescent bulb light. No variations in shade or intensity of color were observed.

Further testing of the films of composition M included testing of absorption which is directly related to concentration. The film was cut into segments each measuring 1.0 in. by 0.75 in., which were consecutively assigned numbers. Approximately 40 mg of the scrap material from which the segments were cut was dissolved in about 10 ml of distilled water and then quantitatively transferred to a 25 ml volumetric flask and brought to volume. The solution was centrifuged and scanned at 3 nm intervals from 203-1200 nm. The frequency of maximum absorption was found to be 530 nm. The solution was then re-centrifuged at a higher RPM (for the same length of time) and re-scanned, which demonstrated no change in the % transmission or frequency.

Each of the segments were weighed to 0.1 mg and then dissolved in 10 ml distilled water and transferred quantitatively to a 25 ml volumetric flask and brought to volume with distilled water. Each segment solution was then centrifuged as above, and then scanned, at first from 203-1200 nm and later from only 500 nm to 550 nm at a 1 nm scanning speed. The value recorded was the % transmission at the lowest wave length, which was most frequently 530 nm.

The absorption values are shown in Table 5 below:

TABLE 5

Segment	mg/% A
1-2	1.717
3-4	1.700
5-6	1.774
7*	1.701
9-10	1.721
11-12	1.729
13-14	1.725
15-16	1.713

*segment 8 was lost

The overall average absorption was 1.724. Of the 15 segments tested, the difference between the highest and lowest values was 0.073 units, or 4% based on the average. This shows excellent control over the uniformity of the dye within the composition because the absorption is directly proportional to the concentration of the dye within each segment.

The film of inventive composition N provided a very flexible film. This film was able to be stretched and exhibited a very high tensile strength.

After forming the film of inventive composition O, the film was removed from the glass by very rapidly stripping the length of the glass with a razor. This provided very tightly wound "toothpick-like" dosage forms. Each dosage form consistently weighed 0.02 g. This demonstrates the uniformity of the dosage forms as well as the superior self-supporting properties of the films.

Examples P-W

Compositions P-W were prepared to demonstrate the interaction among various conditions in production of films as they relate to the present invention. The ingredients in the below Table 6 were combined and formed into a film using the process parameters listed in Table 7 below, prepared in a 6 m drying tunnel designed to incorporate bottom drying of the films. Each of the examples shows the effect of different ingredient formulations and processing techniques on the resultant film products.

TABLE 6

	Weight (g)							
Component	P	Q	R	S	T	U	V	W
Hydroxy propylmethyl cellulose	320	320	320	320	320	320	345	345
Water	1440	1440	1440	1440		1440	999	999
Sweetener						60	60	45
Mint Flavor						80	80	
Propylene Glycol	50	50	50	100	100	100	100	69.3
Xanthan	22		11	11.23	10	10	10	6.9
Water/ Ethanol (60/40)					1440			
Orange Flavor								42

TABLE 7

	Film Thickness (Micron)	Top[1] v (m/sec)	Bot.[1] v (m/sec)	T[1] (° C.)	Top[2] v (m/sec)
P1	100	0	22	75	0
P2	350	0	22	75	0
P3	350	0	40	75	0
P4	350	0	40	75	0
P5	350	10	40	75	10
Q	350	0	40	75	10
R	350	0	40	85	10
S1	250	0	40	100	0
S2	300	0	40	100	0
S3	350	0	40	100	0
T1	250	0	40	100	0
T2	350	0	40	100	0
U1	300	0	40	100	0
U2	250	0	40	100	0
U3	300	0	40	100	0
V1	300	0	40	100	0
V2	300	0	40	100	0
V3	300	0	40	100	0
W1	300	0	40	93	0
W2	250	0	40	90	0
W3	200	0	40	90	0

	Bot.[2] v (m/sec)	T[2] (° C.)	Film Weight (g)	Coater Speed m/min	% Moisture
P1	23	60	109	5	>20
P2	23	60	n/a	5	>20
P3	40	60	161	3	>20
P4	40	75	191	3	>20
P5	40	75	253	3	>20
Q	40	75	n/a	3	>20
R	0	85		2.5	>20
S1	40	90	163	1.5	<5
S2	40	90	193	1.5	<5
S3	40	90	225	1.5	<5
T1	40	90	64	1.5	<5
T2	40	90	83	1.5	<5
U1	40	90	208	1.5	20
U2	40	90	177	1.5	20
U3	40	90	212	1.3	20
V1	40	90	237	1.3	20
V2	40	100	242	1.3	20
V3	40	100	221	1	6
W1	40	90	220	1.3	5
W2	40	90	199	1.3	5
W3	40	90	169	1.3	5

[1]First Heater Section (3 m)
[2]Second Heater Section (3 m)

In Table 7, each of the process parameters contributes to different properties of the films. Film thickness refers to the distance between the blade and the roller in the reverse roll coating apparatus. Bottom velocity and top velocity refer to the speed of air current on the bottom and top sides of the film, respectively. The film weight is a measure of the weight of a circular section of the substrate and the film of 100 cm^2.

Compositions P-R show the effects of visco-elastic properties on the ability to coat the film composition mixture onto the substrate for film formation. Composition P displayed a stringy elastic property. The wet film would not stay level, the coating was uneven, and the film did not dry. In Composition Q, substantially the same formulation as P was used however the xanthan was not included. This product coated the substrate but would not stay level due to the change in the visco-elastic properties of the wet foam. Composition R was prepared using substantially the same formulation, but incorporated one-half of the amount of xanthan of Composition P. This formulation provided a composition that could be evenly coated. Compositions P-Q demonstrate the importance of proper formulation on the ability of the film matrix to conform to a particular coating technique.

The films produced from Composition S contained a large amount of air in the films. This is shown by the dried film thickness which was the same despite that variation in the coated thickness as in Table 7. Microscopic examination of the film revealed a large number of air bubbles in the film. In order to correct for the addition of air in the films, care must be taken in the mixing process to avoid air inclusion.

Composition T included a change in the solvent to 60/40 water ethanol. Composition T was stirred slowly for 45 min. to deaerate the mixture. The dried weight film products T1 and T2 were consistent with the increase in solids from T1 to T2. The films dried much faster with less than 5% moisture. With the particular combination of ingredients in Composition T, the substitution of part ethanol for part water allowed the film to dry more quickly. The elimination of air from the film as a result of the slow stirring also contributed to the uniformity of the final film product and the faster drying time.

Only water was used as a solvent in Composition U. The dried weight of the U1-U3 changed consistently in accordance with the change in coating thickness indicating that no air bubbles were present. However, these films contained 20% moisture upon exit from the oven, unlike the films of Composition T, which included part ethanol and dried completely.

The amount of solids was increased and the amount of water was decreased in Compositions V1 and V2. The dried weight was greater than U1-U3 due to the increase in solids, however the films still contained 20% moisture upon exit from the oven, similar to Composition U.

The coating line speed was reduced for Composition V3, to prevent premature drying of the exposed top film surface. This film product dried to 6% moisture.

While increasing the amount of solids improved the film weight, longer drying times were required. This was due to the surface of the film sealing preventing easy removal of the water. Therefore, for Compositions W1-W3, the temperature in the first 3 m section of the dryer was decreased. This prevented the premature drying of the top surface of the films. Even at greater film thicknesses, the films were dried to 5% moisture even at faster coater line speeds.

Examples X-AA

TABLE 8

	Weight (g)			
Component	X	Y	Z	AA
Loratadine	104.69			
Zomig		52.35		
Paxil			104.69	
Hydroxypropyl methylcellulose	320	320	320	150
Sweetener blend	60	60	60	0.4
Simethicone	1.5	1.5	1.5	1.5
Propylene glycol	100	100	100	
Water	1440	1440	1440	790
Cream essence				0.4
Polyvinyl pyrrolidinone				4
Ethanol				40
Cocoa				55.2
Polyoxyl-40-stearate				7

Compositions X, Y and Z of Table 8 were taste mask coated using a Glatt coater and Eudragit E-100 polymethacrylate

polymer as the coating. The coating was spray coated at a 20% level. Therefore 10 mg of drug 12.5 mg of the final dry product must be weighed.

The base formula which excluded the drug additive was mixed with care to not incorporate air. After initial mixing the formula was slowly mixed to deaerate over 30 min. During this time the drug was weighed and prepared for addition to the base mix.

For Composition X, the Loratadine (80% drug) was added slowly to the mix with stirring. After 5 min. of stirring, the total mix was added to the pan of a three roll coater set (reverse roll coater) at 30 micron coating thickness.

The process bottom temperature was set at 90° C. with no top heat or air, the bottom air velocity was set at 40 m/sec., and the line speed was set at 1.3 m/min. Total drying time for the film was 4.6 min.

The liquid was coated at 30 microns and dried in the oven in less than 5 min. The film was flexible and a 1"×0.75" piece weighed 70 mg and contained 10 mg of Loratadine.

The experiment was repeated for Compositions Y and Z, Zomig and Paxil, respectively. Both produced flexible films with the target weight of 70 mg containing 5 mg of Zomig and 70 mg containing 10 mg of Paxil, respectively.

The products were sweet without any noticeable drug after-taste.

Examples BA-BI

The incorporation of the anti-foaming/de-foaming agent (i.e., simethicone) provided a film that not only provided a uniform film that substantially reduced or eliminated air bubbles in the film product, but also provided other benefits. The films displayed more desirable organoleptic properties. The films had an improved texture that was less "paper-like" provided a better mouth-feel to the consumer.

The compositions in Table 9 were prepared (including the addition of simethicone in inventive compositions BA-BG) and mixed under vacuum to remove air bubbles.

The resultant uncut films of inventive compositions BA-BG exhibited uniformity in content particularly with respect to the insoluble active, as well as unit doses of ¾" by 1" by 5 mils cut therefrom. The inventive compositions also were observed to have a smooth surface, absent of air bubbles. The significantly higher amounts of simethicone present in inventive compositions BF-BG also provided a very uniform film, but not significantly improved from that of inventive compositions BA-BE.

By contrast, comparative examples BH-BI were observed to have a rougher surface, exhibiting the inclusion of air bubbles in the resultant film which provided a less uniform texture and distribution of the ingredients.

TABLE 9

Component	BA	BB	BC	BD	BE	BF	BG	BH	BI
Hydroxypropylmethyl cellulose	0	3.77	3.70	3.84	0	3.67	0	0	3.84
Peppermint oil	2.94	1.93	2.39	0	0	2.67	2.94	2.67	0
Sweetener	2.20	0.32	0.23	0	0.17	1.53	2.20	1.54	0
Polyvinylpyrrolidone	2.68	2.01	2.39	0	0	2.33	2.68	2.34	0
Tween 80[1]	2.24	1.07	1.48	1.42	0.55	1.35	2.24	0	1.42
Simethicone[2]	0.66	0.42	0.68	0.22	0.22	5.00	2.00	0	0
Listerine[3]	0	0	0	0	92.41	0	0	0	0
Methylcellulose	4.03	0	0	0	0	0	4.03	0	0
Cornstarch[4]	2.68	0	0	0	0	0	2.68	0	0
Water	73.53	90.47	89.14	92.22	0	83.45	72.19	93.46	92.44
Loratadine[5]	4.29	0	0	2.31	0	0	4.29	0	2.31
Pullulan[6]	0	0	0	0	6.65	0	0	0	0
Calcium Carbonate	1.43	0	0	0	0	0	1.43	0	0
Xanthan Gum	0.30	0	0	0	0	0	0.30	0	0
Propylene Glycol	3.02	0	0	0	0	0	3.02	0	0

[1]Available from ICI Americas

[2]Available from OSI

[3]Available from Pfizer, Inc. including thymol (0.064%), eucalyptol (0.092%), methyl salicylate (0.060%), menthol (0.042%), water (up to 72.8%), alcohol (26.9%), benzoic acid, poloxamer 407, sodium benzoate, and caramel color

[4]Available from Grain Processing Corporation as Pure Cote B792

[5]Available from Schering Corporation as Claritin

[6]Available from Hayashibara Biochemical Laboratories, Inc., Japan

The ingredients of Composition AA were mixed in order to reduce air captured in the fluid matrix. After mixing 45 g of loratadine coated at a 80% active level and 20% coating using Eudragit E-100, this mixture was added slowing with mixing until the drug was evenly dispersed, approximately 5 min. The liquid was then deposited into the 3 roll coater (reverse roll coater) and coated at 30 microns at a line speed of 1.3 m/min. The oven temperature was set at 90° C. to apply air and heat to the bottom only, with an air velocity set at 40 m/sec. The dried film was 0.005 inch. thick (5 mil) and was cut into 1 in.×0.75 in. pieces weighing 70 mg+/−0.7 mg, demonstrating the uniformity of the composition of the film. The film was flexible with 5% moisture, free of air bubbles, and had uniform drug distribution as seen under the light microscope, as well as shown by the substantially identical weight measurements of the film pieces.

Examples CA-CC

The following examples of the present invention describe films and film-forming compositions that use an ethoxylated caster oil as a surfactant, or alternatively are free of surfactants, plasticizers and/or polyalcohols. Desirably, the films or film-forming compositions of the present invention are essentially free of surfactants. Moreover, the films or film-forming compositions of the present invention are desirably formulated to be essentially free of surfactants. Furthermore, the films or film-forming compositions of the present invention are desirably formulated to be essentially free of plasticizers. Still furthermore, the films or film-forming compositions of the present invention are desirably formulated to be essentially free of polyalcohols. Moreover, the films or film-form-

ing compositions of the present invention are desirably formulated to be essentially free of surfactants and plasticizers. Furthermore, the films or film-forming compositions of the present invention are desirably formulated to be essentially free of surfactants, plasticizers and polyalcohols.

TABLE 10

Component	(parts by wt.) CA
POLYMERS:	
Hydroxypropylmethyl cellulose	15.6
Cornstarch[1]	10.41
Polyvinylpyrrolidone	10.41
Xanthan Gum	1.14
SURFACTANT[2]:	2.0
PLASTICIZER[3]:	11.67
ANTI-FOAM AGENT[4]	2.44
OTHER	
Spearmint Flavor	10.43
Loratadine (drug)	16.62
Calcium Carbonate	5.54
Sweetener	9.36

[1]Available from Grain Processing Corporation as Pure Cote B792
[2]Ethoxylated caster oil, Cremophor ® EL available from BASF
[3]Propylene Glycol
[4]Silicone Emulsion

The above ingredients were added at 30% to 70% water and stirred until polymers were fully hydrated which took 45 min. The mix was then put under vacuum to eliminate entrapped air. Vacuum was added in a steady manner starting at 500 mm and progressing up to 760 mm over 45 min.

After release of the vacuum, 6 grams of the liquid was added to a coating paper using a 200 micron spiral wound rod and a K Control Coater Model 101 (RK Print Coat Inst. Ltd.). The paper substrate onto which the coating was added was a silicone coated paper. The coated paper was then dried at 90° C. until about 5% moisture remained. The formula coated and dried to a film thickness of approx. 60 microns and quickly dissolved in the mouth.

TABLE 11

Component	(parts by wt.) CB
POLYMERS:	
Hydroxypropylmethyl cellulose	15.6
Cornstarch[1]	10.41
Polyvinylpyrrolidone	10.41
PLASTICIZER/SOLVENT[2]:	22.1
ANTI-FOAM AGENT[3]	2.44
OTHER	
Raspberry Flavor	0.3
Calcium Carbonate[4]	30.38
Sweetener	8.36

[1]Available from Grain Processing Corporation as Pure Cote B792
[2]Propylene Glycol
[3]Polydimethyl Siloxane Emulsion
[4]Functioned to mimic drug loading

The above ingredients were added to water at 40% until a homogeneous suspension was made. Vacuum was added over 20 min. starting at 500 mm Hg. and ending at 660 mm Hg. until all air was removed from suspension. Film was made as described in prior experiments. The liquid coated the silicone release substrate and dried to a uniform flexible film. The film passed the 180° bend test without cracking and dissolved in the mouth.

TABLE 12

Component	(parts by wt.) CC
POLYMERS:	
Hydroxypropylmethyl cellulose	7.8
Hydroxypropyl cellulose	7.8
ANTI-FOAM AGENT[1]	0.75
OTHER	
Peppermint & Bittermint Flavor	2.25
Tastemasking Flavor[2]	0.3
Calcium Carbonate[3]	15.2
Sweeteners	0.9

[1]Polydimethyl Siloxane Emulsion
[2]Prosweet from Virginia Dare
[3]Functioned to mimic drug loading

The above ingredients were added at 30% to 70% water and stirred until polymers were fully hydrated which took 20 min. The mix was then put under vacuum to eliminate entrapped air. Vacuum was added in a steady manner up to 760 mm over 35 min.

After release of the vacuum, the liquid was added to a coating paper using a 350 micron smooth bar and a K Control Coater Model 101 (RK Print Coat Inst. Ltd.). The paper substrate onto which the coating was added was a silicone coated paper. The coated paper was then dried at 90° C. until about 4% moisture remained. The formula coated and dried to a film. The film had an acceptable taste and quickly dissolved in the mouth. The taste-masking flavor is an ingredient that affects the taste receptors to mask the receptors from registering a different, typical undesirable, taste. The film passed the 180° bend test without cracking and dissolved in the mouth.

Example CD

The following example of the present invention describes films and film-forming compositions that use a taste-masked, pharmaceutically active agent which also contains flavors and taste-masking aids. A taste-masking flavor is an ingredient that effects taste receptors to mask the receptors from registering a different, typically undesirable, taste.

TABLE 13

Component	(grams) CD
Hydroxypropylmethyl cellulose	4.26
Hydroxypropyl cellulose	1.42
Precipitated calcium Carbonate	1.22
Sweetner[1]	0.6
Taste-Masking flavor[2]	0.08
Taste-masked Acetaminophen[3]	5.86
Cinnamon Flavor	0.9
Spearmint Flavor	0.43
Polydimethylsiloxane emulsion	0.23

[1]Sucralose, available from McNeil Nutritionals
[2]Magna Sweet, available from Mafco Worldwide Corp.
[3]Gutte Enteric, coated acetaminophen, Gatte, LLC

The above ingredients, except for the pharmaceutically active agent and flavors, were added at 35 grams water and stirred until polymers were fully hydrated which took about 20 min. Food coloring (7 drops of red food coloring and 1

drop of yellow fool coloring) was also added. The mix was then put under vacuum to eliminate entrapped air. Vacuum was added in a steady manner starting at 500 mm and progressing up to 760 mm over about 10 to 20 minutes. The taste-masked Acetaminophen was added to the mix in about 4 minutes was stirring under vacuum. The flavors were then added to the mix in about 4 minutes was stirring under vacuum.

After release of the vacuum, the liquid solution was added to a coating paper using a 350 micron smooth bar. The paper substrate onto which the coating was added was a silicone coated paper. The coated paper was then dried at 90° C. for about 11 minutes until about 3% moisture remained.

The formula coated and dried to a film. The film had an acceptable taste and moderately quickly dissolved in the mouth. The film did not curl on standing. The film passed the 180° bend test without cracking and dissolved in the mouth.

Examples CE-CF

Thin film compositions of the present invention were prepared using the amounts described in Table 14.

TABLE 14

Component	Weight (g)
Hydroxypropylmethyl cellulose	3.92
Pullulan	3.92
Trehalose[1]	3.5
Precipitated Calcium Carbonate	3.85
Propylene Glycol	1.96
Simethicone[2]	0.35
Bovine Extract[3]	32.5
Water	q.s.

[1]Available from Cargill Inc.
[2]Available from Sentry
[3]Available from Amarillo Biosciences Inc.

The above ingredients were combined by mixing until a uniform mixture was achieved. A sufficient amount of water was present in the film compositions prior to drying, i.e., q.s., which may range between about 200 g to about 1000 g. The bovine extract protein contained in the compositions is a heat sensitive protein. After mixing, the compositions were cast into films on release paper using a K-Control Coater with a 250 micron smooth bar.

In Example CE, the films subsequently were dried in an oven at approximately 80° C. for about 6 minutes. The films were dried to about 4.3 percent moisture. In Example CF, the films were dried in an oven at approximately 60° C. for about 10 minutes. The films were dried to about 5.06 percent moisture. After drying, the protein derived from bovine extract, which was contained in the films, was tested to determine whether or not it remained substantially active. To test the activity, a film dosage unit of this example was administered to a human. After ingesting the dosage, a microarray on the human's blood was conducted. The results, listed in Appendix A which is incorporated by reference herein, and graphically represented in FIG. **32**, demonstrate that the protein was approximately 100 percent active in the final, dried film products of both Examples CE and CF. Therefore, the heat sensitive active did not substantially degrade or denaturize during the drying process.

Example CG

Thin film compositions of the present invention were prepared using the amounts described in Table 15.

TABLE 15

Component	Weight (g unless otherwise indicated) CG	CH
Hydroxypropylmethyl cellulose	4.59	9.18
Hydroxypropyl cellulose	1.53	3.06
Sucralose[1]	0.7	1.4
Magna Sweet[2]	0.09	0.18
Precipitated calcium carbonate	2.0	4
Fat-coated dextromethorphan hydrobromide	5.96	11.93
Orange concentrate flavor	1.05	2.1
Prosweet MM24[3]	0.18	0.35
Propylene glycol	1.22	2.45
Simethicone[4]	0.18	0.35
Water	32.5	65
Red food color		4 drops
Yellow food color		6 drops

[1]Available from McNeil Nutritional
[2]Taste-masking flavor, available from Mafco Worldwide Corp.
[3]Taste-masking flavor, available from Virginia Dare
[4]Available from Sentry

The above ingredients in the amounts listed for CG were combined by mixing, and then cast into two films on release paper using a K-Control Coater with a 350 micron smooth bar. The films were subsequently dried according to conventional drying techniques, rather than via the uniform drying process of the present invention. One film was dried in an oven at 80° C. for 9 minutes on a wire rack. The second film was dried in an oven at 80° C. for 9 minutes on a wire screen. Both films were dried to about 2.4 percent moisture.

The resulting dried films showed imprints of the wire rack and screen after drying. These configurations comprise imprints of wire supports typically used in the drying process. Without uniform heat diffusion, the wire supports conducted heat more intensely at the points of contact with the substrate, leading to increased evaporation at these points. This caused more vigorous mixing, thereby pulling more particles to the contact points. The result is increased particle density seen as aggregations at the contact points.

The solution was cast into two more films on release paper using the K-Control Coater with a 350 micron smooth bar. These films were dried by the process of the present invention, under the same time and temperature conditions as above. In particular, the films were dried in an 80° C. air oven for 9 minutes on trays lined with furnace filters, which uniformly disperse heat. The films were dried to about 1.89 percent moisture. The resulting films had no streaks, and were homogenous. Due to uniform heat diffusion throughout the film, no particle aggregations developed.

Example CH

The ingredients in Table 15, in the amounts listed for CH, were combined by mixing, and then cast into three films on release paper using a K-Control Coater with a 350 micron smooth bar. The films were dried for 9 minutes in an 80° C. air oven on trays lined with furnace filters, which uniformly distribute heat. The films were dried to about 2.20 percent moisture. As depicted in FIG. **17**, the dried films **200** had no streaks, and were homogenous, i.e., no particle aggregations developed. The active particles appeared intact in the dried films. The films exhibited adequate strength and passed the 180° bend test without cracking, in which the films are bent in half with pressure.

The mixed solution was cast into three more films on release paper using a K-Control Coater with a 350 micron smooth bar. These films similarly were dried for 9 minutes in

an 80° C. air oven, but by conventional top and bottom drying means. Two of the films were dried on wire racks, while the third was dried on a wire screen. All three films were dried to about 2.65 percent moisture. The dried films showed the imprints of the wire racks and screen, for the reasons described above in Example CG.

More particularly, the dried films **100** exhibited aggregations **110** of particles in both line and diamond configurations, as shown in FIGS. **9-16**. These configurations comprise imprints of wire supports used in the drying process to display the disuniformity in heat transfer which occurs in conventional top and bottom drying. As discussed above, the wire supports conducted heat more intensely at the points of contact with the substrate, leading to increased evaporation at these points. This caused more vigorous mixing, thereby pulling more particles to the contact points. The resulting increased particle density at the contact points is depicted in FIGS. **9-16**.

Moreover, the fat-coated dextromethorphan particles contained within the films of this example were not destroyed by the drying processes. FIGS. **28-31** depict fat-coated dextromethorphan particles **500** prior to any processing, and particularly, their substantially spherical shape. After exposure to drying conditions of 80° C. for 9 minutes, the fat-coated drug particles **500** were found to have remained intact within the films, i.e., maintained their spherical shape, as shown in FIGS. **18-25**. Although the active particles were exposed to potentially deleterious temperatures, they did not degrade. In contrast, fat-coated dextromethorphan particles placed in an evaporating dish and heated in an air oven at 80° C. for 9 minutes substantially degrade. As seen in FIGS. **26** and **27**, the fat-coated dextromethorphan particles appear completely melted after the exposure.

Example CI

Thin film compositions of the present invention were prepared using the amounts described in Table 16.

TABLE 16

Component	Weight (g unless otherwise indicated)
Hydroxypropylcellulose	6.00
Polyethylene oxide	2.00
Sucralose[1]	0.84
Magna sweet[2]	0.09
Mixture of microcrystalline cellulose and sodium carboxymethylcellulose[3]	0.18
Precipitated calcium carbonate	1.55
Sildenafil[4]	2.91
Peppermint & bittermint flavor	1.75
Prosweet[5]	0.44
Masking flavor[6]	1.31
N,2,3-trimethyl-2-isopropylbutanamide[7]	0.075
Simethicone[8]	0.035
Water	32.5
Blue food coloring	3 drops

[1]Available from McNeil Nutritional
[2]Taste-masking flavor, available from Mafco Worldwide Corp.
[3]Avicel CL-611, available from FMC Biopolymer
[4]Available from Pfizer, Inc. as Viagra ®
[5]Taste-masking flavor, available from Virginia Dare
[6]Available from Ungerer and Co.
[7]Cooling agent
[8]Available from Sentry

The above ingredients were combined by mixing until a uniform mixture was achieved, and then cast into two films on release paper using a K-Control Coater with a 350 micron smooth bar. One film was dried for 10 minutes in an 80° C. air oven to a moisture level of 3.52%, while the second film was dried for 10 minutes in an 80° C. air oven to a moisture level of 3.95%. The dried films had adequate strength and tear resistance. The films passed the 180° bend test without breaking. The films also dissolved at a moderately fast rate in the mouth and exhibited an acceptable flavor.

As mentioned above, the controlled drying process of the present invention allows for uniform drying to occur, whereby evaporative cooling and thermal mixing contribute to the rapid formation of viscoelastic film and the "locking-in" of uniformity of content throughout the film. One of the additional advantages of the present invention is that the film composition reaches its viscoelastic state, and even the fully dried state, without exposing the components of the composition to temperatures which will cause them to be altered or unusable for their intended purpose. For example, heat sensitive drugs, proteins, flavors, sweeteners, volatile components, antigens, antibodies and the like, readily decompose at certain temperatures become inactive or denature, making them ineffective for their intended use. In the present invention, due to the combination of a short heat history required to dry, and the controlled non-top-skinning drying process, the film composition never need to attain the oven temperature (or other heat source) to reach the dried state. To demonstrate this, films were made in accordance with the present invention and dried as discussed below. A first thermocouple was placed within the film and a second thermocouple was suspended in the oven in order to measure the temperature differential between the oven environment and the film composition during the drying process.

To measure the temperature differentials, a thermocouple, which was connected to a Microtherma 1 thermometer, was placed within the films, and another thermocouple was suspended in the drying oven. Temperature readings in the films and oven were recorded every 30 seconds during the drying of the films.

The thermocouple results for the first film are listed in Table 17 below, and graphically represented in FIG. **33**. The results for the second film are listed in Table 18 below, and graphically represented in FIG. **34**. The results show that even after 10 minutes of drying, the temperatures of the film were substantially below (at least about 5° C.) the oven environment. Films dried for less than 10 minutes may experience significantly greater temperature differentials. For example, drying for 4 to 6 minutes, which is a particularly desirable time frame for many films of the present invention, produces differentials of about 25° C. to about 30° C. Accordingly, films may be dried at high, potentially deleterious temperatures without harming heat sensitive actives contained within the films.

TABLE 17

Time (Min.)	Probe Temp (° C.)	Oven Temp (° C.)
0	42.7	78
1	48.1	80
2	48.8	81
3	50	80
4	51.6	80
5	53.6	80
6	56.8	80
7	61.4	80
8	66.8	80
9	72.7	80
10	76.1	80

TABLE 18

Time (Min.)	Probe Temp (° C.)	Oven Temp (° C.)
0	44.4	77
1	49.8	81
2	49.2	81
3	49.4	80
4	51	80
5	52	80
6	55	80
7	58.9	80
8	64.5	80
9	69.8	80
10	74.4	80

Examples CJ-DB

The following examples describe film compositions of the present invention, which contain water-soluble polymers including polyethylene oxide (PEO) alone or in combination with hydroxypropyl cellulose (HPC) or hydroxypropylmethyl cellulose (HPMC). Thin film compositions were prepared using the polymer amounts listed in Table 19.

TABLE 19

Composition	PEO (g)	HPC (g)	HPMC (g)
CJ		32	8
CK		24	16
CL		16	24
CM		8	32
CN			40
CO	8		32
CP	16		24
CQ	24		16
CR	32		8
CS	40		
CT	4		36
CV	6		34
CV	32	8	
CW	24	16	
CX	16	24	
CY	8	32	
CZ		40	
DA	4	36	
DB	6	34	

The above polymer components were combined with equal amounts of precipitated calcium carbonate (mimics drug loading), simethicone emulsion, and water to form the film compositions. The components were combined by mixing until a uniform mixture was achieved, and then cast into films on release paper using a K-Control Coater with a 350 micron smooth bar. The films then were dried for about 9 minutes at 80° C. in accordance with the present invention. The film compositions were tested for various properties, the results of which are described in Table 20 below.

TABLE 20

Composition	Composition of Polymer in Film	Solution Coating Rating	Solution Leveling Rating	% Moisture in Film	180° Bend Test	Dissolution Test (seconds)	Curl Test
CJ	20% HPMC/ 80% HPC	well	well	2.9	Failed at crease	12, 15	Curl
CK	40% HPMC/ 60% HPC	well	well	1.70	Failed at crease	21, 22	Curl
CL	60% HPMC/ 40% HPC	well	well	2.40	Failed at crease	24, 27	Curl
CM	80% HPMC/ 20% HPC	well	well	2.76	Failed at crease	31, 31	Curl
CN	100% HPMC	reasonably well	well	2.66	Failed at crease	35, 38	Curl
CO	10% PEO/ 90% HPMC	some streaking	well	2.27	Failed at crease	31, 32	Curl
CP	15% PEO/ 85% HPMC	well	well	3.31	Failed	24, 27	Curl
CQ	20% PEO/ 80% HPMC	well	well	2.06	Passed	22, 31	Slight curl
CR	40% PEO/ 60% HPMC	well	well	2.01	Passed	13, 12	Slight curl
CS	60% PEO/ 40% HPMC	well	well	1.40	Passed	5, 6	Very slight curl
CT	80% PEO/ 20% HPMC	well	well	1.35	Passed	5, 6	Very slight curl
CU	100% PEO	well	well	0.98	Passed	5, 5	No curl
CV	20% HPC/ 80% PEO	well	well	1.01	Passed	5, 5	No curl
CW	40% HPC/ 60% PEO	well	well	2.00	Passed	6, 6	No curl
CX	60% HPC/ 40% PEO	well	well	0.97	Passed	7, 7	Slight curl
CY	80% HPC/ 20% PEO	well	well	1.41	Passed	12, 12	Very slight curl
CZ	85% HPC/ 15% PEO	well	well	1.86	Failed at crease	13, 14	Curl
DA	90% HPC/ 10% PEO	well	well	1.62	Failed at crease	14, 13	Curl

TABLE 20-continued

Composition	Composition of Polymer in Film	Solution Coating Rating	Solution Leveling Rating	% Moisture in Film	180° Bend Test	Dissolution Test (seconds)	Curl Test
DB	100% HPC	well	well	2.01	Failed at crease	16, 17	Curl

The solution coating rating and solution leveling rating were both based upon panel observations made during casting of the film compositions.

For the 180° bend test, the dried films were placed in a moisture analyzer (HR73 Moisture Analyzer from Mettler Toledo) to obtain percent moisture and to remove any solvent (e.g. water) remaining in the films after drying at 80° C. in accordance with the present invention. The films then were creased to about 180° and observed for break. Films that broke during creasing were considered a failure. If the film did not break during creasing, a 200 g weight was dropped onto the creased film from a height of about 8.5 mm. Films that broke were considered a failure, and those that did not break were considered a pass. It should be noted, however, that this flexibility test is an extreme test. Films that failed this test are still considered operable within the scope of the present invention. More specifically, there may be certain applications that do not require such extreme flexibility properties.

The films also were tested for dissolution rate. An approximately 20 mm by 100 mm piece of film, having a 2.85 g weight attached, was lowered into a 32.5° C. water bath to a depth of about 50 mm. The time required for the film to dissolve and separate into two pieces was determined (in seconds).

For the curl test, samples of film (about 35 mm by 35 mm) were placed on a glass plate in a laboratory window ledge. The film samples were allowed to stand in the window ledge at room conditions for two to three days and then were observed for curling.

In accordance with the present invention, desirable film compositions are flexible, fast dissolving, and not likely to substantially curl. As indicated by the results in Table 20, Compositions CQ-CY performed best, exhibiting good flexibility, dissolution, and curling properties. In particular, Compositions CQ-CY passed the 180° bend test and dissolved at moderate to fast rates. These compositions also exhibited no or only slight curl. Accordingly, it may be desirable to employ polymer components as in Compositions CQ-CY, particularly about 20% to 100% PEO in the polymer component optionally combined with about 0% to 80% HPC or HPMC.

Examples DC-DG

The following examples of the present invention describe films that include PEO or PEO-polymeric blends and an active component. Thin film compositions with these components were prepared using the amounts described in Table 21.

TABLE 21

Component	Weight (g unless otherwise indicated) DC	DD	DE	DF	DG
PEO[1]	8.75	7	1.75	7	1.75
Sucralose	0.7	0.7	0.7	0.7	0.7
Precipitated calcium carbonate	3.65	3.65	3.65	3.65	3.65
Orange concentrate flavor	1.05	1.05	1.05	1.05	1.05
Vanilla	0.5	0.5	0.5	0.5	0.5
HPMC		1.75	7.0		
HPC				1.75	7.0
Simethicone[2]	0.35	0.35	0.35	0.35	0.35
Water	32.5	32.5	32.5	32.5	32.5
Loratadine[3]	2.5	2.5	2.5	2.5	2.5
Yellow food coloring	3 drops	3 drops	3 drops	3 drops	3 drops
Red food coloring	2 drops	2 drops	2 drops	2 drops	2 drops

[1]Available from the Dow Chemical Company
[2]Available from Sentry
[3]Available from Schering Corporation as Claritin

The above components for each of Compositions DC through DG were combined by mixing until a uniform mixture was achieved, and then cast into films on release paper using a K-Control Coater with a 350 micron smooth bar. The films were dried for about 9 minutes at 80° C. in accordance with the method of the present invention to varying moisture levels.

After drying, the films were tested for various properties, including the 180° bend test, dissolution test, and curl test, as described above in Examples CJ-DB. The films also were tested for resistance to tearing. Tear resistance was measured by a panel test in which members tried to tear the film apart by pulling on opposing ends of the film. Films that tore cleanly received a low grade. Films that stretched a little and began to break received a moderate grade, and films that stretched and were difficult to tear received a high grade.

Composition DC, which included a 100% PEO film base, was dried in accordance with the method of the present invention to about 1.30 percent moisture. The dried film had good strength, and passed the 180° bend test. The film also exhibited good resistance to tearing (high grade). The film dissolved at a fast rate on the tongue, and had a dissolution testing rate of about 3.5 to 4 seconds. The film exhibited no curling.

Composition DD, which included an 80%/20% PEO/HPMC film base, was dried in accordance with the method of the present invention to about 2.30 percent moisture. The dried film exhibited adequate strength, and passed the 180° bend test. The film also exhibited good resistance to tearing. It dissolved at a moderate to fast rate on the tongue, and had a dissolution testing rate of about 5 seconds. The film exhibited slight curling.

Composition DE, which included a 20%/80% PEO/HPMC film base, was dried in accordance with the method of the present invention to about 3.0 percent moisture. The film had good strength, and passed the 180° bend test. The film exhib-

ited moderate tear resistance, dissolved on the tongue at a slow rate, and had a dissolution testing rate of 16 seconds. The film exhibited some curling.

Composition DF, which included an 80%/20% PEO/HPC film base, was dried in accordance with the method of the present invention to about 2.52 percent moisture. The film exhibited good strength, passed the 180° bend test, and exhibited high tear resistance. The film also dissolved at a fast rate on the tongue, and had a dissolution rating of 4 seconds. The film exhibited very slight curling.

Composition DG, which included a 20%/80% PEO/HPC film base, was dried in accordance with the method of the present invention to about 2.81 percent moisture. The film had adequate strength, passed the 180° bend test, and exhibited moderate tear resistance. The film dissolved on the tongue at a fast rate, and had a 10 second dissolution testing rate. The film exhibited no curling.

As indicated above, each of Compositions DC-DG contained about 20% to 100% PEO in the polymer component, optionally in combination with varying levels of HPC or HPMC. The results indicate that varying the polymer component achieved different film properties.

Examples DH-DZ

The following examples of the present invention describe films that include PEO or PEO-HPC polymer blends. The film compositions include PEO of varying molecular weights. Thin film compositions with these components were prepared using the amounts described in Table 22 (listed by weight percent of the polymer component).

TABLE 22

Composition	100,000 PEO (wt. %)	200,000 PEO (wt. %)	300,000 PEO (wt. %)	900,000 PEO (wt. %)	HPC (wt. %)
DH			20		80
DI			50		50
DJ			80		20
DK		50			50
DL		67.5			32.5
DM		70			30
DN		75			25
DO		100			
DP	50				50
DQ	100				
DR				10	90
DS				20	80
DT		40		10	50
DU	25			15	60
DV	20	80			
DW		80		20	
DX		80	20		
DY		50	50		
DZ		20	80		

The above polymer components were combined with sucralose, precipitated calcium carbonate (mimics drug loading), orange concentrate flavor, Tween 80 (available from ICI Americas), vanilla flavor, simethicone emulsion, water, and yellow and red food coloring to form the film compositions. The components were combined by mixing until a uniform mixture was achieved, and then cast into films on release paper using a K-Control Coater with a 350 micron smooth bar. The solution coating and leveling properties were observed. The films then were dried for about 9 minutes at 80° C. in accordance with the method of the present invention. The film compositions were tested for various properties to determine the effect of varying the PEO molecular weight and level in the polymer component, the results of which are described in Table 23 below.

TABLE 23

Composition	Film thickness (mils)	% Moisture	Roof of Mouth Tendency	180° Bend Test	Dissolution Test (seconds)	Tear Resistance
DH	3.5	2.5	low	passed	8	poor
DI	3.8	2.01	low	passed	7	moderate
DJ	2.6	2.63	high	passed	3	excellent
DK	3.4	2.35	low	passed	4	poor
DL	3.5	1.74	low	passed	4	good to excellent
DM	3.5	1.68	low	passed	4	good to excellent
DN	3.3	2.33	moderate	passed	3	good to excellent
DO	3.1	2.14	high	passed	4	excellent
DP	4.1	1.33	high	passed	3.5	poor
DQ	3.2	2.07	high	passed	4	good
DR	3.4	1.90	low	passed	10	poor
DS	3.5	2.04	low	passed	10	poor
DT	3.3	2.25	moderate	passed	5	good
DU	3.6	2.84	low to moderate	passed	6	moderate
DV	2.5	3.45	high	passed	2	excellent
DW	2.5	2.83/1.68	high	passed	3-4	excellent
DX	3.5	2.08	high	passed	5	excellent
DY	2.8	1.67	high	passed	3	excellent
DZ	2.5	1.89/0.93	high	passed	3	excellent

The films were tested for various properties, including the 180° bend test, dissolution test, and tear resistance, as described above. The films also were tested for adhesion, i.e., tendency to go to the roof of the mouth. Adhesion was rated by a panel test in which films that did not stick to the roof of the mouth received a low grade, films that stuck somewhat received a moderate grade, and films that stuck completely received a high grade.

As indicated above, the level and molecular weight of PEO in the polymer component were varied to achieve different film properties. In general, the higher the level of PEO in the polymer component, the greater the adhesiveness and tear resistance exhibited by the film. Film compositions containing about 50% or greater levels of PEO attained higher tear resistance ratings than those with less than 50% PEO. The tear resistance of lower levels of PEO, however, was shown to be improved by combining small amounts of higher molecular weight PEOs with the lower molecular weight PEOs (e.g. Compositions DT and DU).

Compositions containing about 20% to 75% PEO performed best with respect to adhesion prevention (lower tendencies to go to the roof of the mouth). Compositions containing higher levels of PEO performed well when adhesion was desired.

As regards dissolution rate, polymer components containing about 50% or higher levels of PEO performed best, providing faster dissolving film compositions. In those films containing combinations of varying molecular weight PEOs, those with about 60% or higher of the lower molecular weight PEOs (100,000 to 300,000) in the PEO combination dissolved faster.

Example EA

The following example of the present invention describes films that include PEO and polyvinyl pyrrolidone (PVP) polymeric blends. Thin film compositions with these components were prepared using the amounts described in Table 24. In particular, the polymer component of the films contained about 80% PEO and 20% PVP, or a ratio of 4:1 PEO to PVP.

TABLE 24

Component	Weight (g unless otherwise noted)
PVP	3.75
PEO	15
Sucralose[1]	1.5
Precipitated calcium carbonate	14.57
Orange concentrate flavor	2.25
Tween 80[2]	0.056
Simethicone[3]	0.38
Water	62.5
Yellow food color	6 drops
Red food color	4 drops

[1]Available from McNeil Nutritionals
[2]Available from Fisher
[3]Available from Sentry

The above components were combined by mixing until a uniform mixture was achieved, and then cast into films on release paper using a K-Control Coater with a 350 micron smooth bar. The films were dried for about 9 minutes at 80° C. in accordance with the method of the present invention to a moisture level of about 2.19%. The films exhibited good strength, dissolved in the mouth at a moderate to fast rate, had high tear resistance, a thickness of about 4 mils, good flavor, low tendency to adhere to the roof of the mouth, and passed the 180° bend test. The film had a dissolution rate of 4 seconds, according to the test described above. In addition, the film easily released from the release paper.

Example EB-ED

The following examples of the present invention describe extruded films that include PEO-based polymer components. Film compositions were prepared using the amounts described in Table 25 for Example EC and Table 26 for Example ED.

TABLE 25

COMPONENT	WEIGHT (g unless otherwise noted)
HPC	73.78
Polyethylene oxide	153.22
Sucralose	18.16
Precipitated calcium carbonate	176.38
Orange concentrated flavor	27.24
Tween 80	0.68
Simethicone	4.54
Yellow food coloring	27 drops
Red food coloring	18 drops

TABLE 26

COMPONENT	WEIGHT (g unless otherwise noted)
Polyethylene oxide	227
Sucralose	18.16
Precipitated calcium carbonate	176.38
Orange concentrated flavor	27.24
Tween 80	0.68
Simethicone	4.54
Yellow food coloring	27 drops
Red food coloring	18 drops

The films of Examples EB-ED were extruded using a single screw extruder in accordance with the specifications provided in Table 27 below (temperatures are in ° F.).

TABLE 27

		Temp. Barrel	Temp. Barrel	Temp. Barrel	Temp.	Temp.	Temp.	PSI Pressure		
Composition	RPM	Zn. 1	Zn. 2	Zn. 3	Zn. 4	Die	Melt	P1	P2	Amps
EB	73	175	181	185	190	190	194	600	1250	12
EB	153	177	181	199	211	210	217	175	1070	7.8
ED	253	175	181	200	211	210	222	0	761	6.3

TABLE 27-continued

Composition	RPM	Temp. Barrel Zn. 1	Temp. Barrel Zn. 2	Temp. Barrel Zn. 3	Temp. Zn. 4	Temp. Die	Temp. Melt	PSI Pressure P1	PSI Pressure P2	Amps
ED	109	175	181	200	211	210	207	0	1000	6.0
EC	109	175	181	200	211	210	217	0	875	12.1
EC	149	175	200	226	248	239	258	0	583	7.3

More specifically, for Example EB, two pounds of PEO having a molecular weight of about 200,000 were weighed and placed in a polyethylene plastic bag. This PEO flush was then extruded according to the specifications in Table 27.

For Example EC, a blend of the components listed in Table 25 was prepared. The HPC, PEO, sucralose, and precipitated calcium carbonate were placed in a large electric blender and allowed to mix. A solution of orange concentrate flavor and Tween 80 was added to the blender while mixing, after which a solution of simethicone and the food colors was added to the blender while mixing. The blended composition was extruded in accordance with the specifications in Table 27.

For Example ED, a blend of the components listed in Table 26 was prepared. The PEO, sucralose, and precipitated calcium carbonate were placed in a large electric blender and allowed to mix. A solution of orange concentrate flavor and Tween 80 was added to the blender while mixing, after which a solution of simethicone and the food colors was added to the blender while mixing. The blended composition was extruded in accordance with the specifications in Table 27.

The extruded films did not exhibit stickiness to each other during processing. As such, the resulting film could be rolled or wound onto itself without the need for a backing material.

Examples EE-EH

The following examples of the present invention describe films that include a densifying agent. A thin film composition including PEO-polymeric blends and a densifying agent (simethicone) were prepared using the amounts described in Table 28.

TABLE 28

Component	Weight (g unless otherwise indicated) EE	EF	EG	EH
Hydroxypropylcellulose	3.05	3.05	3.05	3.05
Polyethylene oxide	6.33	6.33	6.33	6.33
Sucralose	0.75	0.75	0.75	0.75
Precipitated calcium carbonate	7.47	7.47	7.09	7.09
Orange concentrate flavor	1.12	1.12	1.12	1.12
Tween 80	0.028	0.028	0.028	0.028
Simethicone	0	0	0.38	0.38
Water	31.25	31.25	31.25	31.25
Yellow food coloring	3 drops	3 drops	3 drops	3 drops
Red food coloring	2 drops	2 drops	2 drops	2 drops

The densities of these thin film compositions were measured, the results of which are shown in Table 29.

TABLE 29

Composition	Average Weight of Film/Density
EE	146.5 mg/1.123
EF	126.5 mg/0.969
EG	137 mg/1.057
EH	146 mg/1.119

Vacuum conditions were added to two of the film compositions (EE and EH). Composition EE contained 0% simethicone and vacuum was applied. Composition EF contained 0% simethicone and no vacuum applied. As shown in Table 29 above, the density increased with the addition of vacuum conditions from 0.969 (EF) to 1.123 (EE). Composition EG contained 2% simethicone and no vacuum applied. Composition EH contained 2% simethicone and vacuum was applied. Again, density increased from 1.057 (EG) to 1.119 (EH). Overall, the density of the films increased from 0.969 (EF: no simethicone and no vacuum) to 1.057 (EG: simethicone but no vacuum) to 1.119 (EH: simethicone and vacuum).

Examples EI-EW

The following examples of the present invention describe films that include PEO or PEO-polymeric blends. In particular, PEO was combined with polyvinylpyrrolidone (PVP), starch (pregelatinized modified corn starch), sodium carboxymethyl cellulose (CMC), hydroxypropylcellulose (HPC), hydroxypropylmethyl cellulose (HPMC) or polyvinyl alcohol (PVA) to form the polymer components of the films. Thin film compositions with these components were prepared in accordance with the method of the present invention using the amounts described in FIG. **38**.

In addition to the polymer components listed in FIG. **38**, each of these film compositions included: about 4% sucralose, about 38.85% calcium carbonate, about 6% orange flavor, about 0.15% Tween 80, about 1% simethicone, and food coloring. The PEO included in the polymer component of these examples had a molecular weight of about 200,000.

FIG. **38** also displays certain properties of these films, including: percent solids of solution; viscosity; percent moisture; film thickness; film strength; tear resistance of the film; tendency of the film to go to the roof of the mouth; the 180° bend test; whether molding, or aggregations, are present in the film; dissolution times of the film; rating of dissolution in the mouth; and time in drying oven. Each of these film property tests is described in detail above. The results of these various tests are indicated in FIG. **38**.

Examples EX-FK

The following examples of the present invention describe films that include PEO or PEO-polymeric blends (with HPC)

and different active components. Thin film compositions with these components were prepared in accordance with the method of the present invention using the amounts described in Tables 30 and 31.

TABLE 30

	Weight (in g, unless otherwise indicated)						
Component	EX	EY	EZ	FA	FB	FC	FD
HPC	5.68	5.64	6	6.73	6.22	6.22	
PEO	1.89	1.88	2	2.25	1.78	1.78	9.04
Sucralose	0.84	0.84	0.44	0.66	0.84	0.84	0.44
Magna Sweet	0.08	0.08	0.09	0.10	0.09	0.09	
Avicel CL 611[1]	0.18	0.18	0.18	0.20	0.18	0.18	
Precipitated calcium carbonate	0.67		2.2		0.71	3.07	
Dextromethorphan	5.83	6.94					
Caffeine			3.28				
Tadalafil[2]				4.92			
Sildenafil[3]					4.38		
Loperamide[4]						2.8	
Prosweet	0.18	0.18		0.20	0.61	0.18	
Taste Masking Flavor			0.87		1.31	0.89	
Peppermint			0.87				
Peppermint Bittermask flavor			1.07				
Vanilla flavor				0.56			
Watermelon artificial flavor	1.23	1.23			1.22		
Orange flavor				1.18			
Hawaiian punch flavor						1.22	
Strawberry & cream flavor							1.11
WS-23[5]	0.075	0.075	0.075	0.084	0.075	0.075	
WS-3[6]							0.025
Simethicone	0.08	0.08	0.18	0.39	0.09	0.18	46.43
Propylene glycol	0.76	0.38	0.25	0.22			
Water	32.5	32.5	32.5	32.5	32.5	32.5	
Green color	5 drop	5 drop			5 drop		
Red color				2 drop		5 drop	7 drop
Blue color			3 drop				
Yellow color				3 drop			

[1]Mixture of microcrystalline cellulose and sodium carboxymethylcellulose, available from FMC Biopolymer
[2]Available from Lilly ICOS, LLC, as Cialis ®
[3]Available from Pfizer, Inc. as Viagra ®
[4]Available as Imodium
[5]N-2,3-trimethyl-2-isopropyl butanamide
[6]N-Ethyl-p-menthane-3-carboxamide

TABLE 31

	Weight (in g, unless otherwise indicated)						
Component	FE	FF	FG	FH	FI	FJ	FK
HPC	1.28	3.05	4.5	3.29	2.6	2.92	3.29
PEO	2.66	6.33	3	6.83	5.4	6.08	6.83
Sucralose	0.31	0.9	0.6		0.64		
Magna Sweet		0.09					
Avicel CL 611[1]		0.56	0.45				
Precipitated calcium carbonate	1.07	2.02	0.99	6.05	0.90	2.67	1.39
Meloxicam[2]	1.97						
Risperidone[3]		0.62					
Zyrtec ®[4]			3.75				
Five Grass Powder[5]				2.207			
Tea Tree Oil[6]					4		
Antibacterial concentrate[7]						6.12	
Mite extract[8]							6.87
Prosweet		0.66					
Taste Masking Flavor		1.41					
Peppermint Bittermask flavor		2.81			2.24		
Orange flavor	0.47						
Strawberry & cream flavor			1.5				

TABLE 31-continued

Component	Weight (in g, unless otherwise indicated)						
	FE	FF	FG	FH	FI	FJ	FK
WS-3[9]	0.020	0.081	0.038		0.04		
Tween 80	0.012	0.028	0.022		0.024	0.027	
Simethicone	0.08	0.19	0.15	0.37	0.16	0.18	0.37
Water	14.63	31.25	25	31.25	24	22	31.25
Red color	2 drop		5 drop				
Blue color		3 drop			3 drop		
Yellow color	3 drop						

[1]Mixture of microcrystalline cellulose and sodium carboxymethylcellulose, available from FMC Biopolymer
[2]Available as Mobic ®
[3]Available as Risperdal ®
[4]Available from Pfizer, Inc.
[5]Allergy treatment
[6]Antibiotic
[7]MegaBac ™, available from Nicrosol Technologies
[8]Allergy treatment
[9]N-Ethyl-p-menthane-3-carboxamide

The above components were combined by mixing until a uniform mixture was achieved, and then cast into films on release paper using a K-Control Coater with a 250 or 350 micron smooth bar. The films were dried for about 9 to 10 minutes at 80° C. in accordance with the method of the present invention resulting in dried films having adequate to good strength.

While there have been described what are presently believed to be the preferred embodiments of the invention, those skilled in the art will realize that changes and modifications may be made thereto without departing from the spirit of the invention, and it is intended to include all such changes and modifications as fall within the true scope of the invention.

What is claimed is:

1. A process for making a film having a substantially uniform distribution of components, comprising the steps of:

(a) forming a masterbatch pre-mix comprising a solvent and a polymer selected from the group consisting of water-soluble polymers, water-swellable polymers and combinations thereof;

(b) adding an active to a pre-determined amount of said masterbatch pre-mix to form a flowable polymer matrix, said matrix having a substantially uniform distribution of said active;

(c) casting said flowable polymer matrix;

(d) evaporating at least a portion of said solvent from said flowable polymer matrix to form a visco-elastic film within about 10 minutes or fewer to maintain said substantially uniform distribution of said active by locking-in or substantially preventing migration of said active within said visco-elastic film; and

(e) forming a resulting film from said visco-elastic film, wherein said resulting film has a water content of 10% or less and said substantially uniform distribution of active by said locking-in or substantially preventing migration of said active is maintained.

2. The process of claim **1**, wherein said pre-determined amount of master batch pre-mix is controllably fed via a first metering pump and a control valve to a first mixer and a second mixer.

3. The process of claim **2**, wherein said first mixer and said second mixer are arranged in parallel, series or a combination thereof.

4. The process of claim **1**, wherein said water-soluble polymer comprises polyethylene oxide.

5. The process of claim **1**, wherein said polymer comprises a polymer selected from the group consisting of cellulose, a cellulose derivative, pullulan, polyvinyl pyrrolidone, polyvinyl alcohol, polyethylene glycol, carboxyvinyl copolymers, hydroxypropylmethyl cellulose, hydroxyethyl cellulose, hydroxypropyl cellulose, carboxymethyl cellulose, sodium alginate, xanthan gum, tragacanth gum, guar gum, acacia gum, arabic gum, polyacrylic acid, methylmethacrylate copolymer, carboxyvinyl copolymers, starch, gelatin, and combinations thereof, alone or in combination with polyethylene oxide.

6. The process of claim **5**, wherein said polymer further comprises a water insoluble polymer selected from the group consisting of ethylcellulose, hydroxypropyl ethyl cellulose, cellulose acetate phthalate, hydroxypropyl methyl cellulose phthalate, polyvinylacetatephthalates, phthalated gelatin, crosslinked gelatin, poly(lactic acid)/poly(glycolic acid)/polyethyleneglycol copolymers, polycaprolactone and combinations thereof.

7. The process of claim **5**, wherein said polymer further comprises a polymer selected from the group consisting of methylmethacrylate copolymer, polyacrylic acid polymer, poly(glycolic acid) (PGA), poly(lactic acid) (PLA), poly(lactic acid)/poly(glycolic acid)/polyethyleneglycol copolymers, polydioxanones, polyoxalates, poly(α-esters), polyanhydrides, polyacetates, polycaprolactones, poly(orthoesters), polyamino acids, polyaminocarbonates, polyurethanes, polycarbonates, polyamides, poly(alkyl cyanoacrylates), and mixtures and copolymers thereof.

8. The process of claim **5**, wherein said polymer further comprises a polymer selected from the group consisting of sodium alginate, xanthan gum, tragacanth gum, guar gum, acacia gum, arabic gum, starch, gelatin, carageenan, locust bean gum, dextran, gellan gum and combinations thereof.

9. The process of claim **5**, wherein said polymer further comprises a polymer selected from the group consisting of ethylcellulose, hydroxypropyl ethyl cellulose, cellulose acetate phthalate, hydroxypropyl methyl cellulose phthalate,

polyvinylacetatephthalates, phthalated gelatin, crosslinked gelatin, poly(lactic acid)/poly(glycolic acid)/polyethyleneglycol copolymers, polycaprolactone, methylmethacrylate copolymer, polyacrylic acid polymer, poly(glycolic acid) (PGA), poly(lactic acid) (PLA), poly(lactic acid)/poly(glycolic acid)/polyethyleneglycol copolymers, polydioxanones, polyoxalates, poly(d-esters), polyanhydrides, polyacetates, polycaprolactones, poly(orthoesters), polyamino acids, polyaminocarbonates, polyurethanes, polycarbonates, polyamides, poly(alkyl cyanoacrylates), sodium alginate, xanthan gum, tragacanth gum, guar gum, acacia gum, arabic gum, starch, gelatin, carageenan, locust bean gum, dextran, gellan gum and combinations thereof.

10. The process of claim **1**, wherein said solvent is selected from the group consisting of water, polar organic solvent, and combinations thereof.

11. The process of claim **10**, wherein said solvent is selected from the group consisting of ethanol, isopropanol, acetone, and combinations thereof.

12. The process of claim **1**, wherein said active is selected from the group consisting of bioactive active, pharmaceutical actives, drugs, medicaments and combinations thereof.

13. The process of claim **1**, wherein said active is selected from the group consisting of ace-inhibitors, anti-anginal drugs, anti-arrhythmias, anti-asthmatics, anti-cholesterolemics, analgesics, anesthetics, anti-convulsants, anti-depressants, anti-diabetic agents, anti-diarrhea preparations, antidotes, anti-histamines, anti-hypertensive drugs, anti-inflammatory agents, anti-lipid agents, anti-manics, anti-nauseants, anti-stroke agents, anti-thyroid preparations, anti-tumor drugs, anti-viral agents, acne drugs, alkaloids, amino acid preparations, anti-tussives, anti-uricemic drugs, anti-viral drugs, anabolic preparations, systemic and non-systemic anti-infective agents, anti-neoplastics, anti-parkinsonian agents, anti-rheumatic agents, appetite stimulants, blood modifiers, bone metabolism regulators, cardiovascular agents, central nervous system stimulates, cholinesterase inhibitors, contraceptives, decongestants, dietary supplements, dopamine receptor agonists, endometriosis management agents, enzymes, erectile dysfunction therapies, fertility agents, gastrointestinal agents, homeopathic remedies, hormones, hypercalcemia and hypocalcemia management agents, immunomodulators, immunosuppressives, migraine preparations, motion sickness treatments, muscle relaxants, obesity management agents, osteoporosis preparations, oxytocics, parasympatholytics, parasympathomimetics, prostaglandins, psychotherapeutic agents, respiratory agents, sedatives, smoking cessation aids, sympatholytics, tremor preparations, urinary tract agents, vasodilators, laxatives, antacids, ion exchange resins, anti-pyretics, appetite suppressants, expectorants, anti-anxiety agents, anti-ulcer agents, anti-inflammatory substances, coronary dilators, cerebral dilators, peripheral vasodilators, psycho-tropics, stimulants, anti-hypertensive drugs, vasoconstrictors, migraine treatments, antibiotics, tranquilizers, anti-psychotics, anti-tumor drugs, anti-coagulants, anti-thrombotic drugs, hypnotics, anti-emetics, anti-nauseants, anti-convulsants, neuromuscular drugs, hyper- and hypo-glycemic agents, thyroid and anti-thyroid preparations, diuretics, anti-spasmodics, uterine relaxants, anti-obesity drugs, erythropoietic drugs, anti-asthmatics, cough suppressants, mucolytics, DNA and genetic modifying drugs, and combinations thereof.

14. The process of claim **1**, wherein said active is selected from the group consisting of cosmetic actives, antigens, allergens, spores, microorganisms, seeds, mouthwash components, flavors, fragrances, enzymes, preservatives, sweetening agents, colorants, spices, vitamins and combinations thereof.

15. The process of claim **1**, wherein said active is a bioactive active.

16. The process of claim **1**, wherein said active is a biological response modifier.

17. The process of claim **1**, wherein said active is an opiate or opiate-derivative.

18. The process of claim **1**, wherein said active is an anti-emetic.

19. The process of claim **1**, wherein said active is an amino acid preparation.

20. The process of claim **1**, wherein said active is selected from the group consisting of sildenafils, tadalafils, vardenafils, apomorphines, yohimbine hydrochlorides, alprostadils and combinations thereof.

21. The process of claim **1**, wherein said active is a protein.

22. The process of claim **1**, wherein said active is insulin.

23. The process of claim **1**, wherein said active is an anti-diabetic.

24. The process of claim **1**, wherein said active is an anti-histamine.

25. The process of claim **1**, wherein said active is an anti-tussive.

26. The process of claim **1**, wherein said active is a non-steroidal anti-inflammatory.

27. The process of claim **1**, wherein said active is an anti-asthmatics.

28. The process of claim **1**, wherein said active is an anti-diarrhea.

29. The process of claim **1**, wherein said active is an alkaloid.

30. The process of claim **1**, wherein said active is an anti-psychotic.

31. The process of claim **1**, wherein said active is an anti-spasmodic.

32. The process of claim **1**, wherein said active is a biological response modifier.

33. The process of claim **1**, wherein said active is an anti-obesity drug.

34. The process of claim **1**, wherein said active is an H_2-antagonist.

35. The process of claim **34**, wherein said H_2-antagonist is selected from the group consisting of cimetidine, ranitidine hydrochloride, famotidine, nizatidine, ebrotidine, mifentidine, roxatidine, pisatidine, aceroxatidine and combinations thereof.

36. The process of claim **1**, wherein said active is a smoking cessation aid.

37. The process of claim **1**, wherein said active is an anti-parkinsonian agent.

38. The process of claim **1**, wherein said active is an anti-depressant.

39. The process of claim **1**, wherein said active is an anti-migraine.

40. The process of claim **1**, wherein said active is an anti-Alzheimer's agents.

41. The process of claim **1**, wherein said active is a dopamine receptor agonist.

42. The process of claim **1**, wherein said active is a cerebral dilator.

43. The process of claim **1**, wherein said active is a psychotherapeutic agent.

44. The process of claim **1**, wherein said active is an anti-biotic.

45. The process of claim 1, wherein said active is an anesthetic.

46. The process of claim 1, wherein said active is a contraceptive.

47. The process of claim 1, wherein said active is an antithrombotic drug.

48. The process of claim 1, wherein said active is diphenhydramine.

49. The process of claim 1, wherein said active is nabilone.

50. The process of claim 1, wherein said active is albuterol sulfate.

51. The process of claim 1, wherein said active is an antitumor drug.

52. The process of claim 1, wherein said active is a glycoprotein.

53. The process of claim 1, wherein said active is an analgesic.

54. The process of claim 1, wherein said active is a hormone.

55. The process of claim 1, wherein said active is a decongestant.

56. The process of claim 1, wherein said active is a loratadine.

57. The process of claim 1, wherein said active is dextromethorphan.

58. The process of claim 1, wherein said active is chlorpheniramine maleate.

59. The process of claim 1, wherein said active is selected from the group consisting of an analgesic, an anti-inflammatory, an antihistamine, a decongestant, a cough suppressant and combinations thereof.

60. The process of claim 1, wherein said active is an appetite stimulant.

61. The process of claim 1, wherein said active is a gastrointestinal agent.

62. The process of claim 1, wherein said active is a hypnotic.

63. The process of claim 1, wherein said active is taste-masked.

64. The process of claim 1, wherein said active is taste-masked using a flavor.

65. The process of claim 1, wherein said active is coated with a controlled release composition.

66. The process of claim 65, wherein said controlled release composition provides an immediate release.

67. The process of claim 65, wherein said controlled release composition provides a delayed release.

68. The process of claim 65, wherein said controlled release composition provides a sustained release.

69. The process of claim 65, wherein said controlled release composition provides a sequential release.

70. The process of claim 1, wherein said active is a particulate.

71. The process of claim 1, further comprising adding a degassing agent to said masterbatch premix.

72. The process of claim 1, further comprising a step of providing a second film layer.

73. The process of claim 72, wherein said second film layer is coated onto said resulting film.

74. The process of claim 72, wherein said second film layer is spread onto said resulting film.

75. The process of claim 72, wherein said second film layer is cast onto said resulting film.

76. The process of claim 72, wherein said second film layer is extruded onto said resulting film.

77. The process of claim 72, wherein said second film layer is sprayed onto said resulting film.

78. The process of claim 72, wherein said second film layer is laminated onto said resulting film.

79. The process of claim 72, further comprising laminating said resulting film to another film.

80. The process of claim 72, wherein said second film comprises an active.

81. The process of claim 72, wherein said active in said second film is different than said active in said resulting film.

82. A process for making a film having a substantially uniform distribution of components, comprising the steps of:

(a) forming a flowable polymer matrix comprising a polymer selected from the group consisting of a water-soluble polymer, a water swellable polymer and combinations thereof, a solvent and an active selected from the group consisting of bioactive actives, pharmaceutical actives, drugs, medicaments and combinations thereof, said matrix having a substantially uniform distribution of said active;

(b) casting said flowable polymer matrix;

(c) evaporating at least a portion of said solvent from said flowable polymer matrix to form a visco-elastic film within about 10 minutes or fewer to maintain said substantially uniform distribution of said active by locking-in or substantially preventing migration of said active within said visco-elastic film; and

(d) forming a resulting film from said visco-elastic film, wherein said resulting film has a water content of 10% or less and said substantially uniform distribution of active by said locking-in or substantially preventing migration of said active is maintained.

83. The process of claim 82, wherein said water-soluble polymer comprises polyethylene oxide.

84. The process of claim 82, wherein said polymer comprises a polymer selected from the group consisting of cellulose, a cellulose derivative, pullulan, polyvinyl pyrrolidone, polyvinyl alcohol, polyethylene glycol, carboxyvinyl copolymers, hydroxypropylmethyl cellulose, hydroxyethyl cellulose, hydroxypropyl cellulose, carboxymethyl cellulose, sodium alginate, xanthan gum, tragacanth gum, guar gum, acacia gum, arabic gum, polyacrylic acid, methylmethacrylate copolymer, carboxyvinyl copolymers, starch, gelatin, and combinations thereof, alone or in combination with polyethylene oxide.

85. The process of claim 84, wherein said polymer further comprises a water insoluble polymer selected from the group consisting of ethylcellulose, hydroxypropyl ethyl cellulose, cellulose acetate phthalate, hydroxypropyl methyl cellulose phthalate, polyvinylacetatephthalates, phthalated gelatin, crosslinked gelatin, poly(lactic acid)/poly(glycolic acid)/polyethyleneglycol copolymers, polycaprolactone and combinations thereof.

86. The process of claim 84, wherein said polymer further comprises a polymer selected from the group consisting of methylmethacrylate copolymer, polyacrylic acid polymer, poly(glycolic acid) (PGA), poly(lactic acid) (PLA), poly(lactic acid)/poly(glycolic acid)/polyethyleneglycol copolymers, polydioxanones, polyoxalates, poly(α-esters), polyanhydrides, polyacetates, polycaprolactones, poly(orthoesters), polyamino acids, polyaminocarbonates, polyurethanes, polycarbonates, polyamides, poly(alkyl cyanoacrylates), and mixtures and copolymers thereof.

87. The process of claim 84, wherein said polymer further comprises a polymer selected from the group consisting of sodium alginate, xanthan gum, tragacanth gum, guar gum, acacia gum, arabic gum, starch, gelatin, carageenan, locust bean gum, dextran, gellan gum and combinations thereof.

88. The process of claim 84, wherein said polymer further comprises a polymer selected from the group consisting of ethylcellulose, hydroxypropyl ethyl cellulose, cellulose acetate phthalate, hydroxypropyl methyl cellulose phthalate, polyvinylacetatephthalates, phthalated gelatin, crosslinked gelatin, poly(lactic acid)/poly(glycolic acid)/polyethyleneglycol copolymers, polycaprolactone, methylmethacrylate copolymer, polyacrylic acid polymer, poly(glycolic acid) (PGA), poly(lactic acid) (PLA), poly(lactic acid)/poly(glycolic acid)/polyethyleneglycol copolymers, polydioxanones, polyoxalates, poly(α-esters), polyanhydrides, polyacetates, polycaprolactones, poly(orthoesters), polyamino acids, polyaminocarbonates, polyurethanes, polycarbonates, polyamides, poly(alkyl cyanoacrylates), sodium alginate, xanthan gum, tragacanth gum, guar gum, acacia gum, arabic gum, starch, gelatin, carageenan, locust bean gum, dextran, gellan gum and combinations thereof.

89. The process of claim 82, wherein said solvent is selected from the group consisting of water, polar organic solvent, and combinations thereof.

90. The process of claim 89, wherein said solvent is selected from the group consisting of ethanol, isopropanol, acetone, and combinations thereof.

91. The process of claim 82, wherein said active is selected from the group consisting of bioactive active, pharmaceutical actives, drugs, medicaments and combinations thereof.

92. The process of claim 82, wherein the active is selected from the group consisting of ace-inhibitors, anti-anginal drugs, anti-arrhythmias, anti-asthmatics, anti-cholesterolemics, analgesics, anesthetics, anti-convulsants, anti-depressants, anti-diabetic agents, anti-diarrhea preparations, antidotes, anti-histamines, anti-hypertensive drugs, anti-inflammatory agents, anti-lipid agents, anti-manics, anti-nauseants, anti-stroke agents, anti-thyroid preparations, anti-tumor drugs, anti-viral agents, acne drugs, alkaloids, amino acid preparations, anti-tussives, anti-uricemic drugs, anti-viral drugs, anabolic preparations, systemic and non-systemic anti-infective agents, anti-neoplastics, anti-parkinsonian agents, anti-rheumatic agents, appetite stimulants, blood modifiers, bone metabolism regulators, cardiovascular agents, central nervous system stimulates, cholinesterase inhibitors, contraceptives, decongestants, dietary supplements, dopamine receptor agonists, endometriosis management agents, enzymes, erectile dysfunction therapies, fertility agents, gastrointestinal agents, homeopathic remedies, hormones, hypercalcemia and hypocalcemia management agents, immunomodulators, immunosuppressives, migraine preparations, motion sickness treatments, muscle relaxants, obesity management agents, osteoporosis preparations, oxytocics, parasympatholytics, parasympathomimetics, prostaglandins, psychotherapeutic agents, respiratory agents, sedatives, smoking cessation aids, sympatholytics, tremor preparations, urinary tract agents, vasodilators, laxatives, antacids, ion exchange resins, anti-pyretics, appetite suppressants, expectorants, anti-anxiety agents, anti-ulcer agents, anti-inflammatory substances, coronary dilators, cerebral dilators, peripheral vasodilators, psycho-tropics, stimulants, anti-hypertensive drugs, vasoconstrictors, migraine treatments, antibiotics, tranquilizers, anti-psychotics, anti-tumor drugs, anti-coagulants, anti-thrombotic drugs, hypnotics, anti-emetics, anti-nauseants, anti-convulsants, neuromuscular drugs, hyper- and hypo-glycemic agents, thyroid and anti-thyroid preparations, diuretics, anti-spasmodics, uterine relaxants, anti-obesity drugs, erythropoietic drugs, anti-asthmatics, cough suppressants, mucolytics, DNA and genetic modifying drugs, and combinations thereof.

93. The process of claim 82, wherein said active is selected from the group consisting of cosmetic actives, antigens, allergens, spores, microorganisms, seeds, mouthwash components, flavors, fragrances, enzymes, preservatives, sweetening agents, colorants, spices, vitamins and combinations thereof.

94. The process of claim 82, wherein said active is a bioactive active.

95. The process of claim 82, wherein said active is a biological response modifier.

96. The process of claim 82, wherein said active is an opiate or opiate-derivative.

97. The process of claim 82, wherein said active is an anti-emetic.

98. The process of claim 82, wherein said active is an amino acid preparation.

99. The process of claim 82, wherein said active is selected from the group consisting of sildenafils, tadalafils, vardenafils, apomorphines, yohimbine hydrochlorides, alprostadils and combinations thereof.

100. The process of claim 82, wherein said active is a protein.

101. The process of claim 82, wherein said active is insulin.

102. The process of claim 82, wherein said active is an anti-diabetic.

103. The process of claim 82, wherein said active is an antihistamine.

104. The process of claim 82, wherein said active is an anti-tussive.

105. The process of claim 82, wherein said active is a non-steroidal anti-inflammatory.

106. The process of claim 82, wherein said active is an anti-asthmatics.

107. The process of claim 82, wherein said active is an anti-diarrhea.

108. The process of claim 82, wherein said active is an alkaloid.

109. The process of claim 82, wherein said active is an anti-psychotic.

110. The process of claim 82, wherein said active is an anti-spasmodic.

111. The process of claim 82, wherein said active is a biological response modifier.

112. The process of claim 82, wherein said active is an anti-obesity drug.

113. The process of claim 82, wherein said active is an H_2-antagonist.

114. The process of claim 82, wherein said H_2-antagonist is selected from the group consisting of cimetidine, ranitidine hydrochloride, famotidine, nizatidine, ebrotidine, mifentidine, roxatidine, pisatidine, aceroxatidine and combinations thereof.

115. The process of claim 82, wherein said active is a smoking cessation aid.

116. The process of claim 82, wherein said active is an anti-parkinsonian agent.

117. The process of claim 82, wherein said active is an anti-depressant.

118. The process of claim 82, wherein said active is an anti-migraine.

119. The process of claim 82, wherein said active is an anti-Alzheimer's agents.

120. The process of claim 82, wherein said active is a dopamine receptor agonist.

121. The process of claim 82, wherein said active is a cerebral dilator.

122. The process of claim 82, wherein said active is a psychotherapeutic agent.

123. The process of claim 82, wherein said active is an antibiotic.

124. The process of claim 82, wherein said active is an anesthetic.

125. The process of claim 82, wherein said active is a contraceptive.

126. The process of claim, 82, wherein said active is an anti-thrombotic drug.

127. The process of claim 82, wherein said active is diphenhydramine.

128. The process of claim 82, wherein said active is nabilone.

129. The process of claim 82, wherein said active is albuterol sulfate.

130. The process of claim 82, wherein said active is an anti-tumor drug.

131. The process of claim 82, wherein said active is a glycoprotein.

132. The process of claim 82, wherein said active is an analgesic.

133. The process of claim 82, wherein said active is a hormone.

134. The process of claim 82, wherein said active is a decongestant.

135. The process of claim 82, wherein said active is a loratadine.

136. The process of claim 82, wherein said active is dextromethorphan.

137. The process of claim 82, wherein said active is chlorpheniramine maleate.

138. The process of claim 82, wherein said active is selected from the group consisting of an analgesic, an anti-inflammatory, an antihistamine, a decongestant, a cough suppressant and combinations thereof.

139. The process of claim 82, wherein said active is an appetite stimulant.

140. The process of claim 82, wherein said active is a gastrointestinal agent.

141. The process of claim 82, wherein said active is a hypnotic.

142. The process of claim 82, wherein said active is taste-masked.

143. The process of claim 82, wherein said active is taste-masked using a flavor.

144. The process of claim 82, wherein said active is coated with a controlled release composition.

145. The process of claim 144, wherein said controlled release composition provides an immediate release.

146. The process of claim 144, wherein said controlled release composition provides a delayed release.

147. The process of claim 144, wherein said controlled release composition provides a sustained release.

148. The process of claim 144, wherein said controlled release composition provides a sequential release.

149. The process of claim 82, wherein said active is a particulate.

150. The process of claim 82, further comprising adding a degassing agent to said flowable polymer matrix.

151. The process of claim 82, further comprising a step of providing a second film layer.

152. The process of claim 151, wherein said second film layer is coated onto said resulting film.

153. The process of claim 151, wherein said second film layer is spread onto said resulting film.

154. The process of claim 151, wherein said second film layer is cast onto said resulting film.

155. The process of claim 151, wherein said second film layer is extruded onto said resulting film.

156. The process of claim 151, wherein said second film layer is sprayed onto said resulting film.

157. The process of claim 151, wherein said second film layer is laminated onto said resulting film.

158. The process of claim 151, further comprising laminating said resulting film to another film.

159. The process of claim 151, wherein said second film comprises an active.

160. The process of claim 151, wherein said active in said second film is different than said active in said resulting film.

161. A process for making a film capable of being administered to a body surface having a substantially uniform distribution of components, comprising the steps of:

(a) forming a flowable polymer matrix comprising a water-soluble polymer, a solvent and an active, said matrix having a substantially uniform distribution of said active;

(b) casting said flowable polymer matrix;

(c) evaporating at least a portion of said solvent from said flowable polymer matrix to form a visco-elastic film within about 10 minutes or fewer to maintain said substantially uniform distribution of said active by locking-in or substantially preventing migration of said active within said visco-elastic film;

(d) forming a resulting film from said visco-elastic film, wherein said resulting film has a water content of 10% or less and said substantially uniform distribution of active by said locking-in or substantially preventing migration of said active is maintained; and

(e) administering said resulting film to a body surface.

162. The process of claim 161, wherein said body surface is a mucous membrane.

163. The process of claim 162, wherein said mucous membrane is oral, anal, vaginal or ophthalmological.

164. The process of claim 161, wherein said body surface is the surface of a wound.

165. The process of claim 161, wherein said water-soluble polymer comprises polyethylene oxide.

166. The process of claim 161, wherein said polymer comprises a polymer selected from the group consisting of cellulose, a cellulose derivative, pullulan, polyvinyl pyrrolidone, polyvinyl alcohol, polyethylene glycol, carboxyvinyl copolymers, hydroxypropylmethyl cellulose, hydroxyethyl cellulose, hydroxypropyl cellulose, carboxymethyl cellulose, sodium alginate, xanthan gum, tragacanth gum, guar gum, acacia gum, arabic gum, polyacrylic acid, methylmethacrylate copolymer, carboxyvinyl copolymers, starch, gelatin, and combinations thereof, alone or in combination with polyethylene oxide.

167. The process of claim 166, wherein said polymer further comprises a water insoluble polymer selected from the group consisting of ethylcellulose, hydroxypropyl ethyl cellulose, cellulose acetate phthalate, hydroxypropyl methyl cellulose phthalate, polyvinylacetatephthalates, phthalated gelatin, crosslinked gelatin, poly(lactic acid)/poly(glycolic acid)/polyethyleneglycol copolymers, polycaprolactone and combinations thereof.

168. The process of claim 166, wherein said polymer further comprises a polymer selected from the group consisting of methylmethacrylate copolymer, polyacrylic acid polymer, poly(glycolic acid) (PGA), poly(lactic acid) (PLA), poly(lactic acid)/poly(glycolic acid)/polyethyleneglycol copolymers, polydioxanones, polyoxalates, poly(α-esters), polyanhy-

drides, polyacetates, polycaprolactones, poly(orthoesters), polyamino acids, polyaminocarbonates, polyurethanes, polycarbonates, polyamides, poly(alkyl cyanoacrylates), and mixtures and copolymers thereof.

169. The process of claim **166**, wherein said polymer further comprises a polymer selected from the group consisting of sodium alginate, xanthan gum, tragacanth gum, guar gum, acacia gum, arabic gum, starch, gelatin, carageenan, locust bean gum, dextran, gellan gum and combinations thereof.

170. The process of claim **166**, wherein said polymer further comprises a polymer selected from the group consisting of ethylcellulose, hydroxypropyl ethyl cellulose, cellulose acetate phthalate, hydroxypropyl methyl cellulose phthalate, polyvinylacetatephthalates, phthalated gelatin, crosslinked gelatin, poly(lactic acid)/poly(glycolic acid)/polyethyleneglycol copolymers, polycaprolactone, methylmethacrylate copolymer, polyacrylic acid polymer, poly(glycolic acid) (PGA), poly(lactic acid) (PLA), poly(lactic acid)/poly(glycolic acid)/polyethyleneglycol copolymers, polydioxanones, polyoxalates, poly(α-esters), polyanhydrides, polyacetates, polycaprolactones, poly(orthoesters), polyamino acids, polyaminocarbonates, polyurethanes, polycarbonates, polyamides, poly(alkyl cyanoacrylates), sodium alginate, xanthan gum, tragacanth gum, guar gum, acacia gum, arabic gum, starch, gelatin, carageenan, locust bean gum, dextran, gellan gum and combinations thereof.

171. The process of claim **161**, wherein said solvent is selected from the group consisting of water, polar organic solvent, and combinations thereof.

172. The process of claim **161**, wherein said solvent is selected from the group consisting of ethanol, isopropanol, acetone, and combinations thereof.

173. The process of claim **161**, wherein said active is selected from the group consisting of bioactive active, pharmaceutical actives, drugs, medicaments and combinations thereof.

174. The process of claim **161**, wherein said active is selected from the group consisting of ace-inhibitors, anti-anginal drugs, anti-arrhythmias, anti-asthmatics, anti-cholesterolemics, analgesics, anesthetics, anti-convulsants, anti-depressants, anti-diabetic agents, anti-diarrhea preparations, antidotes, anti-histamines, anti-hypertensive drugs, anti-inflammatory agents, anti-lipid agents, anti-manics, anti-nauseants, anti-stroke agents, anti-thyroid preparations, anti-tumor drugs, anti-viral agents, acne drugs, alkaloids, amino acid preparations, anti-tussives, anti-uricemic drugs, anti-viral drugs, anabolic preparations, systemic and non-systemic anti-infective agents, anti-neoplastics, anti-parkinsonian agents, anti-rheumatic agents, appetite stimulants, blood modifiers, bone metabolism regulators, cardiovascular agents, central nervous system stimulates, cholinesterase inhibitors, contraceptives, decongestants, dietary supplements, dopamine receptor agonists, endometriosis management agents, enzymes, erectile dysfunction therapies, fertility agents, gastrointestinal agents, homeopathic remedies, hormones, hypercalcemia and hypocalcemia management agents, immunomodulators, immunosuppressives, migraine preparations, motion sickness treatments, muscle relaxants, obesity management agents, osteoporosis preparations, oxytocics, parasympatholytics, parasympathomimetics, prostaglandins, psychotherapeutic agents, respiratory agents, sedatives, smoking cessation aids, sympatholytics, tremor preparations, urinary tract agents, vasodilators, laxatives, antacids, ion exchange resins, anti-pyretics, appetite suppressants, expectorants, anti-anxiety agents, anti-ulcer agents, anti-inflammatory substances, coronary dilators, cerebral dilators, peripheral vasodilators, psycho-tropics, stimulants, anti-hypertensive drugs, vasoconstrictors, migraine treatments, antibiotics, tranquilizers, anti-psychotics, anti-tumor drugs, anti-coagulants, anti-thrombotic drugs, hypnotics, anti-emetics, anti-nauseants, anti-convulsants, neuromuscular drugs, hyper- and hypo-glycemic agents, thyroid and anti-thyroid preparations, diuretics, anti-spasmodics, uterine relaxants, anti-obesity drugs, erythropoietic drugs, anti-asthmatics, cough suppressants, mucolytics, DNA and genetic modifying drugs, and combinations thereof.

175. The process of claim **161**, wherein said active is selected from the group consisting of cosmetic actives, antigens, allergens, spores, microorganisms, seeds, mouthwash components, flavors, fragrances, enzymes, preservatives, sweetening agents, colorants, spices, vitamins and combinations thereof.

176. The process of claim **161**, wherein said active is a bioactive active.

177. The process of claim **161**, wherein said active is a biological response modifier.

178. The process of claim **161**, wherein said active is an opiate or opiate-derivative.

179. The process of claim **161**, wherein said active is an anti-emetic.

180. The process of claim **161** wherein said active is an amino acid preparation.

181. The process of claim **161**, wherein said active is selected from the group consisting of sildenafils, tadalafils, vardenafils, apomorphines, yohimbine hydrochlorides, alprostadils and combinations thereof.

182. The process of claim **161**, wherein said active is a protein.

183. The process of claim **161**, wherein said active is insulin.

184. The process of claim **161**, wherein said active is an anti-diabetic.

185. The process of claim **161**, wherein said active is an antihistamine.

186. The process of claim **161**, wherein said active is an anti-tussive.

187. The process of claim **161**, wherein said active is a non-steroidal anti-inflammatory.

188. The process of claim **161**, wherein said active is an anti-asthmatics.

189. The process of claim **161**, wherein said active is an anti-diarrhea.

190. The process of claim **161**, wherein said active is an alkaloid.

191. The process of claim **161**, wherein said active is an anti-psychotic.

192. The process of claim **161**, wherein said active is an anti-spasmodic.

193. The process of claim **161**, wherein said active is a biological response modifier.

194. The process of claim **161**, wherein said active is an anti-obesity drug.

195. The process of claim **161**, wherein said active is an H_2-antagonist.

196. The process of claim **195**, wherein said H_2-antagonist is selected from the group consisting of cimetidine, ranitidine hydrochloride, famotidine, nizatidine, ebrotidine, mifentidine, roxatidine, pisatidine, aceroxatidine and combinations thereof.

197. The process of claim **161**, wherein said active is a smoking cessation aid.

198. The process of claim **161**, wherein said active is an anti-parkinsonian agent.

199. The process of claim 161, wherein said active is an anti-depressant.

200. The process of claim 161, wherein said active is an anti-migraine.

201. The process of claim 161, wherein said active is an anti-Alzheimer's agents.

202. The process of claim 161, wherein said active is a dopamine receptor agonist.

203. The process of claim 161, wherein said active is a cerebral dilator.

204. The process of claim 161, wherein said active is a psychotherapeutic agent.

205. The process of claim 161, wherein said active is an antibiotic.

206. The process of claim 161, wherein said active is an anesthetic.

207. The process of claim 161, wherein said active is a contraceptive.

208. The process of claim 161, wherein said active is an anti-thrombotic drug.

209. The process of claim 161, wherein said active is diphenhydramine.

210. The process of claim 161, wherein said active is nabilone.

211. The process of claim 161, wherein said active is albuterol sulfate.

212. The process of claim 161, wherein said active is an anti-tumor drug.

213. The process of claim 161, wherein said active is a glycoprotein.

214. The process of claim 161, wherein said active is an analgesic.

215. The process of claim 161, wherein said active is a hormone.

216. The process of claim 161, wherein said active is a decongestant.

217. The process of claim 161, wherein said active is a loratadine.

218. The process of claim 161, wherein said active is dextromethorphan.

219. The process of claim 161, wherein said active is chlorpheniramine maleate.

220. The process of claim 161, wherein said active is selected from the group consisting of an analgesic, an anti-inflammatory, an antihistamine, a decongestant, a cough suppressant and combinations thereof.

221. The process of claim 161, wherein said active is an appetite stimulant.

222. The process of claim 161, wherein said active is a gastrointestinal agent.

223. The process of claim 161, wherein said active is a hypnotic.

224. The process of claim 161, wherein said active is taste-masked.

225. The process of claim 161, wherein said active is taste-masked using a flavor.

226. The process of claim 161, wherein said active is coated with a controlled release composition.

227. The process of claim 226, wherein said controlled release composition provides an immediate release.

228. The process of 226, wherein said controlled release composition provides a delayed release.

229. The process of claim 226, wherein said controlled release composition provides a sustained release.

230. The process of claim 226, wherein said controlled release composition provides a sequential release.

231. The process of claim 161, wherein said active is a particulate.

232. The process of claim 161, further comprising adding a degassing agent to said flowable polymer matrix.

233. The process of claim 161, further comprising a step of providing a second film layer.

234. The process of claim 233, wherein said second film layer is coated onto said resulting film.

235. The process of claim 233, wherein said second film layer is spread onto said resulting film.

236. The process of claim 233, wherein said second film layer is cast onto said resulting film.

237. The process of claim 233, wherein said second film layer is extruded onto said resulting film.

238. The process of claim 233, wherein said second film layer is sprayed onto said resulting film.

239. The process of claim 233, wherein said second film layer is laminated onto said resulting film.

240. The process of claim 233, further comprising laminating said resulting film to another film.

241. The process of claim 233, wherein said second film comprises an active.

242. The process of claim 233, wherein said active in said second film is different than said active in said resulting film.

243. The process of claim 1, said active is an anti-nauseant.

244. The process of claim 1, said active is an erectile dysfunction.

245. The process of claim 1, said active is a vasoconstrictor.

246. The process of claim 1, said active is a stimulant.

247. The process of claim 1, said active is a migraine treatment.

248. The process of claim 1, said active is granisetron hydrochloride.

249. The process of claim 1, wherein said resulting film provides administration of said active to an individual through the buccal cavity of said individual.

250. The process of claim 1, wherein said resulting film provides administration of said active through gingival application of said individual.

251. The process of claim 1, wherein said resulting film provides administration of said active through sublingual application of said individual.

252. The process of claim 1, wherein said resulting film provides administration of said active to an individual through a mucosal membrane of said individual.

253. The process of claim 1, wherein said resulting film provides administration of said active to an individual by administration within the body of the individual during surgery.

254. The process of claim 1, wherein said resulting film has a variation of active content of less than 10% per film unit.

255. The process of claim 1, further comprising the step of forming a plurality of individual dosage units of substantially the same size, wherein the active content of individual dosage units has a variance of no more than 10%.

256. The method of claim 1, wherein said resulting film contains less than about 6% by weight solvent.

257. The method of claim 1, wherein said at least one edible polymer, said active, and said at least one polar solvent are each ingestible materials.

258. The method of claim 1, wherein said resulting film is orally administrable.

259. The method of claim 1, wherein said active is in the form of a particle.

260. The method of claim 1, wherein said matrix comprises a dispersion.

261. The process of claim 82, said active is an anti-nauseant.

262. The process of claim 82, said active is an erectile dysfunction.

263. The process of claim 82, said active is a vasoconstrictor.

264. The process of claim 82, said active is a stimulant.

265. The process of claim 82, said active is a migraine treatment.

266. The process of claim 82, said active is granisetron hydrochloride.

267. The process of claim 82, wherein said resulting film provides administration of said active to an individual through the buccal cavity of said individual.

268. The process of claim 82, wherein said resulting film provides administration of said active through gingival application of said individual.

269. The process of claim 82, wherein said resulting film provides administration of said active through sublingual application of said individual.

270. The process of claim 82, wherein said resulting film provides administration of said active to an individual through a mucosal membrane of said individual.

271. The process of claim 82, wherein said resulting film provides administration of said active to an individual by administration within the body of the individual during surgery.

272. The process of claim 82, wherein said resulting film has a variation of active content of less than 10% per film unit.

273. The process of claim 82, further comprising the step of forming a plurality of individual dosage units of substantially the same size, wherein the active content of individual dosage units has a variance of no more than 10%.

274. The method of claim 82, wherein said resulting film contains less than about 6% by weight solvent.

275. The method of claim 82, wherein said at least one edible polymer, said active, and said at least one polar solvent are each ingestible materials.

276. The method of claim 82, wherein said resulting film is orally administrable.

277. The method of claim 82, wherein said active is in the form of a particle.

278. The method of claim 82, wherein said matrix comprises a dispersion.

279. The process of claim 161, said active is an anti-nauseant.

280. The process of claim 161, said active is an erectile dysfunction.

281. The process of claim 161, said active is a vasoconstrictor.

282. The process of claim 161, said active is a stimulant.

283. The process of claim 161, said active is a migraine treatment.

284. The process of claim 161, said active is granisetron hydrochloride.

285. The process of claim 161, wherein said resulting film provides administration of said active to an individual through the buccal cavity of said individual.

286. The process of claim 161, wherein said resulting film provides administration of said active through gingival application of said individual.

287. The process of claim 161, wherein said resulting film provides administration of said active through sublingual application of said individual.

288. The process of claim 161, wherein said resulting film provides administration of said active to an individual through a mucosal membrane of said individual.

289. The process of claim 161, wherein said resulting film provides administration of said active to an individual by administration within the body of the individual during surgery.

290. The process of claim 161, wherein said resulting film has a variation of active content of less than 10% per film unit.

291. The process of claim 161, further comprising the step of forming a plurality of individual dosage units of substantially the same size, wherein the active content of individual dosage units has a variance of no more than 10%.

292. The method of claim 161, wherein said resulting film contains less than about 6% by weight solvent.

293. The method of claim 161, wherein said at least one edible polymer, said active, and said at least one polar solvent are each ingestible materials.

294. The method of claim 161, wherein said resulting film is orally administrable.

295. The method of claim 161, wherein said active is in the form of a particle.

296. The method of claim 161, wherein said matrix comprises a dispersion.

297. The method of claim 1, wherein said matrix comprises an emulsion, a colloid or a suspension.

298. The method of claim 82, wherein said matrix comprises an emulsion, a colloid or a suspension.

299. The method of claim 161, wherein said matrix comprises an emulsion, a colloid or a suspension.

* * * * *

EXHIBIT 3

Docket No.: 117744-00023
(PATENT)

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Inter Partes Reexamination of:	)
US Patent No. 7,897,080	)
Issued: March 1, 2011	) Confirmation No.: 6418
Named Inventor: Robert K. Yang et al.	) Group Art Unit: 3991
Control No.: 95/002,170	) Examiner: Diamond, Alan D.
Filed: September 10, 2012	) M&E Docket: 117744-00023
Title: Polyethylene-oxide based RCE/CON/REX films and Drug delivery systems made therefrom	) H&B Docket: 1199-26

Mail Stop Inter Partes Reexam
Attn: Central Reexamination Unit
Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

Declaration of Jason O. Clevenger under 37 C.F.R. § 1.132

I, Jason O. Clevenger, Ph.D., declare:

1. I am a Principal Scientist at Exponent, a science and engineering consulting firm. My expertise focuses on materials characterization and process engineering for specialty manufacturing, including regulated products such as medical devices and pharmaceuticals. Specifically with regard to pharmaceuticals, my experience includes process engineering and method development for transdermal and solid oral formulations, regulatory compliance and CMC (Chemistry, Manufacturing, and Controls) related issues including root cause analysis, corrective and preventive action plans, and regulatory submissions. Attached is my *curriculum vitae*.

2. While Exponent is being paid for my time, I am not an employee of, nor do I have any financial interest in, BioDelivery Sciences International, Inc.

3. I have carefully reviewed U.S. Patent No. 7,897,080 ("the '080 Patent"), International Publication No. WO 00/42992 ("Chen"), the Declaration of B. Arlie Bogue, Ph.D. submitted to the U.S. Patent Office on March 13, 2013 ("Bogue Declaration") and the Declaration of David T. Lin, Ph.D. submitted to the U.S. Patent Office on March 13, 2013 ("Lin Declaration").

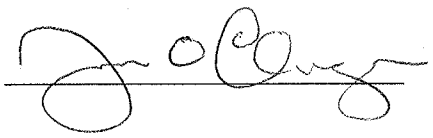
4. In my experience, the route to regulatory approval is an ongoing negotiation with the FDA through the New Drug Application (NDA) process. In this negotiation process, analytical testing and standards are determined for each product depending on its particular properties and characteristics. Different active agents and dosage forms have different properties, and would thus generally have different standards and testing requirements. Also, standardized test methods can change over time (e.g., USP <905> was revised in 2007 and 2011), so regulations from 2000 will not provide adequate information for present approval processes.

5. An FDA New Drug Application ("NDA") is a long and very detailed document. The CMC Section alone is often many hundreds to thousands of pages long. Patents are not intended to be part of an NDA and would not be expected to have the same disclosure, at least because the two documents have different requirements and very different purposes. To the extent that Chen does not provide sufficient information to comply with all of the information required in an NDA, neither does the '080 Patent.

6. The analysis in the Bogue Declaration is not consistent with the currently adopted definition of content uniformity as described in USP <905> Uniformity of Dosage Units. The calculation in paragraphs 9 and 10 of the Bogue Declaration are not included within the definition of content uniformity as described in USP <905> Uniformity of Dosage Units.

All statements herein of my own knowledge are true and all statements made on information and belief are believed to be true; and further these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United States Code and that such willful false statements may jeopardize the validity of this application or any patent issuing thereon

Dated: 12 April 2013

Signature: 

Jason O. Clevenger, Ph.D.
Principal Scientist
Exponent

Exponent
Failure Analysis Associates®

Exponent
9 Strathmore Road
Natick, MA 01760

telephone 508-652-8500
facsimile 508-652-8599
www.exponent.com

Jason O. Clevenger, Ph.D.
Principal Scientist

Professional Profile

Dr. Jason O. Clevenger is a Principal Scientist in Exponent's Polymer Science and Materials Chemistry practice. His expertise focuses on materials characterization and process engineering for specialty manufacturing, with a particular emphasis on regulated products such as medical devices and pharmaceuticals.

Dr. Clevenger's physical chemistry experience is applicable to problems involving materials such as semiconductors, MEMS, metal films, dielectrics, polymers, materials processing, materials characterization, pharmaceutical process chemistry, identification of trace contaminants including organics and particulates, and corrosion processes.

His pharmaceutical experience includes process engineering and optimization for transdermal and solid oral formulations, regulatory compliance and CMC (Chemistry, Manufacturing, and Controls) related issues involving root cause analysis, corrective and preventive action plans, quality assurance, and Quality by Design initiatives. His medical device experience includes method development for regulatory submissions, product development and manufacturing support, and technology due diligence assessment.

His characterization background encompasses a broad range of advanced technologies and techniques including laser spectroscopy, X-ray photoelectron spectroscopy (XPS), Auger spectroscopy, Raman, FTIR, solid/liquid-NMR, optical emission/absorption spectroscopy, energy dispersive spectroscopy (EDS), white-light interferometry, spectroscopic ellipsometry, atomic force microscopy (AFM), and secondary ion mass spectrometry (SIMS). In addition, he has extensive experience with plasma chemistry and spectroscopy, thin film metrology and reliability, high vacuum technology and semiconductor processing.

Academic Credentials and Professional Honors

Ph.D., Physical Chemistry, Massachusetts Institute of Technology, 2002
B.A., Chemistry, Vanderbilt University (*magna cum laude* with *high honors*), 1995

Phi Beta Kappa and Omicron Delta Kappa

High Honors in Chemistry for Undergraduate Thesis, 1995; Outstanding Senior in Chemistry Award, 1995; T.W. Martin Award and D.E. Pearson Award for Excellence in Undergraduate Research and Study of Physical Chemistry, 1995; J.M. Breckenridge Scholarship, 1994; Barry M. Goldwater Foundation Scholarship, Goldwater Excellence in Education Foundation, 1994;

Stephen H. Cook Summer Research Fellowship, 1994; Top-Tennessee Scholars Tuition Scholarship, 1993; Eastman Kodak National Merit Scholarship, 1991

Publications

Kou PM, Clevenger JO. A Coat for All Weathers: A Survey of the Hydrophilic Coatings Market. Med Device Develop 2012; May.

Clevenger JO, Ralston B. Rapid development. Med Device Develop 2009; Oct.

Steffey D, Ostarello A, Clevenger J, Villarraga, M. Troubleshooting analyses of production data. Int J Ind Eng 2009; 16(3):206–213.

Clevenger JO. Sticky situations: Hydrophilic coatings. Med Device Develop 2008; Dec.

Poliskie M, Clevenger JO. FTIR spectroscopy for characterization and failure analysis. Met Finish 2008; 5:44.

Goldsmith C, Forehand D, Scarborough S, Peng Z, Palego C, Hwang J, Clevenger J. Understanding and Improving Longevity in RF MEMS Capacitive Switches. Reliability, Packaging, Testing, and Characterization of MEMS/MOEMS VII, Proc. of SPIE Vol. 6884, 2008.

Clevenger JO. Safe surface—Anti-microbial coatings for implants. Med Device Develop, 2007; Sep.

Ibarreta A, Davis S, Clevenger JO. Flammability of electrical crimp connectors subjected to heating. Proceedings, Fire and Materials 10th International Conference, 2007.

Kay JJ, Byun DS, Clevenger JO, Jiang X, Petrovic VS, Seiler R, Barchi JR, Merer AJ, Field RW. "Spectrum-only" assignment of core-penetrating and core-nonpenetrating Rydberg states of calcium monofluoride. Can J Chem 2004; 82(6):791–803.

Brooks CB, Anderson RB, Clevenger JO, Collard C, Halim M, Sahin T, Mak, AW. Optimization of chrome dry etch in Tetra II using asymmetrically loaded patterns. Proceedings, SPIE-The International Society for Optical Engineering, 2003, 5256 (Pt. 2, 23rd Annual BACUS Symposium on Photomask Technology, 2003), pp. 749–757.

Collard C, Anderson SA, Anderson RB, Clevenger JO, Halim M, Brooks CB, Buie MJ, Sahin T. Examination of various endpoint methods for chrome mask etch. Proceedings, SPIE-The International Society for Optical Engineering, 2003) 5256 (Pt. 2, 23rd Annual BACUS Symposium on Photomask Technology, 2003), pp. 744–748.

Hammond E, Clevenger JO, Buie MJ. Plasma and flow modeling of photomask etch chambers. Proceedings, SPIE-The International Society for Optical Engineering, 5256 (Pt. 2, 23rd Annual BACUS Symposium on Photomask Technology, 2003), pp. 713–723.

Anderson SA, Anderson RB, Buie MJ, Chandrachood M, Clevenger JO, Lee Y, Sandlin NL; Ding J. Optimization of a 65-nm alternating phase-shift quartz etch process. Proceedings, SPIE-The International Society for Optical Engineering, 2003, 5256 (Pt. 1, 23rd Annual BACUS Symposium on Photomask Technology, 2003), pp. 66–75.

Clevenger JO, Buie MJ, Sandlin NL. Effect of chamber seasoning on the chrome dry etch process. Proceedings, SPIE-The International Society for Optical Engineering, 2003, 5130 (Photomask and Next-Generation Lithography Mask Technology X), pp. 92–100.

Li L, Dai X, Liu Y, Clevenger JO, Field RW, Jeung GH, Geum N, Lyyra AM. The Predissociation of the $1^3\Sigma_g^-$ State of $^7Li_2$. J Molecul Spectrosc 2001; 205(1):139–145.

Dai X, Clevenger JO, Liu Y, Song M, Shang J, Chen D, Field RW; Li L. The $2^3\Delta_g$ State of $^7Li_2$. J Molecul Spectrosc 2000; 200(1):120–122.

Clevenger JO, Harris NA, Field RW, Li J. The predissociation mechanism for $^2\Sigma^+$ Rydberg states of CaCl. J Molecul Spectrosc 1999; 193(2):412–417.

Clevenger JO, Tellinghuisen, J. The $B(1/2\ ^2P_{3/2}) - X(1/2\ ^2\Sigma^+)$ transition in XeBr. J Chem Phys 1995; 103(22):9611–9620.

Clevenger JO, Tellinghuisen J. High-resolution spectroscopy with a CCD array detector. The $B - X$ transition in $^{136}Xe^{81}Br$. Chem Phys Lett 1994; 231(4,5,6):515–520.

Clevenger JO, Ray QP, Tellinghuisen J, Zheng X, Heaven MC. Spectroscopy of metastable species in a free-jet expansion: The $\beta - A$ transition in IBr. Can J Phys 1994; 72(11&12):1294–1306.

Radzykewycz DT, Littlejohn CD, Carter MB, Clevenger JO, Purvis JH, Tellinghuisen J. The D' – A' transition in IBr: A deperturbation analysis. J Molecul Spectrosc 1994; 166(2):287–303.

Prior Experience

Process Technologist (Etch and CVD), Applied Materials, Inc., 2002–2004

Professional Affiliations

- American Association of Pharmaceutical Scientists—AAPS
- American Chemical Society—ACS
- Society of Photo-Optical Instrumentation Engineers—SPIE

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re *Inter Partes* Reexamination of:	)	
	)	
US Patent No. 7,897,080	)	Confirmation No.: 6418
	)	
Named Inventor: Robert K. Yang *et al.*	)	Group Art Unit: 3991
	)	
Control No.: 95/002,170	)	Examiner: Alan D. Diamond
	)	
Request Filed: September 10, 2012	)	M&E Docket: 117744-00023
	)	
Title: POLYETHYLENE OXIDE-BASED FILMS AND DRUG DELIVERY SYSTEMS MADE THEREFROM	)	H&B Docket: 1199-26 RCE/CON/REX
	)	
Mailing Date: March 10, 2014	)	

Mail Stop *Inter Partes* Reexam
Attn: Central Reexamination Unit
Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

BDSI'S APPEAL BRIEF IN *INTER PARTES* REEXAMINATION

All claims of the instant patent stand finally rejected by the reexamination panel. BioDelivery Sciences International, Inc. ("BDSI") appeals the decision of the examining panel to not adopt the proposed rejections of all claims under 35 USC §112.

Certificate Regarding Word Count Pursuant to 37 CFR 1.943(c)

I hereby certify that, pursuant to 37 CFR 1.943(c), based on the Word version word count of 10,217 words total, including 8,598 words in the instant brief and 1,619 words in the cited paragraphs of the expert declarations, which does not exceed 14,000 words in length.

Signed: Danielle L. Herritt /Danielle L. Herritt / Reg. No. 43,670 Dated: March 10, 2014

Table of Contents

I. REAL PARTY IN INTEREST

Appellant, BioDelivery Sciences International, Inc. ("BDSI") is the real party in interest for this brief.

II. RELATED APPEALS, INTERFERENCES, AND TRIALS

BDSI is not aware of any related appeals, interferences or judicial proceedings.

III. STATUS OF CLAIMS

Reexamination was initiated with respect to all of the 299 original claims in the '080 patent. But MonoSol cancelled claims 12, 16, 91, 95, 173, 177, 254-255, 257, 272-273, 275, 290-291, and 293. The reexamination now involves 303 claims total—claims 1-11, 13-15, 17-90, 92-94, 96-172, 174-176, 178-253, 256, 258-271, 274, 276-289, 292, 294-299, and new claims 300-318. All of the new and original claims that were not cancelled by MonoSol were finally rejected in the Right of Appeal Notice.

IV. STATUS OF AMENDMENTS

Only one of the three sets of amendments MonoSol proposed was entered. Both the first proposed amendment filed January 29, 2013, and the third proposed amendment filed September 3, 2013, were not entered. See Notice Regarding Defective Paper mailed February 26, 2013 at 3; RAN at 3. A second proposed amendment filed March 13, 2013 was entered. The claims, as amended in the March 13, 2013 filing, are listed in the Claims Appendix.

V. SUMMARY OF CLAIMED SUBJECT MATTER

There are 7 independent claims[1] (*i.e.*, claims 1, 82, 161, 315, 316, 317, and 318) and 296 dependent claims finally rejected in this proceeding. In the RAN, the reexamination panel identified a representative claim (claim 1) and a summary of claimed subject matter. See RAN at 4-9. Because of the substantial similarity of the independent claims, we will address claim 1 as a representative claim, and then address each independent claim separately, to the extent each differs. Referring to claim 1, the rejected claims are directed to a method of making a film with three basic steps: (i) forming a polymer matrix; (ii) casting the matrix; and (iii) drying the matrix to form a film. BDSI could find no disclosure of such a general method, but it did find a description that required specific polymers and excluded plasticizers. See '080 patent at 4:51-58.

The independent claims divide drying into two drying steps (i.e., "controlling drying … to form a visco-elastic film" and then "forming said resulting film from said visco-elastic film"). BDSI could find no conditions that differentiate these two "steps." *Compare* steps (d) and (e) of claim 1 and/or steps

[1] Exhibit A of the April 12, 2013 Comments is a comparison of the independent claims.

(c) and (d) of any of the other independent claims. Accordingly, BDSI cannot provide any support for two distinct drying steps. The "controlled drying" of step (c)/(d) is described as possible "through a variety of methods." Id. at 27:26-27. This variety of methods is described in the section entitled "Drying of Films." Id. at 27:11-28:64. For example, the "Drying of Films" section disclosed a drying method involving an underside water bath, which is admitted to be in the prior art. Id. at 28:2-6. The claims appear to encompass all of the drying methods, including the admitted prior art, disclosed in the "Drying of Films" section. Id.

The independent claims also recite a step—added to each independent claim during reexamination—of "*performing analytical chemical tests*" for uniformity of content of active. See step (f) of claim 1 and step (e) of all other independent claims. The panel correctly found that the term "analytical chemical tests" is neither used nor defined in the '080 patent. See RAN at 7. In the section entitled "Testing Films for Uniformity," uniformity is confirmed by visual inspection and, alternatively, by use of analytical equipment. See '080 patent at 28:65-29:53. Uniformity testing is then exemplified in Examples A-I where visual inspection (use of magnification) and weight testing (a scale for additive weights) are employed as alternatives for confirming uniformity of distribution of the

components within the film. Id. at 31:38-32:45. Dissolution testing is also generally described, as a third alternative for determining the uniformity of active, but not exemplified. Id. at 32:35-39.

Various independent claims add other steps listed here for the sake of completeness. Claim 1 adds the steps of forming a masterbatch pre-mix prior to adding the active to the polymer matrix. See Claim 1, steps (a-b); see id. at 9:64-10:49. Claims 82 and 315 add a step of repeating steps already recited to make and compare "further resulting films." See Claims 82 and 315, step (f); see id. at 29:47-53. Claim 161 oddly adds a step of administering a film to a body surface, even though the claim is recited to be a process for manufacturing a film. See Claim 161, step (f); see id. at 19:6-9.

The other independent claims do not recite any new steps. Claim 315 shifts a desired uniformity result, added to claim 82 in both steps (c) and (e), to steps (d) and (e). Claim 316 is virtually identical to claim 315, except in claim 316, apparently the uniformity is only required in intermediate step (d). Claim 317 is also virtually identical except now the uniformity is only required in intermediate step (c). BDSI found no support in the '080 patent for any methods where

uniformity is transient and/or measured during specific intermediate steps or combination of steps.

Finally, claim 318, as the ACP and RAN has already stated, combines disparate elements unconnected in the specification. See ACP at 26-27; RAN at 27-29.

The independent claims also recite a number of desired results relating to suitability for commercial and regulatory approval and uniformity of the active. These recitations are found in the preamble, and throughout the various claim steps. These recitations are alleged to be supported by nine lines in the '080 patent's background, in a passage disparaging a prior art reference, Fuchs:

> For this reason, dosage forms formed by processes such as Fuchs, would not likely meet the stringent standards of governmental or regulatory agencies, such as the U.S. Federal Drug Administration ("FDA"), relating to the variation of active in dosage forms. Currently, as required by various world regulatory authorities, dosage forms may not vary more than 10% in the amount of active present. When applied to dosage units based on films, this virtually mandates that uniformity in the film be present.
>
> Id. at 2:38-46.

But interestingly, despite Fuchs' disclosure of "uniform" films, and methods and materials for making uniform films—MonoSol argues that Fuchs' films were "inherently non-uniform." Compare id. at 2:10-13 to id. at 2:18-21. In particular,

MonoSol claims to have examined films made in accordance with the process disclosed in Fuchs. Id. at 2:18-19. MonoSol argues the non-uniformity in the examined films "can be attributed to *Fuchs' process parameters*, which although *not disclosed* likely include the use of relatively long drying times." Id. at 2:21-26 (emphasis added). And, MonoSol argues that Fuchs's films are inherently non-uniform due to "relatively long drying times" admittedly not disclosed by Fuchs. Rather than the newly added recitations, the language quoted above appears to support anticipation by Fuchs.

VI. ISSUES TO BE REVIEWED ON APPEAL

A. Whether the panel erred by not holding MonoSol to its interpretation of the new recitation "*suitable for commercialization and regulatory approval…*" as lacking written description and enablement, and by not rejecting the claim as indefinite for being susceptible to at least two interpretations – the PTO's and MonoSol's.

B. Whether the panel erred in declining to adopt the proposed rejections for the term "*analytical chemical tests*" even though the term is not used, not described, not defined, and not exemplified in the '080 patent.

C. Whether the panel erred in declining to adopt the proposed rejections for the step of performing analytical tests to verify specific levels of uniformity, even though this step is not used, not described, not defined, and not exemplified in the '080 patent.

D. Whether the panel erred in declining to adopt the proposed rejections based on limited variation between films even though such limitation is not described, not defined, and not exemplified in the '080 patent.

E. Whether the panel erred in failing to conclude that the scope of the claims cannot be determined because the newly-added "*rapidly increasing the viscosity of said flowable polymer matrix*" includes terms of degree both lacking a reference point and standards for comparison.

F. Whether the panel erred in determining that the "*100 °C or less*" in the "*controlling drying*" step clearly applies throughout the step.

G. (Adopted)

H. Whether the panel erred in declining to adopt the proposed 112 rejections for the newly-added uniformity requirements added to different steps and combinations of steps even though these requirements are not described, not defined, and not exemplified in the '080 patent..

VII. ARGUMENT

Summary

All 300+ claims in this reexamination appeal are directed to methods of making films for delivery of an active. They each recite the same three general steps for making a film: (i) forming a polymer-solvent matrix that includes a bioactive and/or pharmaceutical active; (ii) casting the matrix; and (iii) evaporating at least a portion of the solvent to form a film. But the prior art teaches the same materials and the same film-making process steps. See ACP at 35:12-16; 35-39 (referring to *Chen*[2]); 95:5-8 (referring to *Staab*[3]); RAN at 82 . And, despite multiple opportunities during reexamination, MonoSol has never explained why performing all the claimed process steps with the claimed materials—as the prior art does—would not necessarily produce a film that has the claimed desired results, e.g., the newly recited uniformity results. See RAN at 82.

Instead, MonoSol relies on its new limitations of uniformity—without explaining how the claimed methods differ from those disclosed in the cited prior art. MonoSol never took on its burden to rebut the inherency rejections by

---

[2] International Patent Publication No. WO 00/42992 to Chen *et al.*

[3] US Patent No. 5,393,528 to Staab.

reproducing any examples from, e.g., *Chen* or *Staab*. And it has failed to rebut the obviousness of merely reciting desired results—results MonoSol does not dispute were well known long before its earliest claimed priority date. MonoSol certainly does not recite any new or non-obvious methods of achieving them in its claims. As such, the panel correctly found that all of the new recitations are anticipated and/or obvious in view of the cited prior art.

But in addition to failing to patentably distinguish over the cited prior art, the '080 patent also fails to disclose or enable the new recitations, particularly when MonoSol is held to its own interpretation of these recitations. For example, although iterative sampling and testing throughout one film manufacturing run is briefly mentioned (see the '080 patent at 29:48-53), the '080 patent neither discloses nor exemplifies repetition of steps to satisfy a certain uniformity standard between films, as recited in step (f) of claims 82 and 315. Thus, the '080 patent fails to provide the disclosure that MonoSol itself argues is required of the prior art. In short, in addition to lack of novelty and obviousness over the prior art, the recitation of this new matter is entirely without basis in the specification and has only resulted in invalid claims, the scope of which is unclear.

BDSI files this appeal because, although the non-adopted rejections under 35

USC § 112 might be considered redundant to the final rejections, BDSI wants to make clear that, even if these new recitations did somehow distinguish the methods over the prior art methods (which they do not), the claims are still invalid under 35 USC § 112 for the reasons MonoSol itself advances.

A. Whether the panel erred by not holding MonoSol to its interpretation of the new recitation "*suitable for commercialization and regulatory approval…*" as lacking written description and enablement, and by not rejecting the claim as indefinite for being susceptible to at least two interpretations – the PTO's and MonoSol's.[4]

MonoSol added a new recitation to each of its methods for making a film requiring a resulting film "*suitable for commercialization and regulatory approval including analytical chemical testing which meets the standards of the U.S. Food and Drug Administration relating to variation of an active in individual dosage units*." See Claims Appendix or Reply by Patentee to a Non-Final Office Action Pursuant to 37 CFR 1.111 filed March 13, 2013 (hereinafter "Reply-2") at 2-41. This recitation is in the preamble and is also referred to in the body of the claims in the step requiring performing analytical chemical tests. See step (f) for claim 1, step (e) for all other independent claims. The examining panel correctly

[4] The lettering of the headings is consistent with the lettering of the proposed rejections, the ACP, and the RAN.

determined that this new recitation fails to distinguish the claimed methods over the prior art teachings of the same method steps and the same levels of uniformity. See e.g., ACP at 36-37 (*Chen*) and 56 (*Staab*); RAN at 36-37 (*Chen*) at 57-59 (*Staab*). The panel concluded that the new recitation was satisfied by performing the rest of the step in which the "suitability" language appears:

> The claims do not require commercialization or regulatory approval, they set forth suitability for commercialization and regulatory approval. The bright line test for such suitability is based on performing analytical chemical tests for uniformity of content active, said tests showing a particular variation of active, for example, not more than 10%.
>
> ACP at 13; RAN at 14.

In other words, the examining panel read the new recitation (indicated in bold type below) as satisfied by the rest of the step (indicated with underlining below) in which it appears in the body of the claim.

Exemplary Claim 82: preamble and step (e)
82. A process for manufacturing resulting films **suitable for commercialization and regulatory approval, said regulatory approval including analytical chemical testing which meets the standards of the U.S. Food and Drug Administration relating to variation of an active in individual dosage units**, said films having a substantially uniform distribution of components, comprising a substantially uniform distribution of a desired amount of said active in individual dosage units of said resulting films, comprising the steps of: …. (e) performing analytical chemical tests for uniformity of content of said active in substantially equal sized individual dosage units sampled from different locations of said resulting film, said tests indicating that uniformity of content in the amount of the active varies by no more than 10% and said resulting film is **suitable for commercial and regulatory approval, wherein said regulatory approval is provided by the U.S. Food and Drug Administration**; and

This is one interpretation. But MonoSol argued a different interpretation of this recitation—an interpretation that lacks written description and enablement in the '080 patent by MonoSol's own proposed standards.

To be clear, there is no error in the outstanding final prior art rejections because, where a claim is indefinite because it is subject to multiple interpretations, it is appropriate to make a prior art rejection applying an interpretation of the claims that renders the prior art applicable. See MPEP 2173.06; see also *Ex Parte Mesher*, No. 2012-009669, 2013 WL 6122669 at 3 (PTAB Nov. 25, 2013); *Ex parte Miyazaki*, No. 2007-3300, 2008 WL 5105055 at 5 (BPAI Nov. 19, 2008).

But, in addition, the claims should also have been rejected as lacking clarity with respect to claim scope, and lacking written description and enablement according to the interpretation advanced by MonoSol.

1. *Lack of Enablement*

MonoSol argued that, for the cited art to anticipate this new recitation, it must disclose films meeting all of the requirements for FDA approval. See, e.g., Reply-2 at 66:16-20; 78:6-8; Lin at ¶¶ 17-20. MonoSol's expert states that *Chen* lacked an enabling disclosure because it lacked "sufficient information contained within to allow FDA regulatory approval" of its films. Lin Decl. at ¶ 17. Application of MonoSol's proclaimed standard for determining whether the *prior art* is sufficiently enabled, demonstrates that its own claims are not enabled:

MonoSol argued the following deficiencies in the cited prior art:	**But MonoSol's '080 Patent is similarly deficient:**
"[T]here is insufficient disclosure to allow FDA to determine that a drug product as described can be manufactured for commercial distribution, manufactured in a consistent manner and meet specifications that will ensure the identity, strength, quality, purity, and potency of the drug product." Lin Decl. ¶ 17.	The '080 patent does not qualify as an FDA CMC submission, which is the bar set by MonoSol and its expert, Dr. Lin.

MonoSol argued the following deficiencies in the cited prior art:	**But MonoSol's '080 Patent is similarly deficient:**
"Chen lacks any disclosure which would necessarily lead to the manufacture of films with uniformity of content (strength) of drug active required for FDA approval." Lin Decl. ¶ 17.	Although the '080 patent discloses some uniformity data from physical tests (see '080 patent at 31:38-45 (disclosing data from visual inspection tests) and at 31:46-32:34 (disclosing weight variation tests)), MonoSol argues that these tests are insufficient (see Reply-2 at 58-59). Thus, applying MonoSol's standards, there is no uniformity data in the '080 patent that can be relied upon to satisfy this claim limitation.
"Chen does not disclose sufficient information that the films containing drug can be produced consistently with respect to uniformity of content of the drug." Lin Decl. ¶ 18.	The '080 patent does not include any data or other information regarding the reproducibility of films made according to the methods described.
"No information was disclosed that demonstrated uniformity of content in the amounts of drug in individual dosage units." Lin Decl. ¶ 18.	Again, applying MonoSol's standards, there is no uniformity data that can be relied upon in the '080 patent. See Reply-2 at 58-59.
"Chen discloses no specific test methods, and hence no test results, that could allow for the determination of the actual amount of drug (active) in individual dosage units." Lin Decl. ¶ 18.	While disclosing that a dose may be dissolved and tested for the amount of active (see '080 patent at 32:36-38), the '080 patent specification fails to disclose any specific test methods or exemplify any results that could allow for the determination of the actual amount of drug (active) in individual dosage units.

MonoSol argued the following deficiencies in the cited prior art:	**But MonoSol's '080 Patent is similarly deficient:**
"Chen's patent did not disclose sufficient information regarding the manufacturing process and process controls. The information disclosed by Chen would not ensure that films containing drug could be manufactured to meet specifications that ensure consistent strength." Lin Decl. ¶ 19.	Like *Chen*, the '080 patent fails to disclose or claim any information about manufacturing processes or controls to ensure consistent strength. To the extent that *Chen* is lacking, the '080 patent is also lacking.
"[T]here is no information regarding the test methods that are necessary to determine the amount of drug in individual dosage units." Lin Decl. ¶ 20.	Beyond its so-called physical tests (which MonoSol argues are insufficient in its Reply-2 at 58-59), the '080 patent is devoid of any information regarding "test methods that are necessary to determine the amount of drug in individual dosage units." For example, while disclosing that a dose may be dissolved and tested for the amount of active (see '080 patent at 32:36-38), the '080 patent discloses no such test methods or results.

In short, to the extent that *Chen* lacks an enabling disclosure with respect to this newly added recitation, the '080 patent also lacks an enabling disclosure. See *Inter Partes* Reexamination Comments Under 37 CFR § 1.947 filed April 12, 2013 ("Comments-2") at 11-13.

2. *Lack of Written Description*

In addition, because the new recitation in the pending claims extends beyond what is disclosed in the specification, the amended claims lack written description. See Comments-2 at 14. For example, the '080 patent does not qualify as an FDA CMC submission, which is the bar set by MonoSol and its expert, Dr. Lin, for the prior art to anticipate. See Lin Decl. ¶ 17; Reply-2 at 66:16-20, 78:6-8.

3. *Lack of Clarity*

The claims are indefinite because they subject to at least two very different interpretations—the examining panel's and MonoSol's. The panel interpreted this recitation to only require satisfaction of one uniformity parameter. MonoSol argued that this interpretation requires disclosure equivalent to an FDA submission for a regulatory approval of a new drug product.

In addition, the "suitable for commercial and regulatory approval…." recitation is ambiguous and unclear because there are no set tests or standards that can be applied to determine whether the recitation is satisfied. Indeed, not only do the regulatory standards change over time, but they may differ for each drug

product. As Dr. Clevenger explains, suitability for approval can only be determined through negotiation with the FDA:

> In my experience, the route to regulatory approval is an ongoing negotiation with the FDA through the New Drug Application (NDA) process. In this negotiation process, analytical testing and standards are determined for each product depending on its particular properties and characteristics. Different active agents and dosage forms have different properties, and would thus generally have different standards and testing requirements. Also, standardized test methods can change over time…so regulations from 2000 will not provide adequate information for present approval processes.
>
> Clevenger Decl. ¶ 4.

Without the test methods or standards, it is impossible to understand what is required by the amended claims, particularly when the standards and test methods may differ for each active and the claims potentially cover thousands of actives. And, even with respect to one active, the tests and standards may change over time as the FDA requires.

B. Whether the panel erred in declining to adopt the proposed rejections for the term "*analytical chemical tests*" even though the term is not used, not described, not defined, and not exemplified in the '080 patent.

MonoSol added the step of performing "*analytical chemical tests*" to every independent claim, and took the position that in order for the cited art to anticipate

this new recitation, the cited art must be "supported" by proof that it verified its active uniformity by performing analytical testing. See Reply-2 at 51; Lin Decl. ¶¶ 17-22. The examining panel correctly found the step of performing analytical chemical tests to verify properties does not patentably distinguish the claims. See ACP at 38 (*Chen*) and at 57 (*Staab*); RAN at 39 and 58-59, respectively.

1. *Lack of Written Description*

The examining panel should also have rejected the claims for lacking written description. Nowhere in the '080 patent is the term "analytical chemical testing" employed. And nowhere in the '080 patent is any "analytical chemical test" described or employed to verify the amount of active in any sample. MonoSol's citation of support to an example (Example M) testing a dye—not a bioactive and/or pharmaceutical active—was soundly rejected as evidence of verification of active uniformity by analytical chemical tests. See RAN at 86-87; see also ACP at 6, last two lines (concluding that the '080 patent does not disclose any analytical chemical tests used to verify the amount of active in a sample). In addition, MonoSol proposes the following standard, which the '080 patent fails to meet:

> In the cited prior art, terms such as uniformity, substantial uniformity, and homogeneity are all accepted without real support. They cannot

> be relied upon. What is missing is the support for the statements–that is, having had the amount of active tested by analytical chemical testing, including assaying.
>
> Reply-2 at 51 (citing Lin Decl. ¶¶ 17-22).

Again, MonoSol argues that Example M of the '080 patent includes exemplary analytical chemical testing to verify uniformity. See Reply-2 at 59. But Example M does not verify or even test uniformity of bioactive and/or pharmaceutical active. Indeed, MonoSol admits Example M includes a dye—not the claimed bioactive and/or pharmaceutical actives. See Response by Patentee to Action Closing Prosecution filed September 3, 2013 (hereinafter "Reply-3") at 66. Finally, MonoSol does not explain how the light absorption reading employed in Example M is a "chemical based" test. See generally Reply-2 and Reply-3.

2. *Lack of Clarity*

In addition to the lack of written description, this new recitation renders the scope of the claims unclear. MonoSol's arguments about how uniformity may be appropriately measured contradict the '080 patent. For example, the '080 patent specification provides three alternative tests for confirming uniformity of components (i) visual inspection, (ii) weight measurement, and (iii) dissolution testing. See '080 patent at 31:37-32:39. Weight measurement is even confirmed

as one of several valid methods of confirming active content for the FDA. See Comments-2 at 14-15 and Exhibits J-K (FDA Chapter <905> Uniformity of Dosage Units). But MonoSol now argues that weight measurement is not an acceptable alternative to analytical chemical tests. See Reply-2 at 56-59. So, what exactly is claimed? MonoSol points to the dissolution test, a "chemical based test," as the only type of test that can directly establish the same amount of active. See Reply-2 at 59. But MonoSol does not explain what this dissolution test is or how it differs from that exemplified in, for example, *Chen*.[5]

While an applicant is allowed to be its own lexicographer, it must do so within the patent disclosure (*i.e.*, not after grant), and it must define terms clearly. See MPEP 2111.01(IV) citing *In re Paulsen*, 30 F.3d 1475, 1480 (Fed. Cir. 1994) (inventor may define specific terms used to describe invention, but must do so "with reasonable clarity, deliberateness, and precision" and, if done, must "'set out

[5] Although MonoSol contradicts itself in questioning whether the results in *Chen* verify uniformity (see *Inter Partes* Reexamination Comments Under 37 CFR § 1.947 filed October 3, 2013 ("Comments-3") at 18), Dr. Reitman's reproduction of *Chen* verifies that the claimed uniformity was inherently met (see id. at 19-20; Reitman Decl. ¶ 7).

his uncommon definition in some manner within the patent disclosure so as to give one of ordinary skill in the art notice of the change" in meaning). MonoSol seeks to create a new and undefined category of analytical chemical testing—post grant—in an attempt to avoid the cited prior art. See Reply-2 at 53, last ¶, to 59, last full ¶. But the cited prior art employs the same methods that the '080 patent employs to verify uniformity. See *Chen* at 17:15-16 (disclosing visual inspection), Table 4 (disclosing weight measurement), and Figure 5 (disclosing dissolution testing). While MonoSol clearly argues that the term "analytical chemical tests" does not include the tests described in the prior art, but is superior to those prior tests (in direct contradiction to the teachings of its own specification)—MonoSol has not identified a single test in the '080 patent that meets its newly-invented criteria.

C. Whether the panel erred in declining to adopt the proposed rejections for the step of performing analytical tests to verify specific levels of uniformity, even though this step is not used, not described, not defined, and not exemplified in the '080 patent.

MonoSol added the step of "performing analytical chemical tests…indicating…the amount of active varies by no more than 10%" to every

independent claim, except claim 318.[6] See step (f) of claim 1 and step (e) of all other independent claims. Various new dependent claims recite that "the amount of active varies by no more than 2%, 1% and 0.5%." See e.g., Claims Appendix or Reply-2 at 34-35 (new claims 300-311). MonoSol argued that neither *Chen* nor *Staab* expressly or inherently disclosed this newly-recited desired result. But both references expressly disclose films that satisfy the claimed variation percentages using the '080 patent's own criteria—*i.e.*, weight variation of 0% demonstrated by weight per dosage unit. *Compare* '080 patent at 31:46-66 (reporting consistent 0.04 g, *i.e.,* 40 mg, dosage unit weights) *to Chen* at Table 4 (reporting consistent 28 mg dosage weights rounded to the same decimal place as the '080 patent), and *to Staab* at 11:35-12:3 (reporting consistent 19 mg dosage unit weights).

Indeed, correctly applying the variation/uniformity criteria disclosed in the '080 patent, the examining panel found that all of the claims anticipated and/or obvious in view of the cited art. See, e.g., ACP at 36 and 58-59; RAN at 36-37 and 57. And where a claim is indefinite, it is appropriate to make a prior art rejection over an interpretation of the claims which renders the prior art applicable. See MPEP 2173.06; see also *Ex parte Mesher*, No. 2012-009669, 2013 WL 6122669 at

[6] Claim 318 recites "the amount of active varies by no more than 5%."

3 (PTAB Nov. 25, 2013); *Ex parte Miyazaki*, No. 2007-3300, 2008 WL 5105055 at 5 (BPAI Nov. 19, 2008).

But in addition to the prior art rejections, correctly made and maintained, the examining panel should have also found that the new recitation—explicitly recited in the claims and argued extensively by MonoSol—not only failed to patentably distinguish the claims, but also failed to meet the requirements of 35 USC §112.

1. *Lack of Enablement*

MonoSol argued a different interpretation of its new language—and one that directly contradicts its own specification. MonoSol argued that the prior art does not demonstrate its claimed variation/uniformity because the prior art uniformity has not been verified in accordance with MonoSol's interpretation of its new recitation. MonoSol now insists—post grant—that "physically observable properties of the resulting film product, for example, its appearance and weight … do not indicate that the amount of active in individual dosage units varies by no more than 10%." Reply-2 at 54-55. "Even if the film appears uniform, analytical chemical tests must then be conducted to verify uniformity of content at the prescribed level." Reply-2 at 59. In short, MonoSol argues that to satisfy its new

"variation" recitation, uniformity must be verified by analytical chemical testing of film, not merely by physically observable properties of film.

But there is no evidence in the '080 patent that the disclosed methods result in a film with the claimed variation/uniformity as verified by analytical chemical testing. Despite over 100 examples and 150 pages of specification, the '080 patent discloses no method that results in a film that it states satisfies the new variation/uniformity recitation or which is actually verified by analytical chemical testing as doing so. Indeed, the '080 patent does not even disclose analytical chemical testing. See Section VII.B, *supra*.

MonoSol attempted to remediate its enablement problem by providing new data in the first Bogue Declaration dated March 13, 2013 ("Bogue Declaration"). This is problematic. First, MonoSol asserts that the data supports all 300+ claims, including the 7 independent claims. MonoSol presumably believes that all 300+ claims are not identical methods —yet the data in the Bogue Declaration describes one method—and that method fails to match a single claim. It also fails to disclose the underlying facts that could allow the panel or the Board to independently evaluate if the data is commensurate in scope with the claims. For example, the Bogue Declaration does not identify which polymer or polymers were used—and it

is impossible to tell if these polymers are interchangeable such that the claimed results are achieved with the dozens of other polymers classes claimed or the thousands of polymers covered by the claims.

Second, according to Bogue, "[t]he results shown in the appendices establish … the amount of active varies by no more than 10% between individual dosage units sampled from a particular lot of resulting film." Bogue Decl. at ¶ 11. Thus, it appears that a lot may be a subset of a "resulting film." But there is no certainty as to how a "resulting film" or "resulting films" may relate to one or more "lots." Neither MonoSol nor Bogue equates a "lot" to any recited claim element.

Third, even if the Bogue process were commensurate with a single recited claim, which has not been demonstrated, the results presented in the Bogue Declaration does not fall within the recited desired maximum variance in active content. As can be clearly seen from the data presented in Appendix B, the amount of pharmaceutical active varies between individual dosage units from less than 94% on the far left of the figure, to nearly 106% on the upper right. That is, the amount of pharmaceutical active varies by more than 10%.

Finally, because MonoSol chose only to provide the results of its calculations and not the underlying data, the Office has no way of determining if

the data, analyzed in Appendix A, supports the claims. Unsupported expert testimony may be given little or no weight. See e.g., Rohm & Haas Co. v. Brotech Corp., 127 F.3d 1089, 1092 (Fed. Cir. 1997).

With respect to the recited active variation of 5% or less, Bogue's data does not support these claims. Specifically, for example, Bogue's data demonstrates active variation greater than 5% in 27 of the 73 allegedly relevant lots. See Bogue Decl. ¶ 11; see also id. at Appendices A and C. In other words, 37% have active variation greater than 5%. Bogue's data demonstrates that only one allegedly relevant lot (*i.e.*, 1%) has active variation of 2%. See id. at ¶ 11; see also id. at Appendices A and C. In other words, the active in 99% of the Bogue lots varies by more than 2%. None of the Bogue lots has active variation less than 2%, 1%, or 0.5%. See Bogue Decl. at Appendices A and C.

2. *Lack of Written Description*

Again, despite over 100 examples and 150 total original pages of specification, the '080 patent discloses no method that results in a film that satisfies the new variation/uniformity recitations as verified by analytical chemical testing.

In short, the '080 patent neither describes nor enables verification of any of the recited variation/uniformity levels as verified by so-called "analytical chemical tests." And, by MonoSol's own admission, without verification, there is no indication that the claimed methods meet the newly recited requirements. See Reply-2 at 67, lines 10-15. The physical tests provided in the '080 patent are not enough, according to MonoSol. See id.

3. *Lack of Clarity*

This recitation also lacks clarity. MonoSol's position is that the prior art methods—which are the same as its own disclosed verification methods—are inferior and so somehow not credible. It is not clear how the newly claimed tests may differ from those in the cited prior art.

MonoSol, for example, acknowledges that *Staab* explicitly discloses dosage forms where the amount of active varies by no more than 0%, but dismisses this explicit anticipation of the claims as "suspect." See ACP at 69 citing *Staab* at 11:35-12:3 (reporting consistent 19 mg dosage unit weights). MonoSol's sole reason for its suspicion is that any result with consistent amount of active (in *Staab*, the active is consistently 10% of the total weight) "must always be

considered suspect." Reply-2 at 69. MonoSol dismisses the evidence of Dr. Reitman who recreated an example in *Chen* and reports 0% variation by so-called analytical chemical tests, but could provide no credible reason for doing so. Reply-2 at 66 (referring to the Reitman Decl. ¶ 6 (reporting consistent weights of 34 mg)).[7] In short, MonoSol's overall position with respect to the cited art—art that explicitly anticipates this new recitation—can be summarized as follows: any result that anticipates the '080 patent claims is suspect because it anticipates the '080 patent claims. MonoSol's new recitation lacks disclosure and enablement, and only serves to muddy the waters with respect to claim scope.

D. Whether the panel erred in declining to adopt the proposed rejections based on limited variation between films even though such limitation is not described, not defined, and not exemplified in the '080 patent.

Independent claims 82 and 315, include a new step (f) of "repeating steps (a) through (e) to form additional resulting films, such that … the amount of said active in said resulting film and said additional resulting films varies no more than 10% from the desired amount of the active." Dependent claims 83-90, 92-94, 96-

[7] Although MonoSol implies that Dr. Reitman failed to follow the example exactly, it could provide no example of how Dr. Reitman did not faithfully reproduce the example. See ACP at 66.

160, 261-271, 274, 276-278, 298, 304-307, and 313 each recite a similar "repeating" step.

1. *Lack of Written Description and Enablement*

MonoSol argues there were numerous problems with manufacturing a uniform film in the prior art. Reply-2 at 60 ("Recognition of the Problem"). It asserts that it discovered how to maintain uniformity by "controlling polymer matrix viscosity" and "controlling the drying processes" in order to maintain a lot-to-lot consistency. Reply-2 at 61 ("Solving the Problem"). But, notably, MonoSol does not tell us what step or method condition or conditions are required to "solve the problem." And nowhere does the '080 patent disclose "repeating" these steps, much less verification of resulting variation/uniformity. Logically, repeating a set of steps should produce more of the same film, but not change the quality of the film.

Asserting that there is no requirement to disclose working examples, the examining panel concluded that Example E demonstrates uniformity, by so-called "physical tests", equivalent to the recited variation. See ACP at 18, RAN at 19. But MonoSol argues that assumptions based on the so-called "physical tests," such

as described in Example E, cannot be used as the basis for the claimed variation percentage between films. See Reply-2 at 61. According to MonoSol's proposed standards, the '080 patent does not disclose or enable repeatability of a method to obtain the claimed variation/uniformity. The '080 patent discloses no method involving a "repeating" step and verification of a resulting variation/uniformity.

Accordingly, while the claims were properly rejected as anticipated and/or obvious in view of the cited prior art, the examining panel should also have rejected the claims as lacking written description and enablement. There is simply no support in the '080 patent for a method that achieves one variation percentage within a resulting film, and a second variation percentage between resulting films. This new step is a post-grant idea. "If a claim is amended to include subject matter, limitations, or terminology not present in the application as filed, involving a departure from…the disclosure of the application as filed, the examiner should conclude that the claimed subject matter is not described in that application." MPEP 2163.02.

2. *Lack of Clarity*

With respect to clarity, the new and amended claims indicate that "repeating" produces a variation of up to 20% (± 10% around a target) in active content. This is a much larger variation than the claims indicate are produced each individual time the method is carried out ("varies by no more than 10%, 5%, etc."). The claims suggest and MonoSol argues that its methods do not produce consistent films, *i.e.,* that the method is not repeatable such that each time there is less than 10% variation each time. In sum, it is unclear what uniformity is required and how such uniformity is achieved since the claim only recites known methods and materials.

E. Whether the panel erred in failing to conclude that the scope of the claims cannot be determined because the newly-added "*rapidly increasing the viscosity of said flowable polymer matrix*" includes terms of degree both lacking a reference point and standards for comparison.

Step (d) of claim 1 and step (c) of claims 82 and 161 have been amended to include the relative phrase "*rapidly increasing the viscosity of said flowable polymer matrix*." Each new independent claim recites the same language. MonoSol states its inventive methods avoids the prior art problems by "controlling polymer matrix viscosity" and "controlling the drying processes" to maintain the

recited uniformity. Reply-2 at 61. Both phrases are ambiguous and lacking in any specificity or new teaching not found in the art. Although MonoSol attempts to use this new recitation to overcome the cited prior art, it is unclear how the recitation may do so because no actual method step is recited. The examining panel correctly found the recitation anticipated and/or obvious over the cited prior art. See RAN at 22. *Chen's* method, for example, produces film having less than 10% moisture in 4 minutes and meets the claimed uniformity requirements. See Reitman Decl. ¶¶ 5-8.

But the examining panel should also have rejected these claims for failure to clearly define any process step or condition with the new recitation. First, the term "rapidly" is a relative term with no benchmark for assessment provided in the '080 patent. The term "rapidly" only refers to the timing at which a desired result is obtained, but not how it is achieved. In other words, "rapidly" is a term of degree that requires a standard for measuring the degree; otherwise its scope cannot be determined. See *Sony Corporation v. Network-1 Security Solutions, Inc.*, IPR2013-00092 at 8 (PTAB May 24, 2013) citing *Playtex Prods., Inc. v. Procter & Gamble, Co.*, 400 F.3d 901, 908 (Fed. Cir. 2010). Second, there is no indication of the degree to which the viscosity must be increased. By its very nature, any drying process increases viscosity to some extent and may be deemed to do so

"rapidly" by some benchmark. In short, introduction of this phrase into every independent claim creates ambiguity and indefiniteness and provides no way of determining if the claims is infringed or how it differs from the methods in the cited art. See, e.g., *Amgen, Inc. v. Chugai Pharmaceutical Co., Ltd.*, 927 F.2d 1200, 1217-18 (Fed. Cir. 1991).

F. Whether the panel erred in determining that the "*100 °C or less*" in the "*controlling drying*" step clearly applies throughout the step.

During reexamination, the "controlling drying" step of each independent claim was amended to recite "controlling drying…to form a visco-elastic film…wherein during said drying said flowable polymer matrix temperature is 100 °C or less." See Claims Appendix or Reply-2 at 2-42 (at step (d) in claim 1 and step (c) of every other independent claim). It is unclear whether this new temperature limit applies only to the beginning or throughout the "controlling drying" step. The examining panel concluded that the temperature limitation applied to the entire drying step until the matrix is no longer a flowable polymer matrix, as determined by its viscosity exceeding the range recited in the previous step. See ACP at 22-23; RAN at 23.

The examining panel erred by concluding that the viscosity range recited in the previous casting step clearly defines the metes and bounds of the flowable polymer matrix in the later drying step. The viscosity range recited in a casting step identifies a requirement of the flowable polymer matrix during that step. The upper limit of the viscosity range recited in a casting step does not define when a flowable polymer matrix becomes a visco-elastic film. The '080 patent describes the flowable polymer matrix as already visco-elastic. See, e.g., '080 patent at 9:9-20; 9:31-40; 35:55-57; and 35:61-63. That is, once cast, the flowable polymer matrix is a visco-elastic film—even before drying begins. In short, it is unclear when the 100°C or less temperature limit no longer applies.

G. (Adopted)

H. Whether the panel erred in declining to adopt the proposed 112 rejections for the newly-added uniformity requirements added to different steps and combinations of steps even though these requirements are not described, not defined, and not exemplified in the '080 patent.

Again, MonoSol adds multiple new expressions of its desired variation/uniformity, without reciting what new and non-obvious method steps achieve them. In MonoSol's words, there are numerous factors that can destroy uniformity:

> Even when a wet film matrix is properly formed so as to have a substantially uniform distribution of active within it, there are numerous factors which can destroy that uniformity of content during later processing such as casting and drying.
>
> Reply-2 at 61.

But the claims still recite the same general method steps disclosed in the cited prior art. Although the claimed methods differ in that they require uniformity at different steps, it is impossible to discern any process differences. While MonoSol argues that uniformity can be "destroyed" by "numerous factors," it has not identified any reasonable rationale that supports its assertion that the cited prior art failed to achieve the claimed uniformity.

1. *Lack of clarity*

MonoSol adds so many new and different recitations regarding variation limitations to its independent claims, with multiple uniformity variation levels, even within the same claim, that the claims are mired in ambiguity and uncertainty. For example, if "there are numerous factors which can destroy that uniformity of content during later processing such as casting and drying" (Reply-2 at 61), then what method steps are required to maintain this uniformity that are not already disclosed in the prior art?

In addition, it is unclear where or when analytical tests are required with respect to the various intermediate steps with new recitations regarding uniformity.

In yet another example, to add more confusion, analytical chemical tests are required in a different part of step (e) to "indicate" that the active varies by no more than 10% in individual dosage units. First, this is not the FDA standard for approval. As discussed above, the standard is defined in USP General Chapter <905>. See Exhibit J to Comment-2. Second, what does it mean to "indicate" that the active varies by no more than 10%?

Yet, there is one more layer of confusion. New step (f) of claim 82 also recites "said resulting film and said additional resulting films." How does a "resulting film" differ from "additional resulting films"? Where is that described in the specification? Or demonstrated for that matter? There is simply no discussion of ±10% from a target amount of active anywhere in the specification with respect to a comparison of "resulting films." And why is the amount of variation for merely repeating the method so large compared with the smaller variation required each time a film is made? This new claim amendment, and the data presented in the Bogue Declaration, only serve to demonstrate that repeating the claimed method does not produce consistent films.

Every single independent claim is similarly confusing, each with their own combination of the many shades of "uniformity" that individually and collectively create a hopeless morass of confusion as to the meaning of the claims, the scope of the claims, and what is required by the claims.

Claim 82 is reproduced here with all its varied uniformity requirements underlined:

> 82. (Amended) A process for manufacturing resulting films suitable for commercialization and regulatory approval, said regulatory approval including analytical chemical testing which meets the standards of the U.S. Food and Drug Administration relating to variation of an active in individual dosage units said film having a substantially uniform distribution of components comprising a substantially uniform distribution of a desired amount of said active in individual dosage units of said resulting films, comprising the steps of:
>
> (a) forming a flowable polymer matrix comprising a polymer selected from the group consisting of a water-soluble polymer, a water swellable polymer and combinations thereof, a solvent and said active, said active selected from the group consisting of bioactive actives, pharmaceutical actives and combinations thereof, said matrix having a substantially uniform distribution of said active;
>
> (b) casting said flowable polymer matrix. said flowable polymer matrix having a viscosity from about 400 to about 100,000 cps;

(c) controlling drying through a process comprising conveying said flowable polymer matrix through a drying apparatus and evaporating at least a portion of said solvent from said flowable polymer matrix to form a visco-elastic film, having said active substantially uniformly distributed throughout within about the first 4 minutes by rapidly increasing the viscosity of said flowable polymer matrix upon initiation of drying to maintain said substantially uniform distribution of said active by locking-in or substantially preventing migration of said active within said visco-elastic film, wherein during said drying said flowable polymer matrix temperature is 100°C or less, and wherein uniformity of content of said active in substantially equal sized individual dosage units of said visco-elastic film is such that the amount of the active varies by no more than 10%;

(d) forming said resulting film from said visco-elastic film, wherein said resulting film has a water content of 10% or less and said substantially uniform distribution of active by said locking-in or substantially preventing migration of said active is maintained;

(e) performing analytical chemical tests for uniformity of content of said active in substantially equal sized individual dosage units sampled from different locations of said resulting film, said tests indicating that uniformity of content in the amount of said active varies by no more than 10% and said resulting film is suitable for commercial and regulatory approval, wherein said regulatory approval is provided by the U.S. Food and Drug Administration; and

(f) repeating steps (a) through (e) to form additional resulting films, such that uniformity of content in the amount of said active in said resulting

film and said additional resulting films varies no more than 10% from the desired amount of the active as indicated by said analytical chemical tests.

The vast majority of this claim is dedicated to varied expressions of desired uniformity at intermediate steps, as final desired result of the method, and then in comparing films with additional results films, but with no recitation the actual method step or combination of steps required to achieve them. Not only are the claimed methods unclear, but it is unclear even as to the requirements with respect to various desired uniformity limitations.

2. *Lack of written description.*

MonoSol argues post-grant that uniformity has to be verified by analytical chemical tests. But there is no evidence in the '080 patent that MonoSol verified uniformity at any step, including the intermediate steps where its new recitations require a specific variation/uniformity. See, e.g., '080 patent at 29:10-54 (only referencing uniformity testing of finished film samples). MonoSol has never explained how its methods actually differ from those of the prior art and thereby achieve this allegedly inventive variation/uniformity. No new method step is recited in the claims.

In addition, as discussed above, there is absolutely no support for the recitation of "varying by no more 10% from a desired target" in connection with any inventive method, or film resulting from the method. And certainly none for the claimed variation between "resulting films" and "additional resulting films." And while the '080 patent denigrates the prior art methods in its Background as not meeting this target (see discussion of Fuchs in '080 patent at 2:7-46)—it fails to tell us why and how its own methods achieve what it alleges others could not, apparently with the same methods.

3. *Lack of enablement*

Nowhere in any of the over 100 examples in the '080 Patent is any film demonstrated to meet any of the newly recited "uniformity" limitations. No analytical chemical tests are performed with respect to an active. No results of analytical chemical tests of active are provided. No demonstration is made that the active varies by no more than 10% in individual dosage units. No demonstration is made that "resulting films" and "additional resulting films" vary by no more than 10% from a desired target. In short, the '080 patent cannot withstand application of MonoSol's own proposed statements for written description and enablement.

Conclusion

In a failed attempt to overcome the cited prior art, MonoSol added a variety of recitations to every claim. The new recitations are confusing and unsupported. BDSI files this appeal because although the non-adopted rejections under 35 USC § 112 might be considered redundant to the final rejections, BDSI wants to make clear that, even if these new recitations did somehow distinguish the methods over the cited prior art methods (which they do not), the claims are still invalid under 35 USC § 112 for the reasons MonoSol itself advances.

Respectfully submitted,
Attorneys for Requester, McCarter & English LLP

Dated: March 10, 2014

By: /Danielle L. Herritt/
Danielle L. Herritt Reg. 43,670
Kia Freeman Reg. 47,577
Direct Dial: 617-449-6513

VIII. CLAIMS APPENDIX

1. (Amended) A process for manufacturing a resulting film suitable for commercialization and regulatory approval, said regulatory approval including analytical chemical testing which meets the standards of the U.S. Food and Drug Administration relating to variation of an active in individual dosage units, said [making a]film having a substantially uniform distribution of components comprising a substantially uniform distribution of said active in individual dosage units of said resulting film, comprising the steps of:

(a) forming a masterbatch pre-mix comprising a solvent and a polymer selected from the group consisting of water-soluble polymers, water-swellable polymers and combinations thereof;

(b) adding [an]said active, said active selected from the group consisting of bioactive actives, pharmaceutical actives and combinations thereof, to a pre-determined amount of said masterbatch pre-mix to form a flowable polymer matrix, said matrix having a substantially uniform distribution of said active;

(c) casting said flowable polymer matrix, said flowable polymer matrix having a viscosity from about 400 to about 100,000 cps;

(d) controlling drying through a process comprising conveying said flowable polymer matrix through a drying apparatus and evaporating at least a portion of said solvent from said flowable polymer matrix to form a visco-elastic film, having said active substantially uniformly distributed throughout, within about the first [10]4 minutes [or fewer]by rapidly increasing the viscosity of said flowable polymer matrix upon initiation of drying to maintain said substantially uniform distribution of said active by locking-in or substantially preventing migration of said active within said visco-elastic film, wherein during said drying said flowable polymer matrix temperature is 100 °C or less; [and]

(e) forming [a]said resulting film from said visco-elastic film, wherein said resulting film has a water content of 10% or less and said substantially uniform distribution of active by said locking-in or substantially preventing migration of said active is maintained; and

(f) performing analytical chemical tests for uniformity of content of said active in substantially equal sized individual dosage units sampled from different locations of said resulting film, said tests indicating that uniformity of content in the amount of the active varies by no more than 10% and said resulting film is suitable for commercial and regulatory approval, wherein said regulatory approval is provided by the U.S. Food and Drug Administration.

2. (Original) The process of claim 1, wherein said pre-determined amount of master batch pre-mix is controllably fed via a first metering pump and a control valve to a first mixer and a second mixer.

3. (Original) The process of claim 2, wherein said first mixer and said second mixer are arranged in parallel, series or a combination thereof.

4. (Original) The process of claim 1, wherein said water-soluble polymer comprises polyethylene oxide.

5. (Original) The process of claim 1, wherein said polymer comprises a polymer selected from the group consisting of cellulose, a cellulose derivative, pullulan, polyvinyl pyrrolidone, polyvinyl alcohol, polyethylene glycol, carboxyvinyl copolymers, hydroxypropylmethyl cellulose, hydroxyethyl cellulose, hydroxypropyl cellulose, carboxymethyl cellulose, sodium alginate, xanthan gum, tragacanth gum, guar gum, acacia gum, arabic gum, polyacrylic acid, methylmethacrylate copolymer, carboxyvinyl copolymers, starch, gelatin, and combinations thereof, alone or in combination with polyethylene oxide.

6. (Original) The process of claim 5, wherein said polymer further comprises a water insoluble polymer selected from the group consisting of ethylcellulose, hydroxypropyl ethyl

cellulose, cellulose acetate phthalate, hydroxypropyl methyl cellulose phthalate, polyvinylacetatephthalates, phthalated gelatin, crosslinked gelatin, poly(lactic acid)/poly(glycolic acid)/polyethyleneglycol copolymers, polycaprolactone and combinations thereof.

7. (Original) The process of claim 5, wherein said polymer further comprises a polymer selected from the group consisting of methylmethacrylate copolymer, polyacrylic acid polymer, poly(glycolic acid) (PGA), poly(lactic acid) (PLA), poly(lactic acid)/poly(glycolic acid)/polyethyleneglycol copolymers, polydioxanones, polyoxalates, poly(ά-esters), polyanhydrides, polyacetates, polycaprolactones, poly(orthoesters), polyamino acids, polyaminocarbonates, polyurethanes, polycarbonates, polyamides, poly(alkyl cyanoacrylates), and mixtures and copolymers thereof.

8. (Original) The process of claim 5, wherein said polymer further comprises a polymer selected from the group consisting of sodium alginate, xanthan gum, tragacanth gum, guar gum, acacia gum, arabic gum, starch, gelatin, carageenan, locust bean gum, dextran, gellan gum and combinations thereof.

9. (Original) The process of claim 5, wherein said polymer further comprises a polymer selected from the group consisting of ethylcellulose, hydroxypropyl ethyl cellulose, cellulose acetate phthalate, hydroxypropyl methyl cellulose phthalate, polyvinylacetatephthalates, phthalated gelatin, crosslinked gelatin, poly(lactic acid)/poly(glycolic acid)/polyethyleneglycol copolymers, polycaprolactone, methylmethacrylate copolymer, polyacrylic acid polymer, poly(glycolic acid) (PGA), poly(lactic acid) (PLA), poly(lactic acid)/poly(glycolic acid)/polyethyleneglycol copolymers, polydioxanones, polyoxalates, poly(d-esters), polyanhydrides, polyacetates, polycaprolactones, poly(orthoesters), polyamino acids, polyaminocarbonates, polyurethanes, polycarbonates, polyamides, poly(alkyl cyanoacrylates), sodium alginate, xanthan gum, tragacanth gum, guar gum, acacia gum, arabic gum, starch, gelatin, carageenan, locust bean gum, dextran, gellan gum and combinations thereof.

10. (Original) The process of claim 1, wherein said solvent is selected from the group

consisting of water, polar organic solvent, and combinations thereof.

11. (Original) The process of claim 10, wherein said solvent is selected from the group consisting of ethanol, isopropanol, acetone, and combinations thereof.

12. (Cancelled)

13. (Amended) The process of claim 1, wherein said active is selected from the group consisting of ace-inhibitors, anti-anginal drugs, anti-arrhythmias, anti-asthmatics, anti-cholesterolemics, analgesics, anesthetics, anti-convulsants, anti-depressants, anti-diabetic agents, anti-diarrhea preparations, antidotes, anti-histamines, anti-hypertensive drugs, anti-inflammatory agents, anti-lipid agents, anti-manics, anti-nauseants, anti-stroke agents, anti-thyroid preparations, anti-tumor drugs, anti-viral agents, acne drugs, alkaloids, amino acid preparations, anti-tussives, anti-uricemic drugs, anti-viral drugs, anabolic preparations, systemic and non-systemic anti-infective agents, anti-neoplastics, anti-parkinsonian agents, anti-rheumatic agents, appetite stimulants, blood modifiers, bone metabolism regulators, cardiovascular agents, central nervous system stimulates, cholinesterase inhibitors, contraceptives, decongestants, dietary supplements, dopamine receptor agonists, endometriosis management agents, enzymes, erectile dysfunction therapies, fertility agents, gastrointestinal agents, homeopathic remedies, hormones, hypercalcemia and hypocalcemia management agents, immunomodulators, immunosuppressives, migraine preparations, motion sickness treatments, muscle relaxants, obesity management agents, osteoporosis preparations, oxytocics, parasympatholytics, parasympathomimetics, prostaglandins, psychotherapeutic agents, respiratory agents, sedatives, smoking cessation aids, sympatholytics, tremor preparations, urinary tract agents, vasodilators, laxatives, antacids, ion exchange resins, anti-pyretics, appetite suppressants, expectorants, anti-anxiety agents, anti-ulcer agents, anti-inflammatory substances, coronary dilators, cerebral dilators, peripheral vasodilators, psycho-tropics, stimulants, anti-hypertensive drugs, vasoconstrictors, migraine treatments, antibiotics, tranquilizers, anti-psychotics, [anti-tumor drugs,]anti-coagulants, anti-thrombotic drugs, hypnotics, anti-emetics, anti-nauseants, [anti-convulsants,]neuromuscular drugs, hyper- and hypo-glycemic agents, thyroid and anti-thyroid preparations, diuretics, anti-

spasmodics, uterine relaxants, anti-obesity drugs, erythropoietic drugs, [anti-asthmatics,]cough suppressants, mucolytics, DNA and genetic modifying drugs, and combinations thereof.

14. (Amended) The process of claim 1, wherein said active is selected from the group consisting of [cosmetic actives,]antigens, allergens, spores, microorganisms, seeds, [mouthwash components, flavors, fragrances,]enzymes, [preservatives, sweetening agents, colorants, spices,]vitamins and combinations thereof.

15. (Original) The process of claim 1, wherein said active is a bioactive active.

16. (Cancelled)

17. (Original) The process of claim 1, wherein said active is an opiate or opiate-derivative.

18. (Original) The process of claim 1, wherein said active is an anti-emetic.

19. (Original) The process of claim 1, wherein said active is an amino acid preparation.

20. (Original) The process of claim 1, wherein said active is selected from the group consisting of sildenafils, tadalafils, vardenafils, apomorphines, yohimbine hydrochlorides, alprostadils and combinations thereof.

21. (Original) The process of claim 1, wherein said active is a protein.

22. (Original) The process of claim 1, wherein said active is insulin.

23. (Original) The process of claim 1, wherein said active is an anti-diabetic.

24. (Original) The process of claim 1, wherein said active is an antihistamine.

25. (Original) The process of claim 1, wherein said active is an anti-tussive.

26. (Original) The process of claim 1, wherein said active is a non-steroidal anti-inflammatory.

27. (Original) The process of claim 1, wherein said active is an anti-asthmatics.

28. (Amended) The process of claim 1, wherein said active is an anti-diarrhea preparation.

29. (Original) The process of claim 1, wherein said active is an alkaloid.

30. (Original) The process of claim 1, wherein said active is an anti-psychotic.

31. (Original) The process of claim 1, wherein said active is an anti-spasmodic.

32. (Original) The process of claim 1, wherein said active is a biological response modifier.

33. (Original) The process of claim 1, wherein said active is an anti-obesity drug.

34. (Original) The process of claim 1, wherein said active is an H_2-antagonist.

35. (Original) The process of claim 34, wherein said H_2-antagonist is selected from the group consisting of cimetidine, ranitidine hydrochloride, famotidine, nizatidine, ebrotidine, mifentidine, roxatidine, pisatidine, aceroxatidine and combinations thereof.

36. (Original) The process of claim 1, wherein said active is a smoking cessation aid.

37. (Original) The process of claim 1, wherein said active is an anti-parkinsonian agent.

38. (Original) The process of claim 1, wherein said active is an anti-depressant.

39. (Original) The process of claim 1, wherein said active is an anti-migraine.

40. (Original) The process of claim 1, wherein said active is an anti-Alzheimer's agents.

41. (Original) The process of claim 1, wherein said active is a dopamine receptor agonist.

42. (Original) The process of claim 1, wherein said active is a cerebral dilator.

43. (Original) The process of claim 1, wherein said active is a psychotherapeutic agent.

44. (Original) The process of claim 1, wherein said active is an antibiotic.

45. (Original) The process of claim 1, wherein said active is an anesthetic.

46. (Original) The process of claim 1, wherein said active is a contraceptive.

47. (Original) The process of claim 1, wherein said active is an anti-thrombotic drug.

48. (Original) The process of claim 1, wherein said active is diphenhydramine.

49. (Original) The process of claim 1, wherein said active is nabilone.

50. (Original) The process of claim 1, wherein said active is albuterol sulfate.

51. (Original) The process of claim 1, wherein said active is an anti-tumor drug.

52. (Original) The process of claim 1, wherein said active is a glycoprotein.

53. (Original) The process of claim 1, wherein said active is an analgesic.

54. (Original) The process of claim 1, wherein said active is a hormone.

55. (Original) The process of claim 1, wherein said active is a decongestant.

56. (Original) The process of claim 1, wherein said active is a loratadine.

57. (Original) The process of claim 1, wherein said active is dextromethorphan.

58. (Original) The process of claim 1, wherein said active is chlorpheniramine maleate.

59. (Original) The process of claim 1, wherein said active is selected from the group consisting of an analgesic, an anti-inflammatory, an antihistamine, a decongestant, a cough suppressant and combinations thereof.

60. (Original) The process of claim 1, wherein said active is an appetite stimulant.

61. (Original) The process of claim 1, wherein said active is a gastrointestinal agent.

62. (Original) The process of claim 1, wherein said active is a hypnotic.

63. (Original) The process of claim 1, wherein said active is taste-masked.

64. (Original) The process of claim 1, wherein said active is taste-masked using a flavor.

65. (Original) The process of claim 1, wherein said active is coated with a controlled release composition.

66. (Original) The process of claim 65, wherein said controlled release composition provides an immediate release.

67. (Original) The process of claim 65, wherein said controlled release composition provides a delayed release.

68. (Original) The process of claim 65, wherein said controlled release composition provides a sustained release.

69. (Original) The process of claim 65, wherein said controlled release composition provides a sequential release.

70. (Original) The process of claim 1, wherein said active is a particulate.

71. (Original) The process of claim 1, further comprising adding a degassing agent to said masterbatch premix.

72. (Original) The process of claim 1, further comprising a step of providing a second film layer.

73. (Original) The process of claim 72, wherein said second film layer is coated onto said resulting film.

74. (Original) The process of claim 72, wherein said second film layer is spread onto said resulting film.

75. (Original) The process of claim 72, wherein said second film layer is cast onto said resulting film.

76. (Original) The process of claim 72, wherein said second film layer is extruded onto said resulting film.

77. (Original) The process of claim 72, wherein said second film layer is sprayed onto said resulting film.

78. (Original) The process of claim 72, wherein said second film is laminated onto said resulting film.

79. (Original) The process of claim 72, further comprising laminating said resulting film to another film.

80. (Original) The process of claim 72, wherein said second film layer comprises an active.

81. (Amended) The process of claim [72]80, wherein said active in said second film is different than said active in said resulting film.

82. (Amended) A process for manufacturing resulting films suitable for commercialization and regulatory approval, said regulatory approval including analytical chemical testing which meets the standards of the U.S. Food and Drug Administration relating to variation of an active in individual dosage units, said [making a]films having a substantially uniform distribution of components comprising a substantially uniform distribution of a desired amount of said active in individual dosage units of said resulting films, comprising the steps of:

(a) forming a flowable polymer matrix comprising a polymer selected from the group consisting of a water-soluble polymer, a water swellable polymer and combinations thereof, a solvent and [an]said active, said active selected from the group consisting of bioactive actives, pharmaceutical actives[, drugs, medicaments] and combinations thereof, said matrix having a substantially uniform distribution of said active;

(b) casting said flowable polymer matrix, said flowable polymer matrix having a viscosity from about 400 to about 100,000 cps;

(c) controlling drying through a process comprising conveying said flowable polymer matrix through a drying apparatus and evaporating at least a portion of said solvent from said flowable polymer matrix to form a visco-elastic film, having said active substantially uniformly distributed throughout, within about the first [10]4 minutes [or fewer]by rapidly increasing the viscosity of said flowable polymer matrix upon initiation of drying to maintain said substantially uniform distribution of said active by locking-in or substantially preventing migration of said active within said visco-elastic film, wherein during said drying said flowable polymer matrix temperature is 100 °C or less, and wherein uniformity of content of said active in substantially equal sized individual dosage units of said visco-elastic film is such that the amount of the active varies by no more than 10%; [and]

(d) forming [a]said resulting film from said visco-elastic film, wherein said resulting film has a water content of 10% or less and said substantially uniform distribution of active by said locking-in or substantially preventing migration of said active is maintained;

(e) performing analytical chemical tests for uniformity of content of said active in substantially equal sized individual dosage units sampled from different locations of said resulting film, said tests indicating that uniformity of content in the amount of said active varies by no more than 10% and said resulting film is suitable for commercial and regulatory approval, wherein said regulatory approval is provided by the U.S. Food and Drug Administration; and

(f) repeating steps (a) through (e) to form additional resulting films, such that uniformity of content in the amount of said active in said resulting film and said additional resulting films varies no more than 10% from the desired amount of the active as indicated by said analytical chemical tests.

83. (Original) The process of claim 82, wherein said water-soluble polymer comprises polyethylene oxide.

84. (Original) The process of claim 82, wherein said polymer comprises a polymer selected

from the group consisting of cellulose, a cellulose derivative, pullulan, polyvinyl pyrrolidone, polyvinyl alcohol, polyethylene glycol, carboxyvinyl copolymers, hydroxypropylmethyl cellulose, hydroxyethyl cellulose, hydroxypropyl cellulose, carboxymethyl cellulose, sodium alginate, xanthan gum, tragacanth gum, guar gum, acacia gum, arabic gum, polyacrylic acid, methylmethacrylate copolymer, carboxyvinyl copolymers, starch, gelatin, and combinations thereof, alone or in combination with polyethylene oxide.

85. (Original) The process of claim 84, wherein said polymer further comprises a water insoluble polymer selected from the group consisting of ethylcellulose, hydroxypropyl ethyl cellulose, cellulose acetate phthalate, hydroxypropyl methyl cellulose phthalate, polyvinylacetatephthalates, phthalated gelatin, crosslinked gelatin, poly(lactic acid)/poly(glycolic acid)/polyethyleneglycol copolymers, polycaprolactone and combinations thereof.

86. (Original) The process of claim 84, wherein said polymer further comprises a polymer selected from the group consisting of methylmethacrylate copolymer, polyacrylic acid polymer, poly(glycolic acid) (PGA), poly(lactic acid) (PLA), poly(lactic acid)/poly(glycolic acid)/polyethyleneglycol copolymers, polydioxanones, polyoxalates, poly(ά-esters), polyanhydrides, polyacetates, polycaprolactones, poly(orthoesters), polyamino acids, polyaminocarbonates, polyurethanes, polycarbonates, polyamides, poly(alkyl cyanoacrylates), and mixtures and copolymers thereof.

87. (Original) The process of claim 84, wherein said polymer further comprises a polymer selected from the group consisting of sodium alginate, xanthan gum, tragacanth gum, guar gum, acacia gum, arabic gum, starch, gelatin, carageenan, locust bean gum, dextran, gellan gum and combinations thereof.

88. (Original) The process of claim 84, wherein said polymer further comprises a polymer selected from the group consisting of ethylcellulose, hydroxypropyl ethyl cellulose, cellulose acetate phthalate, hydroxypropyl methyl cellulose phthalate, polyvinylacetatephthalates, phthalated gelatin, crosslinked gelatin, poly(lactic acid)/poly(glycolic acid)/polyethyleneglycol

copolymers, polycaprolactone, methylmethacrylate copolymer, polyacrylic acid polymer, poly(glycolic acid) (PGA), poly(lactic acid) (PLA), poly(lactic acid)/poly(glycolic acid)/polyethyleneglycol copolymers, polydioxanones, polyoxalates, poly(ά-esters), polyanhydrides, polyacetates, polycaprolactones, poly(orthoesters), polyamino acids, polyaminocarbonates, polyurethanes, polycarbonates, polyamides, poly(alkyl cyanoacrylates), sodium alginate, xanthan gum, tragacanth gum, guar gum, acacia gum, arabic gum, starch, gelatin, carageenan, locust bean gum, dextran, gellan gum and combinations thereof.

89. (Original) The process of claim 82, wherein said solvent is selected from the group consisting of water, polar organic solvent, and combinations thereof.

90. (Original) The process of claim 89, wherein said solvent is selected from the group consisting of ethanol, isopropanol, acetone, and combinations thereof.

91. (Cancelled)

92. (Amended) The process of claim 82, wherein the active is selected from the group consisting of ace-inhibitors, anti-anginal drugs, anti-arrhythmias, anti-asthmatics, anti-cholesterolemics, analgesics, anesthetics, anti-convulsants, anti-depressants, anti-diabetic agents, anti-diarrhea preparations, antidotes, anti-histamines, anti-hypertensive drugs, anti-inflammatory agents, anti-lipid agents, anti-manics, anti-nauseants, anti-stroke agents, anti-thyroid preparations, anti-tumor drugs, anti-viral agents, acne drugs, alkaloids, amino acid preparations, anti-tussives, anti-uricemic drugs, anti-viral drugs, anabolic preparations, systemic and non-systemic anti-infective agents, anti-neoplastics, anti-parkinsonian agents, anti-rheumatic agents, appetite stimulants, blood modifiers, bone metabolism regulators, cardiovascular agents, central nervous system stimulates, cholinesterase inhibitors, contraceptives, decongestants, dietary supplements, dopamine receptor agonists, endometriosis management agents, enzymes, erectile dysfunction therapies, fertility agents, gastrointestinal agents, homeopathic remedies, hormones, hypercalcemia and hypocalcemia management agents, immunomodulators, immunosuppressives, migraine preparations, motion sickness treatments, muscle relaxants, obesity management

agents, osteoporosis preparations, oxytocics, parasympatholytics, parasympathomimetics, prostaglandins, psychotherapeutic agents, respiratory agents, sedatives, smoking cessation aids, sympatholytics, tremor preparations, urinary tract agents, vasodilators, laxatives, antacids, ion exchange resins, anti-pyretics, appetite suppressants, expectorants, anti-anxiety agents, anti-ulcer agents, anti-inflammatory substances, coronary dilators, cerebral dilators, peripheral vasodilators, psycho-tropics, stimulants, anti-hypertensive drugs, vasoconstrictors, migraine treatments, antibiotics, tranquilizers, anti-psychotics, [anti-tumor drugs,]anti-coagulants, anti-thrombotic drugs, hypnotics, anti-emetics, anti-nauseants, [anti-convulsants,]neuromuscular drugs, hyper- and hypo-glycemic agents, thyroid and anti-thyroid preparations, diuretics, anti-spasmodics, uterine relaxants, anti-obesity drugs, erythropoietic drugs, [anti-asthmatics,]cough suppressants, mucolytics, DNA and genetic modifying drugs, and combinations thereof.

93. (Amended) The process of claim 82, wherein said active is selected from the group consisting of [cosmetic actives,]antigens, allergens, spores, microorganisms, seeds, [mouthwash components, flavors, fragrances,]enzymes, [preservatives, sweetening agents, colorants, spices,]vitamins and combinations thereof.

94. (Original) The process of claim 82, wherein said active is a bioactive active.

95. (Cancelled)

96. (Original) The process of claim 82, wherein said active is an opiate or opiate-derivative.

97. (Original) The process of claim 82, wherein said active is an anti-emetic.

98. (Original) The process of claim 82, wherein said active is an amino acid preparation.

99. (Original) The process of claim 82, wherein said active is selected from the group consisting of sildenafils, tadalafils, vardenafils, apomorphines, yohimbine hydrochlorides, alprostadils and combinations thereof.

100. (Original) The process of claim 82, wherein said active is a protein.

101. (Original) The process of claim 82, wherein said active is insulin.

102. (Original) The process of claim 82, wherein said active is an anti-diabetic.

103. (Original) The process of claim 82, wherein said active is an antihistamine.

104. (Original) The process of claim 82, wherein said active is an anti-tussive.

105. (Original) The process of claim 82, wherein said active is a non-steroidal anti-inflammatory.

106. (Original) The process of claim 82, wherein said active is an anti-asthmatics.

107. (Amended) The process of claim 82, wherein said active is an anti-diarrhea preparation.

108. (Original) The process of claim 82, wherein said active is an alkaloid.

109. (Original) The process of claim 82, wherein said active is an anti-psychotic.

110. (Original) The process of claim 82, wherein said active is an anti-spasmodic.

111. (Original) The process of claim 82, wherein said active is a biological response modifier.

112. (Original) The process of claim 82, wherein said active is an anti-obesity drug.

113. (Original) The process of claim 82, wherein said active is an H_2-antagonist.

114. (Amended) The process of claim [82]113, wherein said H_2-antagonist is selected from the group consisting of cimetidine, ranitidine hydrochloride, famotidine, nizatidine, ebrotidine, mifentidine, roxatidine, pisatidine, aceroxatidine and combinations thereof.

115. (Original) The process of claim 82, wherein said active is a smoking cessation aid.

116. (Original) The process of claim 82, wherein said active is an anti-parkinsonian agent.

117. (Original) The process of claim 82, wherein said active is an anti-depressant.

118. (Original) The process of claim 82, wherein said active is an anti-migraine.

119. (Original) The process of claim 82, wherein said active is an anti-Alzheimer's agents.

120. (Original) The process of claim 82, wherein said active is a dopamine receptor agonist.

121. (Original) The process of claim 82, wherein said active is a cerebral dilator.

122. (Original) The process of claim 82, wherein said active is a psychotherapeutic agent.

123. (Original) The process of claim 82, wherein said active is an antibiotic.

124. (Original) The process of claim 82, wherein said active is an anesthetic.

125. (Original) The process of claim 82, wherein said active is a contraceptive.

126. (Original) The process of claim 82, wherein said active is an anti-thrombotic drug.

127. (Original) The process of claim 82, wherein said active is diphenhydramine.

128. (Original) The process of claim 82, wherein said active is nabilone.

129. (Original) The process of claim 82, wherein said active is albuterol sulfate.

130. (Original) The process of claim 82, wherein said active is an anti-tumor drug.

131. (Original) The process of claim 82, wherein said active is a glycoprotein.

132. (Original) The process of claim 82, wherein said active is an analgesic.

133. (Original) The process of claim 82, wherein said active is a hormone.

134. (Original) The process of claim 82, wherein said active is a decongestant.

135. (Original) The process of claim 82, wherein said active is a loratadine.

136. (Original) The process of claim 82, wherein said active is dextromethorphan.

137. (Original) The process of claim 82, wherein said active is chlorpheniramine maleate.

138. (Original) The process of claim 82, wherein said active is selected from the group consisting of an analgesic, an anti-inflammatory, an antihistamine, a decongestant, a cough suppressant and combinations thereof.

139. (Original) The process of claim 82, wherein said active is an appetite stimulant.

140. (Original) The process of claim 82, wherein said active is a gastrointestinal agent.

141. (Original) The process of claim 82, wherein said active is a hypnotic.

142. (Original) The process of claim 82, wherein said active is taste-masked.

143. (Original) The process of claim 82, wherein said active is taste-masked using a flavor.

144. (Original) The process of claim 82, wherein said active is coated with a controlled release composition.

145. (Original) The process of claim 144, wherein said controlled release composition provides an immediate release.

146. (Original) The process of claim 144, wherein said controlled release composition provides a delayed release.

147. (Original) The process of claim 144, wherein said controlled release composition provides a sustained release.

148. (Original) The process of claim 144, wherein said controlled release composition provides a sequential release.

149. (Original) The process of claim 82, wherein said active is a particulate.

150. (Original) The process of claim 82, further comprising adding a degassing agent to said flowable polymer matrix.

151. (Original) The process of claim 82, further comprising a step of providing a second film layer.

152. (Original) The process of claim 151, wherein said second film layer is coated onto said resulting film.

153. (Original) The process of claim 151, wherein said second film layer is spread onto said resulting film.

154. (Original) The process of claim 151, wherein said second film layer is cast onto said resulting film.

155. (Original) The process of claim 151, wherein said second film layer is extruded onto said resulting film.

156. (Original) The process of claim 151, wherein said second film layer is sprayed onto said resulting film.

157. (Original) The process of claim 151, wherein said second film layer is laminated onto said resulting film.

158. (Original) The process of claim 151, further comprising laminating said resulting film to another film.

159. (Original) The process of claim 151, wherein said second film comprises an active.

160. (Amended) The process of claim [151]159, wherein said active in said second film is different than said active in said resulting film.

161. (Amended) A process for manufacturing a resulting film suitable for commercialization and regulatory approval, said regulatory approval including analytical chemical testing which meets the standards of the U.S. Food and Drug Administration relating to variation of an active in individual dosage units, said[making a] film capable of being administered to a body surface and having a substantially uniform distribution of components comprising a substantially uniform distribution of said active in individual dosage units of said resulting film, comprising the steps of:

(a) forming a flowable polymer matrix comprising a water-soluble polymer, a solvent and [an]said active, said active selected from the group consisting of bioactive actives, pharmaceutical actives and combinations thereof, said matrix having a substantially uniform distribution of said active;

(b) casting said flowable polymer matrix, said flowable polymer matrix having a viscosity from about 400 to about 100,000 cps;

(c) controlling drying through a process comprising conveying said flowable polymer matrix through a drying apparatus and evaporating at least a portion of said solvent from said flowable polymer matrix to form a visco-elastic film, having said active substantially uniformly distributed throughout, within about the first [10]4 minutes [or fewer]by rapidly increasing the viscosity of said flowable polymer matrix upon initiation of drying to maintain said substantially uniform distribution of said active by locking-in or substantially preventing migration of said active within said visco-elastic film, wherein during said drying said flowable polymer matrix temperature is 100 °C or less, and wherein uniformity of content of said active in substantially equal sized individual dosage units of said visco-elastic film is such that the amount of the active varies by no more than 10%;

(d) forming [a]said resulting film from said visco-elastic film, wherein said resulting film has a water content of 10% or less and said substantially uniform distribution of active by said locking-in or substantially preventing migration of said active is maintained; [and]

(e) performing analytical chemical tests for uniformity of content of said active in substantially equal sized individual dosage units sampled from different locations of said resulting film, said tests indicating that uniformity of content in the amount of said active varies by no more than 10% and said resulting film is suitable for commercial and regulatory approval, wherein said regulatory approval is provided by the U.S. Food and Drug Administration, and

[(e)](f) administering said resulting film to a body surface.

162. (Original) The process of claim 161, wherein said body surface is a mucous membrane.

163. (Original) The process of claim 162, wherein said mucous membrane is oral, anal, vaginal or ophthalmological.

164. (Original) The process of claim 161, wherein said body surface is the surface of a wound.

165. (Original) The process of claim 161, wherein said water-soluble polymer comprises polyethylene oxide.

166. (Original) The process of claim 161, wherein said polymer comprises a polymer selected from the group consisting of cellulose, a cellulose derivative, pullulan, polyvinyl pyrrolidone, polyvinyl alcohol, polyethylene glycol, carboxyvinyl copolymers, hydroxypropylmethyl cellulose, hydroxyethyl cellulose, hydroxypropyl cellulose, carboxymethyl cellulose, sodium alginate, xanthan gum, tragacanth gum, guar gum, acacia gum, arabic gum, polyacrylic acid, methylmethacrylate copolymer, carboxyvinyl copolymers, starch, gelatin, and combinations thereof, alone or in combination with polyethylene oxide.

167. (Original) The process of claim 166, wherein said polymer further comprises a water insoluble polymer selected from the group consisting of ethylcellulose, hydroxypropyl ethyl cellulose, cellulose acetate phthalate, hydroxypropyl methyl cellulose phthalate, polyvinylacetatephthalates, phthalated gelatin, crosslinked gelatin, poly(lactic acid)/poly(glycolic acid)/polyethyleneglycol copolymers, polycaprolactone and combinations thereof.

168. (Original) The process of claim 166, wherein said polymer further comprises a polymer selected from the group consisting of methylmethacrylate copolymer, polyacrylic acid polymer, poly(glycolic acid) (PGA), poly(lactic acid) (PLA), poly(lactic acid)/poly(glycolic

acid)/polyethyleneglycol copolymers, polydioxanones, polyoxalates, poly(ά-esters), polyanhydrides, polyacetates, polycaprolactones, poly(orthoesters), polyamino acids, polyaminocarbonates, polyurethanes, polycarbonates, polyamides, poly(alkyl cyanoacrylates), and mixtures and copolymers thereof.

169. (Original) The process of claim 166, wherein said polymer further comprises a polymer selected from the group consisting of sodium alginate, xanthan gum, tragacanth gum, guar gum, acacia gum, arabic gum, starch, gelatin, caragcenan, locust bean gum, dextran, gellan gum and combinations thereof.

170. (Original) The process of claim 166, wherein said polymer further comprises a polymer selected from the group consisting of ethylcellulose, hydroxypropyl ethyl cellulose, cellulose acetate phthalate, hydroxypropyl methyl cellulose phthalate, polyvinylacetatephthalates, phthalated gelatin, crosslinked gelatin, poly(lactic acid)/poly(glycolic acid)/polyethyleneglycol copolymers, polycaprolactone, methylmethacrylate copolymer, polyacrylic acid polymer, poly(glycolic acid) (PGA), poly(lactic acid) (PLA), poly(lactic acid)/poly(glycolic acid)/polyethyleneglycol copolymers, polydioxanones, polyoxalates, poly(ά-esters), polyanhydrides, polyacetates, polycaprolactones, poly(orthoesters), polyamino acids, polyaminocarbonates, polyurethanes, polycarbonates, polyamides, poly(alkyl cyanoacrylates), sodium alginate, xanthan gum, tragacanth gum, guar gum, acacia gum, arabic gum, starch, gelatin, carageenan, locust bean gum, dextran, gellan gum and combinations thereof.

171. (Original) The process of claim 161, wherein said solvent is selected from the group consisting of water, polar organic solvent, and combinations thereof.

172. (Original) The process of claim 161, wherein said solvent is selected from the group consisting of ethanol, isopropanol, acetone, and combinations thereof.

173. (Cancelled)

174. (Amended) The process of claim 161, wherein said active is selected from the group consisting of ace-inhibitors, anti-anginal drugs, anti-arrhythmias, anti-asthmatics, anti-cholesterolemics, analgesics, anesthetics, anti-convulsants, anti-depressants, anti-diabetic agents, anti-diarrhea preparations, antidotes, anti-histamines, anti-hypertensive drugs, anti-inflammatory agents, anti-lipid agents, anti-manics, anti-nauseants, anti-stroke agents, anti-thyroid preparations, anti-tumor drugs, anti-viral agents, acne drugs, alkaloids, amino acid preparations, anti-tussives, anti-uricemic drugs, anti-viral drugs, anabolic preparations, systemic and non-systemic anti-infective agents, anti-neoplastics, anti-parkinsonian agents, anti-rheumatic agents, appetite stimulants, blood modifiers, bone metabolism regulators, cardiovascular agents, central nervous system stimulates, cholinesterase inhibitors, contraceptives, decongestants, dietary supplements, dopamine receptor agonists, endometriosis management agents, enzymes, erectile dysfunction therapies, fertility agents, gastrointestinal agents, homeopathic remedies, hormones, hypercalcemia and hypocalcemia management agents, immunomodulators, immunosuppressives, migraine preparations, motion sickness treatments, muscle relaxants, obesity management agents, osteoporosis preparations, oxytocics, parasympatholytics, parasympathomimetics, prostaglandins, psychotherapeutic agents, respiratory agents, sedatives, smoking cessation aids, sympatholytics, tremor preparations, urinary tract agents, vasodilators, laxatives, antacids, ion exchange resins, anti-pyretics, appetite suppressants, expectorants, anti-anxiety agents, anti-ulcer agents, anti-inflammatory substances, coronary dilators, cerebral dilators, peripheral vasodilators, psycho-tropics, stimulants, anti-hypertensive drugs, vasoconstrictors, migraine treatments, antibiotics, tranquilizers, anti-psychotics, [anti-tumor drugs,]anti-coagulants, anti-thrombotic drugs, hypnotics, anti-emetics, anti-nauseants, [anti-convulsants,]neuromuscular drugs, hyper- and hypo-glycemic agents, thyroid and anti-thyroid preparations, diuretics, anti-spasmodics, uterine relaxants, anti-obesity drugs, erythropoietic drugs, [anti-asthmatics,]cough suppressants, mucolytics, DNA and genetic modifying drugs, and combinations thereof.

175. (Amended) The process of claim 161, wherein said active is selected from the group consisting of [cosmetic actives,]antigens, allergens, spores, microorganisms, seeds, [mouthwash components, flavors, fragrances,]enzymes, [preservatives, sweetening agents, colorants, spices,

]vitamins and combinations thereof.

176. (Original) The process of claim 161, wherein said active is a bioactive active.

177. (Cancelled)

178. (Original) The process of claim 161, wherein said active is an opiate or opiate-derivative.

179. (Original) The process of claim 161, wherein said active is an anti-emetic.

180. (Original) The process of claim 161 wherein said active is an amino acid preparation.

181. (Original) The process of claim 161, wherein said active is selected from the group consisting of sildenafils, tadalafils, vardenafils, apomorphines, yohimbine hydrochlorides, alprostadils and combinations thereof.

182. (Original) The process of claim 161, wherein said active is a protein.

183. (Original) The process of claim 161, wherein said active is insulin.

184. (Original) The process of claim 161, wherein said active is an anti-diabetic.

185. (Original) The process of claim 161, wherein said active is an antihistamine.

186. (Original) The process of claim 161, wherein said active is an anti-tussive.

187. (Original) The process of claim 161, wherein said active is a non-steroidal anti-inflammatory.

188. (Original) The process of claim 161, wherein said active is an anti-asthmatics.

189. (Amended) The process of claim 161, wherein said active is an anti-diarrhea preparation.

190. (Original) The process of claim 161, wherein said active is an alkaloid.

191. (Original) The process of claim 161, wherein said active is an anti-psychotic.

192. (Original) The process of claim 161, wherein said active is an anti-spasmodic.

193. (Original) The process of claim 161, wherein said active is a biological response modifier.

194. (Original) The process of claim 161, wherein said active is an anti-obesity drug.

195. (Original) The process of claim 161, wherein said active is an H_2-antagonist.

196. (Original) The process of claim 195, wherein said H_2-antagonist is selected from the group consisting of cimetidine, ranitidine hydrochloride, famotidine, nizatidine, ebrotidine, mifentidine, roxatidine, pisatidine, aceroxatidine and combinations thereof.

197. (Original) The process of claim 161, wherein said active is a smoking cessation aid.

198. (Original) The process of claim 161, wherein said active is an anti-parkinsonian agent.

199. (Original) The process of claim 161, wherein said active is an anti-depressant.

200. (Original) The process of claim 161, wherein said active is an anti-migraine.

201. (Original) The process of claim 161, wherein said active is an anti-Alzheimer's agents.

202. (Original) The process of claim 161, wherein said active is a dopamine receptor agonist.

203. (Original) The process of claim 161, wherein said active is a cerebral dilator.

204. (Original) The process of claim 161, wherein said active is a psychotherapeutic agent.

205. (Original) The process of claim 161, wherein said active is an antibiotic.

206. (Original) The process of claim 161, wherein said active is an anesthetic.

207. (Original) The process of claim 161, wherein said active is a contraceptive.

208. (Original) The process of claim 161, wherein said active is an anti-thrombotic drug.

209. (Original) The process of claim 161, wherein said active is diphenhydramine.

210. (Original) The process of claim 161, wherein said active is nabilone.

211. (Original) The process of claim 161, wherein said active is albuterol sulfate.

212. (Original) The process of claim 161, wherein said active is an anti-tumor drug.

213. (Original) The process of claim 161, wherein said active is a glycoprotein.

214. (Original) The process of claim 161, wherein said active is an analgesic.

215. (Original) The process of claim 161, wherein said active is a hormone.

216. (Original) The process of claim 161, wherein said active is a decongestant.

217. (Original) The process of claim 161, wherein said active is a loratadine.

218. (Original) The process of claim 161, wherein said active is dextromethorphan.

219. (Original) The process of claim 161, wherein said active is chlorpheniramine maleate.

220. (Original) The process of claim 161, wherein said active is selected from the group consisting of an analgesic, an anti-inflammatory, an antihistamine, a decongestant, a cough suppressant and combinations thereof.

221. (Original) The process of claim 161, wherein said active is an appetite stimulant.

222. (Original) The process of claim 161, wherein said active is a gastrointestinal agent.

223. (Original) The process of claim 161, wherein said active is a hypnotic.

224. (Original) The process of claim 161, wherein said active is taste-masked.

225. (Original) The process of claim 161, wherein said active is taste-masked using a flavor.

226. (Original) The process of claim 161, wherein said active is coated with a controlled release composition.

227. (Original) The process of claim 226, wherein said controlled release composition provides an immediate release.

228. (Original) The process of 226, wherein said controlled release composition provides a delayed release.

229. (Original) The process of claim 226, wherein said controlled release composition

provides a sustained release.

230. (Original) The process of claim 226, wherein said controlled release composition provides a sequential release.

231. (Original) The process of claim 161, wherein said active is a particulate.

232. (Original) The process of claim 161, further comprising adding a degassing agent to said flowable polymer matrix.

233. (Original) The process of claim 161, further comprising a step of providing a second film layer.

234. (Original) The process of claim 233, wherein said second film layer is coated onto said resulting film.

235. (Original) The process of claim 233, wherein said second film layer is spread onto said resulting film.

236. (Original) The process of claim 233, wherein said second film layer is cast onto said resulting film.

237. (Original) The process of claim 233, wherein said second film layer is extruded onto said resulting film.

238. (Original) The process of claim 233, wherein said second film layer is sprayed onto said resulting film.

239. (Original) The process of claim 233, wherein said second film layer is laminated onto said resulting film.

240. (Original) The process of claim 233, further comprising laminating said resulting film to another film.

241. (Original) The process of claim 233, wherein said second film comprises an active.

242. (Amended) The process of claim [233]241, wherein said active in said second film is different than said active in said resulting film.

243. (Original) The process of claim 1, said active is an anti-nauseant.

244. (Amended) The process of claim 1, said active is an erectile dysfunction drug.

245. (Original) The process of claim 1, said active is a vasoconstrictor.

246. (Original) The process of claim 1, said active is a stimulant.

247. (Original) The process of claim 1, said active is a migraine treatment.

248. (Original) The process of claim 1, said active is granisetron hydrochloride.

249. (Original) The process of claim 1, wherein said resulting film provides administration of said active to an individual through the buccal cavity of said individual.

250. (Original) The process of claim 1, wherein said resulting film provides administration of said active through gingival application of said individual.

251. (Original) The process of claim 1, wherein said resulting film provides administration of said active through sublingual application of said individual.

252. (Original) The process of claim 1, wherein said resulting film provides administration of said active to an individual through a mucosal membrane of said individual.

253. (Original) The process of claim 1, wherein said resulting film provides administration of said active to an individual by administration within the body of the individual during surgery.

254. (Cancelled)

255. (Cancelled)

256. (Original) The method of claim 1, wherein said resulting film contains less than about 6% by weight solvent.

257. (Cancelled)

258. (Original) The method of claim 1, wherein said resulting film is orally administrable.

259. (Original) The method of claim 1, wherein said active is in the form of a particle.

260. (Original) The method of claim 1, wherein said matrix comprises a dispersion.

261. (Original) The process of claim 82, said active is an anti-nauseant.

262. (Amended) The process of claim 82, said active is an erectile dysfunction drug.

263. (Original) The process of claim 82, said active is a vasoconstrictor.

264. (Original) The process of claim 82, said active is a stimulant.

265. (Original) The process of claim 82, said active is a migraine treatment.

266. (Original) The process of claim 82, said active is granisetron hydrochloride.

267. (Original) The process of claim 82, wherein said resulting film provides administration of said active to an individual through the buccal cavity of said individual.

268. (Original) The process of claim 82, wherein said resulting film provides administration of said active through gingival application of said individual.

269. (Original) The process of claim 82, wherein said resulting film provides administration of said active through sublingual application of said individual.

270. (Original) The process of claim 82, wherein said resulting film provides administration of said active to an individual through a mucosal membrane of said individual.

271. (Original) The process of claim 82, wherein said resulting film provides administration of said active to an individual by administration within the body of the individual during surgery.

272. (Cancelled)

273. (Cancelled)

274. (Original) The method of claim 82, wherein said resulting film contains less than about 6% by weight solvent.

275. (Cancelled)

276. (Original) The method of claim 82, wherein said resulting film is orally administrable.

277. (Original) The method of claim 82, wherein said active is in the form of a particle.

278. (Original) The method of claim 82, wherein said matrix comprises a dispersion.

279. (Original) The process of claim 161, said active is an anti-nauseant.

280. (Amended) The process of claim 161, said active is an erectile dysfunction drug.

281. (Original) The process of claim 161, said active is a vasoconstrictor.

282. (Original) The process of claim 161, said active is a stimulant.

283. (Original) The process of claim 161, said active is a migraine treatment.

284. (Original) The process of claim 161, said active is granisetron hydrochloride.

285. (Original) The process of claim 161, wherein said resulting film provides administration of said active to an individual through the buccal cavity of said individual.

286. (Original) The process of claim 161, wherein said resulting film provides administration of said active through gingival application of said individual.

287. (Original) The process of claim 161, wherein said resulting film provides administration of said active through sublingual application of said individual.

288. (Original) The process of claim 161, wherein said resulting film provides administration of said active to an individual through a mucosal membrane of said individual.

289. (Original) The process of claim 161, wherein said resulting film provides administration of said active to an individual by administration within the body of the individual during surgery.

290. (Cancelled)

291. (Cancelled)

292. (Original) The method of claim 161, wherein said resulting film contains less than about 6% by weight solvent.

293. (Cancelled)

294. (Original) The method of claim 161, wherein said resulting film is orally administrable.

295. (Original) The method of claim 161, wherein said active is in the form of a particle.

296. (Original) The method of claim 161, wherein said matrix comprises a dispersion.

297. (Original) The method of claim 1, wherein said matrix comprises an emulsion, a colloid or a suspension.

298. (Original) The method of claim 82, wherein said matrix comprises an emulsion, a colloid or a suspension.

299. (Original) The method of claim 161, wherein said matrix comprises an emulsion, a colloid or a suspension.

300. (New) The process of claim 1, wherein said tests further indicate that the amount of active in said individual dosage units sampled from said resulting film varies by less than 5%.

301. (New) The process of claim 1, wherein said tests further indicate that the amount of active in said individual dosage units sampled from said resulting film varies by less than 2%.

302. (New) The process of claim 1, wherein said tests further indicate that the amount of active in said individual dosage units sampled from said resulting film varies by less than 1%.

303. (New) The process of claim 1, wherein said tests further indicate that the amount of active in said individual dosage units sampled from said resulting film varies by less than 0.5%.

304. (New) The process of claim 82, wherein said tests further indicate that the amount of active in said individual dosage units sampled from said resulting film varies by less than 5%.

305. (New) The process of claim 82, wherein said tests further indicate that the amount of active in said individual dosage units sampled from said resulting film varies by less than 2%.

306. (New) The process of claim 82, wherein said tests further indicate that the amount of active in said individual dosage units sampled from said resulting film varies by less than 1%.

307. (New) The process of claim 82, wherein said tests further indicate that the amount of active in said individual dosage units sampled from said resulting film varies by less than 0.5%.

308. (New) The process of claim 161, wherein said tests further indicate that the amount of active in said individual dosage units sampled from said resulting film varies by less than 5%.

309. (New) The process of claim 161, wherein said tests further indicate that the amount of active in said individual dosage units sampled from said resulting film varies by less than 2%.

310. (New) The process of claim 161, wherein said tests further indicate that the amount of active in said individual dosage units sampled from said resulting film varies by less than 1%.

311. (New) The process of claim 161, wherein said tests further indicate that the amount of active in said individual dosage units sampled from said resulting film varies by less than 0.5%.

312. (New) The process of claim 1, wherein said evaporating is conducted by applying radiant energy selected from the group consisting of hot air currents, heat, infrared radiation, radio frequency radiation and combinations thereof.

313. (New) The process of claim 82, wherein said evaporating is conducted by applying radiant energy selected from the group consisting of hot air currents, heat, infrared radiation, radio frequency radiation and combinations thereof.

314. (New) The process of claim 161, wherein said evaporating is conducted by applying radiant energy selected from the group consisting of hot air currents, heat, infrared radiation, radio frequency radiation and combinations thereof.

315. (New) A process for manufacturing resulting films suitable for commercialization and regulatory approval, said regulatory approval including analytical chemical testing which meets the standards of the U.S. Food and Drug Administration relating to variation of an active in individual dosage units, said films having a substantially uniform distribution of components comprising a substantially uniform distribution of a desired amount of said active in individual dosage units of said resulting films, comprising the steps of:

(a) forming a flowable polymer matrix comprising a water-soluble polymer, a solvent and said active, said active selected from the group consisting of bioactive actives, pharmaceutical actives and combinations thereof, said matrix having a substantially uniform distribution of said active;

(b) casting said flowable polymer matrix, said flowable polymer matrix having a viscosity from about 400 to about 100,000 cps;

(c) controlling drying through a process comprising conveying said polymer matrix through a drying apparatus and evaporating at least a portion of said solvent to form a visco-elastic film, having said active substantially uniformly distributed throughout, within about the first 4 minutes

by rapidly increasing the viscosity of said polymer matrix upon initiation of drying to maintain said substantially uniform distribution of said active by locking-in or substantially preventing migration of said active within said visco-elastic film, wherein during said drying said flowable polymer matrix temperature is 100 °C or less;

(d) forming said resulting film from said visco-elastic film, wherein said resulting film has a water content of 10% or less and said substantially uniform distribution of said active by said locking-in or substantially preventing migration of said active is maintained, such that uniformity of content in the amount of the active in substantially equal sized individual dosage units, sampled from different locations of said resulting film, varies by no more than 10%;

(e) performing analytical chemical tests for uniformity of content of said active in said substantially equal sized individual dosage units of said sampled resulting film, said tests indicating that uniformity of content in the amount of the active varies by no more than 10% and said resulting film is suitable for commercial and regulatory approval, wherein said regulatory approval is provided by the U.S. Food and Drug Administration; and

(f) repeating steps (a) through (e) to form additional resulting films, such that uniformity of content in the amount of said active in said resulting film and said additional resulting films varies no more than 10% from the desired amount of said active as indicated by said analytical chemical tests.

316. (New) A process for manufacturing a resulting film suitable for commercialization and regulatory approval, said regulatory approval including analytical chemical testing which meets the standards of the U.S. Food and Drug Administration relating to variation of an active in individual dosage units, said film having a substantially uniform distribution of components comprising a substantially uniform distribution of said active in individual dosage units of said resulting film, comprising the steps of:

(a) forming a flowable polymer matrix comprising a water-soluble polymer, a solvent and said active, said active selected from the group consisting of bioactive actives, pharmaceutical actives and combinations thereof, said matrix having a substantially uniform distribution of said active;

(b) casting said flowable polymer matrix, said flowable polymer matrix having a viscosity from about 400 to about 100,000 cps;

(c) controlling drying through a process comprising conveying said polymer matrix through a drying apparatus and evaporating at least a portion of said solvent to form a visco-elastic film, having said active substantially uniformly distributed throughout, within about the first 4 minutes by rapidly increasing the viscosity of said polymer matrix upon initiation of drying to maintain said substantially uniform distribution of said active by locking-in or substantially preventing migration of said active within said visco-elastic film, wherein during said drying said flowable polymer matrix temperature is 100 °C or less;

(d) forming said resulting film from said visco-elastic film, wherein said resulting film has a water content of 10% or less and said substantially uniform distribution of active by said locking-in or substantially preventing migration of said active is maintained, such that uniformity of content in the amount of said active in substantially equal sized individual dosage units, sampled from different locations of said resulting film, varies by no more than 10%; and

(e) performing analytical chemical tests for uniformity of content of said active in said substantially equal sized individual dosage units of said sampled resulting film, said tests indicating that uniformity of content in the amount of said active varies by no more than 10% and said resulting film is suitable for commercial and regulatory approval, wherein said regulatory approval is provided by the U.S. Food and Drug Administration.

317. (New) A process for manufacturing a resulting film suitable for commercialization and regulatory approval, said regulatory approval including analytical chemical testing which meets the standards of the U.S. Food and Drug Administration relating to variation of an active in individual dosage units, said film having a substantially uniform distribution of components comprising a substantially uniform distribution of said active in individual dosage units of said resulting film, comprising the steps of:

(a) forming a flowable polymer matrix comprising a water-soluble polymer, a solvent and said active, said active selected from the group consisting of bioactive actives, pharmaceutical actives and combinations thereof, said matrix having a substantially uniform distribution of said active;

(b) casting said flowable polymer matrix, said flowable polymer matrix having a viscosity from about 400 to about 100,000 cps;

(c) controlling drying through a process comprising conveying said flowable polymer matrix through a drying apparatus using air currents, which have forces below a yield value of said flowable polymer matrix during drying, to evaporate at least a portion of said solvent to form a visco-elastic film, having said active substantially uniformly distributed throughout, within about the first 4 minutes by rapidly increasing the viscosity of said flowable polymer matrix upon initiation of drying to maintain said substantially uniform distribution of said active by locking-in or substantially preventing migration of said active within said visco-elastic film, such that uniformity of content in the amount of said active in substantially equal sized individual dosage units, sampled from different locations of said visco-elastic film, varies by no more than 10%, and wherein during said drying said flowable polymer matrix temperature is 100 °C or less;

(d) forming said resulting film from said visco-elastic film by further controlling drying by continuing evaporation to a water content of said resulting film of 10% or less and wherein said substantially uniform distribution of active by said locking-in or substantially preventing migration of said active is maintained, such that uniformity of content in the amount of said

active in substantially equal sized individual dosage units, sampled from different locations of said resulting film, varies by no more than 10%; and

(e) performing analytical chemical tests for uniformity of content of said active in substantially equal sized individual dosage units of said sampled resulting film, said tests indicating that uniformity of content in the amount of said active varies by no more than 10% and said resulting film is suitable for commercial and regulatory approval, wherein said regulatory approval is provided by the U.S. Food and Drug Administration.

318. (New) A process for manufacturing a resulting film suitable for commercialization and regulatory approval, said regulatory approval including analytical chemical testing which meets the standards of the U.S. Food and Drug Administration relating to variation of an active in individual dosage units, said film having a substantially uniform distribution of components comprising a substantially uniform distribution of said active in individual dosage units of said resulting film, comprising the steps of:

(a) forming a flowable polymer matrix comprising a water-soluble polymer, a solvent and said active, said active selected from the group consisting of bioactive actives, pharmaceutical actives and combinations thereof, said matrix having a substantially uniform distribution of said active;

(b) casting said flowable polymer matrix, said flowable polymer matrix having a viscosity from about 400 to about 100,000 cps;

(c) controlling drying through a process comprising conveying said flowable polymer matrix through a drying apparatus at a temperature of about 60 °C and using air currents, which have forces below a yield value of the polymer matrix during drying, to evaporate at least a portion of said solvent to form a visco-elastic film, having said active substantially uniformly distributed throughout, within about the first 4 minutes by rapidly increasing the viscosity of said flowable polymer matrix upon initiation of drying to maintain said substantially uniform distribution of said active by locking-in or substantially preventing migration of said active within said visco-

elastic film, such that uniformity of content in the amount of said active in substantially equal sized individual dosage units, sampled from different locations of said visco-elastic film, varies by less than 5%, and wherein during said drying said flowable polymer matrix temperature is 100 °C or less;

(d) forming said resulting film from said visco-elastic film by further controlling by continuing evaporation to a water content of said resulting film of 10% or less and wherein said substantially uniform distribution of active by said locking-in or substantially preventing migration of said active is maintained, such that uniformity of content in the amount of said active in substantially equal sized individual dosage units, sampled from different locations of said resulting film, varies by less than 5%; and

(e) performing analytical chemical tests for uniformity of content of said active in substantially equal sized individual dosage units of said sampled resulting film, said tests indicating that uniformity of content in the amount of said active varies by less than 5% and said resulting film is suitable for commercial and regulatory approval, wherein said regulatory approval is provided by the U.S. Food and Drug Administration.

IX. EVIDENCE APPENDIX

Exhibit 1: US Patent No. 7,897,080

Exhibit 2: Reitman Declaration filed April 12, 2013

Exhibit 3: Clevenger Declaration filed April 12, 2013

Exhibit 4: Bogue and Lin Declarations filed March 13, 2013

X. RELATED PROCEEDINGS APPENDIX

None.

XI. CERTIFICATE OF SERVICE

CERTIFICATE OF SERVICE

The undersigned hereby certifies that a copy of the foregoing Appellant's Brief was served on March 10, 2014, by first class mail, directed to the patent owner at the correspondence address of record for the subject patent at the following address:

Daniel A. Scola, Jr.

HOFFMANN & BARON, LLP

6900 JERICHO TURNPIKE

SYOSSET, NY 11791,

By: /Danielle L. Herritt/
Danielle L. Herritt
Registration No. 43,670
Attorney for Respondent

EXHIBIT 2

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re *Inter Partes* Reexamination of:	)
US Patent No. 7,897,080	)
Issued: March 1, 2011	) Confirmation No.: 6418
Named Inventor: Robert K. Yang *et al.*	) Group Art Unit: 3991
Control No.: 95/002,170	) Examiner: Diamond, Alan D.
Filed: September 10, 2012	) M&E Docket: 117744-00023
Title: POLYETHYLENE-OXIDE BASED FILMS AND DRUG DELIVERY SYSTEMS MADE THEREFROM	) H&B Docket: 1199-26 RCE/CON/REX

Mail Stop *Inter Partes* Reexam
Attn: Central Reexamination Unit
Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

DECLARATION BY MAUREEN REITMAN, SC.D.
UNDER 37 CFR § 1.132

Sir/Madam:

I, Maureen Reitman, do hereby make the following declaration:

I. Technical Background

1. I am a Principal and the Director of the Polymer Science and Materials Chemistry Practice at Exponent. I hold two academic degrees: (1) a Bachelor of Science in Materials Science and Engineering from the Massachusetts Institute of Technology (MIT), and (2) a Doctor of Science in Materials Science and Engineering, with a thesis in the field of polymers, from MIT. I have been practicing in the field of polymer science and engineering for more than 20 years as a researcher at MIT, in a variety of technical roles at the 3M Company, and as a consultant with Exponent. I provide consulting engineering services in all aspects of polymer science and engineering including, but not limited to material selection, product design and development, mechanical and chemical testing, failure analysis, polymer chemistry, polymer

physics, and polymer processing. My specialties include formulation, processing and performance evaluation of polymeric materials, including films, coatings, adhesives and transdermal drug delivery systems. I have been directly involved in product development, product line extensions, transfer of new products to manufacturing, qualification of alternative materials and manufacturing equipment, evaluating field performance, and assessing intellectual property. I am a past chairman and continue to serve as a member of the board of directors of the Medical Plastics Division of the Society of Plastics Engineers. My *curriculum vitae* is provided in Appendix A.

2. While Exponent is being paid for my time, I am not an employee of, nor do I have any financial interest in, BioDelivery Sciences International, Inc.

3. I have been asked to carefully review International Publication No. WO 00/42992 ("*Chen*"), and manufacture a film as described in *Chen*. I carefully reviewed *Chen*. Under my direction, my team manufactured a film in accordance with Example 7 of *Chen*. I have also been asked to take samples and perform various analytical tests to confirm the uniform distribution of the pharmaceutical active in substantially equal sized individual dosage units of the film, which we did.

4. Manufacturing Example 7 of *Chen*

Chen states: "According to Examples 1-8, the hydrocolloid [Methocel E5(HPMC)] was dissolved in water under agitated mixing to form a uniform and viscous solution." Chen 17:7-8.

- Methocel E5(HPMC) was dissolved in water under agitated mixing to form a uniform and viscous solution, by my team.

Chen states: "Additional ingredients were then added sequentially to the viscous solution such as peppermint, aspartame, propyl[ene] glycol, benzoic acid and citric acid under agitated mixing until they were uniformly dispersed or dissolved in the hydrocolloid." Chen 17:8-11.

- Additional ingredients were then added sequentially to the viscous solution including peppermint oil, aspartame, propylene glycol, benzoic acid and citric acid under agitated mixing until they were uniformly dispersed or dissolved in the hydrocolloid, by my team.

- Kolliphor EL was also added to the viscous solution.

Chen states: "Therapeutic agents were added to the homogeneous mixture (coating solution) prior to forming the film." *Chen* 20:19-20.

- Oxybutynin chloride (the therapeutic agent of Example 7) was added to the homogeneous mixture (coating solution) prior to forming the film, by my team.

Chen's Table 5 specifies the composition for Example 7.

- We used the ingredients in the amounts identified in *Chen*'s Table 5. *See* Table 1.

Table 1			
Formulation, Ex. 7, Table 5, *Chen*	% Weight	Formulation, Prepared by Maureen Reitman Team	% Weight
Oxybutynin	3.71	Oxybutynin chloride	3.71
Methocel E5 (HPMC)	21.06	Methocel E5 Premium LV	21.06
Water	70.72	Water, distilled	70.72
Cremophor EL40	1	Kolliphor EL[1]	1
Propylene glycol	1	Propylene glycol	1
Peppermint	1	Peppermint oil	1
Aspartame	0.8	Aspartame	0.8
Benzoic acid	0.013	Benzoic acid	0.013
Citric acid	0.7	Citric acid, monohydrate	0.7

Chen states: "The resultant mixture was degassed in a vacuum chamber until trapped air bubbles were removed." Chen 17:11-12.

- The resultant mixture was degassed in a vacuum chamber until trapped air bubbles were removed, by my team.

Chen states: "The formulation was then coated on the non-siliconized side of a polyester film at a wet thickness of 10 mil and dried in a hot air circulating oven at 50°C for 9 minutes." Chen 17:13-15.

- The formulation was then coated on a non-siliconized side of a polyester film at a wet thickness of 10 mil and dried in a hot air circulating oven at 50°C for up to 9 minutes, on commercial manufacturing equipment by my team.

Chen states: "Methods for manufacturing the dosage unit include the solvent casting methods as shown in Figure 2." Chen 15:13-14. "The manufacturing process for forming the dosage unit is illustrated in Figure 2. The dry film formed by this process is a glossy, stand alone, self supporting, non-tacky and flexible film (12)." Chen 15:29-31.

- A solvent casting manufacturing process for forming the dosage unit as illustrated in Figure 2 was used[2], by my team.

[1] The Cremophor line of products now owned by BASF and renamed Kolliphor. Based on the naming convention of the Cremophor/ Kolliphor products, EL40 is Polyoxyl 40 Castor Oil and EL is Polyoxyl 35 Castor Oil (*i.e.*, they are based on a 1:40 and 1:35 ratio, respectively, of castor oil:ethylene oxide). They are different materials. However, one of skill in the art would recognize Kolliphor EL as an appropriate substitute, as Cremophor EL40 is no longer available.

- The film was manufactured using a controlled drying process.
- As illustrated in Figure 2, the drying oven featured aeration controller with 3 zones set such that in each successive zone air impingement on the surface of the film increased.
- The dry film formed by the process is a glossy, stand alone, self-supporting, non-tacky and flexible film.

Chen states: "A glossy, substantially transparent, stand alone, self-supporting, non-tacky and flexible film was obtained after drying." Chen 17:15-16.

- A glossy, substantially transparent, stand alone, self-supporting, non-tacky and flexible film was obtained after drying, by my team.

5. Verification of Content Uniformity – Visual Inspection

- By examination with the naked eye, uniformity was verified by my team.

6. Verification of Content Uniformity – Unit Dose Weight

- By weighing individual dosage units of substantially identical size, uniformity was verified by my team. *See* Table 2.

Table 2	
Sample	Weight of 5 cm^2 dosage unit (grams)
1	0.034
2	0.034
3	0.034
4	0.034
5	0.034
6	0.034
7	0.034

7. Verification of Content Uniformity – Dissolution Test (HPLC)

- By dissolution of individual dosage units of substantially identical size and analysis by High Performance Liquid Chromatography (HPLC) active content uniformity was verified by my team. *See* Table 3.

[2] Our backing was not looped and we did not die cut in line, but the solvent casting and drying under aeration is matched.

Table 3	
Sample	Oxybutynin weight (mg)
A	4.4
B	4.4
C	4.3
D	4.4
E	4.1

- As can be seen in Table 3, the active varies by less than 10%.

8. Additional Observations

   - The components of the formulation, including the active component, were uniformly distributed in the viscous solution, which was used to cast the film, as was verified by my team.

   - The viscous solution, which was used to cast the film, exhibited the flow properties of honey (around 10,000 cps), as observed by my team.

   - Water content of the film was less than 10%, as verified by my team.

   - Within about 4 minutes after initiation of drying, the film was self-supporting, non-tacky, flexible and viscoelastic, as verified by my team.

9. I hereby declare that all statements made herein of my own knowledge are true and that all statements made on information and belief are believed to be true; and further that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine, or imprisonment, or both, under section 1001 of Title 18 of the United States Code, and that such willful statements may jeopardize the validity of the application or any patents issued thereon.

Dated: February 28, 2013

Maureen Reitman, Sc.D.

Appendix A

Exponent
Failure Analysis Associates

Exponent
17000 Science Drive
Suite 200
Bowie, Maryland 20715

telephone 301-291-3500
facsimile 301-291-3599
www.exponent.com

Maureen T. F. Reitman, Sc.D.
Principal and Practice Director

Professional Profile

Dr. Maureen Reitman is a Principal and the Director of Exponent's Polymer Science and Material Chemistry practice. Her expertise includes polymer and composite technology, mechanics of materials, adhesion science, fiber mechanics, history and technology of plastics, and material failure analysis. She is skilled in the development and use of testing tools and methods and has applied them to plastic, rubber, textile, metal, glass, ceramic, and composite materials and systems. She is experienced in major aspects of product development, including materials selection, formulation, scale-up, end-use testing, failure analysis, certification procedures and issues related to intellectual property.

Dr. Reitman has conducted research in the areas of packaging and barrier materials; paints and coatings; plastic pipes; transdermal drug delivery; adhesives, sealants, and encapsulants; molding compounds; high temperature resins; nanoparticles; fibers and textiles; protective coatings and finishes; polymer chemical resistance; plastic insulation; connectors and splices; plastic packaging; medical devices; environmental effects on durability; and product aging. She has used her expertise to solve a broad range of problems related to coatings, fibers, films, and extruded and molded products, and their use in the telecom, electronics, electrical, transportation, construction, fire protection, medical, and consumer products markets.

Dr. Reitman is a member of the Board of Directors of the Medical Plastics Division of the Society of Plastics Engineers and an active member of two Underwriters Laboratories Standard Technical Panels, addressing Polymeric Materials (UL 94, UL 746, UL 1694) and Appliance Wiring (UL758).

Prior to joining Exponent, Dr. Reitman worked for the 3M Company in both research and management roles. Her activities included technology identification, materials selection and qualification, product development, customer support, program management, acquisition integration, intellectual property analysis, and patent litigation support.

Academic Credentials and Professional Honors

Sc.D., Materials Science and Engineering/ Program in Polymer Science and Technology, Massachusetts Institute of Technology, 1993
B.S., Materials Science and Engineering, Massachusetts Institute of Technology, 1990

National Academy of Engineering Frontiers of Engineering, 2009; Tau Beta Pi; Sigma Xi
John Wulff Award; Carl Loeb Fellowship; NCAA Postgraduate Scholarship;
Malcolm G. Kispert Award; GTE Academic All-American

02/13

Patents

Patent 6,311,524: Accelerated Method for Increasing the Photosensitivity of a Glassy Material, issued November 6, 2001.

European Patent EP0830428: Tackified Polydiorganosiloxane Polyurea Segmented Copolymers and a Process for Making Same, published March 25, 1998.

Patent 5,371,051: Fiber Optic Fusion Splice Protector Sleeve, issued March 24, 1998.

Publications

Kurtz S, Siskey R, Reitman M. Accelerated aging, natural aging, and small punch testing of gamma-air sterilized polycarbonate urethane acetabular components. Journal of Biomedical Materials Research Part B: Applied Biomaterials 2010 May; 93B(2):422–447.

Hoffman JM, Reitman M, Donthu S, Ledwith P. Complimentary failure analysis methods and their application to CPVC pipe. Proceedings, ANTEC 2010, Society of Plastics Engineers, Orlando, FL, May 2010.

Hoffman JM, Reitman M, Donthu S, Ledwith P, Wills D. Microscopic characterization of CPVC failure modes. Proceedings, ANTEC 2009, Society of Plastics Engineers, Chicago, IL, June 2009. Best Paper Award in Failure Analysis & Prevention.

Kurtz SM, Ebert M, Siskey R, Ciccarelli L, Reitman M, Harper ML, Chan FW. Natural and accelerated aging of polyurethanes in the Bryan cervical disc. Poster No. P158. Transactions of Spineweek 2008, Geneva, Switzerland, May 26–31, 2008.

Reitman M, Ledwith P, Hoffman M, Moalli J, Xu T. Environmentally driven changes in nylon. Proceedings, ANTEC 2008, Milwaukee, WI, Society of Plastics Engineers, May 2008.

Hoffman JM, Reitman M, Ledwith P. Characterization of manufacturing defects in medical balloons. Proceedings, ANTEC 2008, Milwaukee, WI, Society of Plastics Engineers, May 2008.

Reitman, MTF, Moalli JE. Polymeric coatings for medical device. Medical Device and Manufacturing Technology, Touch Briefings, pp. 28–30, 2006.

Moalli JE, Moore CD, Robertson C, Reitman MTF. Failure analysis of nitrile radiant heating tubing. Proceedings, ANTEC 2006, Society of Plastic Engineers, Charlotte, NC, May 2006.

Reitman M, McPeak J. Protective coatings for implantable medical devices. Proceedings, ANTEC 2005, Society of Plastic Engineers, Boston MA, May 2005.

McPeak J, Reitman M, Moalli J. Determination of in-service exposure temperature of thermoformed PVC via TMA. Proceedings, 31st Annual North American Thermal Analysis Society Conference, Williamsburg, VA, 2004.

Reitman MTF, Moalli JE. Product development and standards organizations: Listings and certifications for plastic products. 8th Annual International Conference on Industrial Engineering Theory, Applications and Practice, Las Vegas, NV, 2003.

Potdar YK, Reitman MTF. The role of engineering consultants in failure analysis and product development. 8th Annual International Conference on Industrial Engineering Theory, Applications and Practice, Las Vegas, NV, 2003.

Ezekoye OA, Lowman CD, Hulme-Lowe AG, Fahey MT. Polymer weld strength predictions using a thermal and polymer chain diffusion analysis. Polymer Engineering and Science 1998; 38(6):976–991, June.

Fahey MT. Nonlinear and anisotropic properties of high performance fibers. MIT Thesis, 1993.

Fahey MT. Mechanical property characterization and enhancement of rigid rod polymer fibers. MIT Thesis, 1990.

Book Contributions

Reitman M, Liu D, Rehkopf J. Chapter 38. Mechanical properties of polymers. In: Handbook of Measurement in Science and Engineering. Volume 2. Kutz, M (ed), John Wiley & Sons, Hoboken NJ, 2013. ISBN- 978-1-118-38464-0.

Reitman M, Jaekel D, Siskey R, Kurtz S. Morphology and crystalline architecture of polyarylketones, pp. 49-60. In: PEEK Biomaterials Handbook. Kurtz SM (ed), Elsevier William Andrews, Kidlington, Oxford, UK, 2012. ISBN 13:978-1-4377-4463-7

Tsuji JS, Mowat FS, Donthu S, Reitman M. Application of toxicology studies in assessing the health risks of nanomaterials in consumer products, pp. 543-580. In: Nanotoxicity: From In Vivo and In Vitro Models to Health Risks. Sahu S, and Casciano D. (eds), John Wiley & Sons, Chicester, West Sussex, UK, 2009. ISBN 978-0-470-74137-5.

Reitman MTF. The Plastics Revolution. In: Research and Discovery: Landmarks and Pioneers in American Science. Lawson RM (ed), Armonk NY: Sharpe Reference 2008. ISBN 978-0-7656-8073-0.

Klein SM. Mid-century plastic jewelry. Schiffer Publishing, Atglen, PA, 2005. (Technical advisor to author).

Selected Invited Presentations

Reitman MTF. Failure analysis tools. Workshop on Future Needs for Service Life Prediction of Polymeric Materials. NIST and Underwriters Laboratories, Gaithersburg, MD, October 2012.

Hoffman J, MacLean S, Ralston B, Reitman M, Ledwith P. Fractography of unfilled thermoplastic materials experiencing common mechanical failure modes. Materials Science & Technology 2012 Conference, Pittsburgh PA, October 2012.

Hoffman J, Reitman M, Ledwith P. Microscopic characterization of CPVC failure. Materials Science & Technology 2012 Conference, Pittsburgh PA, October 2012.

Reitman MTF. Polymer material properties for next generation medical devices. Invited Speaker: MedTech Polymers, UBM Canon, Chicago, IL, September 2012.

Reitman MTF. Polymers for medical applications. Fundamentals and Fellows Forum, ANTEC 2012, Orlando FL, April 2012.

Reitman MTF. Plastic and composite product failures. Invited lecture in Failure Analysis of Emerging Technologies. Stanford University Department of Materials Science and Engineering, Menlo Park, CA October 2009.

Reitman MTF. Factors for success: Plastics in injection molded medical devices. Part of *Injection Molding Works for Medical Design*, Design News Webcast, October 2008.

Reitman MTF. Plastic and composite product failures. Keynote Speaker: Third International Conference on Engineering Failure Analysis (ICEFA III), Elsevier, Sitges Spain, July 2008.

Reitman MTF. Multiphase materials for medical device applications, an overview. Medical Device and Manufacturing (MDM), Canon Communications, various locations, January- June 2008.

Reitman MTF. Nanotechnology and plastics for medical devices. Capitalizing on Nanoplastics, Intertek PIRA San Antonio TX, February 2008.

Reitman MTF. Nano additives in composites and coatings for medical device applications. Medical Device and Manufacturing Minneapolis, Canon Communications, Minneapolis MN, October 2007.

Reitman MTF, Swanger LA. Practical tips on how to manage your technical expert in patent disputes. Ropes & Gray IP Master Class, Live Teleconference, June 2007.

Reitman MTF, Kennedy E. Root cause failure analysis and accident investigation. Lorman Educational Services, Live Teleconference, November 2007.

Reitman MTF. Plastics failure analysis: Case studies. Baltimore/ Washington Chapter of SAMPE, October 2006.

Reitman MTF. Plastics failure analysis. Baxter Global Plastics Processing Conference 2005, Schaumburg IL, 2005.

Fahey MT. Fiber mechanics, corrosion, sealants: Tales of a 3M materials scientist. Class of 1960's Scholars Program, Williams College, 1999.

Fahey MT. Adhesives and sealants for the telecommunications industry. Riverwood V Conference, St. Paul MN, 1998.

Current Professional Appointments

- Underwriter's Laboratory Standards Technical Panel STP 746 (Polymeric Materials, includes UL94, UL 746 and UL1694)
- Underwriter's Laboratory Standards Technical Panel STP 758 (Appliance Wires/ UL758)
- Medical Plastics Division Board of Directors, Society of Plastics Engineers

Committee and Review Activities

- UL Forum on Initiatives to Improve the Long Term Aging Program, LTTA Tools Working Groups, Underwriters Laboratories
- Research and Engineering Technology Award Committee, Society of Plastics Engineers
- Reviewer, Medical Plastics Technical Program Committee, Society of Plastics Engineers
- Reviewer, Failure Analysis and Prevention Technical Program Committee, Society of Plastics Engineers
- Reviewer, various book proposals and submissions related to polymer science, ASM International, Elsevier, John Wiley

Professional Affiliations

- American Association for the Advancement of Science (member)
- American Association of Textile Chemists and Colorists—AATCC (senior member)
- American Chemical Society (member)
- ASTM International (member)
- Society for the Advancement of Material and Process Engineering (member)
- Society of Plastics Engineers (senior member)

EXHIBIT 4

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Patentee:	Yang et al.	Examiner:	Diamond, Alan D.
Patent No.:	U.S. 7,897,080	Group Art Unit:	3991
Reexamination Control No.:	95/002,170	Confirmation No.	6418
Filed:	September 10, 2012	H&B Docket:	1199-26 RCE/CON/REX
Dated:	March 13, 2013	M&E Docket:	117744-00023

Mail Stop Inter Partes Reexam
Central Reexamination Unit
Commissioner for Patents
U.S. Patent and Trademark Office
P.O. Box 1450
Alexandria, VA 22313-1450

Certificate of EFS-Web Transmission
I hereby certify that this correspondence is being transmitted via the U.S. Patent and Trademark Office electronic filing system (EFS-Web) to the USPTO on
March 13, 2013.
Signed: Michael I. Chakansky /Michael I Chakansky/

DECLARATION OF B. ARLIE BOGUE, PH.D. UNDER 37 C.F.R. § 1.132

Madame:

I, B. Arlie Bogue, Ph.D., do hereby make the following declaration:

I. Technical Background

1. I have worked in the field of pharmaceutical development, and particularly oral dosage form development, for 22 years. I am employed by MonoSol Rx, LLC. ("Patentee" and/or "MonoSol"), the assignee of issued patent U.S. 7,897,080 ("the '080 Patent"), as Senior Director for Manufacturing Strategy and Innovation.

2. I have a BS in Physical Chemistry from Colorado State University and a Ph.D. in Chemical and BioEngineering from Arizona State University. I have participated in postdoctoral studies in Biochemical Engineering at the University of Virginia. During my career, I have been named as an inventor on over 23 U.S. patents and numerous foreign patents directed to the formulation,

processing and/or packaging of pharmaceutical oral disintegrating unit doses (tablets and film strips). I have direct experience with the commercial scale processing of pharmaceutical film systems as well as an understanding of the uniformity of content of active and methods for testing the same.

3. I have read the '080 Patent and the Office Action issued on November 29, 2012 in the reexamination of the '080 Patent ("Office Action") and the references cited therein, and I have also reviewed the amendment as to the independent claims set forth in Patentee's Reply to the Office Action concurrently filed herewith.

II. Producing resulting films in accordance with the '080 Patent

4. Each of the 73 lots of resulting films (Lots 1-73) containing approximately 2,000,000 individual dosage units per lot discussed herein were manufactured: (i) for commercial use and regulatory approval; (ii) in compliance with U.S Food and Drug Administration ("FDA") standards and regulations, including those relating to analytical chemical testing for variation in active in individual dosage units; and (iii) in accordance with the invention disclosed in the '080 Patent, and as claimed by the '080 Patent both as issued and as amended in the Patentee's Reply to the Office Action; by:

(a) forming a flowable polymer matrix comprising a water-soluble polymer, a solvent and a pharmaceutical active, said matrix having a substantially uniform distribution of said active;

(b) casting said flowable polymer matrix, said flowable polymer matrix having a viscosity from about 400 to about 100,000 cps;

(c) controlling drying through a process comprising conveying said polymer matrix through a drying apparatus and evaporating at least a portion of said solvent to form a visco-elastic film, having said active substantially uniformly distributed throughout, within about the first 4 minutes by rapidly increasing the viscosity of said polymer matrix upon initiation of drying to maintain said substantially uniform distribution of said active by locking-in or substantially preventing migration of said active within said visco-elastic film wherein the polymer matrix temperature is 100 °C or less;

(d) forming the resulting pharmaceutical film from said visco-elastic film, wherein said resulting pharmaceutical film has a water content of 10% or less and said substantially uniform distribution of active by said locking-in or substantially preventing migration of said active is maintained, such that uniformity of content in the amount of the active in substantially equal sized individual dosage units, sampled from different locations of said resulting pharmaceutical film, varies by no more than 10%; and

(e) performing analytical chemical tests for uniformity of content of said active in substantially equal sized individual dosage units of said sampled resulting pharmaceutical film, said tests indicating that uniformity of content in the amount of the active varies by no more than 10%, [see Appendix A] said resulting pharmaceutical film suitable for commercial and regulatory approval, wherein said regulatory approval is provided by the U.S. Food and Drug Administration.

5. Additionally, the uniformity of content in the amount of active as sampled from the 73 lots of resulting film varies no more than 10% from the desired amount of the active as indicated by said analytical chemical tests from 4(e) above. [See Appendix B]

III. Analytical Chemical Testing for Uniformity of Content of Patentee's Resulting Films

6. To demonstrate the uniformity of individual dosage unit films, I compiled individual dosage unit assay data for individual Lots 1- 73, all of which were disclosed in MonoSol's 2012 Annual Product Review to the FDA.

7. Ten (10) individual dosage units all having the same dimensions were cut out from different locations of each of the 73 lots of resulting films using a commercial packaging machine, thus providing 730 randomly sampled individual dosage units, ten each from the 73 separate lots. All samples were analyzed by a validated method, in compliance with FDA guidelines and regulations regarding same, using analytical chemical testing, in which the pharmaceutical active

was extracted and analyzed by High Performance Liquid Chromatography (HPLC) against an external standard to quantify the amount of active present in each individual dosage unit.

8. According to the inventive process set forth and claimed in the '080 Patent, and in accordance with FDA nomenclature, I have prepared tables shown as Appendices A, B and C, reflecting the uniformity of content of active of individual dosage units within particular lots and across different lots.

9. First, the uniformity of content of active in a lot is determined through establishing the amount of active ($A_{N(i)}$) actually present in each sampled individual dosage unit from the same lot (N) as determined by taking the difference between the amount of active in the sample with the most active ($Max_{LOT(N)}$) minus the amount of active in the sample with the least amount of active ($Min_{LOT(N)}$) and dividing the difference by the average amount of active in the lot samples ($Lot_{(N)}$ Sample Average). That is: $(Max_{LOT(N} - Min_{LOT(N)}) / ((A_{N(1)} + A_{N(2)} + + + A_{N(10)})/10)$. The results are shown in Appendix A.

10. Second, the uniformity of content across different lots is determined through establishing the amount of active actually present in each sampled individual dosage unit from all 73 lots and comparing that amount of active with a "target" or "desired" amount of active contained therein. The target amount of active, when it is a pharmaceutical, is referred to as the "Label Claim", thus identifying the amount of pharmaceutical active in the film to a user. The desired amount is 100% of the target amount. Each individual dosage unit film cut from any individual lot must have the desired content of pharmaceutical active, varying no more that 10% from the target or desired amount. See Appendix B.

IV. '080 Patent Process Produces Films With Required Uniformity of Content of Active

11. The results shown in the appendices establish that the resulting films produced by the inventive method of the '080 Patent as disclosed and claimed have the required uniformity of content based on analytical chemical testing. First, the amount of active varies by no more than 10% between individual dosage units sampled from a particular lot of resulting film. See Appendix A.

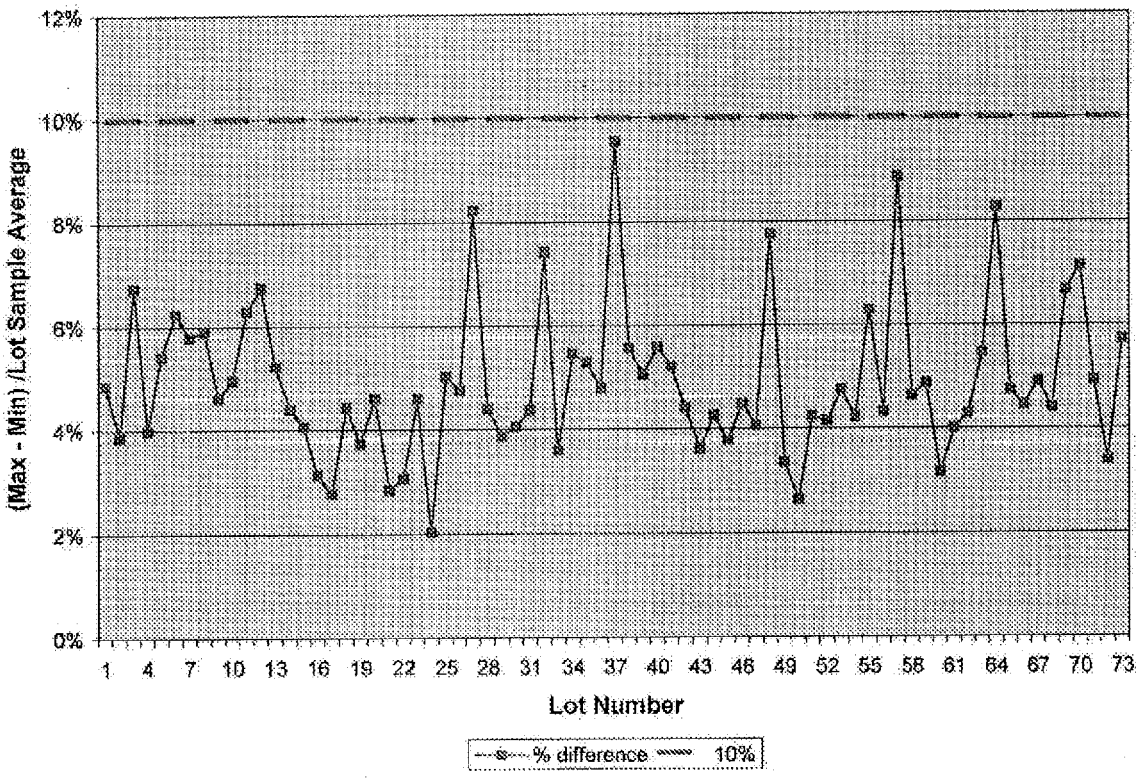
Second, the amount of active across different lots of resulting film varies no more than 10% from the desired amount of the active. See Appendix B. Finally, the uniformity of content of the 73 lots of resulting film meets even more stringent standards, for example, the data shows: (i) 46 lots of resulting film wherein the uniformity of content of active is shown with the amount of active varying by less than 5%; (ii) 15 lots of resulting film wherein the uniformity of content of active is shown with the amount of active varying by less than 4%; 4 lots of resulting film wherein the uniformity of content of active is shown with the amount of active varying by less than 3%; and 1 lot of resulting film wherein the uniformity of content of active is shown with the amount of active varying by only 2%. See Appendix C.

I hereby declare that all statements made herein of my own knowledge are true and that all statements made on information and belief are believed to be true; and further that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United States Code, and. that such statements may jeopardize the validity of the application or any patents issued thereon.

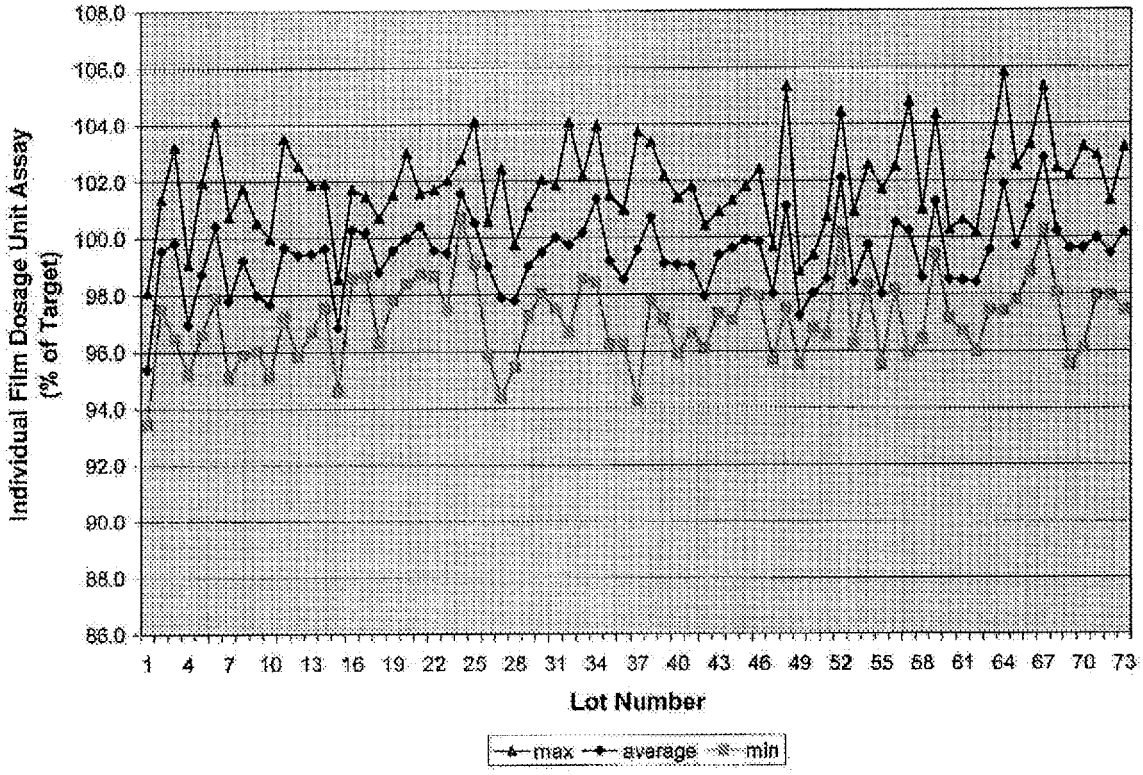
Dated this 13th day of March, 2013

B. Arlie Bogue

APPENDIX A



APPENDIX B



APPENDIX C

Lots less than 5%			lots 5% to 10%	
Lot #	% Difference		Lot #	% Difference
24	2.0%		10	5.0%
45	2.6%		25	5.0%
17	2.8%		39	5.0%
21	2.8%		41	5.2%
22	3.1%		13	5.2%
16	3.1%		35	5.3%
60	3.2%		5	5.4%
50	3.4%		63	5.5%
72	3.4%		34	5.5%
33	3.6%		38	5.6%
43	3.6%		40	5.6%
19	3.7%		73	5.7%
46	3.8%		7	5.8%
29	3.9%		8	5.9%
2	3.9%		6	6.2%
4	4.0%		11	6.3%
61	4.0%		55	6.3%
30	4.0%		69	6.7%
48	4.1%		3	6.7%
15	4.1%		12	6.7%
52	4.2%		70	7.1%
54	4.2%		32	7.4%
51	4.2%		49	7.8%
44	4.3%		27	8.2%
62	4.3%		64	8.3%
56	4.3%		57	8.9%
31	4.4%		37	9.5%
28	4.4%			
14	4.4%			
68	4.4%			
42	4.4%			
18	4.4%			
66	4.5%			
47	4.5%			
23	4.6%			
20	4.6%			
9	4.6%			
58	4.6%			
65	4.7%			
26	4.8%			
53	4.8%			
36	4.8%			
1	4.9%			
59	4.9%			
67	4.9%			
71	4.9%			
total	46		total	27

CERTIFICATE OF FIRST CLASS SERVICE

It is certified that a copy of this **DECLARATION OF B. ARLIE BOGUE, PH.D. UNDER 37 C.F.R. § 1.132** has been served, by first class mail, on March 13, 2013, in its entirety on the third party requester as provided in 37 CFR § 1.903 and 37 CFR § 1.248 at the addess below.

DANIELLE L. HERRITT
McCARTER & ENGLISH LLP
265 FRANKLIN STREET
BOSTON, MASSACHUSETTS 02110

/Daniel A. Scola, Jr./
Daniel A. Scola, Jr.
Registration No.: 29,855
Attorney for the Patentee

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Patentee:	Yang et al.	Examiner:	Diamond, Alan D.
Patent No.:	U.S. 7,897,080	Group Art Unit:	3991
Reexamination Control No.:	95/002,170	Confirmation No.	6418
Filed:	September 10, 2012	H&B Docket:	1199-26 RCE/CON/REX
Dated:	March 13, 2013	M&E Docket:	117744-00023

Mail Stop Inter Partes Reexam
Central Reexamination Unit
Commissioner for Patents
U.S. Patent and Trademark Office
P.O. Box 1450
Alexandria, VA 22313-1450

Certificate of EFS-Web Transmission
I hereby certify that this correspondence is being transmitted via the U.S. Patent and Trademark Office electronic filing system (EFS-Web) to the USPTO on
March 13, 2013.
Signed: Michael I. Chakansky /Michael I Chakansky/

DECLARATION OF DAVID T. LIN, PH.D. UNDER 37 C.F.R. § 1.132

Madame:

I, David T. Lin, Ph.D. do hereby make the following declaration:

I. SUMMARY OF CREDENTIALS AND EXPERIENCE

1. Since January 2005, I have served as a Senior Consultant to Biologics Consulting Group, Inc. ("BCG"), a team of consultants who provide national and international regulatory and product development advice on the development and commercial production of small molecular weight synthetic drug, biotechnological and biological products.

2. While BCG is being paid for my time, I am not an employee of, nor do I have any financial interest in, MonoSol Rx, LLC ("Patentee" and/or "MonoSol").

3. Before joining BCG, I held various positions with the United States Food and Drug Administration ("FDA"). From 1997-2001, I was a Chemistry Reviewer in the Division of Reproductive and Urologic Drug Products, Center for Drug Evaluation and Research ("CDER"). In 2001, I became the Team Leader in the same Division and served in that role until 2003 when I was promoted to the position of acting Deputy Division Director in the Division of New Drug Chemistry III, Office of New Drug Chemistry (currently referred to as Office of New Drug Quality Assessment). In 2004, I was promoted to the position of acting Division Director.

4. As a Chemistry Reviewer at CDER, I was responsible for the comprehensive review of Chemistry, Manufacturing and Controls ("CMC") data for drugs being investigated during Phase 1, 2, and 3 clinical studies. I was also responsible for the review of CMC data in New Drug Applications and provided regulatory input to CMC reviewers responsible for review of Abbreviated New Drug Applications. This included providing scientific and regulatory guidance during development of small molecular weight drugs and biotechnological/biological drugs across a wide variety of dosage forms. I have reviewed CMC data submitted with respect to over 100 Investigational New Drug Applications and New Drug Applications (original and supplemental) as a chemistry reviewer, contributed to decisions regarding the approval of drugs, made presentations before scientific and regulatory conferences and participated in a variety of special FDA projects and committees, including serving as the co-Chair of the CMC Good Review Practices Committee.

5. As Team Leader, acting Deputy Division Director and acting Division Director in the Office of New Drug Chemistry, I was actively involved in directing the content of FDA guidances that pertained to CMC topics. As acting Deputy Division Director and Division Director, I was directly involved in discussions, regarding the content of the 2003 FDA draft guidance on Drug Product-Chemistry, Manufacturing, and Controls Information, with the committee responsible for writing this guidance. I had signatory authority for this draft guidance prior to public issuance by FDA. As acting Deputy Division Director and Division Director, I was involved in regular meetings with the supervisory staff in the Office of Generic Drugs to discuss regulatory and review policy issues that are common to both New Drug Applications and Abbreviated New Drug Applications.

6. I consider myself an expert in the fields of FDA practice and procedure as applicable to the testing requirements for drugs and review of Investigational New Drug Applications (INDs) and New Drug Applications (NDAs).

7. I received my B.A. in Biochemistry from the University of Pennsylvania in 1984, my Ph.D. in Organic Chemistry from the University of Maryland in 1989 and my M.B.A. from the University of Maryland's RH Smith School of Business in 2002. Attached hereto as Exhibit A is my curriculum vitae, including a list of my publications for the past ten years.

8. I have carefully reviewed Chen (WO 00/42992) ("Chen").

II. U.S. STATUTORY AND REGULATORY BACKGROUND FOR TESTING DRUGS FOR POTENCY AND DOSAGE UNITS FOR UNIFORMITY

9. From a US regulatory perspective, for a drug to be approved for commercial marketing and distribution, specifications necessary to ensure the identity, strength, quality, purity, potency, and bioavailability of the drug product must be provided in a New Drug Application.[1] In addition, reference to the current U.S. Pharmacopeia (USP) may satisfy these requirements.

10. Section 501(b) of the Food, Drug, and Cosmetic Act (the Act) deems an official drug (i.e., a drug represented as a drug which is recognized in the U.S. Pharmacopeia) to be adulterated if it fails to conform to compendial standards of quality, strength or purity. Compendial tests or assay methods are used when determining such conformance under 501(b); the standards are stated in individual monographs as well as portions of the General Notices section of the USP/NF. Standards and test methods have been established for such characteristics as potency and content uniformity.

11. Section 501(c) of the Act deems a drug that is not recognized in the USP to be adulterated if it fails to meet the strength, purity or quality which it is represented to possess.

[1] 21 CFR 314.50(d)(1)(ii)(a)

The applicable quality standards for a drug not recognized in the USP can be determined from such sources as the labeling of the drug (or drug product), the manufacturer's written specifications, and new drug applications.

12. The current good manufacturing practice (cGMP) regulations include the minimum requirements for the preparation of drug product for administration to humans. One of the requirements is that the strength[2] of the drug (active ingredient) in the drug product must be determined for each batch of drug product manufactured for commercial distribution.[3] Strength is taken to mean content or assay of the drug.

13. Batch uniformity of the drug products is ensured with procedures that describe the in-process controls, and tests, or examinations to be conducted on appropriate samples of in-process materials of each batch.[4] FDA also describes in guidance that it is expected the sampling plan for drug product is representative of the batch.[5]

14. Controls include the establishment of scientifically sound and appropriate specifications, standards, sampling plans, and test procedures designed to assure that the drug product conform to appropriate standards of identity, strength, quality, and purity.[6]

15. Regulatory specifications must be established to ensure that the dosage form will meet acceptable therapeutic and physicochemical standards throughout the shelf-life of the marketed product.[5] These specifications include tests for strength (content or assay) and uniformity of dosage units.

---

[2] 21 CFR 210.3(b)(16)

[3] 21 CFR 211.165(a)

[4] 21 CFR 211.110(a)

[5] FDA Guideline for Submitting Documentation for the Manufacture and Controls for Drug Products, February 1987

[6] 21 CFR 211.160(b)

16. Testing to establish uniformity of dosage units is defined in the USP under the USP general chapter <905>.[7]

III. CHEN'S DISCLOSURE IS INSUFFICIENT

17. I have been asked to review Chen and render an opinion as to whether there is sufficient information contained within to allow regulatory FDA approval and commercialization of a drug product that is manufactured as described. After review of the patent in light of FDA practice and procedure, it is my opinion that there is insufficient disclosure to allow FDA to determine that a drug product as described can be manufactured for commercial distribution, manufactured in a consistent manner and meet specifications that will ensure the identity, strength, quality, purity, and potency of the drug product. In particular, Chen lacks any disclosure which would necessarily lead to the manufacture of films with uniformity of content (strength) of drug active required for FDA approval.

18. As would be required for FDA approval Chen does not disclose sufficient information that films containing drug can be produced consistently with respect to uniformity of content of the drug. No information was disclosed that demonstrated uniformity of content in the amounts of drug in individual dosage units. Chen discloses no specific test methods, and hence no test results, that could allow for the determination of the actual amount of drug (active) in individual dosage units.

19. As required for FDA approval, Chen's patent did not disclose sufficient information regarding the manufacturing process and process controls. The information disclosed by Chen would not ensure that films containing drug could be manufactured to meet specifications that ensure consistent strength.

20. Even if the information disclosed in Chen could be utilized to develop a manufacturing process for films containing drug, there is no information regarding the test methods that are necessary to determine the amount of drug in individual dosage units.

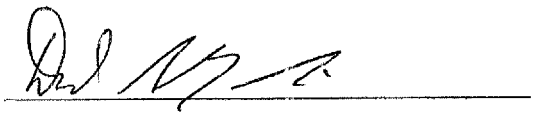
[7] USP General Chapter <905> Uniformity of Dosage Units

21. Therefore, Chen's disclosure is lacking, both explicitly and inherently, the disclosure necessary to provide for the manufacture of drug-containing films with the uniformity of content in amount of drug (active) in individual dosage units to make FDA approvable film products. It is my understanding that an inherent disclosure may not be established by probabilities or possibilities and that the mere fact that a certain thing may result from a given set of circumstances is not sufficient and that to be inherent requires that the missing disclosure is necessarily present.

22. Finally, Chen's patent discloses the release profiles of four active agents from films. See Chen, Figure 5. The release profile data presented in Figure 5 show a high degree of variability at each data point. For example, the release profile for nicotine containing film product show that the amount of nicotine released at the 5 minute and 8 minute time point can be as high as approximately 115-120%. This level of active agent is greater than the 110% level (from an expected amount of 100%) that is considered acceptable to FDA for regulatory approval of a product that purports to be manufactured consistently with acceptable content uniformity. These data indicate that the test method used in the analysis is not reproducible and/or there is a lack of active agent content uniformity between individual dosage units. These deficiencies demonstrate the lack of manufacturing consistency and lack of active agent content uniformity in the film.

23. I hereby declare that all statements made herein of my own knowledge are true and that all statements made on information and belief are believed to be true; and further that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United States Code, and. that such statements may jeopardize the validity of the application or any patents issued thereon.

Dated this 13th day of March, 2013



David T. Lin

CERTIFICATE OF FIRST CLASS SERVICE

It is certified that a copy of this **DECLARATION OF DAVID T. LIN, PH.D. UNDER 37 C.F.R. § 1.132** has been served, by first class mail, on March 13, 2013, in its entirety on the third party requester as provided in 37 CFR § 1.903 and 37 CFR § 1.248 at the addess below.

DANIELLE L. HERRITT
McCARTER & ENGLISH LLP
265 FRANKLIN STREET
BOSTON, MASSACHUSETTS 02110

/Daniel A. Scola, Jr./
Daniel A. Scola, Jr.
Registration No.: 29,855
Attorney for the Patentee

EXHIBIT A

DAVID TSOCHUNG LIN

9121 Fall River Lane, Potomac, MD 20854 (301) 299-2853 dlin@bcg-usa.com

EXPERTISE

- 18+ years pharmaceutical regulatory experience.
  - 7+ years regulatory chemistry, manufacturing and controls (CMC) experience at CDER/FDA on small molecular-weight drugs, botanical drugs, peptide drugs, and protein drugs formulated in a broad range of sterile and non-sterile dosage forms.
  - 3+ years research experience at CBER/FDA.
  - 8+ years experience as regulatory CMC consultant.
- Unique combination of biologic/biotechnological and small molecular-weight drug regulatory experience, including device/drug and device/biologics combination products.
- Understanding of FDA regulatory requirements and expectations for drug development and marketing approval.
- Performed primary CMC review and assessment of drug products for treatment of reproductive and urologic disorders and diseases.
- Supervised CMC review activities in 7 CDER medical reviewing divisions including Reproductive/Urologic, Anti-viral, Dermatologic/Dental, Anti-inflammatory/ Analgesic/Ophthalmologic, Anti-infective, Special Pathogen/Immunologic, and Over-the-Counter drug products.
- Understanding of drug substance and drug product analytical method development and validation.
- Understanding of drug substance and drug product stability protocol development and stability data analysis.
- Understanding of current Good Manufacturing Practices (cGMPs)
- Experienced in chemical synthesis, small-scale and pilot-scale fermentation, biologics/ biotechnology, and protein chemistry.
- Experienced working in cross-functional teams (i.e., Pharmacology/toxicology, Clinical, Biostatistics, Biopharmaceutics, and Analytical).
- Ph.D. in Organic Chemistry; M.B.A. degree and training for managers.

EXPERIENCE

BIOLOGICS CONSULTING GROUP, INC. Alexandria, VA
January 2005 – Present
Senior Consultant

- Evaluate and provide advice on client CMC scientific and regulatory strategies for a wide range of therapeutic drug products (biologic and non-biologic) in dosage forms that include tablets, topicals, injectables, transdermals, implants, sprays, and inhalation, at all stages of product development, from pre-IND through post-NDA/BLA approval.
- Review and provide advice on IND and NDA/BLA submissions for suitability relative to FDA expectations for CMC data.
- Perform gap analysis audits for deficiencies relative to FDA expectations.
- Conduct regulatory and scientific due diligence audits for business acquisitions and licensing partnerships. Provide assessment of strengths and deficiencies.
- Represent clients in interactions with FDA.
- Prepare and write submissions to FDA, with focus on CMC sections.
- Represent client as FDA regulatory expert in legal proceedings.
- Advise clients on manufacturing contractor and vendor evaluation and selection.
- Provide management and technical oversight of contract manufacturing organizations (CMOs).
- Involved in business development to increase client base.
- Provide scientific and regulatory training and presentations at pharmaceutical/biopharmaceutical conferences.

FOOD & DRUG ADMINISTRATION, CENTER FOR DRUG EVALUATION AND RESEARCH, OFFICE OF NEW DRUG CHEMISTRY, DIVISION OF NEW DRUG CHEMISTRY III. Rockville, MD
July 2003 – December 2004
Division Director (acting) *March 2004 – December 2004*
Deputy Division Director (acting) *July 2003 – March 2004*

- Supervised 34 employees in 9 therapeutic product classes, includes 6 Team Leaders, review chemists and administrative staff. Responsible for employee work performance review and career development.
- Planned and set long-range plans and schedules for Division work. Directed and coordinated workload, and assured implementation of Division policies, goals and objectives.
- Evaluated budget and fiscal controls to manage Division functions.
- Made critical decisions and provided expert advice concerning regulatory, scientific and compliance approaches and options consistent with Office policies and objectives.
- Represented FDA in dealing and negotiating with the regulated industry, and professional and industry organizations.
- Participated as invited speaker at regulatory and scientific conferences on behalf of FDA.
- Served as the Chair of the Stability Guidance Technical Committee, Co-chair of the Conjugated Estrogens Working Group and Co-chair of the Good Review Practices Working Group.

FOOD & DRUG ADMINISTRATION, CENTER FOR DRUG EVALUATION AND RESEARCH, DIVISION OF REPRODUCTIVE AND UROLOGIC DRUG PRODUCTS. Rockville, MD
October 2001-July 2003
Lead Chemist (Team Leader)

- Managed a team of 4 review chemists in 2 therapeutic product classes.
- Responsible for secondary review, consistency of CMC reviews and adherence to FDA/ONDC policies and guidances.
- Coordinated reviewers' workload of IND and NDA submissions to ensure that reviews were conducted in timely manner.
- Interacted extensively with the regulated industry to provide regulatory direction during IND drug development and NDA post-approval activities.
- Active in the development of FDA guidances for industry and internal good review practices. Served as the Chair of the Stability Guidance Technical Committee, Co-chair of the Conjugated Estrogens Working Group and Co-chair of the Good Review Practices Working Group.

FOOD & DRUG ADMINISTRATION, CENTER FOR DRUG EVALUATION AND RESEARCH, DIVISION OF REPRODUCTIVE AND UROLOGIC DRUG PRODUCTS. Rockville, MD
April 1997-October 2001
Chemistry Reviewer

- Evaluated the quality of new drug products submitted to the FDA for approval.
- Integral part of a cross-functional review team responsible for evaluating the quality and effectiveness of reproductive and urologic drug products being investigated in clinical studies.
- Major contributor to committees responsible for establishing drug product quality standards and publishing guidances for pharmaceutical companies.
- Provided regulatory guidance to pharmaceutical company representatives during drug development.
- Mentored new reviewers.
- Served as computer focal point to facilitate and troubleshoot computer issues.

FOOD & DRUG ADMINISTRATION, CENTER FOR BIOLOGICS EVALUATION AND RESEARCH, LABORATORY OF PARASITIC BIOLOGY AND BIOCHEMISTRY. Bethesda, MD
February 1994-April 1997
National Research Council Fellow

- Investigated the biological role of specific proteins in the sexual differentiation of the malaria parasite. Published three research papers in peer-reviewed journals.
- Presented research data at three separate scientific conferences.
- Supervised the research projects of college students.
- Responsible for the coordination of instrument repairs and the ordering of laboratory supplies.

GENERAL ELECTRIC CO., CORPORATE RESEARCH & DEVELOPMENT, BIOLOGICAL SCIENCES LABORATORY. Schenectady, NY
July 1989-January 1994
Staff Scientist

- Developed recombinant biphenyl-metabolizing microorganisms capable of degrading environmental contaminants. Marketed this technology to the GE business units and government agencies responsible for environmental clean-up.
- Investigated the factors affecting aerobic biodegradation of indigenous PCBs in Hudson River sediment by various bacterial strains.
- Isolated and conducted mechanistic studies of the dioxygenase enzymes involved in biodegradation.
- Investigated the scientific and economic feasibility of biologically synthesizing aromatic monomers for use as a feedstock to produce biodegradable polymers.
- Supervised research projects of summer interns.
- Published research in peer-reviewed journals.
- Recruited at major East Coast universities. Interviewed and screened graduating science Ph.D. students for second round interviews at the Research Center.

UNIVERSITY OF MARYLAND, Dept. of Chemistry/Biochemistry. College Park, MD
May 1985-May 1989
Research Assistant

- Investigated mechanism of action of two bacterial enzymes, mandelate racemase and D-amino acid oxidase.
- Synthesized and tested novel halogenated aromatic hydroxy- and amino- acid analogs as potential irreversible inhibitors.
- Published research in peer-reviewed journals and co-authored one chapter in a biotechnology book. In addition, the research data was presented at two national scientific conferences.
- Served as the computer expert for the laboratory group.

EDUCATION

ROBERT H. SMITH SCHOOL OF BUSINESS. College Park, MD
University of Maryland
Master of Business Administration (MBA), *2002*
Concentration: Finance

UNIVERSITY OF MARYLAND. College Park, MD
Department of Chemistry and Biochemistry
Ph. D. -- Organic Chemistry, *1989*
Research Advisor -- Dr. John W. Kozarich

UNIVERSITY OF PENNSYLVANIA. Philadelphia, PA
Bachelor of Arts with Honors – Biochemistry, *1984*
Dean's List, Phi Lambda Upsilon Chemical Honor Society

TRAINING

- Facilitation Skills, CDER/FDA (Fall 2002)
- Six Sigma Strategy and Methods, Univ. of MD (Summer 2002)
- Group Decision-Making Techniques, CDER/FDA (Feb. 2002)
- Managing Written Communications for Team Leaders, CDER/FDA (Spring 2002)
- Organizational Behavior and Human Resources, Univ. of MD (Fall 1999)
- Management of Human Resources, Univ. of MD (Fall 1999)
- Introduction to Drug Law and Regulation, CDER/FDA (Nov. 1998)
- Basic Statistical Methods, CDER/FDA (Fall 1998)

HONORS/AWARDS

- CDER's Team Excellence Award (Nov 2004)
- FDA's Group Recognition Award (May 2004)
- CDER's Special Recognition Award (Nov 2002)
- CDER's Team Excellence Award (Nov 2002)
- OPS/ONDC Special Recognition Award (Dec 2001)
- CDER's Team Excellence Award (Nov 2000)
- OPS/ONDC Special Recognition Award (Jun 2000)
- CDER's Excellence in Mentoring Award (Nov 1999)

PRESENTATIONS

- Conducting Effective & Compliant Stability Programs for Pharmaceuticals & Biologics, "Stability Studies During Development", "Stability of Biopharmaceuticals", "Development of Specifications for Biopharmaceuticals", and "Extractables, Leachables, and Particulates – Safety Concern for Biotechnology Products", Dubai, UAE (Sep 2012).
- 4th DIA China Annual Meeting, "ICH Guidelines Q1D, Bracketing and Matrixing Designs for Stability Testing of New Drug Substances and Products", and "Q1E, Evaluation of Stability Data", Shanghai, China (May 2012).
- IPA's Current Trends and Practices in Stability Testing, "Stability Testing Requirements for Biopharmaceutical Products", Montreal, Canada (Oct 2011)
- IPA's Current Trends and Practices in Stability Testing, "Stability Program for Combination Products", Montreal, Canada (Oct 2011)
- 3rd DIA China Annual Meeting, "Thinking About Comparability for Biosimilar Proteins", Beijing, China (May 2011).
- IPA's Current Trends and Practices in Stability Testing, "Stability Challenges for Combination Products", Boston, MA (May 2011).
- IPA's Current Trends and Practices in Stability Testing, "Country Specific Stability Requirements", Boston, MA (May 2011).
- Stability Programs Forum, "Stability Testing for Biotechnology/Biologic Products", Philadelphia, PA (Dec 2010).
- 11th Annual EuroTIDES/EuroPEPTIDES Conference, "Stability Considerations and Testing for Peptide-and Oligo-Based Therapeutics", Barcelona, Spain (Nov 2010).
- International Summit of China Pharmaceutical Industry, "FDA Requirements for Peptide Product Development: Considerations from Small Molecule and Biological Products", Hangzhou, China (Oct 2010).

- 7th Annual Method Validation Conference, "Ensure Method Validation Compliance through a Review of FDA Warning Letters", San Francisco, CA (Jul 2010).
- 6th Annual BioProcess International European Conference, "Extractables, Leachables and Particulates – Safety Concern for Biotechnology Products," Vienna, Austria (May 2010)
- ISPE-CSAC Meeting, "Biotechnological Drug Development and Interactions with CDER," Raleigh, NC (Oct 2009).
- Seminar on China International Bio-medicine Outsourcing Service, "Product Quality Issues with GLPs and GCPs," Hangzhou, China (Sep 2009).
- Informa Stability Testing for Biologics Conference, "Understanding Product Expiry and Shelf-Life," Prague, Czech Republic (Sep 2009).
- Informa Stability Testing for Biologics Conference Workshop, "Stability Testing Performed Over a Product Lifecycle," Prague, Czech Republic (Sep 2009).
- IVT Lab Compliance Conference, "Implement a Comprehensive and Compliant Stability Program," Philadelphia, PA (Aug 2009).
- OKBio ACCELERATE Workshop, "Product Development – Regulatory CMC Considerations," Oklahoma City, OK (Jun 2009).
- IVT Method Validation Conference, "Challenges in Understanding Impurities and Degradants for Biological/Biotechnological Products," San Francisco, CA (Oct 2008).
- IVT Method Validation Conference, "Strategies for Setting Biological Product Specifications," San Francisco, CA (Oct 2008).
- CBI 3rd Annual Stability Programs Conference, "Complex Stability Programs for Biologics," Philadelphia, PA (Jun 2008).
- IVT Lab Compliance Conference, "Stability Testing Fundamentals and Considerations in the Current Regulatory Environment," Baltimore, MD (Apr 2008).
- R&D Direction's 5th Annual Drug Development Summit, "Looking Forward in 2008: Regulatory Priorities and Considerations," Amelia Island, FL (Feb 2008).
- 2007 AAPS Annual Meeting, "Critical Stability Evaluation of Biopharmaceuticals During Clinical Development Stages," San Diego, CA (Nov 2007).
- 2007 DIA Annual Meeting, "The Impact of FDA's Quality by Design Initiative on Biologics Development," Atlanta, GA (Jun 2007).
- Institute for International Research: Formulation and Forced Degradation Strategies for Biomolecules, "Regulatory Requirements for Successful Product Development," San Diego, CA (Mar 2007).
- International Pharmaceutical Academy: Effective Management of Stability Programs, "Stability Design Considerations for Global Regulatory Filings," Toronto, Canada (Feb 2007).
- Cambridge Healthtech Institute's PepTalk: Optimizing Protein and Antibody Therapeutics, "Regulatory Considerations for the Development of Protein Therapeutic Products," San Diego, CA (Jan 2007).
- 2006 AAPS Annual Meeting, "The Impact of FDA Initiatives on the Development of Biological Products," San Antonio, TX (Nov 2006).
- SWE Enterprises: Stability Testing for the FDA Regulated Industry, "In-Use Testing of Biotechnological and Biologic Products," Boston, MA (Oct 2006).
- SWE Enterprises: Stability Testing for the FDA Regulated Industry, "Cost Efficient Design of Stability Studies," Boston, MA (Oct 2006).
- Institute for International Research: Chemistry Manufacturing & Controls, "Clarifying and Understanding ICH Guidance to Help Meet International Requirements for Submissions," Philadelphia, PA (July 2006).
- IVT Stability Testing: Implementing Effective Processes for Stability Program Development, "Cost Efficient Design of Stability Studies," San Diego, CA (June 2006).
- IVT Stability Testing: Implementing Effective Processes for Stability Program Development, "Stability Requirements for Global Regulatory Filings," San Diego, CA (June 2006).

- CBI Stability Programs: New Approaches to Test, Analyze and Document Data for Improved Program Design and Global Compliance, "In Use Testing of Biotechnological and Biological Products," Princeton, NJ (June 2006).
- IBC/TIDES: Oligonucleotide and Peptide Technology and Product Development, "Stability Considerations and Testing for Oligo- and Peptide-Based Therapeutics," Carlsbad, CA (May 2006).
- IBC Biopharm Manufacturing and Distribution Summit: Logistics for Biopharmaceutics, "Stability Studies to Support the Chain of Custody of Biotechnology Products," Reston, VA (Dec 2005).
- 2005 AAPS Annual Meeting: AAPS Short Course on Degradation and Stability in Small Molecule Active Pharmaceutical Ingredients/Stability Testing for Global Filings, "Stability Requirements for Global Regulatory Filings," Nashville, TN (Nov 2005).
- Therapeutic Strategies Against Neurodegenerative Conditions, "The Regulatory Product Development Process," Burlington, MA (Oct 2005).
- International Pharmaceutical Federation (FIP) Workshop: Harmonizing Clinical Trial GMP and Quality Requirements Across the EU and Beyond, "The US Investigational New Drug (IND) System," Noordwijk Zee, The Netherlands (Mar 2005).
- 2004 AAPS Annual Meeting, "Phase 2 and 3 IND CMC Guidance: FDA Perspective," Baltimore, MD (Nov 2004).
- 64th Annual World FIP Congress, "Clinical Trial Application Process – CMC: US FDA Perspective," New Orleans, LA (Sep 2004).
- AAPS Pharmaceutical Technologies 3rd Summer Conference: Optimizing the Global Clinical Trial Process, "IND Applications – FDA Perspective," Cherry Hill, NJ (Aug 2004).
- 2004 DIA Annual Meeting, "FDA Stability Guidance Update," Washington, DC (Jun 2004).
- DIA Meeting on CM&C/Regulatory and Technical Strategies, "Challenges and Opportunities in CMC Requirements for Phase 2-3," Bethesda, MD (Mar 2004).
- 2003 PDA Annual Meeting, "Draft FDA Stability Guidance," Atlanta, GA (Nov 2003).
- 2003 DIA Annual Meeting, "Product Quality of Non-clinical and Clinical Trial Materials," San Antonio, TX (Jun 2003).
- PARCS Meeting, "Managing CMC Requirements during IND," Irvine, CA (Apr 2003).
- PARCS Meeting, "Use of SUPAC Guidances during IND Development," Irvine, CA (Apr 2003).
- DIA Meeting on Global Chemistry, Manufacturing and Controls: Pre IND/CTX and IND/CTX Development Challenges, "FDA Perspective on Stability Testing during IND Development," Philadelphia, PA (Feb 2003).

PUBLICATIONS

- C. Syin, D. Parzy, F. Traincard, I. Boccaccio, M.G. Joshi, D.T. Lin, X.-M. Yang, K. Assemat, C. Doerig, and G. Langeley, "The H89 cAMP-dependent protein kinase inhibitor blocks *Plasmodium falciparum* development in infected erythrocytes," *Eur. J. Biochem. 268*, 4842 (2001).
- J.P. McDaniel, C. Syin, D.T. Lin, M.B. Joshi, S. Li, and N.D. Goldman, "Expression and characterization of a *Plasmodium falciparum* protein containing domains homologous to sarcalumenin and a tyrosine kinase substrate, eps15," *Int. J. Parasitol. 29*, 723 (1999).
- D.T. Lin, N.D. Goldman, and C. Syin, "Stage specific expression of a *Plasmodium falciparum* protein related to the eukaryotic mitogen-activated protein kinase," *Mol. Biochem. Parasitol. 78*, 67 (1995).
- M.R. Harkness, J.B. McDermott, D.A. Abramowicz, J.J. Salvo, W.P. Flanagan, M.L. Stephens, F.J. Mondello, R.J. May, J.H. Lobos, K.M. Carroll, M.J.Brennan, A.A. Bracco, K.M. Fish, G.L. Warner, P.R. Wilson, D.K. Dietrich, D.T. Lin, C.B. Morgan, and W.L. Gately, "*In situ* stimulation of aerobic PCB biodegradation in Hudson River sediments," *Science 259*, 503 (1993).
- D.T. Lin, V.M. Powers, L.J. Reynolds, C.P. Whitman, G.L. Kenyon and J.W. Kozarich, "Evidence for the generation of α-carboxy-α-hydroxy-*p*-xylylene from *p*-(bromomethyl)mandelate by mandelate racemase," *J. Am. Chem. Soc. 110*, 323 (1988).

- M.S. Lakshmikumaran, E. D'Ambrosio, L.A. Laimins, D.T. Lin and A.V. Furano, "Long interspersed repeat DNA(LINE) causes polymorphism at the rat insulin 1 locus," *Mol. Cell. Biol. 5*, 2197 (1985).

BOOK CHAPTER

- N.R. Schmuff and D.T. Lin, "Contents of Module 3 for an Electronic Common Technical Document Investigational New Drug Application," in Preparation and Maintenance of the IND Application in eCTD Format, W.K. Sietsema (ed.), FDAnews, Falls Church, VA, 117-134 (2008).
- N.R. Schmuff and D.T. Lin, "Chemistry, Manufacturing and Controls (CMC)," in Wiley Encyclopedia of Clinical Trials, (2008).
- J.A. Gerlt, G.L. Kenyon, J.W. Kozarich, D.T. Lin, D.C. Neidhart, G.A. Petsko, V.M. Powers, S.C. Ransom and A.Y. Tsou, "Structure-function relationships in mandelate racemase and muconate lactonizing enzyme," in Chemical Aspects of Enzyme Biotechnology, T.O. Baldwin, F.M. Raushel and A.I. Scott (eds.), Plenum, New York, NY, 9-21 (1990).

PROCEEDINGS OF MEETINGS

- D.T. Lin, N.D. Goldman, and C. Syin, "*Plasmodium falciparum* mitogen-activated protein kinase homologue contains an unusually large carboxyl terminal domain which is highly charged and homologous to merozoite surface antigens," Molecular Parasitology Meeting, Woods Hole, MA (1995).
- C. Syin, D. Lin, B. Krzyzanowska, and N.D. Goldman, "*Plasmodium* cGMP-dependent protein kinase," FDA Science Forum on Regulatory Sciences, Washington, D.C. (1994).
- J. H. Lobos, M. J. Brennan, J. T. Jackman and D. T. Lin, "*In situ* stimulation of PCB biodegradation in Hudson River sediment: III. enumeration and characterization of aerobic bacteria," ASM Meeting, New Orleans (1992).
- G.L. Kenyon, D.T. Lin, V.M. Powers, L.J. Reynolds, C.P. Whitman and J.W. Kozarich, "Generation of α-carboxy-α-hydroxy-*p*-xylylene from *p*-bromomethyl-mandelate by mandelate racemase– further evidence for a carbanion mechanism," *FASEB J.* 2, 1329 (1988).
- D.T. Lin, V.M. Powers, L.J. Reynolds, C.P. Whitman, G.L. Kenyon and J.W. Kozarich, "Formation of *p*-xylylene species in the mandelate racemase catalyzed reaction of *p*-(bromomethyl)mandelate," *Fed. Proc. 46*, 2042 (1987)

Electronic Acknowledgement Receipt

EFS ID:	18425655
Application Number:	95002170
International Application Number:	
Confirmation Number:	6418
Title of Invention:	POLYETHYLENE-OXIDE BASED FILMS AND DRUG DELIVERY SYSTEMS MADE THEREFROM
First Named Inventor/Applicant Name:	7897080
Customer Number:	23869
Filer:	Danielle L. Herritt/Maureen Tierney
Filer Authorized By:	Danielle L. Herritt
Attorney Docket Number:	117744-00023
Receipt Date:	10-MAR-2014
Filing Date:	10-SEP-2012
Time Stamp:	19:31:13
Application Type:	inter partes reexam

Payment information:

Submitted with Payment	no

File Listing:

Document Number	Document Description	File Name	File Size(Bytes)/ Message Digest	Multi Part /.zip	Pages (if appl.)
1	Reexam - Affidavit/Decl/Exhibit Filed by 3rd Party	Exhibit_1_US7897080.pdf	11515802 553039d87d2a837a52d99a7fa4116e1f506f040c	no	73

Warnings:	
Information:	

2	Reexam - Affidavit/Decl/Exhibit Filed by 3rd Party	Exhibit_3_Clevenger_Decl.pdf	515093 ee77a994060c8bec1a3614b7786897b4f759a2ac	no	7
Warnings:					
Information:					
3	Appeal Brief - Third Party Requester	117744_00023_Appeal_Brief_FINAL_2014MAR10.pdf	2634267 e4c2ae2fb9c3f9b3d8cb438e0fc5df9e269f1cef	no	91
Warnings:					
Information:					
4	Reexam - Affidavit/Decl/Exhibit Filed by 3rd Party	Exhibit_2_Reitman_Decl--.pdf	712304 9fa5e8f0d31e6e606d68abf4e411f152545ea96a	no	11
Warnings:					
Information:					
5	Reexam - Affidavit/Decl/Exhibit Filed by 3rd Party	Exhibit_4_Bogue_Lin_Decls--.pdf	2317521 54427f6e1c4b137dd028b061e1ca94efc5d0ccc3	no	25
Warnings:					
Information:					
		Total Files Size (in bytes):	17694987		

This Acknowledgement Receipt evidences receipt on the noted date by the USPTO of the indicated documents, characterized by the applicant, and including page counts, where applicable. It serves as evidence of receipt similar to a Post Card, as described in MPEP 503.

New Applications Under 35 U.S.C. 111

If a new application is being filed and the application includes the necessary components for a filing date (see 37 CFR 1.53(b)-(d) and MPEP 506), a Filing Receipt (37 CFR 1.54) will be issued in due course and the date shown on this Acknowledgement Receipt will establish the filing date of the application.

National Stage of an International Application under 35 U.S.C. 371

If a timely submission to enter the national stage of an international application is compliant with the conditions of 35 U.S.C. 371 and other applicable requirements a Form PCT/DO/EO/903 indicating acceptance of the application as a national stage submission under 35 U.S.C. 371 will be issued in addition to the Filing Receipt, in due course.

New International Application Filed with the USPTO as a Receiving Office

If a new international application is being filed and the international application includes the necessary components for an international filing date (see PCT Article 11 and MPEP 1810), a Notification of the International Application Number and of the International Filing Date (Form PCT/RO/105) will be issued in due course, subject to prescriptions concerning national security, and the date shown on this Acknowledgement Receipt will establish the international filing date of the application.

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Inter Partes Reexamination of Yang et al.	Examiner: Alan D. Diamond
U.S. Patent No. 7,897,080	Group Art Unit: 3991
Reexamination Control No. 95/002,170	Confirmation No. 6418
Filed: September 10, 2012	H&B Docket: 1199-26 RCE/CON/REX M&E Docket: 117744-00023

For: POLYETHYLENE-OXIDE BASED FILMS AND
DRUG DELIVERY SYSTEMS MADE THEREFROM

APPELLANT'S APPEAL BRIEF

Mail Stop *Inter Partes* Reexam
Central Reexamination Unit
Commissioner for Patents
U.S. Patent and Trademark Office
P.O. Box 1450
Alexandria, VA 22313-1450

Certificate of EFS-Web Transmission
I hereby certify that this correspondence is being transmitted via the U.S. Patent and Trademark Office electronic filing system (EFS-Web) to the USPTO on March 10, 2014.

Signed: Michael I. Chakansky /Michael I Chakansky/Reg. No. 31,600

I hereby certify that, pursuant to 37 CFR § 1.943(c), based on the WordPerfect word count of 13,976 words, Appellant's brief, counting the words on those pages beginning at page 1 (entitled Appellant's Appeal Brief) and continuing through and including all words of the signature page (entitled Conclusion), does not exceed 14,000 words in length.

Signed: Michael I. Chakansky /Michael I Chakansky/Reg. No. 31,600

Dear Madame:

On December 26, 2013, patent owner MonoSol Rx, LLC ("Appellant") filed its Notice of Appeal to the Patent Trial and Appeal Board (PTAB), appealing all of the Examiner's rejections of all claims delineated as rejected in the Right of Appeal Notice mailed December 6, 2013 ("RAN"), in the above-identified *inter partes* reexamination. On January 9, 2014, Third Party Requester BioDelivery Sciences International, Inc. ("Third Party Requester") filed a Notice of

Cross Appeal regarding certain claims rejections not adopted by the Examiner in the RAN. As March 9, 2014 is a Sunday, this Appeal Brief, filed Monday March 10, 2014 is timely.

Appellant submits this Appeal Brief in support of it appeal, and authorizes the Commissioner to charge all fees associated therewith, including, without limitation, the $2,000.00 fee for filing this brief in support of an appeal in an *inter partes* reexamination proceeding, pursuant to 37 C.F.R. § 41.20(b)(2)(i), to Deposit Account No. 08-2461.

TABLE OF CONTENTS