L117	49	L114 and (estradiol NEAR flux)	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	OFF	2016/08/22 09:57
L118	87	L112 and (estradiol NEAR flux)	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	OFF	2016/08/22 09:57
L119	247	MANTELLE.in. and JUAN.in.	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	OFF	2016/08/22 09:57
L120	38	L119 and estradiol	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	OFF	2016/08/22 09:57
L121	141	L119 and transdermal	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	OFF	2016/08/22 09:57
L122	182	Kanios.in. and David.in.	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	OFF	2016/08/22 09:57
L123	39	L122 NOT L119	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	OFF	2016/08/22 09:57
L124	0	(11/245097).APP.	USPAT; USOCR	OR	OFF	2016/08/22 09:57
L125	687	L112 and ("dipropylene glycol" oleyl)	USPAT; USOCR	OR	OFF	2016/08/22 09:57
L126	127	L114 and ("dipropylene glycol" oleyl)	USPAT; USOCR	OR	OFF	2016/08/22 09:57
L129	57	(("MANTELLE") near3 ("Juan")).INV.	US-PGPUB; USPAT; USOCR	OR	OFF	2016/08/22 10:03
L130	2	12/216811	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	OFF	2016/08/22 10:09
L131	1	(12/216811).APP.	USPAT; USOCR	OR	OFF	2016/08/22 10:09
L133	15907	A61K31/565.cpc.	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	AND	OFF	2016/08/22 10:15
L134	4711	A61K9/70.cpc.	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	AND	OFF	2016/08/22 10:15
L135	33	L133 L134	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	AND	OFF	2016/08/22 10:15
L136	8	L135 and estradiol	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	AND	OFF	2016/08/22 10:16

8/22/2016 10:22:21 AM

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PTO/SB/08 (modified)

	Substitute for form 1449/PTO			Co	omplete if Known
INFORMATION DISCLOSURE			LOSURE	Application Number	13/553972
	STATEMENT BY	Y APP	PLICANT	Filing Date	7/20/2012
Date Submitted: August 2, 2016				First Named Inventor	Juan Mantelle
	Date Gabilitted. 7	rugus	51 2, 2010	Art Unit	1611
	(use as many shee	ts as	necessary)	Examiner Name	Melissa L. Javier
Sheet	1	of	1	Attorney Docket Number	041457-0992

	U.S. PATENT DOCUMENTS						
Examiner	Cite	Document Number	Publication Date	Name of Patentee or Applicant of	Pages, Columns, Lines, Where Relevant		
Initials*	No. ¹	Number-Kind Code ² (if MM-DD-YYYY known)	Cited Document	Passages or Relevant Figures Appear			

	UNPUBLISHED U.S. PATENT APPLICATION DOCUMENTS						
Examiner Initials*	Cite No. ¹	U.S. Patent Application Document Serial Number-Kind Code ² (if known)	Filing Date of Cited Document MM-DD-YYYY	Name of Patentee or Applicant of Cited Document	Pages, Columns, Lines, Where Relevant Passages or Relevant Figures Appear		
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	FOREIGN PATENT DOCUMENTS					
Examiner Initials*	Cite No. ¹	Foreign Patent Document Country Code ³⁻ Number ⁴⁻ Kind Code ⁵ (<i>if known</i>)	Publication Date MM-DD-YYYY	Name of Patentee or Applicant of Cited Documents	Pages, Columns, Lines, Where Relevant Passages or Relevant Figures Appear	T ⁶
	27.75					

		NON PATENT LITERATURE DOCUMENTS	
Examiner Initials*	Cite No. ¹	Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc.) date, page(s), volume-issue number(s), publisher, city and/or country where published.	T ⁶
	A1	MANTELLE, "DOT Matrix® Technology," Modified-Release Drug Delivery Technology, Rathbone et al., eds., Chapter 30, pp. 405-415, May 28, 2008.	TO THE
	A2	Office Action issued on 05/05/2016 in application number 14/024,985 (US 2014-0200530)	
	А3	Notice of Allowance issued on 10/02/2015 in application number 14/024,985 (US 2014-0200530)	
	A4	Office Action issue on 04/29/2016 in application number 14/738,255 (US 2015-0272905)	
	A5	Office Action issue on 10/26/2015 in application number 14/738,255 (US 2015-0272905)	

Examiner Signature /MELISSA L JAVIER/	Date Considered	08/22/2016
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Application/Control No.	Applicant(s)/Patent Under Reexamination
13553972	MANTELLE, JUAN

Examiner Art Unit

MELISSA JAVIER 1611

СРС	PC				
Symbol			Туре	Version	
A61K	9	7 7069	F	2013-01-01	
A61K	9	7 7061	I	2013-01-01	
A61K	31	7 565	I	2013-01-01	
A61K	47	1 10	I	2013-01-01	
A61K	47	<i>i</i> 32	I	2013-01-01	
A61K	9	7 0014	I	2013-01-01	
		<i>f</i>			
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CPC Combination Sets				
Symbol	Туре	Set	Ranking	Version

		Total Claims Allowed:	
(Assistant Examiner)	(Date)	2	1
/MELISSA JAVIER/ Examiner.Art Unit 1611	08/22/2016	O.G. Print Claim(s)	O.G. Print Figure
(Primary Examiner)	(Date)	1	None

Application/Control No.	Applicant(s)/Patent Under Reexamination
13553972	MANTELLE, JUAN
Examiner	Art Unit
MELISSA JAVIER	1611

	US ORI	IGINAL CL	.ASSIFIC	ATION		INTERNATIONAL CLASSIFICATION							ATION	
	CLASS		(SUBCLASS					С	LAIMED		NON-CLAIMED		
						Α	6	1	K	31 / 565 (2006.01.01)				
CROSS REFERENCE(S)					Α	6	1	К	9 / 70 (2006.01.01)					
_		ChO33 REFERENCE(3)												
CLASS	SUB	CLASS (ONE	SUBCLAS	S PER BLO	CK)									
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		Total Clain	ns Allowed:
(Assistant Examiner)	(Date)	2	1
/MELISSA JAVIER/ Examiner.Art Unit 1611	08/22/2016	O.G. Print Claim(s)	O.G. Print Figure
(Primary Examiner)	(Date)	1	None

Application/Control No.	Applicant(s)/Patent Under Reexamination
13553972	MANTELLE, JUAN
Examiner	Art Unit
MELISSA IAVIER	I 1611

	Claims re	numbere	d in the sa	ame orde	r as prese	ented by a	applicant		СР	A 🗵	T.D.		R.1.4	17	
Final	Original	Final	Original	Final	Original	Final	Original	Final	Original	Final	Original	Final	Original	Final	Origina
	1	16	17	12	33										
	2		18	13	34										
	3		19	14	35										
	4		20	17	36										
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	11		27												
	12	8	28												
	13	9	29												
1	14		30												
	15	10	31												
15	16	11	32												

		Total Claims Allowed:	
(Assistant Examiner)	(Date)	2	1
/MELISSA JAVIER/ Examiner.Art Unit 1611	08/22/2016	O.G. Print Claim(s)	O.G. Print Figure
(Primary Examiner)	(Date)	1	None

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

First Inventor Name:

Juan Mantelle

Title:

Transdermal Estrogen Device and Delivery

Appl. No.:

13/553972

Appl. Filing Date:

7/20/2012

Examiner:

Melissa L. Javier

Art Unit:

1611

Confirmation Number:

3635

REQUEST FOR CONTINUED EXAMINATION (RCE) TRANSMITTAL

Mail Stop RCE Commissioner for Patents P.O. Box 1450 Alexandria, VA 22313-1450

Commissioner:

This is a Request for Continued Examination (RCE) under 37 C.F.R. § 1.114 of the above-identified application. This RCE and the enclosed items listed below are being filed prior to the earliest of: (1) payment of the issue fee (unless a petition under 37 C.F.R. § 1.313 is granted); (2) abandonment of the application; or (3) the filing of a notice of appeal to the U.S. Court of Appeals for the Federal Circuit under 35 U.S.C. §141, or the commencement of a civil action under 35 U.S.C. §145 or §146 (unless the appeal or civil action is terminated).

Submission required under 37 C.F.R. §1.114:

- [X] Information Disclosure Statement.
- [X] Form PTO/SB/08 with copies of 9 listed reference(s).

The filing fee is calculated below at the large entity rate:

	Claims as Amended	Previ Paid l	•	Extra Claims Present		Rate		Fee Totals
RCE Fee 1.17(e):						\$1,700.0	=	\$1,700.00
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T				0		ф о о оо		Φ0.00
Total Claims:	13	- 2	6 =	0	X	\$80.00		\$0.00
Independents	3	- 5	; =	0	x	\$420.00	=	\$0.00
First p	resentation of	any Mul	tiple Dep	endent Claims:	+	\$780.00	=	\$0.00
			RC	E and CLAIMS	FEE	TOTAL:	_	\$1,700.00

The above-identified fees of \$1700.00 are being paid by credit card via EFS-Web.

The Commissioner is hereby authorized to charge any additional fees which may be required regarding this application under 37 C.F.R. §§ 1.16-1.17, or credit any overpayment, to Deposit Account No. 19-0741. Should no proper payment be enclosed herewith, as by the credit card payment instructions in EFS-Web being incorrect or absent, resulting in a rejected or incorrect credit card transaction, the Commissioner is authorized to charge the unpaid amount to Deposit Account No. 19-0741.

Please direct all correspondence to the undersigned attorney or agent at the address indicated below.

Respectfully submitted,

Courtenay C. Brinckerhoff

Attorney for Applicant

Registration No. 37,288

Date NN 28, 2016

FOLEY & LARDNER LLP Customer Number: 22428 Telephone: (202) 295-4094

Facsimile: (202) 672-5399

-3-

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

First Inventor Name: Juan Mantelle

Title: Transdermal Estrogen Device

and Delivery

Application No.: 13/553,972

Filing Date: 7/20/2012

Examiner: Melissa L. Javier

Art Unit: 1611

Confirmation No.: 3635

INFORMATION DISCLOSURE STATEMENT UNDER 37 CFR §1.56

Commissioner for Patents P.O. Box 1450 Alexandria, VA 22313-1450

Commissioner:

Applicant submits herewith documents for the Examiner's consideration in accordance with 37 CFR §§1.56, 1.97 and 1.98.

Applicant respectfully requests that each listed document be considered by the Examiner and be made of record in the present application and that an initialed copy of Form PTO/SB/08 be returned in accordance with MPEP §609.

The submission of any document herewith is not an admission that such document constitutes prior art against the claims of the present application or that such document is considered material to patentability as defined in 37 CFR §1.56(b). Applicant does not waive any rights to take any action which would be appropriate to antedate or otherwise remove as a competent reference any document submitted herewith.

4823-6143-6221.1 __1_

TIMING OF THE DISCLOSURE

The listed documents are being submitted in compliance with 37 CFR §1.97(b), before the mailing of a first Office action after the filing of a RCE.

Although Applicant believes that no fee is required, the Commissioner is hereby authorized to charge any additional fees which may be due for this application to Deposit Account Number 19-0741.

Respectfully submitted,

Date November 28, 2016

By /Courtenay C. Brinckerhoff/

FOLEY & LARDNER LLP Customer Number: 22428 (202) 295-4094

Telephone: Facsimile:

(202) 672-5399

Courtenay C. Brinckerhoff Attorney for Applicant Registration No. 37,288

Substitute for form 1449/PTO Complete if Known 13/553972 INFORMATION DISCLOSURE Application Number STATEMENT BY APPLICANT Filing Date 7/20/2012 First Named Inventor Juan Mantelle Date Submitted: November 28, 2016 Art Unit 1611 Examiner Name (use as many sheets as necessary) Melissa L. Javier 041457-0992 Sheet 2 Attorney Docket Number

	U.S. PATENT DOCUMENTS									
Examiner	Cite	Document Number	Publication Date	Name of Patentee or Applicant of	Pages, Columns, Lines, Where Relevant					
Initials*	No. ¹	Number-Kind Code ² (if known)	MM-DD-YYYY	Cited Document	Passages or Relevant Figures Appear					

	UNPUBLISHED U.S. PATENT APPLICATION DOCUMENTS									
Examiner Initials*	Cite No. ¹	U.S. Patent Application Document Serial Number-Kind Code ² (if known)	Filing Date of Cited Document MM-DD-YYYY	Name of Patentee or Applicant of Cited Document	Pages, Columns, Lines, Where Relevant Passages or Relevant Figures Appear					

FOREIGN PATENT DOCUMENTS									
Examiner Initials*	Cite No. ¹	Foreign Patent Document Country Code ³⁻ Number ⁴⁻ Kind Code ⁵ (<i>if known</i>)	Publication Date MM-DD-YYYY	Name of Patentee or Applicant of Cited Documents	Pages, Columns, Lines, Where Relevant Passages or Relevant Figures Appear	Τ ⁶			

		NON PATENT LITERATURE DOCUMENTS	
Examiner Initials*	Cite No. ¹	Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc.) date, page(s), volume-issue number(s), publisher, city and/or country where published.	T ⁶
	A1	TOOLE ET AL., "Evaluation of irritation and sensitisation of two 50 μg/day oestrogen patches," Maturitas, Vol. 43, pp. 257-263, December 2002.	
	A2	MARTY, "New trends in transdermal technologies: Development of the skin patch, Menorest®," International Journal of Gynecology & Obstetrics, Vol. 52, Suppl. 1, pp. S17-S20, March 1996.	
	А3	NOVARTIS, "Estraderm®," Prescribing information, June 2004.	
	A4	NOVARTIS, "Vivelle®," Prescribing information, June 2004.	
	A5	NOVARTIS, "Vivelle-Dot®," Prescribing information, June 2004.	
	A6	BAYER HEALTHCARE, "Climara®," Prescribing information, 2007	
	A7	3M PHARMACEUTICALS, "Menostar™," Prescribing information, June 2004.	THE REAL PROPERTY OF THE PERSON OF THE PERSO
	A8	WATSON PHARMA, INC., "Alora®," Prescribing information, May 2005.	

Examiner	Date	
Signature	Considered	

PTO/SB/08 (modified)

Substitute for form 1449/PTO				C	Complete if Known			
	INFORMATION	DISC	LOSURE	Application Number	13/553972			
STATEMENT BY APPLICANT				Filing Date	7/20/2012			
Date Submitted: November 28, 2016 (use as many sheets as necessary)			or 20 2016	First Named Inventor	Juan Mantelle			
			ei 26, 2016	Art Unit	1611			
			necessary)	Examiner Name	Melissa L. Javier			
Sheet	2	of	2	Attorney Docket Number	041457-0992			

NON PATENT LITERATURE DOCUMENTS							
Examiner Initials*	Cite No. ¹	Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc.) date, page(s), volume-issue number(s), publisher, city and/or country where published.	T⁵				
	A9	SERONO LABORATORIES, INC., "Esclim®," Prescribing information, August 1998.					

	(
Examiner	Date	
Signature	Considered	

Electronic Patent Application Fee Transmittal						
Application Number:	13.	553972				
Filing Date:	20	-Jul-2012				
Title of Invention:	TRANSDERMAL ESTROGEN DEVICE AND DELIVERY					
First Named Inventor/Applicant Name:	Juan Mantelle					
Filer:	Courtenay C. Brinckerhoff					
Attorney Docket Number:	04	1457-0992				
Filed as Large Entity						
Filing Fees for Utility under 35 USC 111(a)						
Description		Fee Code	Quantity	Amount	Sub-Total in USD(\$)	
Basic Filing:						
Pages:						
Claims:						
Miscellaneous-Filing:						
Petition:						
Patent-Appeals-and-Interference:						
Post-Allowance-and-Post-Issuance:						
Extension-of-Time:						

Description	Fee Code	Quantity	Amount	Sub-Total in USD(\$)
Miscellaneous:				
RCE- 2ND AND SUBSEQUENT REQUEST	1820	1	1700	1700
	Tot	1700		

Electronic Acknowledgement Receipt					
EFS ID:	27619812				
Application Number:	13553972				
International Application Number:					
Confirmation Number:	3635				
Title of Invention:	TRANSDERMAL ESTROGEN DEVICE AND DELIVERY				
First Named Inventor/Applicant Name:	Juan Mantelle				
Customer Number:	22428				
Filer:	Courtenay C. Brinckerhoff/Christine Arthur				
Filer Authorized By:	Courtenay C. Brinckerhoff				
Attorney Docket Number:	041457-0992				
Receipt Date:	28-NOV-2016				
Filing Date:	20-JUL-2012				
Time Stamp:	14:02:26				
Application Type:	Utility under 35 USC 111(a)				

Payment information:

Submitted with Payment	yes
Payment Type	CARD
Payment was successfully received in RAM	\$1700
RAM confirmation Number	112916INTEFSW14032600
Deposit Account	190741
Authorized User	Christine Arthur

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

37 CFR 1.17 (Patent application and reexamination processing fees)

37 CFR 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.)	
			245161			
1		rceids.pdf	a6b73ea014c20b5b86f6327612b3fe1cd19 2e9eb	yes	7	
	Multip	ı Dart Description/PDF files in	.zip description			
	Document De	scription	Start	E	nd	
	Request for Continued E	1		3		
	Transmittal	4	5			
	Information Disclosure Stater	6		7		
Warnings:						
Information:						
			77843		7	
2	Non Patent Literature	toole2002.pdf	c70337f8aec67eb6cdf1f41477645405053c 0c21	no		
Warnings:			'			
Information:						
			7295311		_	
3	Non Patent Literature	Marty 1996.pdf	050613821102d409c0ad0da289a45d6fe93 1183e	no	4	
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Information:						
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4	4 Non Patent Literature estradermjune 20		1d97460ef7b258eaf4b26e416aef8d93dd1e dcac	no	22	
Warnings:						
Information:						
5	Non Patent Literature	vivelle 2004. pdf	522915 bed5c72638aff66d5b0122934eb17e6a87d	no	28	
			1a437			

Warnings:					
Information:					
			391153		
6	Non Patent Literature	vivelledot 2004. pdf	e91f07c4d292c518223c7e77c6e7f5a77b8f cd58	no	28
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7	Non Patent Literature	climara 2007. pdf	2ba61920dd4d73a49f6fb4d41bcbfe26301 42296	no	23
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8	Non Patent Literature	menostar 2004. pdf	818aaf0be23f41cea4bd2d53eaa23d4da1f9 1b4a	no	28
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9	Non Patent Literature	alora 2005. pdf	3150b28ac9894d475dc8d1b1cef0578a7ba a05af	no	29
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10	Non Patent Literature	esclim98.pdf	6ae80f7cc7ce83f0531c33289500eeff0b71e 423	no	19
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11	Fee Worksheet (SB06)	fee-info.pdf	62c13ec7b0cc5c97fa0bf42d451c06e96e8d 5e71	no	2
Warnings:		•			
Information:					
		Total Files Size (in byte	1175	5902	

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.go

NOTICE OF ALLOWANCE AND FEE(S) DUE

12/09/2016 Foley & Lardner LLP 3000 K STREET N.W. SUITE 600 WASHINGTON, DC 20007-5109

EXAMINER JAVIER, MELISSA L ART UNIT PAPER NUMBER 1611

DATE MAILED: 12/09/2016

APPLICATION NO.			ATTORNEY DOCKET NO.	CONFIRMATION NO.
13/553,972	07/20/2012	Juan Mantelle	041457-0992	3635

TITLE OF INVENTION: TRANSDERMAL ESTROGEN DEVICE AND DELIVERY

	APPLN. TYPE	ENTITY STATUS	ISSUE FEE DUE	PUBLICATION FEE DUE	PREV. PAID ISSUE FEE	TOTAL FEE(S) DUE	DATE DUE
Ξ	nonprovisional	UNDISCOUNTED	\$960	\$0	\$0	\$960	03/09/2017

THE APPLICATION IDENTIFIED ABOVE HAS BEEN EXAMINED AND IS ALLOWED FOR ISSUANCE AS A PATENT. PROSECUTION ON THE MERITS IS CLOSED. THIS NOTICE OF ALLOWANCE IS NOT A GRANT OF PATENT RIGHTS. THIS APPLICATION IS SUBJECT TO WITHDRAWAL FROM ISSUE AT THE INITIATIVE OF THE OFFICE OR UPON PETITION BY THE APPLICANT. SEE 37 CFR 1.313 AND MPEP 1308.

THE ISSUE FEE AND PUBLICATION FEE (IF REQUIRED) MUST BE PAID WITHIN THREE MONTHS FROM THE MAILING DATE OF THIS NOTICE OR THIS APPLICATION SHALL BE REGARDED AS ABANDONED. STATUTORY PERIOD CANNOT BE EXTENDED. SEE 35 U.S.C. 151. THE ISSUE FEE DUE INDICATED ABOVE DOES NOT REFLECT A CREDIT FOR ANY PREVIOUSLY PAID ISSUE FEE IN THIS APPLICATION. IF AN ISSUE FEE HAS PREVIOUSLY BEEN PAID IN THIS APPLICATION (AS SHOWN ABOVE), THE RETURN OF PART B OF THIS FORM WILL BE CONSIDERED A REQUEST TO REAPPLY THE PREVIOUSLY PAID ISSUE FEE TOWARD THE ISSUE FEE NOW DUE.

HOW TO REPLY TO THIS NOTICE:

I. Review the ENTITY STATUS shown above. If the ENTITY STATUS is shown as SMALL or MICRO, verify whether entitlement to that entity status still applies.

If the ENTITY STATUS is the same as shown above, pay the TOTAL FEE(S) DUE shown above.

If the ENTITY STATUS is changed from that shown above, on PART B - FEE(S) TRANSMITTAL, complete section number 5 titled "Change in Entity Status (from status indicated above)".

For purposes of this notice, small entity fees are 1/2 the amount of undiscounted fees, and micro entity fees are 1/2 the amount of small entity

II. PART B - FEE(S) TRANSMITTAL, or its equivalent, must be completed and returned to the United States Patent and Trademark Office (USPTO) with your ISSUE FEE and PUBLICATION FEE (if required). If you are charging the fee(s) to your deposit account, section "4b" of Part B - Fee(s) Transmittal should be completed and an extra copy of the form should be submitted. If an equivalent of Part B is filed, a request to reapply a previously paid issue fee must be clearly made, and delays in processing may occur due to the difficulty in recognizing the paper as an equivalent of Part B.

III. All communications regarding this application must give the application number. Please direct all communications prior to issuance to Mail Stop ISSUE FEE unless advised to the contrary.

IMPORTANT REMINDER: Utility patents issuing on applications filed on or after Dec. 12, 1980 may require payment of maintenance fees. It is patentee's responsibility to ensure timely payment of maintenance fees when due.

PART B - FEE(S) TRANSMITTAL

Complete and send this form, together with applicable fee(s), to: Mail Mail Stop ISSUE FEE

Mail Stop ISSUE FEE Commissioner for Patents P.O. Box 1450 Alexandria, Virginia 22313-1450

or <u>Fax</u> (571)-273-2885

INSTRUCTIONS: This form should be used for transmitting the ISSUE FEE and PUBLICATION FEE (if required). Blocks 1 through 5 should be completed where appropriate. All further correspondence including the Patent, advance orders and notification of maintenance fees will be mailed to the current correspondence address as indicated unless corrected below or directed otherwise in Block 1, by (a) specifying a new correspondence address; and/or (b) indicating a separate "FEE ADDRESS" for maintenance fee notifications.

maintenance fee notifica	tions.								
CURRENT CORRESPOND	ENCE ADDRESS (Note: Use Bl	ock 1 for a	any change of address)		Note: A certificate of mailing can only be used for domestic mailings of the Fee(s) Transmittal. This certificate cannot be used for any other accompanying papers. Each additional paper, such as an assignment or formal drawing, mus have its own certificate of mailing or transmission.				
Foley & Lardn 3000 K STREE SUITE 600		/2016			I her State addr trans	reby certify that th	is Feel	e of Mailing or Trans s) Transmittal is being ficient postage for firs ISSUE FEE address 1) 273-2885, on the da	unission g deposited with the United st class mail in an envelope above, or being facsimile ate indicated below.
	I, DC 20007-5109								(Depositor's name)
							(Signature)		
									(Date)
APPLICATION NO.	FILING DATE			FIRST NAMED INVEN	TOR		ATTC	RNEY DOCKET NO.	CONFIRMATION NO.
13/553,972	07/20/2012	•		Juan Mantelle				041457-0992	3635
ΠΤLE OF INVENTION	: TRANSDERMAL EST	ΓROGE	N DEVICE AND	DELIVERY					
APPLN. TYPE	ENTITY STATUS	ISS	SUE FEE DUE	PUBLICATION FEE I	UE	PREV. PAID ISSUI	E FEE	TOTAL FEE(S) DUE	DATE DUE
nonprovisional	UNDISCOUNTED		\$960	\$0		\$0		\$960	03/09/2017
EXAM	INER		ART UNIT	CLASS-SUBCLASS	S				
JAVIER, M			1611	424-487000					
·		n of "Fe			the n	atent front page lis	rt		
 1. Change of correspondence address or indication of "Fee Address" (37 CFR 1.363). 1. Change of correspondence address (or Change of Correspondence Address form PTO/SB/122) attached. 1. "Fee Address" indication (or "Fee Address" Indication form PTO/SB/47; Rev 03-02 or more recent) attached. Use of a Customer Number is required. 				(1) The names of up to 3 registered patent attorneys or agents OR, alternatively, (2) The name of a single firm (having as a member a registered attorney or agent) and the names of up to					
	ND RESIDENCE DATA	A TO B	E PRINTED ON T	L ΓΗΕ PATENT (print α	or typ	ne)			
PLEASE NOTE: Un recordation as set fort	less an assignee is ident h in 37 CFR 3.11. Comp	ified be pletion o	low, no assignee of this form is NO	data will appear on t I a substitute for filin	he pa	ntent. If an assign	ee is io	dentified below, the d	ocument has been filed for
(A) NAME OF ASSI	GNEE			(B) RESIDENCE: (C	CITY	and STATE OR C	OUN]	TRY)	
Please check the appropr	iate assignee category or	catego	ries (will not be pr	inted on the patent):	۵	Individual 🖵 Co	orporat	ion or other private gro	oup entity 🚨 Government
4a. The following fee(s)	are submitted:		46			se first reapply ar	ıy prev	viously paid issue fee	shown above)
Issue Fee	T 10 10	•	1/2	A check is enclose		1 E PEO 2020			
	No small entity discount p of Copies			☐ Payment by credit card. Form PTO-2038 is attached. ☐ The director is hereby authorized to charge the required fee(s), any deficiency, or credits any					ficiency, or credits any
Travance order	or copies			overpayment, to l	Depo	sit Account Number	er	(enclose a	n extra copy of this form).
5. Change in Entity Sta	tus (from status indicated	d above)						
Applicant certifyin	FR 1.29	NOTE: Absent a val	id ce	rtification of Micro entity amount will	Entity not be	Status (see forms PTC accepted at the risk of	O/SB/15A and 15B), issue application abandonment.		
Applicant assertin	NOTE: If the application was previously under micro entity status, checking this box will be taken to be a notification of loss of entitlement to micro entity status.								
Applicant changing to regular undiscounted fee status. NOTE: Checking this box will be taken to be a notification of loss of entitlement to small or mic entity status, as applicable.							tlement to small or micro		
NOTE: This form must b	e signed in accordance v	vith 37	CFR 1.31 and 1.33	3. See 37 CFR 1.4 for	signa	nture requirements	and ce	rtifications.	
Authorized Signature						Date			
Typed or printed nam	Registration No								

Page 2 of 3



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DATE MAILED: 12/09/2016

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
13/553,972	07/20/2012 Juan Mantelle		041457-0992	3635
22428 75	90 12/09/2016		EXAM	INER
Foley & Lardner		JAVIER, M	ELISSA L	
3000 K STREET N SUITE 600	N.W.		ART UNIT	PAPER NUMBER
WASHINGTON, I	OC 20007-5109		1611	

Determination of Patent Term Adjustment under 35 U.S.C. 154 (b)

(Applications filed on or after May 29, 2000)

The Office has discontinued providing a Patent Term Adjustment (PTA) calculation with the Notice of Allowance.

Section 1(h)(2) of the AIA Technical Corrections Act amended 35 U.S.C. 154(b)(3)(B)(i) to eliminate the requirement that the Office provide a patent term adjustment determination with the notice of allowance. See Revisions to Patent Term Adjustment, 78 Fed. Reg. 19416, 19417 (Apr. 1, 2013). Therefore, the Office is no longer providing an initial patent term adjustment determination with the notice of allowance. The Office will continue to provide a patent term adjustment determination with the Issue Notification Letter that is mailed to applicant approximately three weeks prior to the issue date of the patent, and will include the patent term adjustment on the patent. Any request for reconsideration of the patent term adjustment determination (or reinstatement of patent term adjustment) should follow the process outlined in 37 CFR 1.705.

Any questions regarding the Patent Term Extension or Adjustment determination should be directed to the Office of Patent Legal Administration at (571)-272-7702. Questions relating to issue and publication fee payments should be directed to the Customer Service Center of the Office of Patent Publication at 1-(888)-786-0101 or (571)-272-4200.

OMB Clearance and PRA Burden Statement for PTOL-85 Part B

The Paperwork Reduction Act (PRA) of 1995 requires Federal agencies to obtain Office of Management and Budget approval before requesting most types of information from the public. When OMB approves an agency request to collect information from the public, OMB (i) provides a valid OMB Control Number and expiration date for the agency to display on the instrument that will be used to collect the information and (ii) requires the agency to inform the public about the OMB Control Number's legal significance in accordance with 5 CFR 1320.5(b).

The information collected by PTOL-85 Part B is required by 37 CFR 1.311. 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 1.14. 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, Virginia 22313-1450. DO NOT SEND FEES OR COMPLETED FORMS TO THIS ADDRESS. SEND TO: Commissioner for Patents, P.O. Box 1450, Alexandria, Virginia 22313-1450. Under the Paperwork Reduction Act of 1995, no persons are required to respond to a collection of information unless it displays a valid OMB control number.

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.

	Application No.	Applicant(s)	
	13/553,972	MANTELLE,	JUAN
Notice of Allowability	Examiner Melissa Javier	Art Unit 1611	AIA (First Inventor to File) Status No

The MAILING DATE of this communication appears on the All claims being allowable, PROSECUTION ON THE MERITS IS (OR REM herewith (or previously mailed), a Notice of Allowance (PTOL-85) or other a NOTICE OF ALLOWABILITY IS NOT A GRANT OF PATENT RIGHTS. Tof the Office or upon petition by the applicant. See 37 CFR 1.313 and MPE	AINS) CLOSED in this application. If not included appropriate communication will be mailed in due course. THIS his application is subject to withdrawal from issue at the initiative					
 This communication is responsive to <u>11/28/2016</u>. A declaration(s)/affidavit(s) under 37 CFR 1.130(b) was/were filed 	don					
 An election was made by the applicant in response to a restriction recrequirement and election have been incorporated into this action. 	quirement set forth during the interview on; the restriction					
☑ The allowed claim(s) is/are 14,16,17,21-26,28,29 and 31-40. As a result of the allowed claim(s), you may be eligible to benefit from the Patent Prosecution Highway program at a participating intellectual property office for the corresponding application. For more information, please see http://www.uspto.gov/patents/init_events/pph/index.jsp or send an inquiry to PPHfeedback@uspto.gov.						
4. Acknowledgment is made of a claim for foreign priority under 35 U.S.	C. § 119(a)-(d) or (f).					
Certified copies:						
a) All b) Some *c) None of the:						
 Certified copies of the priority documents have been rec 						
2. Certified copies of the priority documents have been rec	• • • • • • • • • • • • • • • • • • • •					
Copies of the certified copies of the priority documents h	nave been received in this national stage application from the					
International Bureau (PCT Rule 17.2(a)).						
* Certified copies not received:						
Applicant has THREE MONTHS FROM THE "MAILING DATE" of this connoted below. Failure to timely comply will result in ABANDONMENT of the THIS THREE-MONTH PERIOD IS NOT EXTENDABLE.						
5. CORRECTED DRAWINGS (as "replacement sheets") must be subm	itted.					
including changes required by the attached Examiner's Amenda Paper No./Mail Date	nent / Comment or in the Office action of					
Identifying indicia such as the application number (see 37 CFR 1.84(c)) sho each sheet. Replacement sheet(s) should be labeled as such in the header						
 DEPOSIT OF and/or INFORMATION about the deposit of BIOLOGIC attached Examiner's comment regarding REQUIREMENT FOR THE D 						
Attach mont/o)						
Attachment(s) 1. ☐ Notice of References Cited (PTO-892)	5. 🛛 Examiner's Amendment/Comment					
2. ☑ Information Disclosure Statements (PTO/SB/08), Paper No./Mail Date	6. Examiner's Statement of Reasons for Allowance					
Examiner's Comment Regarding Requirement for Deposit	7. Other					
of Biological Material 4. ☐ Interview Summary (PTO-413), Paper No./Mail Date						
/Melissa Javier/ Examiner, Art Unit 1611						

U.S. Patent and Trademark Office PTOL-37 (Rev. 08-13) 20161202

Notice of Allowability

Part of Paper No./Mail Date

DETAILED ACTION

The present application is being examined under the pre-AIA first to invent provisions.

Continued Examination Under 37 CFR 1.114

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after allowance or after an Office action under *Ex Parte Quayle*, 25 USPQ 74, 453 O.G. 213 (Comm'r Pat. 1935). Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, prosecution in this application has been reopened pursuant to 37 CFR 1.114. Applicant's submission filed on 11/28/2016 has been entered.

Information Disclosure Statement

The Information Disclosure Statement (IDS) filed 11/28//2016 has been considered by the examiner.

Conclusion

Any comments considered necessary by applicant must be submitted no later than the payment of the issue fee and, to avoid processing delays, should preferably accompany the issue fee. Such submissions should be clearly labeled "Comments on Statement of Reasons for Allowance."

Art Unit: 1611

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Melissa Javier whose telephone number is (571)270-7430. The examiner can normally be reached on Monday-Thursday, 8am-6pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Bethany Barham can be reached on 571-272-6175. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Melissa Javier/ Examiner, Art Unit 1611



Application/Control No.	Applicant(s)/Patent Under Reexamination
13553972	MANTELLE, JUAN
Examiner	Art Unit
MELISSA JAVIER	1611

CPC				
Symbol			Туре	Version
A61K	9	7069	F	2013-01-01
A61K	9	7061	I	2013-01-01
A61K	31	565	I	2013-01-01
A61K	47	/ 10	I	2013-01-01
A61K	47	32	I	2013-01-01
A61K	9	0014	I	2013-01-01

CPC Combination Sets								
Symbol	Туре	Set	Ranking	Version				

		Total Clain	ns Allowed:
(Assistant Examiner)	(Date)	2	1
/MELISSA JAVIER/ Examiner.Art Unit 1611	12/2/2016	O.G. Print Claim(s)	O.G. Print Figure
(Primary Examiner)	(Date)	1	None

Application/Control No.	Applicant(s)/Patent Under Reexamination
13553972	MANTELLE, JUAN
Examiner	Art Unit
MELISSA JAVIER	1611

US ORIGINAL CLASSIFICATION								INTERNATIONAL	CLA	SSI	FIC	ATION			
	CLASS SUBCLASS						С	LAIMED			N	ON-CLAIMED			
						Α	6	1	К	31 / 565 (2006.01.01)					
CROSS REFERENCE(S)		A	6	1	К	9 / 70 (2006.0)									
CLASS	SUB	CLASS (ONE	SUBCLAS	S PER BLO	CK)										

		Total Clain	ns Allowed:
(Assistant Examiner)	(Date)	2	1
/MELISSA JAVIER/ Examiner.Art Unit 1611	12/2/2016	O.G. Print Claim(s)	O.G. Print Figure
(Primary Examiner)	(Date)	1	None

Application/Control No.	Applicant(s)/Patent Under Reexamination
13553972	MANTELLE, JUAN
Examiner	Art Unit
MELISSA IAVIER	I 1611

☐ Claims renumbered in the same order as presented by applicant						☐ CPA ⊠ T.D. ☐ R.1.47									
Final	Original	Final	Original	Final	Original	Final	Original	Final	Original	Final	Original	Final	Original	Final	Origina
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15	16	11	32												

			ns Allowed:
(Assistant Examiner)	(Date)	21	
/MELISSA JAVIER/ Examiner.Art Unit 1611	12/2/2016	O.G. Print Claim(s)	O.G. Print Figure
(Primary Examiner)	(Date)	1	None

PTO/SB/08 (modified)

	Substitute for fo	rm 144	49/PTO	С	Complete if Known			
	INFORMATION	DISC	LOSURE	Application Number	13/553972			
	STATEMENT BY	Y APF	PLICANT	Filing Date	7/20/2012			
r	Date Submitted: No	womb	or 20, 2016	First Named Inventor	Juan Mantelle			
L	Date Submitted, No	veill	ei 20, 2010	Art Unit	1611			
	(use as many shee	ts as	necessary)	Examiner Name	Melissa L. Javier			
Sheet	1	of	2	Attorney Docket Number	041457-0992			

U.S. PATENT DOCUMENTS									
Examiner Initials*	Cite	Document Number	Publication Date	Name of Patentee or Applicant of	Pages, Columns, Lines, Where Relevant				
	No. ¹	Number-Kind Code ² (if known)	MM-DD-YYYY	Cited Document	Passages or Relevant Figures Appear				

	UNPUBLISHED U.S. PATENT APPLICATION DOCUMENTS										
Examiner Initials*	Cite No. ¹	U.S. Patent Application Document Serial Number-Kind Code ² (if known)	Filing Date of Cited Document MM-DD-YYYY	Name of Patentee or Applicant of Cited Document	Pages, Columns, Lines, Where Relevant Passages or Relevant Figures Appear						

	FOREIGN PATENT DOCUMENTS										
Examiner Initials*	Cite No. ¹	Foreign Patent Document Country Code ³ Number ⁴ Kind Code ⁵ (<i>if known</i>)	Publication Date MM-DD-YYYY	Name of Patentee or Applicant of Cited Documents	Pages, Columns, Lines, Where Relevant Passages or Relevant Figures Appear	T ₆					

		NON PATENT LITERATURE DOCUMENTS	
Examiner Initials*	Cite No.1	Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc.) date, page(s), volume-issue number(s), publisher, city and/or country where published.	T⁵
	A1	TOOLE ET AL., "Evaluation of irritation and sensitisation of two 50 μg/day oestrogen patches," Maturitas, Vol. 43, pp. 257-263, December 2002.	
	A2	MARTY, "New trends in transdermal technologies: Development of the skin patch, Menorest®," International Journal of Gynecology & Obstetrics, Vol. 52, Suppl. 1, pp. S17-S20, March 1996.	
	А3	NOVARTIS, "Estraderm®," Prescribing information, June 2004.	
	A4	NOVARTIS, "Vivelle®," Prescribing information, June 2004.	
	A5	NOVARTIS, "Vivelle-Dot®," Prescribing information, June 2004.	
	A6	BAYER HEALTHCARE, "Climara®," Prescribing information, 2007	
	A7	3M PHARMACEUTICALS, "Menostar™," Prescribing information, June 2004.	
	A8	WATSON PHARMA, INC., "Alora®," Prescribing information, May 2005.	A CONTRACTOR OF THE CONTRACTOR

Examiner Date Considered
digitation

13553972 - GAU: 1611

PTO/SB/08 (modified)

	Substitute for fo	rm 144	19/PTO	C	Complete if Known		
	INFORMATION	DISC	LOSURE	Application Number	13/553972		
	STATEMENT BY	Y APF	PLICANT	Filing Date	7/20/2012		
_	Date Submitted: No	wamh	or 20 2016	First Named Inventor	Juan Mantelle		
L	date Submitted, No	veniu	ei 26, 2016	Art Unit	1611		
(use as many sheets as necessary)				Examiner Name	Melissa L. Javier		
Sheet 2 of 2		Attorney Docket Number	041457-0992				

		NON PATENT LITERATURE DOCUMENTS	
Examiner Initials*	Cite No. ¹	Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc.) date, page(s), volume-issue number(s), publisher, city and/or country where published.	T ⁶
	A9	SERONO LABORATORIES, INC., "Esclim®," Prescribing information, August 1998.	

4				
	Examiner Signature	/MELISSA L JAVIER/	Date Considered	12/02/2016

EAST Search History

EAST Search History (Prior Art)

Ref Hits #		Search Query	DBs	Default Operator	Plurals	Time Stamp	
L1	15404	estradiol and transdermal	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	OFF	2016/12/02 16:37	
L2	5333	L1 and ("surface area" flux)	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	OFF	2016/12/02 16:37	
L3	886	L2 and acrylic and silicone and (PVP polyvinyl pyrrolidone)	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	OFF	2016/12/02 16:37	
L4	34	L3 and estradiol.ab.	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	OFF	2016/12/02 16:37	
L5	260	L3 and transdermal.ab.	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	OFF	2016/12/02 16:37	
L6	50	L3 and (estradiol NEAR flux)	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	OFF	2016/12/02 16:37	
L7	88	L1 and (estradiol NEAR flux)	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	OFF	2016/12/02 16:37	
L8	257	MANTELLE.in. and JUAN.in.	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	OFF	2016/12/02 16:37	
L9	42	L8 and estradiol	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	OFF	2016/12/02 16:37	
L10	149	L8 and transdermal	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	OFF	2016/12/02 16:37	
L11	184	Kanios.in. and David.in.	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	OFF	2016/12/02 16:37	
L12	39	L11 NOT L8	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	OFF	2016/12/02 16:37	
L13	0	(11/245097).APP.	USPAT; USOCR	OR	OFF	2016/12/02 16:37	
L14	699	L1 and ("dipropylene glycol" oleyl)	USPAT; USOCR	OR	OFF	2016/12/02 16:37	
L15	129	L3 and ("dipropylene glycol" oleyl)	USPAT; USOCR	OR	OFF	2016/12/02 16:37	
L16	15404	estradiol and transdermal	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	OFF	2016/12/02 16:37	
L17	5333	L16 and ("surface area" flux)	US-PGPUB; USPAT; USOCR; FPRS; EPO;	OR	OFF	2016/12/02 16:37	

			JPO; DERWENT			***************************************
L18	886	L17 and acrylic and silicone and (PVP polyvinyl pyrrolidone)	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	OFF	2016/12/02 16:37
L19	34	L18 and estradiol.ab.	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	OFF	2016/12/02 16:37
L20	260	L18 and transdermal.ab.	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	OFF	2016/12/02 16:37
L21	50	L18 and (estradiol NEAR flux)	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	OFF	2016/12/02 16:37
L22	88	L16 and (estradiol NEAR flux)	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	OFF	2016/12/02 16:37
L23	257	MANTELLE.in. and JUAN.in.	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	OFF	2016/12/02 16:37
L24	42	L23 and estradiol	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	OFF	2016/12/02 16:37
L25	149	L23 and transdermal	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	OFF	2016/12/02 16:37
L26	184	Kanios.in. and David.in.	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	OFF	2016/12/02 16:37
L27	39	L26 NOT L23	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	OFF	2016/12/02 16:37
L28	0	(11/245097).APP.	USPAT; USOCR	OR	OFF	2016/12/02 16:37
L29	699	L16 and ("dipropylene glycol" oleyl)	USPAT; USOCR	OR	OFF	2016/12/02 16:37
L30	129	L18 and ("dipropylene glycol" oleyl)	USPAT; USOCR	OR	OFF	2016/12/02 16:37
L31	2	"6638528".pn.	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	OFF	2016/12/02 16:37
L32	4	"4624665".pn.	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	OFF	2016/12/02 16:37
L33	3	"20090041831".pn.	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	OFF	2016/12/02 16:37
L34	15404	estradiol and transdermal	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	OFF	2016/12/02 16:37
L35	5333	L34 and ("surface area" flux)	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	OFF	2016/12/02 16:37
L36	886	L35 and acrylic and silicone and (PVP polyvinyl pyrrolidone)	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	OFF	2016/12/02 16:37
L37	34	L36 and estradiol.ab.	US-PGPUB; USPAT;	OR	OFF	2016/12/02

			USOCR; FPRS; EPO; JPO; DERWENT		Proportion of the Control of the Con	16:37
L38	260	L36 and transdermal.ab.	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	OFF	2016/12/02 16:37
L39	50	L36 and (estradiol NEAR flux)	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	OFF	2016/12/02 16:37
L40	88	L34 and (estradiol NEAR flux)	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	OFF	2016/12/02 16:37
L41	257	MANTELLE.in. and JUAN.in.	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	OFF	2016/12/02 16:37
L42	42	L41 and estradiol	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	OFF	2016/12/02 16:37
L43	149	L41 and transdermal	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	OFF	2016/12/02 16:37
L44	184	Kanios.in. and David.in.	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	OFF	2016/12/02 16:37
L45	39	L44 NOT L41	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	OFF	2016/12/02 16:37
L46	0	(11/245097).APP.	USPAT; USOCR	OR	OFF	2016/12/02 16:37
L47	699	L34 and ("dipropylene glycol" oleyl)	USPAT; USOCR	OR	OFF	2016/12/02 16:37
L48	129	L36 and ("dipropylene glycol" oleyl)	USPAT; USOCR	OR	OFF	2016/12/02 16:37
L49	15404	estradiol and transdermal	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	OFF	2016/12/02 16:37
L50	5333	L49 and ("surface area" flux)	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	OFF	2016/12/02 16:37
L51	886	L50 and acrylic and silicone and (PVP polyvinyl pyrrolidone)	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	OFF	2016/12/02 16:37
L52	34	L51 and estradiol.ab.	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	OFF	2016/12/02 16:37
L53	260	L51 and transdermal.ab.	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	OFF	2016/12/02 16:37
L54	50	L51 and (estradiol NEAR flux)	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	OFF	2016/12/02 16:37
L55	88	L49 and (estradiol NEAR flux)	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	OFF	2016/12/02 16:37
L56	257	MANTELLE.in. and JUAN.in.	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	OFF	2016/12/02 16:37

L57	42	L56 and estradiol	US-PGPUB; USPAT; USOCR; FPRS; EPO;	OR	OFF	2016/12/02 16:37
			JPO; DERWENT			
L58	149	L56 and transdermal	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	OFF	2016/12/02 16:37
L59	184	Kanios.in. and David.in.	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	OFF	2016/12/02 16:37
L60	39	L59 NOT L56	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	OFF	2016/12/02 16:37
L61	0	(11/245097).APP.	USPAT; USOCR	OR	OFF	2016/12/02 16:37
L62	699	L49 and ("dipropylene glycol" oleyl)	USPAT; USOCR	OR	OFF	2016/12/02 16:37
L63	129	L51 and ("dipropylene glycol" oleyl)	USPAT; USOCR	OR	OFF	2016/12/02 16:37
L64	15404	estradiol and transdermal	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	OFF	2016/12/02 16:37
L65	5333	L64 and ("surface area" flux)	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	OFF	2016/12/02 16:37
L66	886	L65 and acrylic and silicone and (PVP polyvinyl pyrrolidone)	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	OFF	2016/12/02 16:37
L67	34	L66 and estradiol.ab.	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	OFF	2016/12/02 16:37
L68	260	L66 and transdermal.ab.	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	OFF	2016/12/02 16:37
L69	50	L66 and (estradiol NEAR flux)	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	OFF	2016/12/02 16:37
L70	88	L64 and (estradiol NEAR flux)	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	OFF	2016/12/02 16:37
L71	257	MANTELLE.in. and JUAN.in.	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	OFF	2016/12/02 16:37
L72	42	L71 and estradiol	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	OFF	2016/12/02 16:37
L73	149	L71 and transdermal	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	OFF	2016/12/02 16:37
L74	184	Kanios.in. and David.in.	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	OFF	2016/12/02 16:37
L75	39	L74 NOT L71	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	OFF	2016/12/02 16:37
L76	0	(11/245097).APP.	USPAT; USOCR	OR	OFF	2016/12/02 16:37

L77	699	L64 and ("dipropylene glycol" oleyl)	USPAT; USOCR	OR	OFF	2016/12/02 16:37
L78	129	L66 and ("dipropylene glycol" oleyl)	USPAT; USOCR	OR	OFF	2016/12/02 16:37
L79	15404	estradiol and transdermal	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	OFF	2016/12/02 16:37
L80	5333	L79 and ("surface area" flux)	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	OFF	2016/12/02 16:37
L81	886	L80 and acrylic and silicone and (PVP polyvinyl pyrrolidone)	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	OFF	2016/12/02 16:37
L82	34	L81 and estradiol.ab.	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	OFF	2016/12/02 16:37
L83	260	L81 and transdermal.ab.	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	OFF	2016/12/02 16:37
L84	50	L81 and (estradiol NEAR flux)	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	OFF	2016/12/02 16:37
L85	88	L79 and (estradiol NEAR flux)	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	OFF	2016/12/02 16:37
L86	257	MANTELLE.in. and JUAN.in.	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	OFF	2016/12/02 16:37
L87	42	L86 and estradiol	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	OFF	2016/12/02 16:37
L88	149	L86 and transdermal	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	OFF	2016/12/02 16:37
L89	184	Kanios.in. and David.in.	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	OFF	2016/12/02 16:37
L90	39	L89 NOT L86	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	OFF	2016/12/02 16:37
L91	0	(11/245097).APP.	USPAT; USOCR	OR	OFF	2016/12/02 16:37
L92	699	L79 and ("dipropylene glycol" oleyl)	USPAT; USOCR	OR	OFF	2016/12/02 16:37
L93	129	L81 and ("dipropylene glycol" oleyl)	USPAT; USOCR	OR	OFF	2016/12/02 16:37
L94	2	"6638528".pn.	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	OFF	2016/12/02 16:37
L95	4	"4624665".pn.	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	OFF	2016/12/02 16:37
L96	3	"20090041831".pn.	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	OFF	2016/12/02 16:37
L97	15404	estradiol and transdermal	US-PGPUB; USPAT;	OR	OFF	2016/12/02

			USOCR; FPRS; EPO; JPO; DERWENT		Parlamenta property of the Control o	16:37
L98	5333	L97 and ("surface area" flux)	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	OFF	2016/12/02 16:37
L99	886	L98 and acrylic and silicone and (PVP polyvinyl pyrrolidone)	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	OFF	2016/12/02 16:37
L100	34	L99 and estradiol.ab.	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	OFF	2016/12/02 16:37
L101	260	L99 and transdermal.ab.	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	OFF	2016/12/02 16:37
L102	50	L99 and (estradiol NEAR flux)	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	OFF	2016/12/02 16:37
L103	88	L97 and (estradiol NEAR flux)	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	OFF	2016/12/02 16:37
L104	257	MANTELLE.in. and JUAN.in.	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	OFF	2016/12/02 16:37
L105	42	L104 and estradiol	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	OFF	2016/12/02 16:37
L106	149	L104 and transdermal	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	OFF	2016/12/02 16:37
L107	184	Kanios.in. and David.in.	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	OFF	2016/12/02 16:37
L108	39	L107 NOT L104	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	OFF	2016/12/02 16:37
L109	0	(11/245097).APP.	USPAT; USOCR	OR	OFF	2016/12/02 16:37
L110	699	L97 and ("dipropylene glycol" oleyl)	USPAT; USOCR	OR	OFF	2016/12/02 16:37
L111	129	L99 and ("dipropylene glycol" oleyl)	USPAT; USOCR	OR	OFF	2016/12/02 16:37
L112	15404	estradiol and transdermal	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	OFF	2016/12/02 16:37
L113	5333	L112 and ("surface area" flux)	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	OFF	2016/12/02 16:37
L114	886	L113 and acrylic and silicone and (PVP polyvinyl pyrrolidone)	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	OFF	2016/12/02 16:37
L115	34	L114 and estradiol.ab.	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	OFF	2016/12/02 16:37
L116	260	L114 and transdermal.ab.	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	OFF	2016/12/02 16:37

L117	17 50 L114 and (estradiol NEAR flux)		US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	OFF	2016/12/02 16:37
L118	88	L112 and (estradiol NEAR flux)	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	OFF	2016/12/02 16:37
L119	257	MANTELLE.in. and JUAN.in.	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	OFF	2016/12/02 16:37
L120	0 42 L119 and estradiol		US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	OFF	2016/12/02 16:37
L121	149	L119 and transdermal	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	OFF	2016/12/02 16:37
L122	184	Kanios.in. and David.in.	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	OFF	2016/12/02 16:37
L123	39	L122 NOT L119	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	OFF	2016/12/02 16:37
L124	0	(11/245097).APP.	USPAT; USOCR	OR	OFF	2016/12/02 16:37
L125	699 L112 and ("dipropylene glycol" oleyl)		USPAT; USOCR	OR	OFF	2016/12/02 16:37
L126	129	L114 and ("dipropylene glycol" oleyl)	USPAT; USOCR	OR	OFF	2016/12/02 16:37
L129	/h/h/h/h/h/h/		US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	OFF	2016/12/02 16:37
L130	5333	L129 and ("surface area" flux)	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	OFF	2016/12/02 16:37
L131	886	L130 and acrylic and silicone and (PVP polyvinyl pyrrolidone)	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	OFF	2016/12/02 16:37
L132	34	L131 and estradiol.ab.	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	OFF	2016/12/02 16:37
L133	260	L131 and transdermal.ab.	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	OFF	2016/12/02 16:37
L134	50	L131 and (estradiol NEAR flux)	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	OFF	2016/12/02 16:37
L135	88	L129 and (estradiol NEAR flux)	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	OFF	2016/12/02 16:37
L136	257	MANTELLE.in. and JUAN.in.	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	OFF	2016/12/02 16:37
L137	42	L136 and estradiol	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	OFF	2016/12/02 16:37
L138	149	L136 and transdermal	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	OFF	2016/12/02 16:37

L139	184	Kanios.in. and David.in.	US-PGPUB; USPAT;	OR	OFF	2016/12/02
LISS	104	ranios.in. and David.in.	USOCR; FPRS; EPO; JPO; DERWENT	On	0 1	16:37
L140	39	L139 NOT L136	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	OFF	2016/12/02 16:37
L141	1 0 (11/245097).APP.		USPAT; USOCR	OR	OFF	2016/12/02 16:37
L142	699	L129 and ("dipropylene glycol" oleyl)	USPAT; USOCR	OR	OFF	2016/12/02 16:37
L143	129	L131 and ("dipropylene glycol" oleyl)	USPAT; USOCR	OR	OFF	2016/12/02 16:37
L144	15404	estradiol and transdermal	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	OFF	2016/12/02 16:37
L145	5333	L144 and ("surface area" flux)	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	OFF	2016/12/02 16:37
L146	886	L145 and acrylic and silicone and (PVP polyvinyl pyrrolidone)	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	OFF	2016/12/02 16:37
L147			US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	OFF	2016/12/02 16:37
L148	260 L146 and transdermal.ab.		US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	OFF	2016/12/02 16:37
L149	50	L146 and (estradiol NEAR flux)	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	OFF	2016/12/02 16:37
L150	88	L144 and (estradiol NEAR flux)	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	OFF	2016/12/02 16:37
L151	257	MANTELLE.in. and JUAN.in.	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	OFF	2016/12/02 16:37
L152	42	L151 and estradiol	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	OFF	2016/12/02 16:37
L153	149	L151 and transdermal	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	OFF	2016/12/02 16:37
L154	184	Kanios.in. and David.in.	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	OFF	2016/12/02 16:37
L155	39	L154 NOT L151	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	OFF	2016/12/02 16:37
L156	0	(11/245097).APP.	USPAT; USOCR	OR	OFF	2016/12/02 16:37
L157	699	L144 and ("dipropylene glycol" oleyl)	USPAT; USOCR	OR	OFF	2016/12/02 16:37
L158	129	L146 and ("dipropylene glycol" oleyl)	USPAT; USOCR	OR	OFF	2016/12/02 16:37
L159	2	"6638528".pn.	US-PGPUB; USPAT; USOCR; FPRS; EPO;	OR	OFF	2016/12/02 16:37

			JPO; DERWENT			
L160	4	"4624665".pn.	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	OFF	2016/12/02 16:37
L161	3	"20090041831".pn.	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	OFF	2016/12/02 16:37
L162	2 15404 estradiol and transdermal		US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	OFF	2016/12/02 16:37
L163	5333	L162 and ("surface area" flux)	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	OFF	2016/12/02 16:37
L164	886	L163 and acrylic and silicone and (PVP polyvinyl pyrrolidone)	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	OFF	2016/12/02 16:37
L165	34	L164 and estradiol.ab.	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	OFF	2016/12/02 16:37
L166	260	L164 and transdermal.ab.	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	OFF	2016/12/02 16:37
L167	L164 and (estradiol NEAR flux)		US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	OFF	2016/12/02 16:37
L168	88	L162 and (estradiol NEAR flux)	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	OFF	2016/12/02 16:37
L169	257	MANTELLE.in. and JUAN.in.	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	OFF	2016/12/02 16:37
L170	42	L169 and estradiol	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	OFF	2016/12/02 16:37
L171	149	L169 and transdermal	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	OFF	2016/12/02 16:37
L172	184	Kanios.in. and David.in.	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	OFF	2016/12/02 16:37
L173	39	L172 NOT L169	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	OFF	2016/12/02 16:37
L174	0	(11/245097).APP.	USPAT; USOCR	OR	OFF	2016/12/02 16:37
L175	699	L162 and ("dipropylene glycol" oleyl)	USPAT; USOCR	OR	OFF	2016/12/02 16:37
L176	129	L164 and ("dipropylene glycol" oleyl)	USPAT; USOCR	OR	OFF	2016/12/02 16:37
L177	15404	estradiol and transdermal	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	OFF	2016/12/02 16:37
L178	5333 L177 and ("surface area" flux)		US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	OFF	2016/12/02 16:37
L179	886	L178 and acrylic and	US-PGPUB; USPAT;	OR	OFF	2016/12/02

		silicone and (PVP polyvinyl pyrrolidone)	USOCR; FPRS; EPO; JPO; DERWENT		Appropriate of the control of the co	16:37
L180	34	L179 and estradiol.ab.	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	OFF	2016/12/02 16:37
L181	260	L179 and transdermal.ab.	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	OFF	2016/12/02 16:37
L182	182 50 L179 and (estradiol NEAR flux)		US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	OFF	2016/12/02 16:37
L183	183 88 L177 and (estradiol NEAR flux)		US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	OFF	2016/12/02 16:37
L184	184 257 MANTELLE.in. and JUAN.in.		US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	OFF	2016/12/02 16:37
L185	42	L184 and estradiol	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	OFF	2016/12/02 16:37
L186	149	L184 and transdermal	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	OFF	2016/12/02 16:37
L187	184	Kanios.in. and David.in.	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	OFF	2016/12/02 16:37
L188	39	L187 NOT L184	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	OFF	2016/12/02 16:37
L189	0	(11/245097).APP.	USPAT; USOCR	OR	OFF	2016/12/02 16:37
L190	699	L177 and ("dipropylene glycol" oleyl)	USPAT; USOCR	OR	OFF	2016/12/02 16:37
L191	129	L179 and ("dipropylene glycol" oleyl)	USPAT; USOCR	OR	OFF	2016/12/02 16:37
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L193	5333	L192 and ("surface area" flux)	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	OFF	2016/12/02 16:37
L194	886	L193 and acrylic and silicone and (PVP polyvinyl pyrrolidone)	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	OFF	2016/12/02 16:37
L195	95 34 L194 and estradiol.ab.		US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	OFF	2016/12/02 16:37
L196	260	L194 and transdermal.ab.	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	OFF	2016/12/02 16:37
L197	50	L194 and (estradiol NEAR flux)	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	OFF	2016/12/02 16:37
L198	88	L192 and (estradiol NEAR flux)	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	OFF	2016/12/02 16:37

L199 257		MANTELLE.in. and JUAN.in.	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	OFF	2016/12/02 16:37
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L202	02 184 Kanios.in. and David.in.		US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	OFF	2016/12/02 16:37
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L204	0	(11/245097).APP.	USPAT; USOCR	OR	OFF	2016/12/02 16:37
L205	699	L192 and ("dipropylene glycol" oleyl)	USPAT; USOCR	OR	OFF	2016/12/02 16:37
L206	129	L194 and ("dipropylene glycol" oleyl)	USPAT; USOCR	OR	OFF	2016/12/02 16:37
L207	\\\\\\.\.\.\.\.\.\.\.\		US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	OFF	2016/12/02 16:37
L208	5333 L207 and ("surface area" flux)		US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	OFF	2016/12/02 16:37
L209	886 L208 and acrylic and silicone and (PVP polyvinyl pyrrolidone)		US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	OFF	2016/12/02 16:37
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L212	50	L209 and (estradiol NEAR flux)	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	OFF	2016/12/02 16:37
L213	88	L207 and (estradiol NEAR flux)	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	OFF	2016/12/02 16:37
L214	257	MANTELLE.in. and JUAN.in.	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	OFF	2016/12/02 16:37
L215	15 42 L214 and estradiol		US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	OFF	2016/12/02 16:37
L216	16 149 L214 and transdermal		US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	OFF	2016/12/02 16:37
L217	17 184 Kanios.in. and David.in.		US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	OFF	2016/12/02 16:37
L218	39	L217 NOT L214	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	OFF	2016/12/02 16:37

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L220	699	L207 and ("dipropylene glycol" oleyl)	USPAT; USOCR	OR	OFF	2016/12/02 16:37
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L226	5333	L225 and ("surface area" flux)	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	OFF	2016/12/02 16:37
L227	886	L226 and acrylic and silicone and (PVP polyvinyl pyrrolidone)	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	OFF	2016/12/02 16:37
L228	34	34 L227 and estradiol.ab. US-PGPL USOCR; JPO; DE		OR	OFF	2016/12/02 16:37
L229	260	L227 and transdermal.ab.	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	OFF	2016/12/02 16:37
L230	50	L227 and (estradiol NEAR flux)	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	OFF	2016/12/02 16:37
L231	88	L225 and (estradiol NEAR flux)	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	OFF	2016/12/02 16:37
L232	257	MANTELLE.in. and JUAN.in.	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	OFF	2016/12/02 16:37
L233	42	L232 and estradiol	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	OFF	2016/12/02 16:37
L234	149	L232 and transdermal	US-PGPUB; USPAT; OR USOCR; FPRS; EPO; JPO; DERWENT		OFF	2016/12/02 16:37
L235	184	Kanios.in. and David.in.	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	OFF	2016/12/02 16:37
L236	39	L235 NOT L232	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	OFF	2016/12/02 16:37
L237	0	(11/245097).APP.	USPAT; USOCR	OR	OFF	2016/12/02 16:37
L238	699	L225 and ("dipropylene glycol" oleyl)	USPAT; USOCR	OR	OFF	2016/12/02 16:37
L239	129	L227 and ("dipropylene	USPAT; USOCR	OR	OFF	2016/12/02

		glycol" oleyl)				16:37
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L241	5333	L240 and ("surface area" flux)	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	OFF	2016/12/02 16:37
L242	12 886 L241 and acrylic and silicone and (PVP polyvinyl pyrrolidone)		US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	OFF	2016/12/02 16:37
L243	34	L242 and estradiol.ab.	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	OFF	2016/12/02 16:37
L244	260	L242 and transdermal.ab.	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	OFF	2016/12/02 16:37
L245	50	L242 and (estradiol NEAR flux)	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	OFF	2016/12/02 16:37
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L247	257			OR	OFF	2016/12/02 16:37
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L249	149	L247 and transdermal	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	OFF	2016/12/02 16:37
L250	184	Kanios.in. and David.in.	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	OFF	2016/12/02 16:37
L251	39	L250 NOT L247	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	OFF	2016/12/02 16:37
L252	0	(11/245097).APP.	USPAT; USOCR	OR	OFF	2016/12/02 16:37
L253	699	L240 and ("dipropylene glycol" oleyl)	USPAT; USOCR	OR	OFF	2016/12/02 16:37
L254	129	L242 and ("dipropylene glycol" oleyl)	USPAT; USOCR	OR	OFF	2016/12/02 16:37
L255	58	(("MANTELLE") near3 ("Juan")).INV.	US-PGPUB; USPAT; USOCR	OR	OFF	2016/12/02 16:37
L256	2	12/216811	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	OFF	2016/12/02 16:37
L257	1	(12/216811).APP.	USPAT; USOCR	OR	OFF	2016/12/02 16:37
L258	16305	A61K31/565.cpc.	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	AND	OFF	2016/12/02 16:37
L259	5074	A61K9/70.cpc.	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	AN D	OFF	2016/12/02 16:37

L260	33	L258 L259	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	AND	OFF	2016/12/02 16:37
L261	8	L260 and estradiol	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	AND	OFF	2016/12/02 16:37

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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

BIB DATA SHEET

CONFIRMATION NO. 3635

SERIAL NUME	BER	FILING or 371(c) DATE		CLASS	GROUP ART	UNIT	ROUP ART UNIT ATTORNEY DOCKE NO.				
13/553,972	2	07/20/2012		424	1611	1611)41457-0992			
		RULE									
APPLICANTS											
INVENTORS Juan Mantelle, Miami, FL;											
	** CONTINUING DATA ***********************************										
** FOREIGN AP	PLICA	TIONS ***********	*****	*							
** IF REQUIRED 07/31/2012		EIGN FILING LICENS	E GRA	ANTED **							
Foreign Priority claimed		Yes No	G	STATE OR	SHEETS	TOT		INDEPENDENT			
35 USC 119(a-d) condition Verified and /N	//FLISSAI	JAVIER/	ance	COUNTRY	DRAWINGS	CLAII		CLAIMS			
Acknowledged E	xaminer's	Signature Initials		FL	1	16	5	4			
ADDRESS											
Foley & La 3000 K ST											
SUITE 600		IN.VV.									
WASHING UNITED S		DC 20007-5109									
TITLE	TAIL	,									
TRANSDE	RMAL	ESTROGEN DEVICE	AND [DELIVERY							
					☐ All Fe	es					
					☐ 1.16 F	ees (Fil	ina)				
	FILING FEE FEES: Authority has been given in Paper										
	RECEIVED No to charge/credit DEPOSIT ACCOUNT 1.17 Fees (Processing Ext. of time) No to charge/credit DEPOSIT ACCOUNT 1.18 Fees (Issue)										
2010	2540 Other										
					☐ Credit						
					0.00m						

Search Notes



Application/Control No.	Applicant(s)/Patent Under Reexamination
13553972	MANTELLE, JUAN
Examiner	Art Unit
MELISSA JAVIER	1611

CPC- SEARCHED		
Symbol	Date	Examiner

CPC COMBINATION SETS - SEARCHED							
Symbol Date Examiner							

US CLASSIFICATION SEARCHED						
Class	Subclass	Date	Examiner			

SEARCH NOTES						
Search Notes	Date	Examiner				
EAST search (see attached history)	8/25/2013	MJ				
Inventor search in EAST	8/25/2013	MJ				
Google Scholar search (keywords used: transdermal monolithic estradiol)	8/25/2013	MJ				
Updated EAST search	2/21/2014	MJ				
Updated Google Scholar search	2/21/2014	MJ				
Updated EAST search	4/29/2015	MJ				
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Updated EAST search	8/22/2016	MJ				
Updated Google Scholar search	8/22/2016	MJ				
(A61K31/565 A61K9/70).cpc. and estradiol	8/22/2016	MJ				
Updated EAST search	12/2/2016	MJ				
Updated Google Scholar search	12/2/2016	MJ				
(A61K31/565 A61K9/70).cpc. and estradiol	12/2/2016	MJ				

/M.J./ Examiner.Art Unit 1611	

INTERFERENCE SEARCH						
US Class/ CPC Symbol	US Subclass / CPC Group	Date	Examiner			
_	(monolith\$2 estradiol transdermal adhesive coat weight flux).clm.	9/28/2015	MJ			
	(monolith\$2 estradiol transdermal system adhesive coat weight flux).clm.	8/22/2016	MJ			
	(monolith\$2 estradiol transdermal system adhesive coat weight flux).clm.	12/2/2016	MJ			

U.S. Patent and Trademark Office Part of Paper No.: 20161202



Atty. Dkt. No. 041457-0992

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

First Inventor Name:

Juan Mantelle

Title:

Transdermal Estrogen Device and Delivery

Appl. No.:

13/553,972

Appl. Filing Date:

7/20/2012

Examiner:

Melissa L. Javier

Art Unit:

1611

Confirmation Number:

3635

REQUEST FOR CONTINUED EXAMINATION (RCE) TRANSMITTAL

Mail Stop RCE Commissioner for Patents P.O. Box 1450 Alexandria, VA 22313-1450

Commissioner:

This is a Request for Continued Examination (RCE) under 37 C.F.R. § 1.114 of the above-identified application. This RCE and the enclosed items listed below are being filed prior to the earliest of: (1) payment of the issue fee (unless a petition under 37 C.F.R. § 1.313 is granted); (2) abandonment of the application; or (3) the filing of a notice of appeal to the U.S. Court of Appeals for the Federal Circuit under 35 U.S.C. §141, or the commencement of a civil action under 35 U.S.C. §145 or §146 (unless the appeal or civil action is terminated).

03/09/2017 SMOHAMME 00000002 13553972 01 FC:1820 1700.00 OP

Submission required under 37 C.F.R. §1.114:

- [X] Information Disclosure Statement.
- [X] Form PTO/SB/08 with copies of 3 listed reference(s).

The filing fee is calculated below at the large entity rate:

	Claims as Amended		viously d For		Extra Claims Present	,	Rate		Fee Totals
RCE Fee 1.17(e):							\$1,700.0	=	\$1,700.00
							0		
Total Claims:	13	-	26	=	0	x	\$80.00	=	\$0.00
Independents	3	-	5	===	0	x	\$420.00	=	\$0.00
First p	resentation of	any M	ultiple I	Depe	ndent Claims:	+	\$780.00	=	\$0.00
				RCE	and CLAIMS	FEE	TOTAL:	_	\$1,700.00

The above-identified fees of \$1700.00 are being paid by credit card via EFS-Web.

The Commissioner is hereby authorized to charge any additional fees which may be required regarding this application under 37 C.F.R. §§ 1.16-1.17, or credit any overpayment, to Deposit Account No. 19-0741. Should no proper payment be enclosed herewith, as by the credit card payment instructions in EFS-Web being incorrect or absent, resulting in a rejected or incorrect credit card transaction, the Commissioner is authorized to charge the unpaid amount to Deposit Account No. 19-0741.

Please direct all correspondence to the undersigned attorney or agent at the address indicated below.

Respectfully submitted,

By Conf CMM

Date March 8,207

FOLEY & LARDNER LLP Customer Number: 22428 Telephone: (202) 295-4094

Facsimile: (202) 672-5399

Courtenay C. Brinckerhoff Attorney for Applicant

Registration No. 37,288



IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

First Inventor Name: Juan Mantelle

Title: Transdermal Estrogen Device

and Delivery

Application No.: 13/553972

Filing Date: 7/20/2012

Examiner: Melissa L. Javier

Art Unit: 1611

Confirmation No.: 3635

<u>UNDER 37 CFR §1.56</u>

Commissioner for Patents P.O. Box 1450 Alexandria, VA 22313-1450

Commissioner:

Applicant submits herewith documents for the Examiner's consideration in accordance with 37 CFR §§1.56, 1.97 and 1.98.

Applicant respectfully requests that each listed document be considered by the Examiner and be made of record in the present application and that an initialed copy of Form PTO/SB/08 be returned in accordance with MPEP §609.

The submission of any document herewith is not an admission that such document constitutes prior art against the claims of the present application or that such document is considered material to patentability as defined in 37 CFR §1.56(b). Applicant does not waive any rights to take any action which would be appropriate to antedate or otherwise remove as a competent reference any document submitted herewith.

TIMING OF THE DISCLOSURE

The listed documents are being submitted in compliance with 37 CFR §1.97(b), before the mailing of a first Office action after the filing of a RCE.

RELEVANCE OF LISTED DOCUMENTS

Documents A1 and A2 are Office Actions which were issued in the child applications.

Document A3 is a Decision issued in an Opposition of a corresponding European patent. Although the patent was revoked because certain claim language not present in the pending claims was found to constitute an impermissible generalization of the original disclosure, the EPO Opposition Division rejected the Opponent's prior art and enablement-type arguments.

Although Applicant believes that no fee is required, the Commissioner is hereby authorized to charge any additional fees which may be due to Deposit Account Number 19-0741.

Respectfully submitted,

By aig com

Date Maich 8, 2M

FOLEY & LARDNER LLP Customer Number: 22428

Telephone: (202) 295-4094

Facsimile: (202) 672-5399

Courtenay C. Brinckerhoff

Attorney for Applicant

Registration No. 37,288

Substitute for form 1449/PTO

INFORMATION DISCLOSURE STATEMENT BY APPLICANT

Date Submitted: March 8, 2017

(use as many sheets as necessary)

Sheet 1 of 1

***		PTO/SB/98 (modified)
	Complete if Known	CIPAD
Application Number	13/553972	/
Filing Date	7/20/2012	MAR 0 8 2017 2
First Named Inventor	Juan Mantelle	2 . /
Art Unit	1611	The state of the s
Examiner Name	Melissa L. Javier	RADEMARKU
Attorney Docket Number	041457-0992	

U.S. PATENT DOCUMENTS								
Examiner Initials*	Cite No. ¹	Document Number Number-Kind Code ² (if known)	Publication Date MM-DD-YYYY	Name of Patentee or Applicant of Cited Document	Pages, Columns, Lines, Where Relevant Passages or Relevant Figures Appear			

	UNPUBLISHED U.S. PATENT APPLICATION DOCUMENTS						
Examiner Initials*	Cite No. ¹	U.S. Patent Application Document Serial Number-Kind Code ² (if known)	Filing Date of Cited Document MM-DD-YYYY	Name of Patentee or Applicant of Cited Document	Pages, Columns, Lines, Where Relevant Passages or Relevant Figures Appear		

	FOREIGN PATENT DOCUMENTS						
Examiner Initials*	Cite No.1	Foreign Patent Document Country Code ³ Number ⁴ Kind Code ⁵ (if known)	Publication Date MM-DD-YYYY	Name of Patentee or Applicant of Cited Documents	Pages, Columns, Lines, Where Relevant Passages or Relevant Figures Appear	Τ6	

	NON PATENT LITERATURE DOCUMENTS				
Examiner Initials*	Cite No. ¹	Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc.) date, page(s), volume-issue number(s), publisher, city and/or country where published.	T⁰		
	A1	Notice of Allowance issued on 01/10/2017 in application number 14/024,985 (US 2014-0200530)			
	A2	Office Action issued on 09/07/2016 in application number 14/870,574 (US 2016-0015655)			
	A3	European Office Action issued on 02/14/2017 in application number EP 09790211.8			

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Examiner Signature	Date Considered	
Cignatare	00	



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NOTICE OF ALLOWANCE AND FEE(S) DUE

03/23/2017 Foley & Lardner LLP 3000 K STREET N.W. SUITE 600 WASHINGTON, DC 20007-5109

EXAMINER FISHER, MELISSA L ART UNIT PAPER NUMBER

1611 DATE MAILED: 03/23/2017

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
13/553,972	07/20/2012	Juan Mantelle	041457-0992	3635

TITLE OF INVENTION: TRANSDERMAL ESTROGEN DEVICE AND DELIVERY

APPLN. TYPE	ENTITY STATUS	ISSUE FEE DUE	PUBLICATION FEE DUE	PREV. PAID ISSUE FEE	TOTAL FEE(S) DUE	DATE DUE
nonprovisional	UNDISCOUNTED	\$960	\$0	\$0	\$960	06/23/2017

THE APPLICATION IDENTIFIED ABOVE HAS BEEN EXAMINED AND IS ALLOWED FOR ISSUANCE AS A PATENT. PROSECUTION ON THE MERITS IS CLOSED. THIS NOTICE OF ALLOWANCE IS NOT A GRANT OF PATENT RIGHTS. THIS APPLICATION IS SUBJECT TO WITHDRAWAL FROM ISSUE AT THE INITIATIVE OF THE OFFICE OR UPON PETITION BY THE APPLICANT. SEE 37 CFR 1.313 AND MPEP 1308.

THE ISSUE FEE AND PUBLICATION FEE (IF REQUIRED) MUST BE PAID WITHIN THREE MONTHS FROM THE MAILING DATE OF THIS NOTICE OR THIS APPLICATION SHALL BE REGARDED AS ABANDONED. STATUTORY PERIOD CANNOT BE EXTENDED. SEE 35 U.S.C. 151. THE ISSUE FEE DUE INDICATED ABOVE DOES NOT REFLECT A CREDIT FOR ANY PREVIOUSLY PAID ISSUE FEE IN THIS APPLICATION. IF AN ISSUE FEE HAS PREVIOUSLY BEEN PAID IN THIS APPLICATION (AS SHOWN ABOVE), THE RETURN OF PART B OF THIS FORM WILL BE CONSIDERED A REQUEST TO REAPPLY THE PREVIOUSLY PAID ISSUE FEE TOWARD THE ISSUE FEE NOW DUE.

HOW TO REPLY TO THIS NOTICE:

I. Review the ENTITY STATUS shown above. If the ENTITY STATUS is shown as SMALL or MICRO, verify whether entitlement to that entity status still applies.

If the ENTITY STATUS is the same as shown above, pay the TOTAL FEE(S) DUE shown above.

If the ENTITY STATUS is changed from that shown above, on PART B - FEE(S) TRANSMITTAL, complete section number 5 titled "Change in Entity Status (from status indicated above)".

For purposes of this notice, small entity fees are 1/2 the amount of undiscounted fees, and micro entity fees are 1/2 the amount of small entity

II. PART B - FEE(S) TRANSMITTAL, or its equivalent, must be completed and returned to the United States Patent and Trademark Office (USPTO) with your ISSUE FEE and PUBLICATION FEE (if required). If you are charging the fee(s) to your deposit account, section "4b" of Part B - Fee(s) Transmittal should be completed and an extra copy of the form should be submitted. If an equivalent of Part B is filed, a request to reapply a previously paid issue fee must be clearly made, and delays in processing may occur due to the difficulty in recognizing the paper as an equivalent of Part B.

III. All communications regarding this application must give the application number. Please direct all communications prior to issuance to Mail Stop ISSUE FEE unless advised to the contrary.

IMPORTANT REMINDER: Utility patents issuing on applications filed on or after Dec. 12, 1980 may require payment of maintenance fees. It is patentee's responsibility to ensure timely payment of maintenance fees when due.

PART B - FEE(S) TRANSMITTAL

Complete and send this form, together with applicable fee(s), to: Mail Mail Stop ISSUE FEE

Mail Stop ISSUE FEE Commissioner for Patents P.O. Box 1450 Alexandria, Virginia 22313-1450

or <u>Fax</u> (571)-273-2885

INSTRUCTIONS: This form should be used for transmitting the ISSUE FEE and PUBLICATION FEE (if required). Blocks 1 through 5 should be completed where appropriate. All further correspondence including the Patent, advance orders and notification of maintenance fees will be mailed to the current correspondence address as indicated unless corrected below or directed otherwise in Block 1, by (a) specifying a new correspondence address; and/or (b) indicating a separate "FEE ADDRESS" for maintenance fee notifications.

maintenance fee notifica	tions.	(, - <u>F</u> ,		,		
CURRENT CORRESPOND	ENCE ADDRESS (Note: Use Bl	ock 1 for any change of address)		Fee(s) Transmi	ittal This c	ertificate cannot be used f	or domestic mailings of the for any other accompanying ent or formal drawing, must
Foley & Lardn 3000 K STREE SUITE 600		/2017		I hereby certify States Postal S addressed to t transmitted to t	Certifiy that this I ervice with he Mail St the USPTO	icate of Mailing or Trans Fee(s) Transmittal is being a sufficient postage for fir top ISSUE FEE address (571) 273-2885, on the di	mission g deposited with the United st class mail in an envelope above, or being facsimile ate indicated below.
	N, DC 20007-5109						(Depositor's name)
	,						(Signature)
							(Date)
APPLICATION NO.	FILING DATE		FIRST NAMED INVEN	TOR	A	TTORNEY DOCKET NO.	CONFIRMATION NO.
13/553,972	07/20/2012		Juan Mantelle			041457-0992	3635
TITLE OF INVENTION	I: TRANSDERMAL EST	TROGEN DEVICE AND	DELIVERY				
APPLN. TYPE	ENTITY STATUS	ISSUE FEE DUE	PUBLICATION FEE D	UE PREV. PA	ID ISSUE F	EE TOTAL FEE(S) DUE	DATE DUE
nonprovisional	UNDISCOUNTED	\$960	\$0		\$0	\$960	06/23/2017
EXAM	IINER	ART UNIT	CLASS-SUBCLASS				
FISHER, M	ÆLISSA L	1611	424-487000				
CFR 1.363). Change of corresp Address form PTO/Sl "Fee Address" ind	ence address or indication condence address (or Cha B/122) attached. lication (or "Fee Address' 32 or more recent) attached.	nge of Correspondence	2. For printing on t (1) The names of a or agents OR, alter (2) The name of a registered attorney 2 registered patent listed, no name wil	up to 3 registered natively, single firm (have or agent) and the attorneys or agent	ed patent a		
3. ASSIGNEE NAME A	ND RESIDENCE DATA	A TO BE PRINTED ON	THE PATENT (print o	r type)			
PLEASE NOTE: Un recordation as set fort	less an assignee is ident ih in 37 CFR 3.11. Comr	ified below, no assignee pletion of this form is NO	data will appear on the	ne patent. If an	n assignee	is identified below, the d	ocument has been filed for
(A) NAME OF ASSI		, 	(B) RESIDENCE: (C	_			
Please check the appropr	riate assignee category or	categories (will not be pr	rinted on the patent):	☐ Individual	l 🖵 Corpo	oration or other private gro	oup entity 📮 Government
4a. The following fee(s)	are submitted:	41	b. Payment of Fee(s): (Please first rea	apply any i	previously paid issue fee	shown above)
☐ Issue Fee			A check is enclos		-FF-33 I	Freeze and Freeze and Tree	210 H1 10 10 10 1
	No small entity discount p		Payment by credi				
■ Advance Order - ‡	of Copies		The director is her overpayment, to I	reby authorized Deposit Accoun	to charge t t Number _	the required fee(s), any de (enclose a	ficiency, or credits any n extra copy of this form).
	itus (from status indicated ng micro entity status. Se		NOTE: Absent a vali	d certification of	of Micro Er	ntity Status (see forms PT	O/SB/15A and 15B), issue application abandonment.
Applicant asserting	g small entity status. See	37 CFR 1.27	1 2	tion was previo	ously under	micro entity status, check	11
Applicant changing	ng to regular undiscounted	d fee status.		s box will be ta		notification of loss of enti	itlement to small or micro
NOTE: This form must b	oe signed in accordance v	vith 37 CFR 1.31 and 1.3	3. See 37 CFR 1.4 for s	signature requir	rements and	d certifications.	
Authorized Signature				Date _			
Typed or printed nam	e			Regist	tration No.		

Page 2 of 3



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.
13/553,972	07/20/2012	Juan Mantelle	041457-0992	3635
22428 75	90 03/23/2017		EXAM	INER
Foley & Lardner			FISHER, M	ELISSA L
3000 K STREET N SUITE 600	N.W.		ART UNIT	PAPER NUMBER
WASHINGTON, I	OC 20007-5109		1611	
			DATE MAILED: 03/23/201	7

Determination of Patent Term Adjustment under 35 U.S.C. 154 (b)

(Applications filed on or after May 29, 2000)

The Office has discontinued providing a Patent Term Adjustment (PTA) calculation with the Notice of Allowance.

Section 1(h)(2) of the AIA Technical Corrections Act amended 35 U.S.C. 154(b)(3)(B)(i) to eliminate the requirement that the Office provide a patent term adjustment determination with the notice of allowance. See Revisions to Patent Term Adjustment, 78 Fed. Reg. 19416, 19417 (Apr. 1, 2013). Therefore, the Office is no longer providing an initial patent term adjustment determination with the notice of allowance. The Office will continue to provide a patent term adjustment determination with the Issue Notification Letter that is mailed to applicant approximately three weeks prior to the issue date of the patent, and will include the patent term adjustment on the patent. Any request for reconsideration of the patent term adjustment determination (or reinstatement of patent term adjustment) should follow the process outlined in 37 CFR 1.705.

Any questions regarding the Patent Term Extension or Adjustment determination should be directed to the Office of Patent Legal Administration at (571)-272-7702. Questions relating to issue and publication fee payments should be directed to the Customer Service Center of the Office of Patent Publication at 1-(888)-786-0101 or (571)-272-4200.

OMB Clearance and PRA Burden Statement for PTOL-85 Part B

The Paperwork Reduction Act (PRA) of 1995 requires Federal agencies to obtain Office of Management and Budget approval before requesting most types of information from the public. When OMB approves an agency request to collect information from the public, OMB (i) provides a valid OMB Control Number and expiration date for the agency to display on the instrument that will be used to collect the information and (ii) requires the agency to inform the public about the OMB Control Number's legal significance in accordance with 5 CFR 1320.5(b).

The information collected by PTOL-85 Part B is required by 37 CFR 1.311. 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 1.14. 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, Virginia 22313-1450. DO NOT SEND FEES OR COMPLETED FORMS TO THIS ADDRESS. SEND TO: Commissioner for Patents, P.O. Box 1450, Alexandria, Virginia 22313-1450. Under the Paperwork Reduction Act of 1995, no persons are required to respond to a collection of information unless it displays a valid OMB control number.

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.

	Application No.	Applicant(s)	
	13/553,972	MANTELLE,	JUAN
Notice of Allowability	Examiner Melissa Javier	Art Unit 1611	AIA (First Inventor to File) Status No

The MAILING DATE of this communication appears on the All claims being allowable, PROSECUTION ON THE MERITS IS (OR REM herewith (or previously mailed), a Notice of Allowance (PTOL-85) or other a NOTICE OF ALLOWABILITY IS NOT A GRANT OF PATENT RIGHTS. Tof the Office or upon petition by the applicant. See 37 CFR 1.313 and MPE	AINS) CLOSED in this application. If not included appropriate communication will be mailed in due course. THIS his application is subject to withdrawal from issue at the initiative
1. This communication is responsive to <u>3/8/2017</u> .	
A declaration(s)/affidavit(s) under 37 CFR 1.130(b) was/were filed	d on
 An election was made by the applicant in response to a restriction recrequirement and election have been incorporated into this action. 	uirement set forth during the interview on; the restriction
 The allowed claim(s) is/are <u>14,16,17,21-26,28,29 and 31-40</u>. As a res the Patent Prosecution Highway program at a participating intellectu information, please see http://www.uspto.gov/patents/init_events/pph/ 	ual property office for the corresponding application. For more
4. Acknowledgment is made of a claim for foreign priority under 35 U.S.	C. § 119(a)-(d) or (f).
Certified copies:	
a) All b) Some *c) None of the:	
1. Certified copies of the priority documents have been rec	
2. Certified copies of the priority documents have been rec	
3. Copies of the certified copies of the priority documents h	nave been received in this national stage application from the
International Bureau (PCT Rule 17.2(a)). * Certified copies not received:	
Certified copies flot received:	
Applicant has THREE MONTHS FROM THE "MAILING DATE" of this connoted below. Failure to timely comply will result in ABANDONMENT of the THIS THREE-MONTH PERIOD IS NOT EXTENDABLE.	
5. CORRECTED DRAWINGS (as "replacement sheets") must be subm	itted.
including changes required by the attached Examiner's Amendn Paper No./Mail Date	nent / Comment or in the Office action of
Identifying indicia such as the application number (see 37 CFR 1.84(c)) sho each sheet. Replacement sheet(s) should be labeled as such in the header	
 DEPOSIT OF and/or INFORMATION about the deposit of BIOLOGIC attached Examiner's comment regarding REQUIREMENT FOR THE D 	
Attachment(s)	
1. Notice of References Cited (PTO-892)	5. ⊠ Examiner's Amendment/Comment
2. Information Disclosure Statements (PTO/SB/08),	6. ☐ Examiner's Statement of Reasons for Allowance
Paper No./Mail Date 3.	7. Other
4. ☐ Interview Summary (PTO-413), Paper No./Mail Date	
/Melissa Javier/ Primary Examiner, Art Unit 1611	

U.S. Patent and Trademark Office PTOL-37 (Rev. 08-13) 20170318

Notice of Allowability

Part of Paper No./Mail Date

DETAILED ACTION

The present application is being examined under the pre-AIA first to invent provisions.

Continued Examination Under 37 CFR 1.114

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after allowance or after an Office action under *Ex Parte Quayle*, 25 USPQ 74, 453 O.G. 213 (Comm'r Pat. 1935). Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, prosecution in this application has been reopened pursuant to 37 CFR 1.114. Applicant's submission filed on 3/8/2017 has been entered.

Information Disclosure Statement

The Information Disclosure Statement (IDS) filed 3/8/2017 has been considered by the examiner.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Melissa Javier whose telephone number is (571)270-7430. The examiner can normally be reached on Monday-Friday, 8am-5pm.

Art Unit: 1611

Examiner interviews are available via telephone, in-person, and video conferencing using a USPTO supplied web-based collaboration tool. To schedule an interview, applicant is encouraged to use the USPTO Automated Interview Request (AIR) at http://www.uspto.gov/interviewpractice.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Bethany Barham can be reached on 571-272-6175. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Melissa Javier/ Primary Examiner, Art Unit 1611

Issue Classification



Application/Control No.	Applicant(s)/Patent Under Reexamination
13553972	MANTELLE, JUAN
Examiner	Art Unit
MELISSA JAVIER	1611

CPC							
Symbol				Туре	Version		
A61K	9	7069		F	2013-01-01		
A61K	9	7061		I	2013-01-01		
A61K	31	/ 565		I	2013-01-01		
A61K	47	/ 10		I	2013-01-01		
A61K	47	/ 32		I	2013-01-01		
A61K	9	/ 0014		I	2013-01-01		
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CPC Combination Sets				
Symbol	Туре	Set	Ranking	Version

		Total Clain	ns Allowed:
(Assistant Examiner)	(Date)	21	
/MELISSA JAVIER/ Primary Examiner.Art Unit 1611	03/18/2017	O.G. Print Claim(s)	O.G. Print Figure
(Primary Examiner)	(Date)	1	None

U.S. Patent and Trademark Office Part of Paper No. 20170318

Issue Classification

Application/Control No.	Applicant(s)/Patent Under Reexamination
13553972	MANTELLE, JUAN
Examiner	Art Unit
MELISSA JAVIER	1611

US ORIGINAL CLASSIFICATION					INTERNATIONAL CLASSIFICAT						ATION		
CLASS SUBCLASS							С	LAIMED		NC	ON-CLAIMED		
						Α	6	1	К	31 / 565 (2006.01.01)			
	CR	OSS REF	-BENCE(S)		Α	6	1	К	9 / 70 (2006.01.01)			
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		Total Claims Allowed:		
(Assistant Examiner)	(Date)	21		
/MELISSA JAVIER/ Primary Examiner.Art Unit 1611	03/18/2017	O.G. Print Claim(s)	O.G. Print Figure	
(Primary Examiner)	(Date)	1	None	

U.S. Patent and Trademark Office Part of Paper No. 20170318

Issue Classification



Application/Control No.	Applicant(s)/Patent Under Reexamination
13553972	MANTELLE, JUAN
Examiner	Art Unit
MELISSA JAVIER	1611

☐ Claims renumbered in the same order as presented by applicant ☐ CPA ☒ T.D. ☐ R.1.47															
Final	Original	Final	Original	Final	Original	Final	Original	Final	Original	Final	Original	Final	Original	Final	Origina
	1	16	17	12	33										
	2		18	13	34										
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	4		20	17	36										
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	11		27												
	12	8	28												
	13	9	29												
1	14		30												
	15	10	31												
15	16	11	32												

		Total Claims Allowed:		
(Assistant Examiner)	(Date)	21		
/MELISSA JAVIER/ Primary Examiner.Art Unit 1611	03/18/2017	O.G. Print Claim(s)	O.G. Print Figure	
(Primary Examiner)	(Date)	1	None	

U.S. Patent and Trademark Office Part of Paper No. 20170318

EAST Search History

EAST Search History (Prior Art)

Ref #	Hits	Search Query	DBs	Default Operator	Plurals	Time Stamp
L1	15742	estradiol and transdermal	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	OFF	2017/03/18 12:01
L2	5455	L1 and ("surface area" flux)	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	OFF	2017/03/18 12:01
L3	916	L2 and acrylic and silicone and (PVP polyvinyl pyrrolidone)	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	OFF	2017/03/18 12:01
L4	35	L3 and estradiol.ab.	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	OFF	2017/03/18 12:01
L5	262	L3 and transdermal.ab.	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	OFF	2017/03/18 12:01
L6	51	L3 and (estradiol NEAR flux)	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	OFF	2017/03/18 12:01
L7	90	L1 and (estradiol NEAR flux)	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	OFF	2017/03/18 12:01
L8	259	MANTELLE.in. and JUAN.in.	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	OFF	2017/03/18 12:01
L9	42	L8 and estradiol	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	OFF	2017/03/18 12:01
L10	151	L8 and transdermal	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	OFF	2017/03/18 12:01
L11	186	Kanios.in. and David.in.	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	OFF	2017/03/18 12:01
L12	40	L11 NOT L8	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	OFF	2017/03/18 12:01
L13	0	(11/245097).APP.	USPAT; USOCR	OR	OFF	2017/03/18 12:01
L14	714	L1 and ("dipropylene glycol" oleyl)	USPAT; USOCR	OR	OFF	2017/03/18 12:01
L15	132	L3 and ("dipropylene glycol" oleyl)	USPAT; USOCR	OR	OFF	2017/03/18 12:01
L16	15742	estradiol and transdermal	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	OFF	2017/03/18 12:01
L17	5455	L16 and ("surface area" flux)	US-PGPUB; USPAT; USOCR; FPRS; EPO;	OR	OFF	2017/03/18 12:01

			JPO; DERWENT			
L18	916	L17 and acrylic and silicone and (PVP polyvinyl pyrrolidone)	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	OFF	2017/03/18 12:01
L19	35	L18 and estradiol.ab.	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	OFF	2017/03/18 12:01
L20	262	L18 and transdermal.ab.	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	OFF	2017/03/18 12:01
L21	51	L18 and (estradiol NEAR flux)	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	OFF	2017/03/18 12:01
L22	90	L16 and (estradiol NEAR flux)	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	OFF	2017/03/18 12:01
L23	259	MANTELLE.in. and JUAN.in.	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	OFF	2017/03/18 12:01
L24	42	L23 and estradiol	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	OFF	2017/03/18 12:01
L25	151	L23 and transdermal	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	OFF	2017/03/18 12:01
L26	186	Kanios.in. and David.in.	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	OFF	2017/03/18 12:01
L27	40	L26 NOT L23	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	OFF	2017/03/18 12:01
L28	0	(11/245097).APP.	USPAT; USOCR	OR	OFF	2017/03/18 12:01
L29	714	L16 and ("dipropylene glycol" oleyl)	USPAT; USOCR	OR	OFF	2017/03/18 12:01
L30	132	L18 and ("dipropylene glycol" oleyl)	USPAT; USOCR	OR	OFF	2017/03/18 12:01
L31	2	"6638528".pn.	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	OFF	2017/03/18 12:01
L32	4	"4624665".pn.	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	OFF	2017/03/18 12:01
L33	3	"20090041831".pn.	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	OFF	2017/03/18 12:01
L34	15742	estradiol and transdermal	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	OFF	2017/03/18 12:01
L35	5455	L34 and ("surface area" flux)	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	OFF	2017/03/18 12:01
L36	916	L35 and acrylic and silicone and (PVP polyvinyl pyrrolidone)	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	OFF	2017/03/18 12:01
L37	35	L36 and estradiol.ab.	US-PGPUB; USPAT;	OR	OFF	2017/03/18

			USOCR; FPRS; EPO; JPO; DERWENT			12:01
L38	262	L36 and transdermal.ab.	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	OFF	2017/03/18 12:01
L39	51	L36 and (estradiol NEAR flux)	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	OFF	2017/03/18 12:01
L40	90	L34 and (estradiol NEAR flux)	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	OFF	2017/03/18 12:01
L41	259	MANTELLE.in. and JUAN.in.	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	OFF	2017/03/18 12:01
L42	42	L41 and estradiol	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	OFF	2017/03/18 12:01
L43	151	L41 and transdermal	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	OFF	2017/03/18 12:01
L44	186	Kanios.in. and David.in.	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	OFF	2017/03/18 12:01
L45	40	L44 NOT L41	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	OFF	2017/03/18 12:01
L46	0	(11/245097). A PP.	USPAT; USOCR	OR	OFF	2017/03/18 12:01
L47	714	L34 and ("dipropylene glycol" oleyl)	USPAT; USOCR	OR	OFF	2017/03/18 12:01
L48	132	L36 and ("dipropylene glycol" oleyl)	USPAT; USOCR	OR	OFF	2017/03/18 12:01
L49	15742	estradiol and transdermal	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	OFF	2017/03/18 12:01
L50	5455	L49 and ("surface area" flux)	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	OFF	2017/03/18 12:01
L51	916	L50 and acrylic and silicone and (PVP polyvinyl pyrrolidone)	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	OFF	2017/03/18 12:01
L52	35	L51 and estradiol.ab.	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	OFF	2017/03/18 12:01
L53	262	L51 and transdermal.ab.	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	OFF	2017/03/18 12:01
L54	51	L51 and (estradiol NEAR flux)	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	OFF	2017/03/18 12:01
L55	90	L49 and (estradiol NEAR flux)	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	OFF	2017/03/18 12:01
L56	259	MANTELLE.in. and JUAN.in.	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	OFF	2017/03/18 12:01

L57	42	L56 and estradiol	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	OFF	2017/03/18 12:01
L58	151	L56 and transdermal	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	OFF	2017/03/18 12:02
L59	186	Kanios.in. and David.in.	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	OFF	2017/03/18 12:02
L60	40	L59 NOT L56	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	OFF	2017/03/18 12:02
L61	0	(11/245097).APP.	USPAT; USOCR	OR	OFF	2017/03/18 12:02
L62	714	L49 and ("dipropylene glycol" oleyl)	USPAT; USOCR	OR	OFF	2017/03/18 12:02
L63	132	L51 and ("dipropylene glycol" oleyl)	USPAT; USOCR	OR	OFF	2017/03/18 12:02
L64	15742	estradiol and transdermal	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	OFF	2017/03/18 12:02
L65	5455	L64 and ("surface area" flux)	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	OFF	2017/03/18 12:02
L66	916	L65 and acrylic and silicone and (PVP polyvinyl pyrrolidone)	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	OFF	2017/03/18 12:02
L67	35	L66 and estradiol.ab.	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	OFF	2017/03/18 12:02
L68	262	L66 and transdermal.ab.	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	OFF	2017/03/18 12:02
L69	51	L66 and (estradiol NEAR flux)	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	OFF	2017/03/18 12:02
L70	90	L64 and (estradiol NEAR flux)	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	OFF	2017/03/18 12:02
L71	259	MANTELLE.in. and JUAN.in.	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	OFF	2017/03/18 12:02
L72	42	L71 and estradiol	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	OFF	2017/03/18 12:02
L73	151	L71 and transdermal	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	OFF	2017/03/18 12:02
L74	186	Kanios.in. and David.in.	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	OFF	2017/03/18 12:02
L75	40	L74 NOT L71	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	OFF	2017/03/18 12:02
L76	0	(11/245097).APP.	USPAT; USOCR	OR	OFF	2017/03/18 12:02

L77	714	L64 and ("dipropylene glycol" oleyl)	USPAT; USOCR	OR	OFF	2017/03/18 12:02
L78	132	L66 and ("dipropylene glycol" oleyl)	USPAT; USOCR	OR	OFF	2017/03/18 12:02
L79	15742	estradiol and transdermal	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	OFF	2017/03/18 12:02
L80	5455	L79 and ("surface area" flux)	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	OFF	2017/03/18 12:02
L81	916	L80 and acrylic and silicone and (PVP polyvinyl pyrrolidone)	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	OFF	2017/03/18 12:02
L82	35	L81 and estradiol.ab.	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	OFF	2017/03/18 12:02
L83	262	L81 and transdermal.ab.	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	OFF	2017/03/18 12:02
L84	51	L81 and (estradiol NEAR flux)	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	OFF	2017/03/18 12:02
L85	90	L79 and (estradiol NEAR flux)	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	OFF	2017/03/18 12:02
L86	259	MANTELLE.in. and JUAN.in.	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	OFF	2017/03/18 12:02
L87	42	L86 and estradiol	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	OFF	2017/03/18 12:02
L88	151	L86 and transdermal	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	OFF	2017/03/18 12:02
L89	186	Kanios.in. and David.in.	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	OFF	2017/03/18 12:02
L90	40	L89 NOT L86	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	OFF	2017/03/18 12:02
L91	0	(11/245097).APP.	USPAT; USOCR	OR	OFF	2017/03/18 12:02
L92	714	L79 and ("dipropylene glycol" oleyl)	USPAT; USOCR	OR	OFF	2017/03/18 12:02
L93	132	L81 and ("dipropylene glycol" oleyl)	USPAT; USOCR	OR	OFF	2017/03/18 12:02
L94	2	"6638528".pn.	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	OFF	2017/03/18 12:02
L95	4	"4624665".pn.	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	OFF	2017/03/18 12:02
L96	3	"20090041831".pn.	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	OFF	2017/03/18 12:02
L97	15742	estradiol and transdermal	US-PGPUB; USPAT;	OR	OFF	2017/03/18

			USOCR; FPRS; EPO; JPO; DERWENT		Parameter Control	12:02
L98	5455	L97 and ("surface area" flux)	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	OFF	2017/03/18 12:02
L99	916	L98 and acrylic and silicone and (PVP polyvinyl pyrrolidone)	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	OFF	2017/03/18 12:02
L100	35	L99 and estradiol.ab.	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	OFF	2017/03/18 12:02
L101	262	L99 and transdermal.ab.	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	OFF	2017/03/18 12:02
L102	51	L99 and (estradiol NEAR flux)	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	OFF	2017/03/18 12:02
L103	90	L97 and (estradiol NEAR flux)	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	OFF	2017/03/18 12:02
L104	259	MANTELLE.in. and JUAN.in.	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	OFF	2017/03/18 12:02
L105	42	L104 and estradiol	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	OFF	2017/03/18 12:02
L106	151	L104 and transdermal	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	OFF	2017/03/18 12:02
L107	186	Kanios.in. and David.in.	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	OFF	2017/03/18 12:02
L108	40	L107 NOT L104	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	OFF	2017/03/18 12:02
L109	0	(11/245097).APP.	USPAT; USOCR	OR	OFF	2017/03/18 12:02
L110	714	L97 and ("dipropylene glycol" oleyl)	USPAT; USOCR	OR	OFF	2017/03/18 12:02
L111	132	L99 and ("dipropylene glycol" oleyl)	USPAT; USOCR	OR	OFF	2017/03/18 12:02
L112	15742	estradiol and transdermal	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	OFF	2017/03/18 12:02
L113	5455	L112 and ("surface area" flux)	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	OFF	2017/03/18 12:02
L114	916	L113 and acrylic and silicone and (PVP polyvinyl pyrrolidone)	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	OFF	2017/03/18 12:02
L115	35	L114 and estradiol.ab.	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	OFF	2017/03/18 12:02
L116	262	L114 and transdermal.ab.	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	OFF	2017/03/18 12:02

L117	51	L114 and (estradiol NEAR flux)	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	OFF	2017/03/18 12:02
L118	90	L112 and (estradiol NEAR flux)	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	OFF	2017/03/18 12:02
L119	259	MANTELLE.in. and JUAN.in.	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	OFF	2017/03/18 12:02
L120	42	L119 and estradiol	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	OFF	2017/03/18 12:02
L121	151	L119 and transdermal	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	OFF	2017/03/18 12:02
L122	186	Kanios.in. and David.in.	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	OFF	2017/03/18 12:02
L123	40	L122 NOT L119	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	OFF	2017/03/18 12:02
L124	0	(11/245097).APP.	USPAT; USOCR	OR	OFF	2017/03/18 12:02
L125	714	L112 and ("dipropylene glycol" oleyl)	USPAT; USOCR	OR	OFF	2017/03/18 12:02
L126	132	L114 and ("dipropylene glycol" oleyl)	USPAT; USOCR	OR	OFF	2017/03/18 12:02
L129	15742	estradiol and transdermal	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	OFF	2017/03/18 12:02
L130	5455	L129 and ("surface area" flux)	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	OFF	2017/03/18 12:02
L131	916	L130 and acrylic and silicone and (PVP polyvinyl pyrrolidone)	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	OFF	2017/03/18 12:02
L132	35	L131 and estradiol.ab.	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	OFF	2017/03/18 12:02
L133	262	L131 and transdermal.ab.	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	OFF	2017/03/18 12:02
L134	51	L131 and (estradiol NEAR flux)	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	OFF	2017/03/18 12:02
L135	90	L129 and (estradiol NEAR flux)	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	OFF	2017/03/18 12:02
L136	259	MANTELLE.in. and JUAN.in.	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	OFF	2017/03/18 12:02
L137	42	L136 and estradiol	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	OFF	2017/03/18 12:02
L138	151	L136 and transdermal	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	OFF	2017/03/18 12:02

L139	186	Kanios.in. and David.in.	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	OFF	2017/03/18 12:02
L140	40	L139 NOT L136	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	OFF	2017/03/18 12:02
L141	0	(11/245097).APP.	USPAT; USOCR	OR	OFF	2017/03/18 12:02
L142	714	L129 and ("dipropylene glycol" oleyl)	USPAT; USOCR	OR	OFF	2017/03/18 12:02
L143	132	L131 and ("dipropylene glycol" oleyl)	USPAT; USOCR	OR	OFF	2017/03/18 12:02
L144	15742	estradiol and transdermal	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	OFF	2017/03/18 12:02
L145	5455	L144 and ("surface area" flux)	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	OFF	2017/03/18 12:02
L146	916	L145 and acrylic and silicone and (PVP polyvinyl pyrrolidone)	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	OFF	2017/03/18 12:02
L147	35	L146 and estradiol.ab.	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	OFF	2017/03/18 12:02
L148	262	L146 and transdermal.ab.	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	OFF	2017/03/18 12:02
L149	51	L146 and (estradiol NEAR flux)	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	OFF	2017/03/18 12:02
L150	90	L144 and (estradiol NEAR flux)	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	OFF	2017/03/18 12:02
L151	259	MANTELLE.in. and JUAN.in.	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	OFF	2017/03/18 12:02
L152	42	L151 and estradiol	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	OFF	2017/03/18 12:02
L153	151	L151 and transdermal	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	OFF	2017/03/18 12:02
L154	186	Kanios.in. and David.in.	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	OFF	2017/03/18 12:02
L155	40	L154 NOT L151	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	OFF	2017/03/18 12:02
L156	0	(11/245097). A PP.	USPAT; USOCR	OR	OFF	2017/03/18 12:02
L157	714	L144 and ("dipropylene glycol" oleyl)	USPAT; USOCR	OR	OFF	2017/03/18 12:02
L158	132	L146 and ("dipropylene glycol" oleyl)	USPAT; USOCR	OR	OFF	2017/03/18 12:02
L159	2	"6638528".pn.	US-PGPUB; USPAT; USOCR; FPRS; EPO;	OR	OFF	2017/03/18 12:02

	<u> </u>		JPO; DERWENT			
L160	4	"4624665".pn.	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	OFF	2017/03/18 12:02
L161	3	"20090041831".pn.	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	OFF	2017/03/18 12:02
L162	15742	estradiol and transdermal	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	OFF	2017/03/18 12:02
L163	5455	L162 and ("surface area" flux)	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	OFF	2017/03/18 12:02
L164	916	L163 and acrylic and silicone and (PVP polyvinyl pyrrolidone)	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	OFF	2017/03/18 12:02
L165	35	L164 and estradiol.ab.	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	OFF	2017/03/18 12:02
L166	262	L164 and transdermal.ab.	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	OFF	2017/03/18 12:02
L167	51	L164 and (estradiol NEAR flux)	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	OFF	2017/03/18 12:02
L168	90	L162 and (estradiol NEAR flux)	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	OFF	2017/03/18 12:02
L169	259	MANTELLE.in. and JUAN.in.	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	OFF	2017/03/18 12:02
L170	42	L169 and estradiol	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	OFF	2017/03/18 12:02
L171	151	L169 and transdermal	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	OFF	2017/03/18 12:02
L172	186	Kanios.in. and David.in.	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	OFF	2017/03/18 12:02
L173	40	L172 NOT L169	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	OFF	2017/03/18 12:02
L174	0	(11/245097). A PP.	USPAT; USOCR	OR	OFF	2017/03/18 12:02
L175	714	L162 and ("dipropylene glycol" oleyl)	USPAT; USOCR	OR	OFF	2017/03/18 12:02
L176	132	L164 and ("dipropylene glycol" oleyl)	USPAT; USOCR	OR	OFF	2017/03/18 12:02
L177	15742	estradiol and transdermal	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	OFF	2017/03/18 12:02
L178	5455	L177 and ("surface area" flux)	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	OFF	2017/03/18 12:02
L179	916	L178 and acrylic and	US-PGPUB; USPAT;	OR	OFF	2017/03/18

		silicone and (PVP polyvinyl pyrrolidone)	USOCR; FPRS; EPO; JPO; DERWENT		***************************************	12:02
L180	35	L179 and estradiol.ab.	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	OFF	2017/03/18 12:02
L181	262	L179 and transdermal.ab.	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	OFF	2017/03/18 12:02
L182	51	L179 and (estradiol NEAR flux)	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	OFF	2017/03/18 12:02
L183	90	L177 and (estradiol NEAR flux)	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	OFF	2017/03/18 12:02
L184	259	MANTELLE.in. and JUAN.in.	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	OFF	2017/03/18 12:02
L185	42	L184 and estradiol	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	OFF	2017/03/18 12:02
L186	151	L184 and transdermal	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	OFF	2017/03/18 12:02
L187	186	Kanios.in. and David.in.	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	OFF	2017/03/18 12:02
L188	40	L187 NOT L184	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	OFF	2017/03/18 12:02
L189	0	(11/245097).APP.	USPAT; USOCR	OR	OFF	2017/03/18 12:02
L190	714	L177 and ("dipropylene glycol" oleyl)	USPAT; USOCR	OR	OFF	2017/03/18 12:02
L191	132	L179 and ("dipropylene glycol" oleyl)	USPAT; USOCR	OR	OFF	2017/03/18 12:02
L192	15742	estradiol and transdermal	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	OFF	2017/03/18 12:02
L193	5455	L192 and ("surface area" flux)	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	OFF	2017/03/18 12:02
L194	916	L193 and acrylic and silicone and (PVP polyvinyl pyrrolidone)	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	OFF	2017/03/18 12:02
L195	35	L194 and estradiol.ab.	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	OFF	2017/03/18 12:02
L196	262	L194 and transdermal.ab.	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	OFF	2017/03/18 12:02
L197	51	L194 and (estradiol NEAR flux)	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	OFF	2017/03/18 12:02
L198	90	L192 and (estradiol NEAR flux)	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	OFF	2017/03/18 12:02

L199	OEO	MANTELLE in and HANLin	LIC DODLID, LICDAT,	OR	OFF	2017/03/18
L199	259	MANTELLE.in. and JUAN.in.	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	OFF	12:02
L200	42	L199 and estradiol	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	OFF	2017/03/18 12:02
L201	151	L199 and transdermal	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	OFF	2017/03/18 12:02
L202	186	Kanios.in. and David.in.	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	OFF	2017/03/18 12:02
L203	40	L202 NOT L199	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	OFF	2017/03/18 12:02
L204	0	(11/245097).APP.	USPAT; USOCR	OR	OFF	2017/03/18 12:02
L205	714	L192 and ("dipropylene glycol" oleyl)	USPAT; USOCR	OR	OFF	2017/03/18 12:02
L206	132	L194 and ("dipropylene glycol" oleyl)	USPAT; USOCR	OR	OFF	2017/03/18 12:02
L207	15742	estradiol and transdermal	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	OFF	2017/03/18 12:02
L208	5455	L207 and ("surface area" flux)	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	OFF	2017/03/18 12:02
L209	916	L208 and acrylic and silicone and (PVP polyvinyl pyrrolidone)	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	OFF	2017/03/18 12:02
L210	35	L209 and estradiol.ab.	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	OFF	2017/03/18 12:02
L211	262	L209 and transdermal.ab.	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	OFF	2017/03/18 12:02
L212	51	L209 and (estradiol NEAR flux)	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	OFF	2017/03/18 12:02
L213	90	L207 and (estradiol NEAR flux)	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	OFF	2017/03/18 12:02
L214	259	MANTELLE.in. and JUAN.in.	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	OFF	2017/03/18 12:02
L215	42	L214 and estradiol	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	OFF	2017/03/18 12:02
L216	151	L214 and transdermal	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	OFF	2017/03/18 12:02
L217	186	Kanios.in. and David.in.	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	OFF	2017/03/18 12:02
L218	40	L217 NOT L214	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	OFF	2017/03/18 12:02

L219	0	(11/245097). A PP.	USPAT; USOCR	OR	OFF	2017/03/18 12:02
L220	714	L207 and ("dipropylene glycol" oleyl)	USPAT; USOCR	OR	OFF	2017/03/18 12:02
L221	132	L209 and ("dipropylene glycol" oleyl)	USPAT; USOCR	OR	OFF	2017/03/18 12:02
L222	2	"6638528".pn.	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	OFF	2017/03/18 12:02
L223	4	"4624665".pn.	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	OFF	2017/03/18 12:02
L224	3	"20090041831".pn.	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	OFF	2017/03/18 12:02
L225	15742	estradiol and transdermal	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	OFF	2017/03/18 12:02
L226	5455	L225 and ("surface area" flux)	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	OFF	2017/03/18 12:02
L227	916	L226 and acrylic and silicone and (PVP polyvinyl pyrrolidone)	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	OFF	2017/03/18 12:02
L228	35	L227 and estradiol.ab.	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	OFF	2017/03/18 12:02
L229	262	L227 and transdermal.ab.	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	OFF	2017/03/18 12:02
L230	51	L227 and (estradiol NEAR flux)	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	OFF	2017/03/18 12:02
L231	90	L225 and (estradiol NEAR flux)	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	OFF	2017/03/18 12:02
L232	259	MANTELLE.in. and JUAN.in.	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	OFF	2017/03/18 12:02
L233	42	L232 and estradiol	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	OFF	2017/03/18 12:02
L234	151	L232 and transdermal	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	OFF	2017/03/18 12:02
L235	186	Kanios.in. and David.in.	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	OFF	2017/03/18 12:02
L236	40	L235 NOT L232	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	OFF	2017/03/18 12:02
L237	0	(11/245097).APP.	USPAT; USOCR	OR	OFF	2017/03/18 12:02
L238	714	L225 and ("dipropylene glycol" oleyl)	USPAT; USOCR	OR	OFF	2017/03/18 12:02
L239	132	L227 and ("dipropylene	USPAT; USOCR	OR	OFF	2017/03/18

		glycol" oleyl)				12:02
L240	15742	estradiol and transdermal	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	OFF	2017/03/18 12:02
L241	5455	L240 and ("surface area" flux)	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	OFF	2017/03/18 12:02
L242	916	L241 and acrylic and silicone and (PVP polyvinyl pyrrolidone)	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	OFF	2017/03/18 12:02
L243	35	L242 and estradiol.ab.	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	OFF	2017/03/18 12:02
L244	262	L242 and transdermal.ab.	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	OFF	2017/03/18 12:02
L245	51	L242 and (estradiol NEAR flux)	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	OFF	2017/03/18 12:02
L246	90	L240 and (estradiol NEAR flux)	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	OFF	2017/03/18 12:02
L247	259	MANTELLE.in. and JUAN.in.	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	OFF	2017/03/18 12:02
L248	42	L247 and estradiol	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	OFF	2017/03/18 12:02
L249	151	L247 and transdermal	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	OFF	2017/03/18 12:02
L250	186	Kanios.in. and David.in.	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	OFF	2017/03/18 12:02
L251	40	L250 NOT L247	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	OFF	2017/03/18 12:02
L252	0	(11/245097).APP.	USPAT; USOCR	OR	OFF	2017/03/18 12:02
L253	714	L240 and ("dipropylene glycol" oleyl)	USPAT; USOCR	OR	OFF	2017/03/18 12:02
L254	132	L242 and ("dipropylene glycol" oleyl)	USPAT; USOCR	OR	OFF	2017/03/18 12:02
L255	58	(("MANTELLE") near3 ("Juan")).INV.	US-PGPUB; USPAT; USOCR	OR	OFF	2017/03/18 12:02
L256	2	12/216811	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	OFF	2017/03/18 12:02
L257	1	(12/216811). A PP.	USPAT; USOCR	OR	OFF	2017/03/18 12:02
L258	16747	A61K31/565.cpc.	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	AND	OFF	2017/03/18 12:02
L259	5310	A61K9/70.cpc.	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	AND	OFF	2017/03/18 12:02

L260	33	L258 L259	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	AND	OFF	2017/03/18 12:02
L261	8	L260 and estradiol	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	AND	OFF	2017/03/18 12:02
L265	15742	estradiol and transdermal	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	OFF	2017/03/18 12:02
L266	5455	L265 and ("surface area" flux)	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	OFF	2017/03/18 12:02
L267	916	L266 and acrylic and silicone and (PVP polyvinyl pyrrolidone)	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	OFF	2017/03/18 12:02
L268	35	L267 and estradiol.ab.	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	OFF	2017/03/18 12:02
L269	262	L267 and transdermal.ab.	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	OFF	2017/03/18 12:02
L270	51	L267 and (estradiol NEAR flux)	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	OFF	2017/03/18 12:02
L271	90	L265 and (estradiol NEAR flux)	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	OFF	2017/03/18 12:02
L272	259	MANTELLE.in. and JUAN.in.	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	OFF	2017/03/18 12:02
L273	42	L272 and estradiol	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	OFF	2017/03/18 12:02
L274	151	L272 and transdermal	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	OFF	2017/03/18 12:02
L275	186	Kanios.in. and David.in.	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	OFF	2017/03/18 12:02
L276	40	L275 NOT L272	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	OFF	2017/03/18 12:02
L277	0	(11/245097).APP.	USPAT; USOCR	OR	OFF	2017/03/18 12:02
L278	714	L265 and ("dipropylene glycol" oleyl)	USPAT; USOCR	OR	OFF	2017/03/18 12:02
L279	132	L267 and ("dipropylene glycol" oleyl)	USPAT; USOCR	OR	OFF	2017/03/18 12:02
L280	15742	estradiol and transdermal	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	OFF	2017/03/18 12:02
L281	5455	L280 and ("surface area" flux)	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	OFF	2017/03/18 12:02
L282	916	L281 and acrylic and silicone and (PVP polyvinyl pyrrolidone)	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	OFF	2017/03/18 12:02

L283	35	L282 and estradiol.ab.	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	OFF	2017/03/18 12:02
L284	262	L282 and transdermal.ab.	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	OFF	2017/03/18 12:02
L285	51	L282 and (estradiol NEAR flux)	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	OFF	2017/03/18 12:02
L286	90	L280 and (estradiol NEAR flux)	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	OFF	2017/03/18 12:02
L287	259	MANTELLE.in. and JUAN.in.	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	OFF	2017/03/18 12:02
L288	42	L287 and estradiol	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	OFF	2017/03/18 12:02
L289	151	L287 and transdermal	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	OFF	2017/03/18 12:02
L290	186	Kanios.in. and David.in.	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	OFF	2017/03/18 12:02
L291	40	L290 NOT L287	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	OFF	2017/03/18 12:02
L292	0	(11/245097).APP.	USPAT; USOCR	OR	OFF	2017/03/18 12:02
L293	714	L280 and ("dipropylene glycol" oleyl)	USPAT; USOCR	OR	OFF	2017/03/18 12:02
L294	132	L282 and ("dipropylene glycol" oleyl)	USPAT; USOCR	OR	OFF	2017/03/18 12:02
L295	2	"6638528".pn.	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	OFF	2017/03/18 12:02
L296	4	"4624665".pn.	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	OFF	2017/03/18 12:02
L297	3	"20090041831".pn.	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	OFF	2017/03/18 12:02
L298	15742	estradiol and transdermal	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	OFF	2017/03/18 12:02
L299	5455	L298 and ("surface area" flux)	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	OFF	2017/03/18 12:02
L300	916	L299 and acrylic and silicone and (PVP polyvinyl pyrrolidone)	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	OFF	2017/03/18 12:02
L301	35	L300 and estradiol.ab.	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	OFF	2017/03/18 12:02
L302	262	L300 and transdermal.ab.	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	OFF	2017/03/18 12:02

L303	51	L300 and (estradiol NEAR	US-PGPUB; USPAT;	OR	OFF	2017/03/18
		flux)	USOCR; FPRS; EPO; JPO; DERWENT			12:02
	90	L298 and (estradiol NEAR flux)	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	OFF	2017/03/18 12:02
L305	259	MANTELLE.in. and JUAN.in.	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	OFF	2017/03/18 12:02
L306	42	L305 and estradiol	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	OFF	2017/03/18 12:02
L307	151	L305 and transdermal	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	OFF	2017/03/18 12:02
L308	186	Kanios.in. and David.in.	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	OFF	2017/03/18 12:02
L309	40	L308 NOT L305	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	OFF	2017/03/18 12:02
L310	0	(11/245097).APP.	USPAT; USOCR	OR	OFF	2017/03/18 12:02
L311	714	L298 and ("dipropylene glycol" oleyl)	USPAT; USOCR	OR	OFF	2017/03/18 12:02
L312	132	L300 and ("dipropylene glycol" oleyl)	USPAT; USOCR	OR	OFF	2017/03/18 12:02
L313	15742	estradiol and transdermal	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	OFF	2017/03/18 12:02
L314	5455	L313 and ("surface area" flux)	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	OFF	2017/03/18 12:02
L315	916	L314 and acrylic and silicone and (PVP polyvinyl pyrrolidone)	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	OFF	2017/03/18 12:02
L316	35	L315 and estradiol.ab.	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	OFF	2017/03/18 12:02
L317	262	L315 and transdermal.ab.	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	OFF	2017/03/18 12:02
L318	51	L315 and (estradiol NEAR flux)	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	OFF	2017/03/18 12:02
L319	90	L313 and (estradiol NEAR flux)	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	OFF	2017/03/18 12:02
L320	259	MANTELLE.in. and JUAN.in.	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	OFF	2017/03/18 12:02
L321	42	L320 and estradiol	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	OFF	2017/03/18 12:02
L322	151	L320 and transdermal	US-PGPUB; USPAT; USOCR; FPRS; EPO;	OR	OFF	2017/03/18 12:02

			JPO; DERWENT			
L323	186	Kanios.in. and David.in.	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	OFF	2017/03/18 12:02
L324	40	L323 NOT L320	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	OFF	2017/03/18 12:02
L325	0	(11/245097).APP.	USPAT; USOCR	OR	OFF	2017/03/18 12:02
L326	714	L313 and ("dipropylene glycol" oleyl)	USPAT; USOCR	OR	OFF	2017/03/18 12:02
L327	132	L315 and ("dipropylene glycol" oleyl)	USPAT; USOCR	OR	OFF	2017/03/18 12:02
L328	15742	estradiol and transdermal	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	OFF	2017/03/18 12:02
L329	5455	L328 and ("surface area" flux)	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	OFF	2017/03/18 12:02
L330	916	L329 and acrylic and silicone and (PVP polyvinyl pyrrolidone)	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	OFF	2017/03/18 12:02
L331	35	L330 and estradiol.ab.	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	OFF	2017/03/18 12:02
L332	262	L330 and transdermal.ab.	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	OFF	2017/03/18 12:02
L333	51	L330 and (estradiol NEAR flux)	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	OFF	2017/03/18 12:02
L334	90	L328 and (estradiol NEAR flux)	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	OFF	2017/03/18 12:02
L335	259	MANTELLE.in. and JUAN.in.	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	OFF	2017/03/18 12:02
L336	42	L335 and estradiol	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	OFF	2017/03/18 12:02
L337	151	L335 and transdermal	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	OFF	2017/03/18 12:02
L338	186	Kanios.in. and David.in.	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	OFF	2017/03/18 12:02
L339	40	L338 NOT L335	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	OFF	2017/03/18 12:02
L340	0	(11/245097).APP.	USPAT; USOCR	OR	OFF	2017/03/18 12:02
L341	714	L328 and ("dipropylene glycol" oleyl)	USPAT; USOCR	OR	OFF	2017/03/18 12:02
L342	132	L330 and ("dipropylene glycol" oleyl)	USPAT; USOCR	OR	OFF	2017/03/18 12:02
L343	15742	estradiol and transdermal	US-PGPUB; USPAT;	OR	OFF	2017/03/18

			USOCR; FPRS; EPO; JPO; DERWENT			12:02
L344	5455	L343 and ("surface area" flux)	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	OFF	2017/03/18 12:02
L345	916	L344 and acrylic and silicone and (PVP polyvinyl pyrrolidone)	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	OFF	2017/03/18 12:02
L346	35	L345 and estradiol.ab.	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	OFF	2017/03/18 12:02
L347	262	L345 and transdermal.ab.	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	OFF	2017/03/18 12:02
L348	51	L345 and (estradiol NEAR flux)	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	OFF	2017/03/18 12:02
L349	90	L343 and (estradiol NEAR flux)	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	OFF	2017/03/18 12:02
L350	259	MANTELLE.in. and JUAN.in.	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	OFF	2017/03/18 12:02
L351	42	L350 and estradiol	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	OFF	2017/03/18 12:02
L352	151	L350 and transdermal	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	OFF	2017/03/18 12:02
L353	186	Kanios.in. and David.in.	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	OFF	2017/03/18 12:02
L354	40	L353 NOT L350	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	OFF	2017/03/18 12:02
L355	0	(11/245097).APP.	USPAT; USOCR	OR	OFF	2017/03/18 12:02
L356	714	L343 and ("dipropylene glycol" oleyl)	USPAT; USOCR	OR	OFF	2017/03/18 12:02
L357	132	L345 and ("dipropylene glycol" oleyl)	USPAT; USOCR	OR	OFF	2017/03/18 12:02
L358	2	"6638528".pn.	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	OFF	2017/03/18 12:02
L359	4	"4624665".pn.	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	OFF	2017/03/18 12:02
L360	3	"20090041831".pn.	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	OFF	2017/03/18 12:02
L361	15742	estradiol and transdermal	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	OFF	2017/03/18 12:02
L362	5455	L361 and ("surface area" flux)	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	OFF	2017/03/18 12:02

L363	916	L362 and acrylic and silicone and (PVP polyvinyl pyrrolidone)	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	OFF	2017/03/18 12:02
L364		L363 and estradiol.ab.	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	OFF	2017/03/18 12:02
L365	262	L363 and transdermal.ab.	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	OFF	2017/03/18 12:02
L366	51	L363 and (estradiol NEAR flux)	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	OFF	2017/03/18 12:02
L367	90	L361 and (estradiol NEAR flux)	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	OFF	2017/03/18 12:02
L368	259	MANTELLE.in. and JUAN.in.	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	OFF	2017/03/18 12:02
L369	42	L368 and estradiol	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	OFF	2017/03/18 12:02
L370	151	L368 and transdermal	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	OFF	2017/03/18 12:02
L371	186	Kanios.in. and David.in.	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	OFF	2017/03/18 12:02
L372	40	L371 NOT L368	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	OFF	2017/03/18 12:02
L373	0	(11/245097).APP.	USPAT; USOCR	OR	OFF	2017/03/18 12:02
L374	714	L361 and ("dipropylene glycol" oleyl)	USPAT; USOCR	OR	OFF	2017/03/18 12:02
L375	132	L363 and ("dipropylene glycol" oleyl)	USPAT; USOCR	OR	OFF	2017/03/18 12:02
L376	15742	estradiol and transdermal	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	OFF	2017/03/18 12:02
L377	5455	L376 and ("surface area" flux)	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	OFF	2017/03/18 12:02
L378	916	L377 and acrylic and silicone and (PVP polyvinyl pyrrolidone)	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	OFF	2017/03/18 12:02
L379	35	L378 and estradiol.ab.	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	OFF	2017/03/18 12:02
L380	262	L378 and transdermal.ab.	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	OFF	2017/03/18 12:02
L381	51	L378 and (estradiol NEAR flux)	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	OFF	2017/03/18 12:02
L382	90	L376 and (estradiol NEAR flux)	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	OFF	2017/03/18 12:02

L383	259	MANTELLE.in. and JUAN.in.	US-PGPUB; USPAT;	OR	OFF	2017/03/18
			USOCR; FPRS; EPO; JPO; DERWENT			12:02
	42	L383 and estradiol	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	OFF	2017/03/18 12:02
L385	151	L383 and transdermal	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	OFF	2017/03/18 12:02
L386	186	Kanios.in. and David.in.	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	OFF	2017/03/18 12:02
L387	40	L386 NOT L383	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	OFF	2017/03/18 12:02
L388	0	(11/245097).APP.	USPAT; USOCR	OR	OFF	2017/03/18 12:02
L389	714	L376 and ("dipropylene glycol" oleyl)	USPAT; USOCR	OR	OFF	2017/03/18 12:02
L390	132	L378 and ("dipropylene glycol" oleyl)	USPAT; USOCR	OR	OFF	2017/03/18 12:02
L391	15742	estradiol and transdermal	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	OFF	2017/03/18 12:02
L392	5455	L391 and ("surface area" flux)	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	OFF	2017/03/18 12:02
L393	916	L392 and acrylic and silicone and (PVP polyvinyl pyrrolidone)	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	OFF	2017/03/18 12:02
L394	35	L393 and estradiol.ab.	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	OFF	2017/03/18 12:02
L395	262	L393 and transdermal.ab.	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	OFF	2017/03/18 12:02
L396	51	L393 and (estradiol NEAR flux)	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	OFF	2017/03/18 12:02
L397	90	L391 and (estradiol NEAR flux)	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	OFF	2017/03/18 12:02
L398	259	MANTELLE.in. and JUAN.in.	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	OFF	2017/03/18 12:02
L399	42	L398 and estradiol	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	OFF	2017/03/18 12:02
L400	151	L398 and transdermal	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	OFF	2017/03/18 12:02
L401	186	Kanios.in. and David.in.	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	OFF	2017/03/18 12:02
L402	40	L401 NOT L398	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	OFF	2017/03/18 12:02

L403	0	(11/245097). A PP.	USPAT; USOCR	OR	OFF	2017/03/18 12:02
L404	714	L391 and ("dipropylene glycol" oleyl)	USPAT; USOCR	OR	OFF	2017/03/18 12:02
L405	132	L393 and ("dipropylene glycol" oleyl)	USPAT; USOCR	OR	OFF	2017/03/18 12:02
L406	15742	estradiol and transdermal	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	OFF	2017/03/18 12:02
L407	5455	L406 and ("surface area" flux)	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	OFF	2017/03/18 12:02
L408	916	L407 and acrylic and silicone and (PVP polyvinyl pyrrolidone)	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	OFF	2017/03/18 12:02
L409	35	L408 and estradiol.ab.	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	OFF	2017/03/18 12:02
L410	262	L408 and transdermal.ab.	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	OFF	2017/03/18 12:02
L411	51	L408 and (estradiol NEAR flux)	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	OFF	2017/03/18 12:02
L412	90	L406 and (estradiol NEAR flux)	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	OFF	2017/03/18 12:02
L413	259	MANTELLE.in. and JUAN.in.	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	OFF	2017/03/18 12:02
L414	42	L413 and estradiol	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	OFF	2017/03/18 12:02
L415	151	L413 and transdermal	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	OFF	2017/03/18 12:02
L416	186	Kanios.in. and David.in.	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	OFF	2017/03/18 12:02
L417	40	L416 NOT L413	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	OFF	2017/03/18 12:02
L418	0	(11/245097).APP.	USPAT; USOCR	OR	OFF	2017/03/18 12:02
L419	714	L406 and ("dipropylene glycol" oleyl)	USPAT; USOCR	OR	OFF	2017/03/18 12:02
L420	132	L408 and ("dipropylene glycol" oleyl)	USPAT; USOCR	OR	OFF	2017/03/18 12:02
L421	2	"6638528".pn.	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	OFF	2017/03/18 12:02
L422	4	"4624665".pn.	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	OFF	2017/03/18 12:02
L423	3	"20090041831".pn.	US-PGPUB; USPAT; USOCR; FPRS; EPO;	OR	OFF	2017/03/18 12:02

			JPO; DERWENT			
L424	15742	estradiol and transdermal	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	OFF	2017/03/18 12:02
L425	5455	L424 and ("surface area" flux)	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	OFF	2017/03/18 12:02
L426	916	L425 and acrylic and silicone and (PVP polyvinyl pyrrolidone)	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	OFF	2017/03/18 12:02
L427	35	L426 and estradiol.ab.	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	OFF	2017/03/18 12:02
L428	262	L426 and transdermal.ab.	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	OFF	2017/03/18 12:02
L429	51	L426 and (estradiol NEAR flux)	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	OFF	2017/03/18 12:02
L430	90	L424 and (estradiol NEAR flux)	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	OFF	2017/03/18 12:02
L431	259	MANTELLE.in. and JUAN.in.	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	OFF	2017/03/18 12:02
L432	42	L431 and estradiol	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	OFF	2017/03/18 12:02
L433	151	L431 and transdermal	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	OFF	2017/03/18 12:02
L434	186	Kanios.in. and David.in.	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	OFF	2017/03/18 12:02
L435	40	L434 NOT L431	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	OFF	2017/03/18 12:02
L436	0	(11/245097).APP.	USPAT; USOCR	OR	OFF	2017/03/18 12:02
L437	714	L424 and ("dipropylene glycol" oleyl)	USPAT; USOCR	OR	OFF	2017/03/18 12:02
L438	132	L426 and ("dipropylene glycol" oleyl)	USPAT; USOCR	OR	OFF	2017/03/18 12:02
L439	15742	estradiol and transdermal	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	OFF	2017/03/18 12:02
L440	5455	L439 and ("surface area" flux)	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	OFF	2017/03/18 12:02
L441	916	L440 and acrylic and silicone and (PVP polyvinyl pyrrolidone)	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	OFF	2017/03/18 12:02
L442	35	L441 and estradiol.ab.	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	OFF	2017/03/18 12:02
L443	262	L441 and transdermal.ab.	US-PGPUB; USPAT;	OR	OFF	2017/03/18

			USOCR; FPRS; EPO; JPO; DERWENT			12:02
L444	51	L441 and (estradiol NEAR flux)	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	OFF	2017/03/18 12:02
L445	90	L439 and (estradiol NEAR flux)	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	OFF	2017/03/18 12:02
L446	259	MANTELLE.in. and JUAN.in.	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	OFF	2017/03/18 12:02
L447	42	L446 and estradiol	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	OFF	2017/03/18 12:02
L448	151	L446 and transdermal	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	OFF	2017/03/18 12:02
L449	186	Kanios.in. and David.in.	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	OFF	2017/03/18 12:02
L450	40	L449 NOT L446	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	OFF	2017/03/18 12:02
L451	0	(11/245097).APP.	USPAT; USOCR	OR	OFF	2017/03/18 12:02
L452	714	L439 and ("dipropylene glycol" oleyl)	USPAT; USOCR	OR	OFF	2017/03/18 12:02
L453	132	L441 and ("dipropylene glycol" oleyl)	USPAT; USOCR	OR	OFF	2017/03/18 12:02
L454	15742	estradiol and transdermal	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	OFF	2017/03/18 12:02
L455	5455	L454 and ("surface area" flux)	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	OFF	2017/03/18 12:02
L456	916	L455 and acrylic and silicone and (PVP polyvinyl pyrrolidone)	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	OFF	2017/03/18 12:02
L457	35	L456 and estradiol.ab.	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	OFF	2017/03/18 12:02
L458	262	L456 and transdermal.ab.	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	OFF	2017/03/18 12:02
L459	51	L456 and (estradiol NEAR flux)	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	OFF	2017/03/18 12:02
L460	90	L454 and (estradiol NEAR flux)	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	OFF	2017/03/18 12:02
L461	259	MANTELLE.in. and JUAN.in.	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	OFF	2017/03/18 12:02
L462	42	L461 and estradiol	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	OFF	2017/03/18 12:02

L463	151	L461 and transdermal	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	OFF	2017/03/18 12:02
L464	186	Kanios.in. and David.in.	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	OFF	2017/03/18 12:02
L465	40	L464 NOT L461	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	OFF	2017/03/18 12:02
L466	0	(11/245097).APP.	USPAT; USOCR	OR	OFF	2017/03/18 12:02
L467	714	L454 and ("dipropylene glycol" oleyl)	USPAT; USOCR	OR	OFF	2017/03/18 12:02
L468	132	L456 and ("dipropylene glycol" oleyl)	USPAT; USOCR	OR	OFF	2017/03/18 12:02
L469	15742	estradiol and transdermal	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	OFF	2017/03/18 12:02
L470	5455	L469 and ("surface area" flux)	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	OFF	2017/03/18 12:02
L471	916	L470 and acrylic and silicone and (PVP polyvinyl pyrrolidone)	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	OFF	2017/03/18 12:02
L472	35	L471 and estradiol.ab.	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	OFF	2017/03/18 12:02
L473	262	L471 and transdermal.ab.	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	OFF	2017/03/18 12:02
L474	51	L471 and (estradiol NEAR flux)	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	OFF	2017/03/18 12:02
L475	90	L469 and (estradiol NEAR flux)	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	OFF	2017/03/18 12:02
L476	259	MANTELLE.in. and JUAN.in.	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	OFF	2017/03/18 12:02
L477	42	L476 and estradiol	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	OFF	2017/03/18 12:02
L478	151	L476 and transdermal	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	OFF	2017/03/18 12:02
L479	186	Kanios.in. and David.in.	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	OFF	2017/03/18 12:02
L480	40	L479 NOT L476	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	OFF	2017/03/18 12:02
L481	0	(11/245097).APP.	USPAT; USOCR	OR	OFF	2017/03/18 12:02
L482	714	L469 and ("dipropylene glycol" oleyl)	USPAT; USOCR	OR	OFF	2017/03/18 12:02
L483	132	L471 and ("dipropylene	USPAT; USOCR	OR	OFF	2017/03/18

		glycol" oleyl)				12:02
L484	2	"6638528".pn.	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	OFF	2017/03/18 12:02
L485	4	"4624665".pn.	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	OFF	2017/03/18 12:02
L486	3	"20090041831".pn.	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	OFF	2017/03/18 12:02
L487	15742	estradiol and transdermal	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	OFF	2017/03/18 12:02
L488	5455	L487 and ("surface area" flux)	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	OFF	2017/03/18 12:02
L489	916	L488 and acrylic and silicone and (PVP polyvinyl pyrrolidone)	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	OFF	2017/03/18 12:02
L490	35	L489 and estradiol.ab.	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	OFF	2017/03/18 12:02
L491	262	L489 and transdermal.ab.	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	OFF	2017/03/18 12:02
L492	51	L489 and (estradiol NEAR flux)	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	OFF	2017/03/18 12:02
L493	90	L487 and (estradiol NEAR flux)	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	OFF	2017/03/18 12:02
L494	259	MANTELLE.in. and JUAN.in.	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	OFF	2017/03/18 12:02
L495	42	L494 and estradiol	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	OFF	2017/03/18 12:02
L496	151	L494 and transdermal	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	OFF	2017/03/18 12:02
L497	186	Kanios.in. and David.in.	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	OFF	2017/03/18 12:02
L498	40	L497 NOT L494	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	OFF	2017/03/18 12:02
L499	0	(11/245097).APP.	USPAT; USOCR	OR	OFF	2017/03/18 12:02
L500		L487 and ("dipropylene glycol" oleyl)	USPAT; USOCR	OR	OFF	2017/03/18 12:02
L501	132	L489 and ("dipropylene glycol" oleyl)	USPAT; USOCR	OR	OFF	2017/03/18 12:02
L502	15742	estradiol and transdermal	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	OFF	2017/03/18 12:02
L503	5455	L502 and ("surface area"	US-PGPUB; USPAT;	OR	OFF	2017/03/18

		flux)	USOCR; FPRS; EPO; JPO; DERWENT		Parameter Control of C	12:02
L504	916	L503 and acrylic and silicone and (PVP polyvinyl pyrrolidone)	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	OFF	2017/03/18 12:02
L505	35	L504 and estradiol.ab.	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	OFF	2017/03/18 12:02
L506	262	L504 and transdermal.ab.	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	OFF	2017/03/18 12:02
L507	51	L504 and (estradiol NEAR flux)	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	OFF	2017/03/18 12:02
L508	90	L502 and (estradiol NEAR flux)	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	OFF	2017/03/18 12:02
L509	259	MANTELLE.in. and JUAN.in.	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	OFF	2017/03/18 12:02
L510	42	L509 and estradiol	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	OFF	2017/03/18 12:02
L511	151	L509 and transdermal	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	OFF	2017/03/18 12:02
L512	186	Kanios.in. and David.in.	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	OFF	2017/03/18 12:02
L513	40	L512 NOT L509	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	OFF	2017/03/18 12:02
L514	0	(11/245097).APP.	USPAT; USOCR	OR	OFF	2017/03/18 12:02
L515	714	L502 and ("dipropylene glycol" oleyl)	USPAT; USOCR	OR	OFF	2017/03/18 12:02
L516	132	L504 and ("dipropylene glycol" oleyl)	USPAT; USOCR	OR	OFF	2017/03/18 12:02
L517	58	(("MANTELLE") near3 ("Juan")).INV.	US-PGPUB; USPAT; USOCR	OR	OFF	2017/03/18 12:02
L518	2	12/216811	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	OFF	2017/03/18 12:02
L519	1	(12/216811).APP.	USPAT; USOCR	OR	OFF	2017/03/18 12:02
L520	16747	A61K31/565.cpc.	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	AND	OFF	2017/03/18 12:02
L521	5310	A61K9/70.cpc.	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	AND	OFF	2017/03/18 12:02
L522	33	L520 L521	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	AND	OFF	2017/03/18 12:02
L523	8	L522 and estradiol	US-PGPUB; USPAT; USOCR; FPRS; EPO;	AND	OFF	2017/03/18 12:02

JPO; DERWENT

3/ 18/ 2017 12:11:11 PM C:\ Users\ mjavier\ Documents\ EAST\ Workspaces\ 13553972.wsp



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

BIB DATA SHEET

CONFIRMATION NO. 3635

SERIAL NUM	IBER	FILING or 371(c) DATE	CLASS	GI	ROUP ART	UNIT	ATTC	RNEY DOCKET NO.
13/553,97	'2	07/20/2012	424		1611		С	41457-0992
		RULE						
APPLICANT	S							
INVENTORS Juan Mai		1iami, FL;						
		A ************************************		231906	5			
** FOREIGN A	PPLICA	ATIONS ***********	*****					
** IF REQUIRE 07/31/20		REIGN FILING LICENS	E GRANTED **					
Foreign Priority claim		Yes No	STATE O		SHEETS	TOT		INDEPENDENT
35 USC 119(a-d) con Verified and	MELISSA	I JAVIER/	ance COUNTY	Y DF	RAWINGS	CLAII		CLAIMS
Acknowledged	Examiner's	Signature Initials	FL		1	16	i	4
ADDRESS								
Foley & L 3000 K S								
SUITE 60	00							
WASHIN UNITED		DC 20007-5109						
TITLE	OTATIE	<u> </u>						
TRANSD	ERMAL	ESTROGEN DEVICE	AND DELIVERY					
					☐ All Fe	es		
	_				☐ 1.16 F	ees (Fil	ing)	
		Authority has been give to charge/cr	•	OUNT	☐ 1.17 F	ees (Pr	ocessi	ng Ext. of time)
RECEIVED 2540		for following		CONT	☐ 1.18 F	ees (lss	sue)	
		- -			☐ Other			
					☐ Credit			
								-



Atty. Dkt. No. 041457-0992

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

First Inventor Name: Juan Mantelle

Title: Transdermal Estrogen Device

and Delivery

Application No.: 13/553972

Filing Date: 7/20/2012

Examiner: Melissa L. Javier

Art Unit: 1611

Confirmation No.: 3635

INFORMATION DISCLOSURE STATEMENT UNDER 37 CFR §1.56

Commissioner for Patents P.O. Box 1450 Alexandria, VA 22313-1450

Commissioner:

Applicant submits herewith documents for the Examiner's consideration in accordance with 37 CFR §§1.56, 1.97 and 1.98.

Applicant respectfully requests that each listed document be considered by the Examiner and be made of record in the present application and that an initialed copy of Form PTO/SB/08 be returned in accordance with MPEP §609.

The submission of any document herewith is not an admission that such document constitutes prior art against the claims of the present application or that such document is considered material to patentability as defined in 37 CFR §1.56(b). Applicant does not waive any rights to take any action which would be appropriate to antedate or otherwise remove as a competent reference any document submitted herewith.

4850-4765-8308.1

Atty. Dkt. No. 041457-0992

TIMING OF THE DISCLOSURE

The listed documents are being submitted in compliance with 37 CFR §1.97(b), before the mailing of a first Office action after the filing of a RCE.

RELEVANCE OF LISTED DOCUMENTS

Documents A1 and A2 are Office Actions which were issued in the child applications.

Document A3 is a Decision issued in an Opposition of a corresponding European patent. Although the patent was revoked because certain claim language not present in the pending claims was found to constitute an impermissible generalization of the original disclosure, the EPO Opposition Division rejected the Opponent's prior art and enablement-type arguments.

Although Applicant believes that no fee is required, the Commissioner is hereby authorized to charge any additional fees which may be due to Deposit Account Number 19-0741.

Respectfully submitted,

By algon

FOLEY & LARDNER LLP

Date Maide 8, 2M

Customer Number: 22428

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(202) 295-4094

Facsimile:

(202) 672-5399

Courtenay C. Brinckerhoff Attorney for Applicant Registration No. 37,288

PTO/SB/99 (modified) Substitute for form 1449/PTO Complete if Known 13/553972 **Application Number** INFORMATION DISCLOSURE MAR 0 8 2017 7/20/2012 STATEMENT BY APPLICANT Filing Date Juan Mantelle First Named Inventor Date Submitted: March 8, 2017 Art Unit 1611 PRADEMARKUR Examiner Name Melissa L. Javier (use as many sheets as necessary) 041457-0992 Sheet of 1 **Attorney Docket Number**

<u>.</u>	U.S. PATENT DOCUMENTS								
Examiner	0.14	Document Number	Publication Date	Name of Patentee or Applicant of	Pages, Columns, Lines, Where Relevant				
Initials*	Cite No. ¹	Number-Kind Code ² (if known)	MM-DD-YYYY	Cited Document	Passages or Relevant Figures Appear				

	UNPUBLISHED U.S. PATENT APPLICATION DOCUMENTS								
Examiner Initials*	Cite No. ¹	U.S. Patent Application Document Serial Number-Kind Code ² (if known)	Filing Date of Cited Document MM-DD-YYYY	Name of Patentee or Applicant of Cited Document	Pages, Columns, Lines, Where Relevant Passages or Relevant Figures Appear				

	FOREIGN PATENT DOCUMENTS							
Examiner Initials*	Cite No. ¹	Foreign Patent Document Country Code ³ Number ⁴ Kind Code ⁵ (<i>if known</i>)	Publication Date MM-DD-YYYY	Name of Patentee or Applicant of Cited Documents	Pages, Columns, Lines, Where Relevant Passages or Relevant Figures Appear	T ⁶		

		NON PATENT LITERATURE DOCUMENTS	
Examiner Initials*	Cite No. ¹	Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc.) date, page(s), volume-issue number(s), publisher, city and/or country where published.	T [®]
	A1	Notice of Allowance issued on 01/10/2017 in application number 14/024,985 (US 2014-0200530)	
<u> </u>	A2	Office Action issued on 09/07/2016 in application number 14/870,574 (US 2016-0015655)	
	A3	European Office Action issued on 02/14/2017 in application number EP 09790211.8	

			0011010010
	/MELISSA L JAVIER/	1 <u> </u>	03/18/2017
Examiner	y a more market and a second a	Date	
		Considered	
Signature		Considered	l i

Search Notes



Application/Control No.	Applicant(s)/Patent Under Reexamination
13553972	MANTELLE, JUAN
Examiner	Art Unit
MELISSA JAVIER	1611

CPC- SEARCHED		
Symbol	Date	Examiner

CPC COMBINATION SETS - SEARC	CHED		
Symbol Date Examiner			

	US CLASSIFICATION SEA	RCHED		
Class Subclass Date Examine				

SEARCH NOTES					
Search Notes	Date	Examiner			
EAST search (see attached history)	8/25/2013	MJ			
Inventor search in EAST	8/25/2013	MJ			
Google Scholar search (keywords used: transdermal monolithic estradiol)	8/25/2013	MJ			
Updated EAST search	2/21/2014	MJ			
Updated Google Scholar search	2/21/2014	MJ			
Updated EAST search	4/29/2015	MJ			
Updated Google Scholar search	4/29/2015	MJ			
Updated EAST search	9/28/2015	MJ			
Updated Google Scholar search	9/28/2015	MJ			
Updated EAST search	4/22/2016	MJ			
Updated Google Scholar search	4/22/2016	MJ			
Updated EAST search	8/22/2016	MJ			
Updated Google Scholar search	8/22/2016	MJ			
(A61K31/565 A61K9/70).cpc. and estradiol	8/22/2016	MJ			
Updated EAST search	12/2/2016	MJ			
Updated Google Scholar search	12/2/2016	MJ			
(A61K31/565 A61K9/70).cpc. and estradiol	12/2/2016	MJ			
Updated EAST search	3/18/2017	MJ			
Updated Google Scholar search	3/18/2017	MJ			

	/M.J./ Primary Examiner.Art Unit 1611

	INTERFERENCE SEARCH					
US Class/ CPC Symbol	US Subclass / CPC Group	Date	Examiner			
CFC Symbol	(monolith\$2 estradiol transdermal adhesive coat weight flux).clm.	9/28/2015	MJ			
	(monolith\$2 estradiol transdermal system adhesive coat weight flux).clm.	8/22/2016	MJ			
	(monolith\$2 estradiol transdermal system adhesive coat weight flux).clm.	12/2/2016	MJ			
	(monolith\$2 estradiol transdermal system adhesive coat weight flux).clm.	3/18/2017	MJ			

/M.J./ Primary Examiner.Art Unit 1611

U.S. Patent and Trademark Office Part of Paper No. : 20170318

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

First Inventor Name: Juan Mantelle

Title: Transdermal Estrogen Device and Delivery

Appl. No.: 13/553,972

Appl. Filing Date: 7/20/2012

Examiner: Melissa L. Fisher

Art Unit: 1611

Confirmation Number: 3635

REQUEST FOR CONTINUED EXAMINATION (RCE) TRANSMITTAL

Mail Stop RCE Commissioner for Patents P.O. Box 1450 Alexandria, VA 22313-1450

Commissioner:

This is a Request for Continued Examination (RCE) under 37 C.F.R. § 1.114 of the above-identified application. This RCE and the enclosed items listed below are being filed prior to the earliest of: (1) payment of the issue fee (unless a petition under 37 C.F.R. § 1.313 is granted); (2) abandonment of the application; or (3) the filing of a notice of appeal to the U.S. Court of Appeals for the Federal Circuit under 35 U.S.C. §141, or the commencement of a civil action under 35 U.S.C. §145 or §146 (unless the appeal or civil action is terminated).

Submission required under 37 C.F.R. §1.114:

[X] Amendment/Reply.

The filing fee is calculated below at the large entity rate:

	Claims as Amended	Previous Paid For	ly Extra Claims Present		Rate		Fee Totals
RCE Fee 1.17(e):					\$1,700.0	=	\$1,700.00
					0		
Total Claims:	23	- 26	= 0	X	\$80.00	=	\$0.00
Independents	2	- 5	= 0	X	\$420.00	=	\$0.00
First p	resentation of	any Multiplo	e Dependent Claims:	+	\$780.00	=	\$0.00
			RCE and CLAIMS	FEE	E TOTAL:	=	\$1,700.00

The above-identified fees of \$1,700.00 are being paid by credit card via EFS-Web.

The Commissioner is hereby authorized to charge any additional fees which may be required regarding this application under 37 C.F.R. §§ 1.16-1.17, or credit any overpayment, to Deposit Account No. 19-0741. Should no proper payment be enclosed herewith, as by the credit card payment instructions in EFS-Web being incorrect or absent, resulting in a rejected or incorrect credit card transaction, the Commissioner is authorized to charge the unpaid amount to Deposit Account No. 19-0741.

Please direct all correspondence to the undersigned attorney or agent at the address indicated below.

Respectfully submitted,

Date June 6, 2017

By / Courtenay C. Brinckerhoff/

FOLEY & LARDNER LLP Customer Number: 22428 Telephone: (202) 295-4094 Facsimile: (202) 672-5399 Courtenay C. Brinckerhoff Attorney for Applicant Registration No. 37,288

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicant: Juan Mantelle

Title: Transdermal Estrogen Device and Delivery

13/553,972 Appl. No.:

Filing Date: 7/20/2012

Examiner: Melissa L. Javier

Art Unit: 1611

Confirmation 3635

Number:

AMENDMENT

MAIL STOP: Amendment Commissioner for Patents P.O. Box 1450

Alexandria, VA 22313-1450

Commissioner:

This paper is filed with a Request for Continued Examination. If any extensions of time are required for timely acceptance, Applicant hereby petitions for such extension of time. The Commissioner is hereby authorized to charge any fees which may be due for this application, including any extension of time fees or excess claim fees not submitted herewith, to Deposit Account No. 19-0741.

Amendments to the claims are set forth in the **Listing of Claims** which begins on page 2.

Remarks/Arguments begin on page 6.

Listing of Claims:

Claims 1-13 (Cancelled)

14. (Previously Presented) A method for administering estradiol, comprising applying to the skin or mucosa of a subject in need thereof a monolithic transdermal drug delivery system consisting of (i) a backing layer and (ii) a single adhesive polymer matrix layer defining an active surface area and comprising an adhesive polymer matrix comprising estradiol as the only drug, wherein the polymer matrix has a coat weight of greater than about 10 mg/cm² and includes greater than 0.156 mg/cm² estradiol, and the system achieves an estradiol flux of from about 0.0125 to about 0.05 mg/cm²/day, based on the active surface area.

15. (Canceled)

- 16. (Previously Presented) A method of making a monolithic transdermal drug delivery system for administering estradiol consisting of (i) a backing layer, (ii) a single adhesive polymer matrix layer and, optionally, (iii) a release liner, comprising forming an adhesive polymer matrix comprising estradiol as the only drug and a polymer blend comprising an acrylic adhesive, a silicone adhesive, and soluble PVP, and applying the adhesive polymer matrix to a support layer to form a single adhesive polymer matrix layer such that the adhesive polymer matrix layer has a coat weight of greater than about 10 mg/cm² and includes greater than 0.156 mg/cm² estradiol, wherein the system achieves an estradiol flux of from about 0.0125 to about 0.05 mg/cm²/day, based on the active surface area.
- 17. (Original) The method of claim 16, wherein the system has an active surface area that is about 60% of a size selected from the group consisting of 2.5, 3.75, 5.0, 7.5 and 10.0 cm².

18-20 (Canceled)

21. (Previously Presented) The method of claim 14, wherein the adhesive polymer matrix comprises a polymer blend comprising an acrylic adhesive, a silicone adhesive, and soluble polyvinylpyrrolidone (PVP).

- 22. (Previously Presented) The method of claim 14, wherein the adhesive polymer matrix comprises about 2-25% by weight acrylic adhesive, about 45-70% by weight silicone adhesive, about 2-25% by weight soluble PVP, about 5-15% penetration enhancer, and about 0.1-10% by weight estradiol, all based on the total dry weight of the adhesive polymer matrix.
- 23. (Previously Presented) The method of claim 22, wherein the penetration enhancer comprises oleyl alchol.
- 24. (Previously Presented) The method of claim 22, wherein the penetration enhancer comprises dipropylene glycol.
- 25. (Previously Presented) The method of claim 22, wherein the penetration enhancer comprises oleyl alcohol and dipropylene glycol.
- 26. (Previously Presented) The method of claim 22, wherein the acrylic adhesive and silicone adhesive are present in a ratio of from about 1:2 to about 1:6, based on the total weight of the acrylic and silicone adhesives.

27. (Canceled)

- 28. (Previously Presented) The method of claim 14, wherein the adhesive polymer matrix comprises an amount of estradiol effective to deliver a therapeutically effective amount of estradiol over a period of time selected from the group consisting of at least 1 day, at least 2 days, at least 3 days, at least 4 days, at least 5 days, at least 6 days and at least 7 days.
- 29. (Previously Presented) The method of claim 14, wherein the adhesive polymer matrix comprises an amount of estradiol effective to deliver an amount of estradiol selected from the group consisting of about 0.025, 0.0375, 0.05, 0.075 and 0.1 mg/day.

30. (Canceled)

- 31. (Previously Presented) The method of claim 14, wherein the system achieves an estradiol flux of about 0.0125 mg/cm²/day, based on the active surface area.
- 32. (Previously Presented) The method of claim 14, wherein the system achieves an estradiol flux of about 0.0133 mg/cm²/day, based on the active surface area.
- 33. (Previously Presented) The method of claim 14, wherein the system achieves an estradiol flux of about 0.015 mg/cm²/day, based on the active surface area.
- 34. (Previously Presented) The method of claim 14, wherein the system achieves an estradiol flux of about 0.0167 mg/cm²/day, based on the active surface area.
- 35. (Previously Presented) The method of claim 14, wherein the system achieves an estradiol flux of about 0.0175 mg/cm²/day, based on the active surface area.
- 36. (Previously Presented) The method of claim 16, wherein the system achieves an estradiol flux of about 0.0125 mg/cm²/day, based on the active surface area.
- 37. (Previously Presented) The method of claim 16, wherein the system achieves an estradiol flux of about 0.0133 mg/cm²/day, based on the active surface area.
- 38. (Previously Presented) The method of claim 16, wherein the system achieves an estradiol flux of about 0.015 mg/cm²/day, based on the active surface area.
- 39. (Previously Presented) The method of claim 16, wherein the system achieves an estradiol flux of about 0.0167 mg/cm²/day, based on the active surface area.
- 40. (Previously Presented) The method of claim 16, wherein the system achieves an estradiol flux of about 0.0175 mg/cm²/day, based on the active surface area.
- 41. (New) The method of claim 14, wherein the adhesive polymer matrix comprises about 1.6% by weight estradiol, based on the total dry weight of the adhesive polymer matrix.

42. (New) The method of claim 16, wherein the adhesive polymer matrix comprises about 1.6% by weight estradiol, based on the total dry weight of the adhesive polymer matrix.

REMARKS

A Notice of Allowance allowing claims 14, 16, 17, 21-26, 28, 29, and 31-40 was mailed March 23, 2017.

Claims 41 and 42 are added to recite specific embodiment described in the specification as filed, including in paragraphs [0011], [0069] and [0082]. No new matter is added.

Upon entry of these amendments claims 14, 16-17, 21-26, and 28-29 and 31-42 will be pending. Applicant believes that these claims are in condition for allowance.

Should there be any questions regarding this submission, or should any issue remain, the Examiner is urged to contact the undersigned by telephone to advance prosecution.

Respectfully submitted,

Date: June 6, 2017

By /Courtenay C. Brinckerhoff/

FOLEY & LARDNER LLP Customer Number: 22428 Telephone: (202) 295-4094 Facsimile: (202) 672-5399 Courtenay C. Brinckerhoff Attorney for Applicant Registration No. 37,288

Electronic Patent Application Fee Transmittal					
Application Number:	13.	13553972			
Filing Date:	20	-Jul-2012			
Title of Invention:	TR.	ANSDERMAL ESTRC	OGEN DEVICE AN	ID DELIVERY	
First Named Inventor/Applicant Name:	Juan Mantelle				
Filer:	Courtenay C. Brinckerhoff				
Attorney Docket Number:	04	1457-0992			
Filed as Large Entity					
Filing Fees for Utility under 35 USC 111(a)					
Description		Fee Code	Quantity	Amount	Sub-Total in USD(\$)
Basic Filing:					
Pages:					
Claims:					
Miscellaneous-Filing:					
Petition:					
Patent-Appeals-and-Interference:					
Post-Allowance-and-Post-Issuance:					
Extension-of-Time:					

Description	Fee Code	Quantity	Amount	Sub-Total in USD(\$)
Miscellaneous:				
RCE- 2ND AND SUBSEQUENT REQUEST	1820	1	1700	1700
	Tot	al in USD	(\$)	1700

Electronic Acknowledgement Receipt		
EFS ID:	29406722	
Application Number:	13553972	
International Application Number:		
Confirmation Number:	3635	
Title of Invention:	TRANSDERMAL ESTROGEN DEVICE AND DELIVERY	
First Named Inventor/Applicant Name:	Juan Mantelle	
Customer Number:	22428	
Filer:	Courtenay C. Brinckerhoff/Christine Arthur	
Filer Authorized By:	Courtenay C. Brinckerhoff	
Attorney Docket Number:	041457-0992	
Receipt Date:	06-JUN-2017	
Filing Date:	20-JUL-2012	
Time Stamp:	12:39:47	
Application Type:	Utility under 35 USC 111(a)	

Payment information:

Submitted with Payment	yes
Payment Type	CARD
Payment was successfully received in RAM	\$1700
RAM confirmation Number	060617INTEFSW12400900
Deposit Account	
Authorized User	

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

File Listing	j :				
Document Number	Document Description	File Name	File Size(Bytes)/ Message Digest	Multi Part /.zip	Pages (if appl.)
			102546		
1	Request for Continued Examination (RCE)	RCE.pdf	ad5731ba910b235b2e92279226e9734a57 443a31	no	3
Warnings:	-		-	l	
This is not a USF	PTO supplied RCE SB30 form.				
Information:					
			104738		6
2	Amendment Submitted/Entered with Filing of CPA/RCE	amendment.pdf	795ff5b7be0cd2a5135e87b03f0fdda1dce0 6931	no	
Warnings:					
Information:					
			30373		
3	Fee Worksheet (SB06)	fee-info.pdf	7afa426d28fac95b6a98b120e36ac4ae36d4 abec	no	2
Warnings:			1		
Information:					
		Total Files Size (in bytes): 23		

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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.

Approved for use through 1/31/2014. OMB 0651-0032

U.S. Patent and Trademark Office; U.S. DEPARTMENT OF COMMERCE

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P	PATENT APPLICATION FEE DETERMINATION RECORD Substitute for Form PTO-875						on or Docket Number 3/553,972	Filing Date 07/20/2012	To be Mailed
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				APPLICA	ATION AS FIL	ED – PAI	RTI		
			(Column 1						
	FOR		NUMBER FIL	.ED	NUMBER EXTRA		RATE (\$)	F	FEE (\$)
	BASIC FEE (37 CFR 1.16(a), (b),	or (c))	N/A		N/A		N/A		
	SEARCH FEE (37 CFR 1.16(k), (i), (or (m))	N/A		N/A		N/A		
	EXAMINATION FE (37 CFR 1.16(o), (p),	EE or (q))	N/A		N/A		N/A		
	TAL CLAIMS CFR 1.16(i))		min	us 20 = *			X \$ =		
	EPENDENT CLAIM CFR 1.16(h))	IS	mi	nus 3 = *			X \$ =		
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	MULTIPLE DEPEN	IDENT CLAIM	1 PRESENT (3	7 CFR 1.16(j))					
* If t	* If the difference in column 1 is less than zero, enter "0" in column 2.								
		(Column 1	1)	APPLICAT	ION AS AMEN		ART II		
_N:	06/06/2017	CLAIMS REMAINING AFTER AMENDME		HIGHEST NUMBER PREVIOUSLY PAID FOR	PRESENT EX	TRA	RATE (\$)	ADDITIO	ONAL FEE (\$)
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This collection of information is required by 37 CFR 1.16. 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 1.14. 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.

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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
13/553,972	07/20/2012	Juan Mantelle	041457-0992	3635
22428 Foley & Lardne	7590 06/14/201 er LLP	7	EXAM	INER
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WASHINGTO	N, DC 20007-5109		ART UNIT	PAPER NUMBER
			1611	
			NOTIFICATION DATE	DELIVERY MODE
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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.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

ipdocketing@foley.com

Applicant-Initiated Interview Summary	13/553,972	MANTELLE, JUAN						
Applicant-initiated interview Summary	Examiner	Art Unit						
	Melissa Fisher	1611						
All participants (applicant, applicant's representative, PTO p	ersonnel):							
(1) <u>Melissa Fisher</u> .	(3) <i>Richard Guy</i> .							
(2) <u>Courtenay Brinckerhoff</u> .	(4)							
Date of Interview: <u>08 June 2017</u> .								
Type: ☐ Telephonic ☐ Video Conference ☐ Personal [copy given to: ☐ applicant ☐	applicant's representative]							
Exhibit shown or demonstration conducted: Yes If Yes, brief description:] No.							
Issues Discussed 101 112 1102 103 Other (For each of the checked box(es) above, please describe below the issue and detailed								
Claim(s) discussed:								
Identification of prior art discussed: None.								
Substance of Interview (For each issue discussed, provide a detailed description and indicate if agreement vereference or a portion thereof, claim interpretation, proposed amendments, arguments	÷ •	entification or clarifica	tion of a					
Discussed the attached agenda.								
Specifically, Applicant's representative and Dr. Guy explained that increasing the coat weight of the drug-containing adhesi permitted the development of smaller transdermal drug deliver	ve layer resulted in an increas	ed flux per unit a	rea, and					
Applicant recordation instructions: The formal written reply to the last Office action must include the substance of the interview. (See MPEP ection 713.04). If a reply to the last Office action has already been filed, applicant is given a non-extendable period of the longer of one month or nirty days from this interview date, or the mailing date of this interview summary form, whichever is later, to file a statement of the substance of the atterview. In a statement of the substance of the substance of any interview of record. A complete and proper recordation of the substance of an interview should include the items listed in MPEP 713.04 for complete and proper recordation including the identification of the eneral thrust of each argument or issue discussed, a general indication of any other pertinent matters discussed regarding patentability and the eneral results or outcome of the interview, to include an indication as to whether or not agreement was reached on the issues raised.								
Attachment /Melissa Fisher/								
Primary Examiner, Art Unit 1611								

Application No.

Applicant(s)

U.S. Patent and Trademark Office PTOL-413 (Rev. 8/11/2010) Interview Summary

Paper No. 20170609

Summary of Record of Interview Requirements

Manual of Patent Examining Procedure (MPEP), Section 713.04, Substance of Interview Must be Made of Record

A complete written statement as to the substance of any face-to-face, video conference, or telephone interview with regard to an application must be made of record in the application whether or not an agreement with the examiner was reached at the interview.

Title 37 Code of Federal Regulations (CFR) § 1.133 Interviews

Paragraph (b)

In every instance where reconsideration is requested in view of an interview with an examiner, a complete written statement of the reasons presented at the interview as warranting favorable action must be filed by the applicant. An interview does not remove the necessity for reply to Office action as specified in §§ 1.111, 1.135. (35 U.S.C. 132)

37 CFR §1.2 Business to be transacted in writing.

All business with the Patent or Trademark Office should be transacted in writing. The personal attendance of applicants or their attorneys or agents at the Patent and Trademark Office is unnecessary. The action of the Patent and Trademark Office will be based exclusively on the written record in the Office. No attention will be paid to any alleged oral promise, stipulation, or understanding in relation to which there is disagreement or doubt.

The action of the Patent and Trademark Office cannot be based exclusively on the written record in the Office if that record is itself incomplete through the failure to record the substance of interviews.

It is the responsibility of the applicant or the attorney or agent to make the substance of an interview of record in the application file, unless the examiner indicates he or she will do so. It is the examiner's responsibility to see that such a record is made and to correct material inaccuracies which bear directly on the question of patentability.

Examiners must complete an Interview Summary Form for each interview held where a matter of substance has been discussed during the interview by checking the appropriate boxes and filling in the blanks. Discussions regarding only procedural matters, directed solely to restriction requirements for which interview recordation is otherwise provided for in Section 812.01 of the Manual of Patent Examining Procedure, or pointing out typographical errors or unreadable script in Office actions or the like, are excluded from the interview recordation procedures below. Where the substance of an interview is completely recorded in an Examiners Amendment, no separate Interview Summary Record is required.

The Interview Summary Form shall be given an appropriate Paper No., placed in the right hand portion of the file, and listed on the "Contents" section of the file wrapper. In a personal interview, a duplicate of the Form is given to the applicant (or attorney or agent) at the conclusion of the interview. In the case of a telephone or video-conference interview, the copy is mailed to the applicant's correspondence address either with or prior to the next official communication. If additional correspondence from the examiner is not likely before an allowance or if other circumstances dictate, the Form should be mailed promptly after the interview rather than with the next official communication.

The Form provides for recordation of the following information:

- Application Number (Series Code and Serial Number)
- Name of applicant
- Name of examiner
- Date of interview
- Type of interview (telephonic, video-conference, or personal)
- Name of participant(s) (applicant, attorney or agent, examiner, other PTO personnel, etc.)
- An indication whether or not an exhibit was shown or a demonstration conducted
- An identification of the specific prior art discussed
- An indication whether an agreement was reached and if so, a description of the general nature of the agreement (may be by
 attachment of a copy of amendments or claims agreed as being allowable). Note: Agreement as to allowability is tentative and does
 not restrict further action by the examiner to the contrary.
- The signature of the examiner who conducted the interview (if Form is not an attachment to a signed Office action)

It is desirable that the examiner orally remind the applicant of his or her obligation to record the substance of the interview of each case. It should be noted, however, that the Interview Summary Form will not normally be considered a complete and proper recordation of the interview unless it includes, or is supplemented by the applicant or the examiner to include, all of the applicable items required below concerning the substance of the interview.

A complete and proper recordation of the substance of any interview should include at least the following applicable items:

- 1) A brief description of the nature of any exhibit shown or any demonstration conducted,
- 2) an identification of the claims discussed,
- 3) an identification of the specific prior art discussed,
- 4) an identification of the principal proposed amendments of a substantive nature discussed, unless these are already described on the Interview Summary Form completed by the Examiner.
- 5) a brief identification of the general thrust of the principal arguments presented to the examiner,
 - (The identification of arguments need not be lengthy or elaborate. A verbatim or highly detailed description of the arguments is not required. The identification of the arguments is sufficient if the general nature or thrust of the principal arguments made to the examiner can be understood in the context of the application file. Of course, the applicant may desire to emphasize and fully describe those arguments which he or she feels were or might be persuasive to the examiner.)
- 6) a general indication of any other pertinent matters discussed, and
- if appropriate, the general results or outcome of the interview unless already described in the Interview Summary Form completed by the examiner.

Examiners are expected to carefully review the applicant's record of the substance of an interview. If the record is not complete and accurate, the examiner will give the applicant an extendable one month time period to correct the record.

Examiner to Check for Accuracy

If the claims are allowable for other reasons of record, the examiner should send a letter setting forth the examiner's version of the statement attributed to him or her. If the record is complete and accurate, the examiner should place the indication, "Interview Record OK" on the paper recording the substance of the interview along with the date and the examiner's initials.

Outline for June 8, 2017 Examiner Interview

Summary Of Claimed Subject Matter

The claimed subject matter includes transdermal drug delivery systems estradiol that have a smaller active surface area than the prior art Vivelle-Dot® patches, but achieve daily dosages that are about equal to or greater than the Vivelle-Dot® patches. That is, the subject matter includes transdermal drug delivery systems that achieve daily dosages that are about equal to a Vivelle-Dot® patch, in a smaller size. *See, e.g.*, Specification, at paragraph [0014].

As stated in the specification, "the Applicant surprisingly discovered that increasing the coat weight of the drug-containing adhesive layer resulted in an increased flux per unit area, and thus permitted the development of smaller transdermal drug delivery systems that achieve comparable daily dosages." Specification, at paragraph [0014].

All claims recite a monolithic transdermal drug delivery system consisting of (i) a backing layer and (ii) a single adhesive polymer matrix layer defining an active surface area and comprising an adhesive polymer matrix comprising estradiol as the only drug.¹

The claims of the '972, '985, and '255 applications recite that the polymer matrix has a coat weight of greater than about 10 mg/cm² and includes greater than 0.156 mg/cm² estradiol, and that the transdermal drug delivery system achieves an estradiol flux of from about 0.0125 to about 0.05 g/cm²/day, based on the active surface area.

The claims of the '574 application recite that the coat weight of the polymer matrix is adjusted such that system includes greater than 0.156 mg/cm² estradiol, and that the transdermal drug delivery achieves an estradiol flux of from about 0.0125 to about 0.05 g/cm²/day, based on the active surface area.

1

¹ Some claims recite an optional release liner that is removed prior to use.

Summary Of Issues To Be Discussed

- Understanding in the art regarding passive drug flux from a transdermal drug delivery system (Fick's 1st Law of Diffusion)
- Impact of polymer components on drug flux (predicted by Fick's 1st Law)
- Additional experimental data demonstrating surprising and unexpected result that increasing coat weight increases estradiol flux (not predicted by Fick's 1st Law)

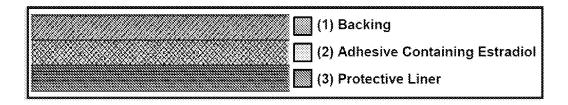
Introduction of Expert

Dr. Richard Guy, Professor of Pharmaceutical Sciences, University of Bath (UK) (in the Department of Pharmacy & Pharmacology)

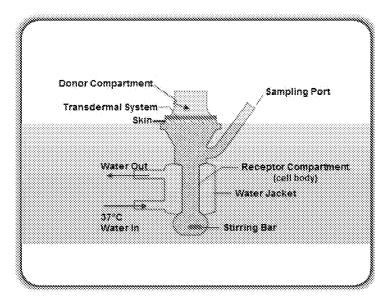
- over 30 years' research experience in the field of topical and transdermal drug delivery, including the study of drug absorption into and through the skin
- Bachelor of Arts in chemistry from Oxford University (UK) (1977)
- Master of Arts in chemistry from Oxford University (1980)
- Ph.D. in pharmaceutical chemistry from the University of London (UK) (1980).
- D.Sc. from Oxford University (2016).
- co-author on over 350 peer-reviewed articles and over 70 book chapters.
- experience as a consultant (and scientific advisory board member) to numerous pharmaceutical companies involved in the development of transdermal drug delivery formulations (including patches and other gels)
- engaged by the Applicant (Noven Pharmaceuticals, Inc.) to serve as an expert witness in ANDA litigation involving U.S. Patent No.8,231,906 (the '906 Patent), in the U.S. District Court for the District of Delaware (C.A. No. 15-249) (the "ANDA litigation).
- engaged by the Applicant to prepare a Declaration for U.S. patent applications 13/553,972, 14/024,985, 14/738,255, and 14/870,574 and attend the Patent Office Interview
- His compensation does not depend in any way on the outcome of the examination of the pending applications or on the outcome of the ANDA litigation.

TECHNICAL BACKGROUND

The inventions claimed in the pending applications generally relate to transdermal drug delivery systems (*e.g.*, transdermal "patches") for the delivery of estradiol, methods of administering estradiol to a patient using the claimed transdermal drug delivery systems, and delivering estradiol using them, and methods of making them. The claimed transdermal drug delivery systems are "monolithic" drug-in-adhesive systems that consist of (i) a backing layer; (ii) a drug-in-adhesive polymer matrix layer, and, optionally, (iii) a release liner that is removed prior to use, as illustrated below.



The claims recite that the adhesive polymer matrix layers include a certain amount estradiol per unit area and achieve a certain estradiol flux. The flux of a drug is the rate at which it diffuses through the skin. An *in vitro* flux study may be conducted to assess the flux of a drug from a transdermal drug delivery system. The image below shows a typical Franz diffusion cell set up used to conduct an *in vitro* flux study.



In general, the receptor compartment is filled with a receiver solution that is stirred and held at a constant (typically, physiological) temperature. A transdermal system is placed on a skin sample in the donor compartment, and the contents of the receptor compartment are sampled (withdrawn) periodically and analyzed for drug (for example, estradiol) content. From this information, the cumulative amount of drug delivered over time and the flux of drug across the skin as a function of time is calculated.

An illustration of the type of experimental data collected with this approach is shown below for one particular formulation; the results are presented as the average cumulative amounts of drug delivered, and the average drug flux, as a function of time, with the corresponding standard deviations for 4 replicate Franz diffusion cells.

(hours)	(mcg/cm2)	(mcg/cm2)	(mcg/cm2 hr)	(mcg/cm2 hr)
Average Time	Average Cum.	Cum. Stdev	Average Flux	Flux Stdev
0.00	0.00	0.00	0.00	0.00
9.92	2.55	0.49	0.26	0.05
23.95	12.64	1.99	0.72	0.11
33.65	20.85	2.91	0.85	0.10
48.03	33.45	4.10	0.88	0.08
57.58	41.70	4.81	0.86	0.08
72.20	54.23	5.71	0.86	0.06
81.02	61,43	6.07	0.82	0.04

These results may be plotted graphically as illustrated in the specification and the additional experimental data that will be discussed.

U.S. Patent Application Nos. 13/553,972; 14/024,985; 14/738,255; 14/870,574 Atty. Docket Nos. 041457-0992, -1016, -1133, -1160

FICK'S FIRST LAW OF DIFFUSION

As of June 10, 2008, a person of ordinary skill in the art understood that the passive flux of a drug can be quantitatively described and modelled by Fick's 1st law. Fick's 1st law is often used to describe drug delivery (in units of amount per time, *e.g.*, mg/day or µg/hour) from a transdermal patch across the skin:

$$J = A \times k_p \times \Delta C$$

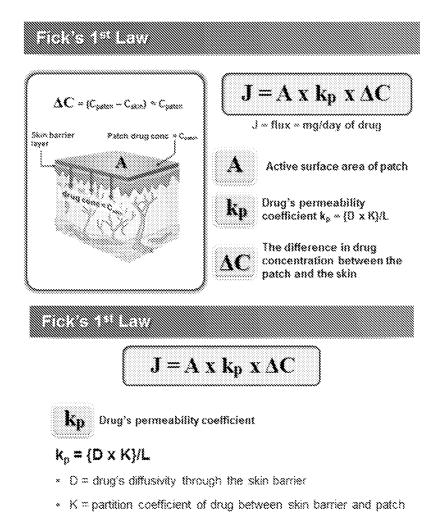
In this formula:

A is the active surface area of the patch.

 k_p is the drug's permeability coefficient across the skin, and can be defined as $k_p = \{D \ x \ K\}/L$, where D is the drug's diffusivity through the skin barrier, K is its partition coefficient between the skin barrier and the patch, and L is the path length for diffusion across the skin barrier.

 ΔC is the difference in concentration of the drug between that in the patch (C_{patch}) and that on the "downstream" side of the skin barrier ($C_{downstream}$). In many examples of transdermal delivery, when depletion of drug from the patch is limited, ΔC can be approximated to C_{patch} .

The following images illustrate these factors:



Fick's 1st law indicates that there are four general ways to increase flux:

• Increase the active surface area of the patch to cause a proportional change in flux.

L = path length for drug diffusion across skin barrier

- Increase the drug concentration in the patch until it reaches its limiting solubility.
- Adjust the formulation to increase K, *e.g.*, cause drug concentration to approach more closely its limiting solubility.
- Introduce a penetration enhancer into the formulation to increase D and/or alter the value of K.

U.S. Patent Application Nos. 13/553,972; 14/024,985; 14/738,255; 14/870,574 Atty. Docket Nos. 041457-0992, -1016, -1133, -1160

Nothing in Fick's 1st law indicates or predicts that increasing the coat weight (thickness) of a polymer matrix would increase flux. This is because no factor in Fick's 1st law embodies or includes coat weight.

THE UNEXPECTED DISCOVERY OF THE INVENTION

As noted above, "the Applicant surprisingly discovered that increasing the coat weight of the drug-containing adhesive layer resulted in an increased flux per unit area, and thus permitted the development of smaller transdermal drug delivery systems that achieve comparable daily dosages." Specification, at paragraph [0014]. As stated in paragraph [0015] in the specification:

This result was surprising because coat weight is typically selected to control the duration of delivery, but is not generally understood to impact delivery rate. Thus, while it is known in the art to increase coat weight to provide delivery over a longer period of time, it was not known that increasing coat weight could increase delivery rate or flux, and thus permit the development of a smaller system while maintaining daily dosage.

Indeed, as explained above, nothing in Fick's 1st law indicates or predicts that increasing the coat weight (thickness) of a polymer matrix would increase flux.

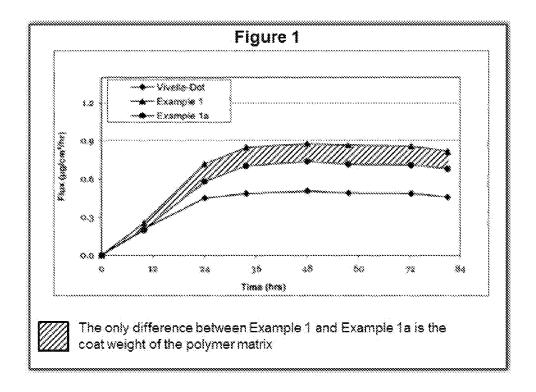
THE EXAMPLE IN THE SPECIFICATION

The specification illustrates this surprising and unexpected effect in Example 1, which describes an *in vitro* flux study conducted to assess the flux of estradiol from different systems. Figure 1 reports the flux of drug across the skin for the systems tested in Example 1.

Example 1 sets forth the polymer matrix formulation used to prepare Example 1 and Example 1a. As noted in the prosecution history of the '906 Patent, in the Amendment and Reply filed April 20, 2011, the specification as filed had a clerical error in the formulation listed (see below), but the flux data presented in Figure 1 is correct.

	Example 1	Actual Formulation
Silicone (4502)	36.9	66.9
Acrylic (Gelva 788)	20	10
PVP (Kollidon K-30)	7.5	7.5
DPG	8	8
Oleyl Alcohol	6	6
Estradiol	1.6	1.6

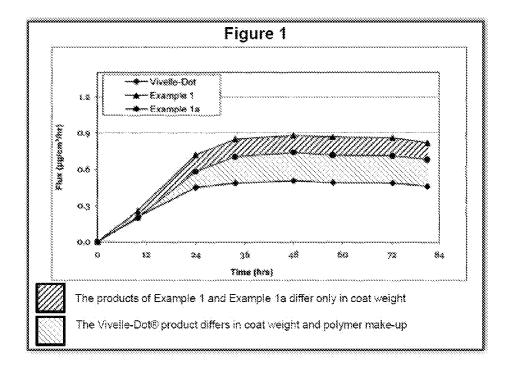
As described in the specification, test systems were prepared by applying the polymer matrix to a release liner at two different coat weights: 12.5 mg/cm² (Example 1a, ●) and 15 mg/cm² (Example 1, ▲), and estradiol flux was assessed in an *in vitro* flux study. As reported in Figure 1, the system with the higher coat weight exhibited a greater flux.



The only experimental variable different between Example 1a and Example 1 is the coat weight of the polymer matrix. The difference in flux reported in Figure 1 between Example 1a and Example 1 can only be attributed, therefore, to the difference in coat weight, which is a surprising and unexpected result that is not predicted by Fick's 1st Law.

Figure 1 also reports results achieved with a Vivelle-Dot® system. As described in the prescribing information, Vivelle-Dot® is a monolithic transdermal drug delivery system for estradiol with a polymer matrix layer that includes estradiol as the only drug, acrylic adhesive, silicone adhesive, oleyl alcohol, povidone, and dipropylene glycol. The specification states that each Vivelle-Dot® patch includes 0.156 mg/cm² estradiol and has a polymer matrix coat weight of 10 mg/cm². See, e.g., Specification at paragraph [0013]; [0074]. Although Vivelle-Dot® includes the same polymer matrix components of the Example 1 formulation, I have been informed that the Vivelle-Dot® formulation includes different amounts of some components, including different relative amounts of acrylic adhesive and silicone adhesive, with a greater relative amount of acrylic adhesive. That is, the formulation of Examples 1 and 1a have less acrylic adhesive and more silicone adhesive than the Vivelle-Dot® formulation.

Prior art such as U.S. Patent No. 6,024,976 (the "'976 Patent") and Mantelle, et al., Effect of Silicone/Acrylic PSA Blends on Skin Permeation, 26 Proc. Internat'l Symp. Controlled Release of Bioactive Materials 5123, 415-16 (Revised July 1999) (the "Mantelle Article"), and post-filing date publications such as Juan A. Mantelle, "Dot Matrix® Technology," in Modified Release Drug Delivery Technology (2nd ed. 2008) 405-14 (the "Mantelle Chapter") teach that the difference in relative amounts of acrylic adhesive and silicone adhesive between the formulation of Examples 1/1a and the Vivelle-Dot® formulation contributes to the difference in flux seen in Figure 1 between Vivelle-Dot® and Example 1 and between Vivelle-Dot® and Example 1a.



It is not possible to quantify from available data the relative contributions of coat weight and polymer composition to the differences in flux observed between the Vivelle-Dot® system and Examples 1/1a systems. However, based on the difference in flux between the Example 1 and 1a systems (which, as explained above, can only be due to the difference in coat weight), and in view of other experimental data discussed below, it is Dr. Guy's expert opinion that the difference in coat weight is contributing to the difference in flux.

EXPERIMENTAL DATA – IMPACT OF POLYMER MAKE-UP ON FLUX

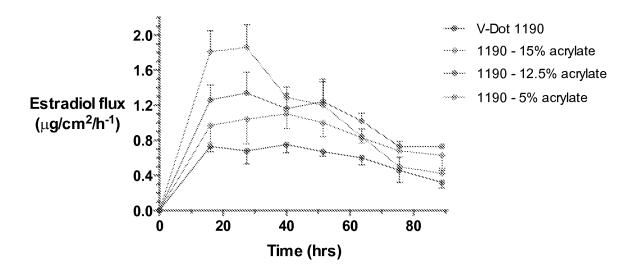
As noted above, it was known in the art that the relative amounts of acrylic adhesive and silicone adhesive used in an estradiol polymer matrix can impact the flux of estradiol. This is described in the '976 Patent, which explains that this is because estradiol's solubility in acrylic adhesives differs from that in silicone adhesives. The potential effect of the relative amounts of acrylic adhesive and silicone adhesive is illustrated in Examples 10-13 and Figure 6 of the '976 patent, and in the Mantelle Article. Thus, it was known in the art that the relative amounts of acrylic adhesive and silicone adhesive in an estradiol polymer matrix can impact estradiol flux, and that

increasing the relative amount of silicone polymer generally increased the flux but may alter the drug delivery profile such that the increased flux is not sustained.

Flux Study 1190 conducted by Noven also illustrates this effect. Flux Study 1190 tested five different formulations at the same target coat weight (15 mg/cm²) and used a Vivelle-Dot® system (*) as an internal control. The five formulations differed in the relative amounts of acrylic adhesive and silicone adhesive.

Component	5% Acrylic	10% Acrylic	12.5% Acrylic	15% Acrylic	17.5% Acrylic
(% by weight)					
Acrylic Adhesive	5	10	12.5	15	17.5
Silicon Adhesive	71.9	66.9	64.5	61.9	59.4
Dipropylene Glycol	8	8	8	8	8
Oleyl Alcohol	6	6	6	6	6
PVP	7.5	7.5	7.5	7.5	7.5
Estradiol	1.6	1.6	1.6	1.6	1.6

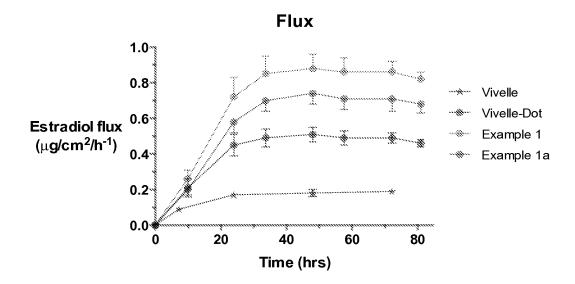
A representative sample of the data from this Flux Study are shown in the figure below. The results show that initial flux increased as the relative amount of acrylic polymer decreased but the initially higher flux from the 5% acrylic composition was not sustained:

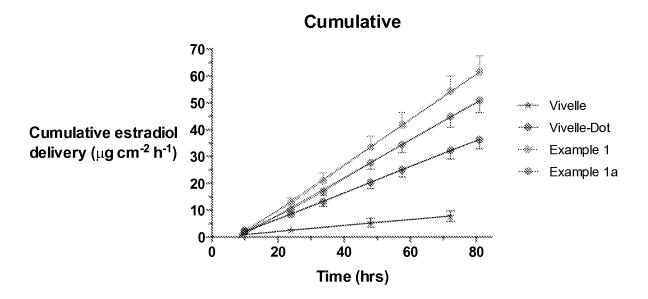


EXPERIMENTAL DATA – IMPACT OF COAT WEIGHT ON FLUX

As noted above, while it was known in the art that the relative amounts of acrylic adhesive and silicone adhesive in an estradiol polymer matrix can impact estradiol flux, it was not known or expected that the coat weight of the polymer matrix would impact flux, but Noven conducted a number of other flux studies that showed this effect with monolithic transdermal drug delivery systems for estradiol as described in the pending applications.

Flux Study 1326 is the flux study reported in Example 1 of the pending applications. As discussed above, the same formulation (1.6 % estradiol, 10% acrylic adhesive, 66.9% silicone adhesive, 6% oleyl alcohol, 7.5% povidone, and 8% dipropylene glycol) was tested at coat weights of 12.5 mg/cm² and 15 mg/cm². Both Vivelle® and Vivelle-Dot® were used as internal controls. As noted above, the results (see below) show that the increase in the coat weight of the polymer matrix from Example 1a to Example 1 resulted in an increased flux of estradiol.



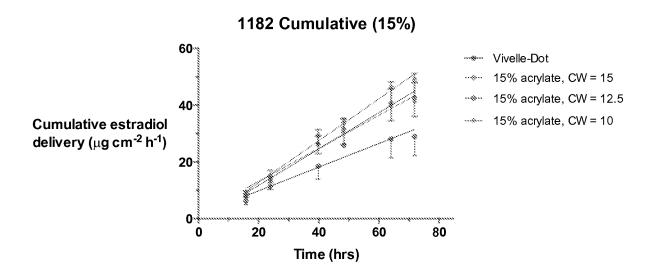


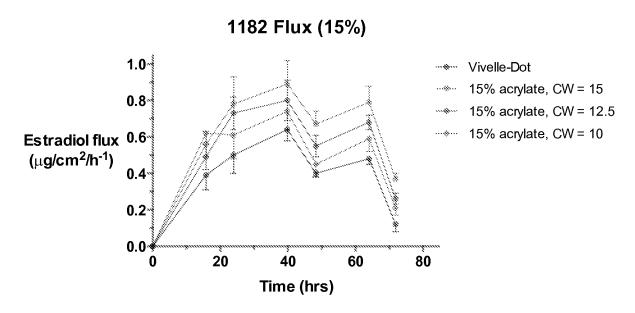
Flux Study 1182 conducted by Noven tested four different formulations at three different target coat weights and used a Vivelle-Dot® system as an internal control. The four formulations differed in the relative amounts of acrylic adhesive and silicone adhesive, as follows:

Component	10% Acrylic	15% Acrylic	17.5% Acrylic	20% Acrylic
(% by weight)				
Acrylic	10	15	17.5	20
Adhesive				
Silicon	66.9	61.9	59.4*	56.9
Adhesive				
Dipropylene	8	8	8	8
Glycol				
Oleyl Alcohol	6	6	6	6
PVP	7.5	7.5	7.5	7.5
Estradiol	1.6	1.6	1.6	1.6

^{*}Reported as 59.9%, but likely used 59.4% Silicone Adhesive.

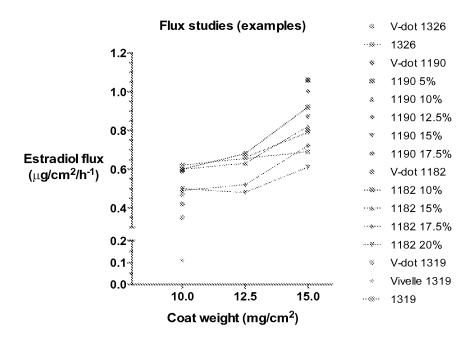
The different target coat weights assessed were 10 mg/cm², 12.5 mg/cm² and 15 mg/cm². The overall results show that increasing coat weight from 10 mg/cm² to 15 mg/cm² surprisingly and unexpectedly increased flux. For illustration, results for the composition with 15% acrylic polymer at a coat weight of 10 mg/cm², 12.5 mg/cm², and 15 mg/cm² (ℕ) are set forth below (Vivelle-Dot® was used as an internal control).





Collectively, the results from Flux Studies 1190 and 1182 indicate that while the relative amounts of acrylic adhesive and silicone adhesive impact the flux of estradiol—as was known in the art—the coat weight of the polymer matrix also impacts flux—which was not known in the art, and indeed was a surprising and unexpected result not predicted by Fick's 1st law of diffusion.

The estimated estradiol fluxes from Flux Studies 1190 and 1182 are shown below:

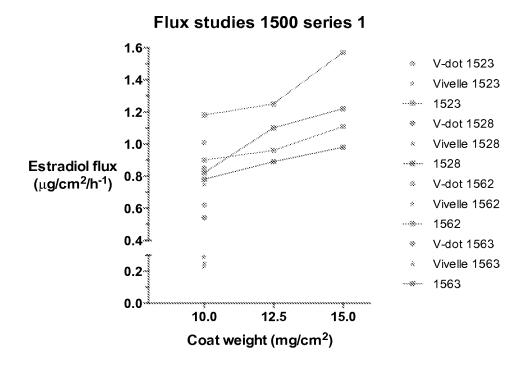


Flux Studies 1523, 1528, 1562 and 1563 assessed other formulations at different target coat weights, as outlined in the following table.

Elver Cturder	Fori	nulation C	ompone	ents (%	by wei	ght)	Coat Wt.	Drug Flux
Flux Study	Acrylate	Silicone	DPG	OAlc	PVP	Estradiol	(mg/cm ²)	(µg/cm ² •h)
	10	69.4	8	6	5	1.6	15	1.57
	10	69.4	8	6	5	1.6	12.5	1.25
1523	10	69.4	8	6	5	1.6	10	1.18
	Control (fl	lux): Vivel	le-Dot®) (1. 0 1 μ	ug/cm ²	•h)		
	10	60.4	0		_	1.6	1.5	0.00
	10	69.4	8	6	5	1.6	15	0.98
	10	69.4	8	6	5	1.6	12.5	0.89
1528	10	69.4	8	6	5	1.6	10	0.78
	Control (fl	lux): Vivel	le-Dot®	(0.54 µ	ug/cm ²	•h)		
1562	10	69.4	8	6	5	1.6	15	1.11
1562 (Form 1)	10	69.4	8	6	5	1.6	12.5	0.96
(Form. 1)	10	69.4	8	6	5	1.6	10	0.90

Elvy Study	Forn	nulation Co	Coat Wt.	Drug Flux				
Flux Study	Acrylate	Silicone	DPG	OAlc	PVP	Estradiol	(mg/cm ²)	(µg/cm ² •h)
	Control (fl	ux): Vivell	le-Dot®) (0.62 µ	ıg/cm²•	rh)		
	10	69.4	8	6	5	1.6	15	1.22
1562	10	69.4	8	6	5	1.6	12.5	1.10
1563 10 69.4 8 6 5 1.6 10 0.8							0.82	
(Form. 1)	Control (flux): Vivelle-Dot® (0.85 µg/cm ² •h)							

The estimated estradiol fluxes from Flux Studies 1523, 1528, 1562, and 1563 are illustrated below, and again show the surprising and unexpected impact of polymer matrix coat weight on flux:



Flux Studies 1562 and 1563 were repeated with different formulations at coat weights of 12.5 mg/cm² and 15 mg/cm² using both Vivelle and Vivelle-Dot® as internal controls.

E1 C4 4	For	Formulation Components (% by weight) Coat Wt. Drug							
Flux Study	Acrylate	Silicone	DPG	OAlc	PVP	Estradiol	(mg/cm ²)	(µg/cm ² •h)	
1560	10	60.4	0			1.6	1.5	1.01	
1562	10	69.4	8	6	5	1.6	15	1.01	
(Form. 1)	10	69.4	8	6	5	1.6	12.5	0.85	
1562 (Form. 2)	7	72.6	8	6	5	1.4	15	1.12	
	7	72.6	8	6	5	1.4	12.5	0.92	
1 - 12									
1562 (Form. 3)	7	74.6	8	6	3	1.4	15	1.07	
	7	74.6	8	6	3	1.4	12.5	0.96	
1562 Contro	ol (flux): Vi	velle-Dot®	(0.62μ)	ig/cm²•l	1)	1		•	
1563	10	69.4	8	6	5	1.6	15	1.12	
(Form. 1)	10	69.4	8	6	5	1.6	12.5	1.04	
1563 (Form. 2)	7	72.6	8	6	5	1.4	15	1.08	
	7	72.6	8	6	5	1.4	12.5	1.01	
1563 (Form. 3)	7	74.6	8	6	3	1.4	15	1.05	
	7	74.6	8	6	3	1.4	12.5	0.81	
1563 Contro	l ol (flux): Vi	l velle-Dot®	Ι (0.85 μ	l ıg/cm²•l	l 1)				

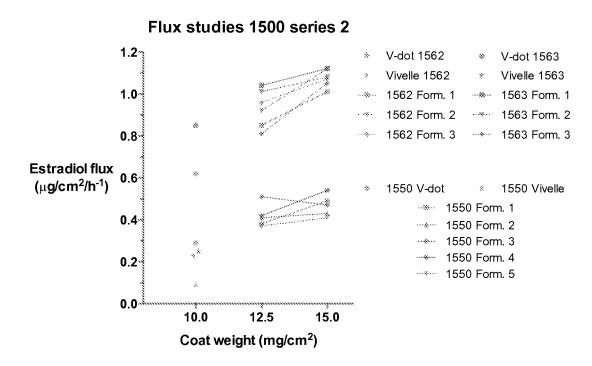
Flux Study 1550 assessed other formulations at different target coat weights, as outlined in the following table.

Formulation	Formulation Components (% by weight)						Coat Wt.	Drug Flux	
	Acrylate	Silicone	Silicone DPG OAlc PVP Estradiol					Drug Flux (μg/cm ² •h)	
Form. 1	10	71.6	8	6	3	1.4	15	0.49	
	10	71.6	8	6	3	1.4	12.5	0.38	

U.S. Patent Application Nos. 13/553,972; 14/024,985; 14/738,255; 14/870,574 Atty. Docket Nos. 041457-0992, -1016, -1133, -1160

Formulation	Formulati	on Compo	Coat Wt.	Drug Flux				
	Acrylate	Silicone	DPG	OAlc	PVP	Estradiol	(mg/cm ²)	$(\mu g/cm^2 \cdot h)$
Form. 2	10	69.4	8	6	5	1.6	15	0.43
	10	69.4	8	6	5	1.6	12.5	0.41
Form. 3	7	72.6	8	6	5	1.4	15	0.47
	7	72.6	8	6	5	1.4	12.5	0.51
Form. 4	7	74.6	8	6	3	1.4	15	0.54
	7	74.6	8	6	3	1.4	12.5	0.42
Form. 5	10	73.4	6	6	3	1.6	15	0.41
	10	73.4	6	6	3	1.6	12.5	0.41

The estimated estradiol fluxes from 1562 and 1563 (second series) and 1550 are illustrated below, and again show the surprising and unexpected impact of polymer matrix coat weight on flux:



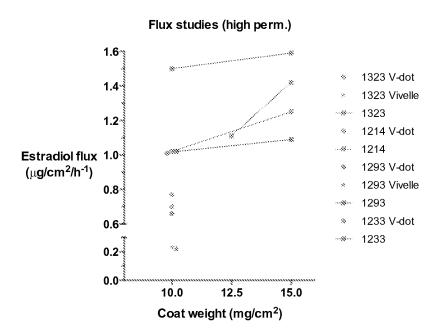
EXPERIMENTAL DATA - IMPACT OF SKIN PERMEABILITY ON FLUX

Since drug flux is a measure of the rate at which drug passes through the skin, the permeability of the skin sample used in a flux study can impact the results. The permeability of human skin varies from person to person and region of skin to region of skin. Noven accounted for this variability by using internal controls, such as Vivelle®-Dot or Vivelle®, since it was very familiar with the flux of these FDA-approved systems which were developed at Noven.

The impact of skin permeability on flux and the usefulness of an internal control in this context is illustrated in Flux Studies 1214, 1233, and 1293, which assessed the flux of formulations having the same components as the Example 1 formulation at target coat weights of 10 mg/cm² and 15 mg/cm² (and used Vivelle-Dot® and Vivelle as internal controls).

Study #	Fo	rmulation	Coat Wt.	Drug Flux				
	Acrylate	Silicone	DPG	OAlc	PVP	Estradiol	(mg/cm ²)	$(\mu g/cm^2 \cdot h)$
1323	10	66.9	8	6	7.5	1.6	15	1.42
	10	66.9	8	6	7.5	1.6	12.5	1.11
Control (flux): Vivel	le-Dot® (().77 μg/	/cm ² •h)				
	flux): Vivel							
1214	10	66.9	8	6	7.5	1.6	15	1.25
	10	66.9	8	6	7.5	1.6	10	1.02
Control (flux): Vivel	lle-Dot® (0).7 μg/c	m ² •h)				
1293	10	66.9	8	6	7.5	1.6	15	1.09
	10	66.9	8	6	7.5	1.6	10	1.02
Control (flux): Vivel	lle-Dot® (0).66 µg/	/cm ² •h)				
Control (flux): Vivel	lle® (0.22	μg/cm²	•h)				
1233	10	66.9	8	6	7.5	1.6	15	1.59
	10	66.9	8	6	7.5	1.6	10	1.50
Control (flux): Vivel	lle-Dot® (1	1.01 μg/	/cm ² •h)	_			-

The cumulative flux results are illustrated below:



In these studies, the estradiol flux from Vivelle-Dot® was higher than usual, indicating that the donor skin had a higher permeability than usual. While the product label and the patient information leaflet indicate that the estradiol transdermal flux from the Vivelle®-Dot system is nominally $0.4~\mu g~cm^{-2}~h^{-1}$, the values observed in these flux studies were 1.5 to 2.5-fold higher. The high fluxes seen from the test formulations are therefore completely consistent with that from the Vivelle®-Dot control (and reinforce the clear benefit of including this system as an internal check in experiments such as these).

Pending Independent Claims

U.S. Patent Application Nos. 13/553,972 (041457-0992)

- 14. **(Allowed)** A method for administering estradiol, comprising applying to the skin or mucosa of a subject in need thereof a monolithic transdermal drug delivery system consisting of (i) a backing layer and (ii) a single adhesive polymer matrix layer defining an active surface area and comprising an adhesive polymer matrix comprising estradiol as the only drug, wherein the polymer matrix has a coat weight of greater than about 10 mg/cm² and includes greater than 0.156 mg/cm² estradiol, and the system achieves an estradiol flux of from about 0.0125 to about 0.05 g/cm²/day, based on the active surface area.
- 16. **(Allowed)** A method of making a monolithic transdermal drug delivery system for administering estradiol consisting of (i) a backing layer, (ii) a single adhesive polymer matrix layer and, optionally, (iii) a release liner, comprising forming an adhesive polymer matrix comprising estradiol as the only drug and a polymer blend comprising an acrylic adhesive, a silicone adhesive, and soluble PVP, and applying the adhesive polymer matrix to a support layer to form a single adhesive polymer matrix layer such that the adhesive polymer matrix layer has a coat weight of greater than about 10 mg/cm² and includes greater than 0.156 mg/cm² estradiol, wherein the system achieves an estradiol flux of from about 0.0125 to about 0.05 mg/cm²/day, based on the active surface area.

U.S. Patent Application Nos. 14/024,985 (041457-1016)

1. **(Allowed)** A monolithic transdermal drug delivery system for estradiol, consisting of (i) a backing layer, (ii) a single adhesive polymer matrix layer defining an active surface area and, optionally, (iii) a release liner, wherein the single adhesive polymer matrix layer comprises an adhesive polymer matrix comprising estradiol as the only drug, wherein the adhesive polymer matrix layer has a coat weight of greater than about 10 mg/cm² and includes greater than 0.156 mg/cm² estradiol, and the system achieves an estradiol flux of from about 0.0125 to about 0.05 mg/cm²/day, based on the active surface area.

U.S. Patent Application Nos. 14/738,255 (041457-1133)

- 45. (New) A monolithic transdermal drug delivery system for estradiol, consisting of:
- (i) a backing layer;
- (ii) an adhesive polymer matrix layer comprising an adhesive polymer matrix comprising estradiol as the only drug and defining an active surface area, and

optionally, (iii) a release liner,

wherein the adhesive polymer matrix layer includes from about 0.195 to about 0.260 mg/cm² estradiol and achieves an estradiol flux of from about 0.0125 to about 0.0167 mg/cm²/day, based on the active surface area.

- 59. (New) A transdermal drug delivery system for estradiol, consisting of:
- (i) a backing layer,
- (ii) an adhesive polymer matrix layer defining an active surface area and, optionally, (iii) a release liner,

wherein the adhesive polymer matrix layer comprises an adhesive polymer matrix comprising about 2-25% by weight acrylic adhesive, about 45-70% by weight silicone adhesive, about 2-25% by weight soluble PVP, about 5-15% penetration enhancer, and about 0.1-10% by weight estradiol as the only drug, and includes from about 0.195 to about 0.260 mg/cm² estradiol, achieves an estradiol flux of from about 0.0125 to about 0.0167 mg/cm²/day, based on the active

surface area, and comprises an amount of estradiol effective to deliver a therapeutically effective amount of estradiol over a period of time of at least 1 day.

U.S. Patent Application Nos. 14/870,575 (041457-1160)

21. (New) A monolithic transdermal drug delivery system for estradiol, consisting of (i) a backing layer, (ii) a single adhesive polymer matrix layer defining an active surface area and, optionally, (iii) a release liner,

wherein the single adhesive polymer matrix layer comprises 2-25% by weight acrylic adhesive, 45-70% by weight silicone adhesive, 2-25% by weight soluble PVP, 5-15% by weight penetration enhancer, and 0. 1-10% by weight estradiol as the only drug, and

wherein the coat weight of the adhesive polymer matrix layer is adjusted such that the system includes greater than 0.156 mg/cm² estradiol and achieves an estradiol flux of from about 0.0125 to about 0.05 mg/cm²/day, based on the active surface area.

35. (New) A method of making a transdermal drug delivery system according to claim 21, comprising forming an adhesive polymer matrix comprising 2-25% by weight acrylic adhesive, 45-70% by weight silicone adhesive, 2-25% by weight soluble PVP, 5-15% by weight penetration enhancer, and 0. 1-10% by weight estradiol as the only drug, and applying the adhesive polymer matrix to support layer to form a single adhesive polymer matrix layer,

wherein the coat weight of the adhesive polymer matrix is adjusted such that the system includes greater than $0.156~\text{mg/cm}^2$ estradiol and achieves an estradiol flux of from about 0.0125 to about $0.05~\text{mg/cm}^2$ /day, based on the active surface area.

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicant:

Juan Mantelle

Title:

Transdermal Estrogen Device and Delivery

Appl. No.:

13/553,972

Filing Date:

7/20/2012

Examiner:

Melissa L. Javier

Art Unit:

1611

Confirmation

3635

Number:

SUPPLEMENTAL RESPONSE

Commissioner for Patents P.O. Box 1450 Alexandria, VA 22313-1450

Commissioner:

This paper is filed subsequent to the Request for Continued Examination filed June 6, 2017. If any extensions of time are required for timely acceptance, Applicant hereby petitions for such extension of time. The Commissioner is hereby authorized to charge any fees which may be due for this application, including any extension of time fees or excess claim fees not submitted herewith, to Deposit Account No. 19-0741.

A Listing of Claims begins on page 2.

Remarks begin on page 6.

Listing of Claims:

Claims 1-13 (Cancelled)

14. (Previously Presented) A method for administering estradiol, comprising applying to the skin or mucosa of a subject in need thereof a monolithic transdermal drug delivery system consisting of (i) a backing layer and (ii) a single adhesive polymer matrix layer defining an active surface area and comprising an adhesive polymer matrix comprising estradiol as the only drug, wherein the polymer matrix has a coat weight of greater than about 10 mg/cm² and includes greater than 0.156 mg/cm² estradiol, and the system achieves an estradiol flux of from about 0.0125 to about 0.05 mg/cm²/day, based on the active surface area.

15. (Canceled)

- 16. (Previously Presented) A method of making a monolithic transdermal drug delivery system for administering estradiol consisting of (i) a backing layer, (ii) a single adhesive polymer matrix layer and, optionally, (iii) a release liner, comprising forming an adhesive polymer matrix comprising estradiol as the only drug and a polymer blend comprising an acrylic adhesive, a silicone adhesive, and soluble PVP, and applying the adhesive polymer matrix to a support layer to form a single adhesive polymer matrix layer such that the adhesive polymer matrix layer has a coat weight of greater than about 10 mg/cm² and includes greater than 0.156 mg/cm² estradiol, wherein the system achieves an estradiol flux of from about 0.0125 to about 0.05 mg/cm²/day, based on the active surface area.
- 17. (Original) The method of claim 16, wherein the system has an active surface area that is about 60% of a size selected from the group consisting of 2.5, 3.75, 5.0, 7.5 and 10.0 cm².

18-20 (Canceled)

21. (Previously Presented) The method of claim 14, wherein the adhesive polymer matrix comprises a polymer blend comprising an acrylic adhesive, a silicone adhesive, and soluble polyvinylpyrrolidone (PVP).

- 22. (Previously Presented) The method of claim 14, wherein the adhesive polymer matrix comprises about 2-25% by weight acrylic adhesive, about 45-70% by weight silicone adhesive, about 2-25% by weight soluble PVP, about 5-15% penetration enhancer, and about 0.1-10% by weight estradiol, all based on the total dry weight of the adhesive polymer matrix.
- 23. (Previously Presented) The method of claim 22, wherein the penetration enhancer comprises oleyl alchol.
- 24. (Previously Presented) The method of claim 22, wherein the penetration enhancer comprises dipropylene glycol.
- 25. (Previously Presented) The method of claim 22, wherein the penetration enhancer comprises oleyl alcohol and dipropylene glycol.
- 26. (Previously Presented) The method of claim 22, wherein the acrylic adhesive and silicone adhesive are present in a ratio of from about 1:2 to about 1:6, based on the total weight of the acrylic and silicone adhesives.

27. (Canceled)

- 28. (Previously Presented) The method of claim 14, wherein the adhesive polymer matrix comprises an amount of estradiol effective to deliver a therapeutically effective amount of estradiol over a period of time selected from the group consisting of at least 1 day, at least 2 days, at least 3 days, at least 4 days, at least 5 days, at least 6 days and at least 7 days.
- 29. (Previously Presented) The method of claim 14, wherein the adhesive polymer matrix comprises an amount of estradiol effective to deliver an amount of estradiol selected from the group consisting of about 0.025, 0.0375, 0.05, 0.075 and 0.1 mg/day.

30. (Canceled)

- 31. (Previously Presented) The method of claim 14, wherein the system achieves an estradiol flux of about 0.0125 mg/cm²/day, based on the active surface area.
- 32. (Previously Presented) The method of claim 14, wherein the system achieves an estradiol flux of about 0.0133 mg/cm²/day, based on the active surface area.
- 33. (Previously Presented) The method of claim 14, wherein the system achieves an estradiol flux of about 0.015 mg/cm²/day, based on the active surface area.
- 34. (Previously Presented) The method of claim 14, wherein the system achieves an estradiol flux of about 0.0167 mg/cm²/day, based on the active surface area.
- 35. (Previously Presented) The method of claim 14, wherein the system achieves an estradiol flux of about 0.0175 mg/cm²/day, based on the active surface area.
- 36. (Previously Presented) The method of claim 16, wherein the system achieves an estradiol flux of about 0.0125 mg/cm²/day, based on the active surface area.
- 37. (Previously Presented) The method of claim 16, wherein the system achieves an estradiol flux of about 0.0133 mg/cm²/day, based on the active surface area.
- 38. (Previously Presented) The method of claim 16, wherein the system achieves an estradiol flux of about 0.015 mg/cm²/day, based on the active surface area.
- 39. (Previously Presented) The method of claim 16, wherein the system achieves an estradiol flux of about 0.0167 mg/cm²/day, based on the active surface area.
- 40. (Previously Presented) The method of claim 16, wherein the system achieves an estradiol flux of about 0.0175 mg/cm²/day, based on the active surface area.
- 41. (Previously Presented) The method of claim 14, wherein the adhesive polymer matrix comprises about 1.6% by weight estradiol, based on the total dry weight of the adhesive polymer matrix.

42. (Previously Presented) The method of claim 16, wherein the adhesive polymer matrix comprises about 1.6% by weight estradiol, based on the total dry weight of the adhesive polymer matrix.

REMARKS

A Notice of Allowance allowing claims 14, 16-17, 21-26, and 28-29 and 31-40 was mailed March 9, 2017. Claims 41-42 were added in the response filed June 6, 2017. No claims are amended, added or canceled herein. Thus, claims 14, 16-17, 21-26, and 28-29 and 31-42 are pending and presented for reconsideration.

Applicant thanks Examiner Fisher for the courtesies extended during the Patent Office Interview on June 8, 2017. Applicant's Statement of the Substance of the Interview is provided here, in accordance with MPEP § 713.04. Applicant concurs with the Examiner's summary of the substance of the Applicant-Initiated Interview held June 8, 2017, and confirms that the substance of the agenda attached to the Examiner's summary was discussed.

Applicant submits herewith a Declaration under 37 C.F.R. § 1.132 of Dr. Richard H. Guy that presents the evidence discussed during the interview.

Applicant submits herewith an Information Disclosure Statement that makes of record the Mantelle Article discussed in Dr. Guy's Declaration. The other references discussed in Dr. Guy's Declaration already are of record.

Applicant believes that the application is in condition for allowance. If there are any questions regarding this submission, or if any issue remain, the Examiner is urged to contact the undersigned by telephone in order to advance prosecution.

Respectfully submitted,

Date: June 15, 2017

By /Courtenay C. Brinckerhoff/

FOLEY & LARDNER LLP

Customer Number: 22428

Telephone: Facsimile:

(202) 295-4094

(202) 672-5399

Courtenay C. Brinckerhoff Attorney for Applicant Registration No. 37,288

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

First Inventor Name: Juan Mantelle

Title: Transdermal Estrogen Device and Delivery

Application No.: 13/553972

Filing Date: 7/20/2012

Examiner: Melissa L. Fisher

Art Unit: 1611

Confirmation No.: 3635

INFORMATION DISCLOSURE STATEMENT UNDER 37 CFR §1.56

Commissioner for Patents P.O. Box 1450 Alexandria, VA 22313-1450

Commissioner:

Applicant submits herewith documents for the Examiner's consideration in accordance with 37 CFR §§1.56, 1.97 and 1.98.

Applicant respectfully requests that each listed document be considered by the Examiner and be made of record in the present application and that an initialed copy of Form PTO/SB/08 be returned in accordance with MPEP §609.

The submission of any document herewith is not an admission that such document constitutes prior art against the claims of the present application or that such document is considered material to patentability as defined in 37 CFR §1.56(b). Applicant does not waive any rights to take any action which would be appropriate to antedate or otherwise remove as a competent reference any document submitted herewith.

4847-2557-9594.1 -1-

TIMING OF THE DISCLOSURE

The listed documents are being submitted in compliance with 37 CFR §1.97(b), before the mailing of a first Office action after the filing of a RCE.

RELEVANCE OF LISTED DOCUMENT

Document A1 is discussed in the Rule 132 Declaration of Dr. Richard H. Guy submitted herewith. The other references discussed in the Declaration are already of record.

Documents A2 and A3 are Office Actions which issued in child applications.

Although Applicant believes that no fee is required, the Commissioner is hereby authorized to charge any additional fees which may be due to Deposit Account Number 19-0741.

Respectfully submitted,

Date June 15, 2017

FOLEY & LARDNER LLP Customer Number: 22428

Telephone: (202) 295-4094 Facsimile: (202) 672-5399 By /Courtenay C. Brinckerhoff/

Courtenay C. Brinckerhoff Attorney for Applicant Registration No. 37,288

4847-2557-9594.1 -2-

Substitute for form 1449/PTO Complete if Known INFORMATION DISCLOSURE **Application Number** 13/553972 Filing Date STATEMENT BY APPLICANT 7/20/2012 First Named Inventor Juan Mantelle Date Submitted: June 15, 2017 Art Unit 1611 Examiner Name (use as many sheets as necessary) Melissa L. Javier Attorney Docket Number 041457-0992 Sheet of

	U.S. PATENT DOCUMENTS							
Examiner	Cite	Document Number	Publication Date MM-DD-YYYY	Name of Patentee or Applicant of	Pages, Columns, Lines, Where Relevant			
	No. ¹	Number-Kind Code ² (if known)		Cited Document	Passages or Relevant Figures Appear			

UNPUBLISHED U.S. PATENT APPLICATION DOCUMENTS							
Examiner Initials* Cite Document Cite No.1 Serial Number-Kind Code2 (if known) Cited Document MM-DD-YYYY		Name of Patentee or Applicant of Cited Document	Pages, Columns, Lines, Where Relevant Passages or Relevant Figures Appear				

	FOREIGN PATENT DOCUMENTS								
Examiner Initials*	Cite No. ¹	Foreign Patent Document Country Code ³⁻ Number ⁴⁻ Kind Code ⁵ (<i>if known</i>)	Publication Date MM-DD-YYYY	Name of Patentee or Applicant of Cited Documents	Pages, Columns, Lines, Where Relevant Passages or Relevant Figures Appear	T€			

		NON PATENT LITERATURE DOCUMENTS	
Examiner Initials*	Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc.) date, page(s), volume-issue number(s), publisher, city and/or country where published.	T⁵	
	A1	MANTELLE ET AL., "Effect of Silicone/Acrylic PSA Blends on Skin Permation," Procced. Int'l. Symp. Control. Rel. Bioact. Mater., June 20-23, 1999	
***************************************	A2	Notice of Allowance issued on 04/26/2017 in application number 14/024,985 (US 2014/0200530)	
	А3	Office Action issued on 06/15/2017 in application number 14/870,574 (US 2016/0015655)	

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Examiner	Date	
Signature	Considered	

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

First Inventor Name: Juan Mantelle

Title: Transdermal Estrogen Device and Delivery

Examiner: Javier

Art Unit: 1611

App. No.	13/553,972	Filing Date: 7/20/2012	Conf. No.: 3635	Atty. Dkt No.041457-0992
App. No.	14/024,985	Filing Date: 9/12/2013	Conf. No.: 7031	Atty. Dkt No.041457-1016
App. No.	14/738,255	Filing Date: 6/12/2015	Conf. No.: 5737	Atty. Dkt No.041457-1133
App. No.	14/870,574	Filing Date: 9/30/2015	Conf. No.: 5148	Atty. Dkt No.041457-1160

DECLARATION UNDER 37 CFR § 1.132 OF RICHARD H. GUY, PH.D.

I, Richard H. Guy, Ph.D., hereby declare and say that:

I. QUALIFICATIONS AND EXPERIENCE

- 1. I have more than 30 years' research experience in the field of topical and transdermal drug delivery, including the study of drug absorption into and through the skin. During that time my research interests have spanned a wide range of subjects including the characterization of skin barrier function, transdermal drug delivery, enhancement of percutaneous absorption, iontophoresis, noninvasive biosensing, and the prediction and assessment of skin penetration and topical bioavailability.
- 2. I am currently Professor of Pharmaceutical Sciences at the University of Bath (UK) in the Department of Pharmacy & Pharmacology. I have held this position since 2004. From 2006-2008, I also served as Head of the Department of Pharmacy & Pharmacology at the University of Bath. Prior to joining the faculty at the University of Bath in 2004, I was Scientific Director of the Centre interuniversitaire de recherche et d'enseignement (Universities of Geneva (CH) and Lyon (FR)), and Professor of Biopharmaceutics in the Faculty of Sciences at the University of Geneva (CH). I held these positions between 1996 and 2004. Prior to that, I served as an

Assistant (1980-87), Associate (1987-1991) and Full Professor (1991-96) of Biopharmaceutical Sciences and Pharmaceutical Chemistry at the University of California, San Francisco ("UCSF"). During my time at UCSF (1987-1996), I was also Vice-Chair of the Department of Biopharmaceutical Sciences.

- 3. I obtained my Bachelor of Arts degree in chemistry from Oxford University (UK) in 1977, my Master of Arts degree in chemistry from Oxford University in 1980, and my Ph.D. in pharmaceutical chemistry from the University of London (UK) in 1980. I was awarded a D.Sc. by Oxford University in 2016.
- 4. I have co-authored more than 350 peer-reviewed articles and over 70 book chapters. Many of my peer-reviewed articles describe my research into understanding the mechanisms of topical and transdermal drug delivery. For example, in early work, I was involved in the development of diffusion and pharmacokinetic models of skin penetration and their application to the feasibility assessment of candidates for transdermal drug delivery. Subsequently, my research centered on a sustained effort to understand the mechanisms of skin penetration enhancement induced by chemical enhancers and other approaches, including (in particular) iontophoresis, and sonophoresis.
- 5. I have served as the Associate Editor of the Journal of Pharmaceutical Sciences (2002-2007) and currently serve on the editorial advisory boards of the European Journal of Pharmaceutical Sciences, Skin Pharmacology & Physiology, and the European Journal of Pharmaceutics and Biopharmaceutics.
- 6. Over the course of my career, I have earned numerous professional awards and honors, which are described in my curriculum vitae. For example, I am an elected Fellow of the Royal Society of Chemistry (UK, 1988), the American Association of Pharmaceutical Scientists (US, 1990), the American Association for the Advancement of Science (US, 1992), the Academy of Pharmaceutical Sciences, Great Britain (UK, 2007) and the Controlled Release Society College of Fellows (UK, 2010). More recently, I became a Fellow of the UCL School of Pharmacy,

University College, London, in recognition of my "distinguished contribution to the pharmaceutical sciences."

- 7. I am also a co-inventor of 12 issued U.S. patents in the field of transdermal drug delivery and glucose biosensing.
- 8. In the course of my career, I have served as a consultant (and scientific advisory board member) to numerous pharmaceutical companies, which have been involved in the development of transdermal drug delivery formulations (including both patches and other vehicles, such as gels). My role has involved assisting with the identification and evaluation of potential drug candidates for transdermal delivery and, quite often, with offering advice on formulation and/or enhancement strategies by which the skin absorption of target compounds might be increased to ensure therapeutic activity. I have authored or co-authored more than 30 articles and book chapters on aspects of transdermal delivery (including, most recently, "Transdermal Drug Delivery: 30+ Years of War and Still Fighting! S. Wiedersberg and R.H. Guy. J. Control. Release 190: 150-156 (2014)") and I have co-edited two books on the subject: [1] Transdermal Delivery Systems: Developmental Issues and Research Initiatives. Edited by J. Hadgraft and R.H. Guy. New York: Marcel Dekker, 1989; reprinted 1993. A 2nd Edition, revised and expanded, was published in 2003. [2] Mechanisms of Transdermal Drug Delivery. Edited by R.O. Potts and R.H. Guy. New York: Marcel Dekker, 1997. Several publications and book chapters address the manner in which drug pharmacokinetics can be modified and controlled by transdermal delivery, and describe the different patch designs, which have been used, their performance and benefits. The feasibility of transdermal delivery for certain drugs has been explored as well in this body of work, a subject which has been the focus of multiple interactions with the pharmaceutical industry as a consultant and scientific advisor.
- 9. A copy of my curriculum vitae, which includes my education background, work and research history, and a list of selected publications and presentations, is attached to this declaration as Exhibit 1.

- 10. Any opinions expressed herein are based on my education, research, knowledge and experience over the past 30 years in the field of transdermal drug delivery.
- I was engaged by Noven Pharmaceuticals, Inc. ("Noven"), to serve as an expert witness in ANDA litigation involving U.S. Patent No.8,231,906 (the '906 Patent), in the U.S. District Court for the District of Delaware (C.A. No. 15-249) (the "ANDA litigation). I understand that U.S. patent applications 13/553,972, 14/024,985, 14/738,255, and 14/870,574 (the "pending applications") claim priority to the '906 Patent, and are assigned to Noven. I was engaged by Noven to prepare this declaration for the pending applications.
- 12. Noven is compensating me for my time associated with the pending applications at my customary consulting rate of \$400 per hour. My compensation does not depend in any way on the outcome of the examination of the pending applications or on the outcome of the ANDA litigation.

II. THE PENDING CLAIMS

13. I understand that the claims of the pending applications are directed to monolithic transdermal drug delivery systems for estradiol consisting of (i) a backing layer, (ii) a single adhesive polymer matrix layer defining an active surface area and comprising an adhesive polymer matrix comprising estradiol as the only drug, and, optionally, (iii) a release liner, methods for administering estradiol using such systems, and methods for making such systems. With regard to the adhesive polymer matrix, I understand that the claims of the '972, '985, and '255 applications recite that the adhesive polymer matrix has a coat weight of greater than about 10 mg/cm², includes greater than 0.156 mg/cm² estradiol, and achieves an estradiol flux of from about 0.0125 to about 0.05 mg/cm²/day, based on the active surface area, with some claims reciting additional features. I understand that the claims of the '574 application recite that the coat weight of the adhesive polymer matrix layer is adjusted such that the system includes greater than 0.156 mg/cm² estradiol and achieves an estradiol flux of from about 0.0125 to about 0.05 mg/cm²/day, based on the active surface area.

III. TECHNICAL BACKGROUND

- 14. I understand that the '906 Patent and the pending applications have a priority date of July 10, 2008. Thus, I discuss below what would have been known to a person of ordinary skill in the field of transdermal drug delivery as of July 10, 2008.
- 15. The inventions claimed in the pending applications generally relate to transdermal drug delivery systems (*e.g.*, transdermal "patches") for the delivery of estradiol, methods of administering estradiol to a patient using the claimed transdermal drug delivery systems, and delivering estradiol using them, and methods of making them. The claimed transdermal drug delivery systems are "monolithic" drug-in-adhesive systems that consist of (i) a backing layer; (ii) a drug-in-adhesive polymer matrix layer, and, optionally, (iii) a release liner that is removed prior to use, as illustrated below.

	(1)	Backing
	(2)	Adhesive Containing Estradiol
	(3)	Protective Liner

- 16. The claims recite that the adhesive polymer matrix layers include a certain amount estradiol per unit area and achieve a certain estradiol flux.
- 17. The flux of a drug is the rate at which it diffuses through the skin. As of June 10, 2008, a person of ordinary skill in the art understood that the passive flux of a drug can be quantitatively described and modelled by Fick's 1st law. Fick's 1st law is often used to describe drug delivery (in units of amount per time, e.g., mg/day or μ g/hour) from a transdermal patch across the skin:

$$J = A \times k_p \times \Delta C$$

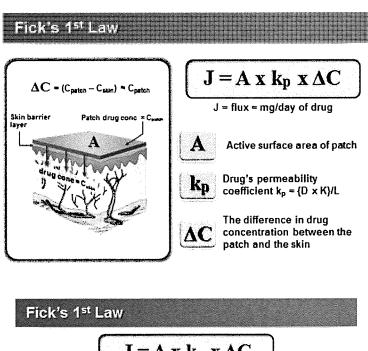
In this formula:

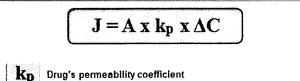
A is the active surface area of the patch.

 k_p is the drug's permeability coefficient across the skin, and can be defined as $k_p = \{D \ x \ K\}/L$, where D is the drug's diffusivity through the skin barrier, K is its partition coefficient between the skin barrier and the patch, and L is the path length for diffusion across the skin barrier.

 ΔC is the difference in concentration of the drug between that in the patch (C_{patch}) and that on the "downstream" side of the skin barrier ($C_{downstream}$). In many examples of transdermal delivery, when depletion of drug from the patch is limited, ΔC can be approximated to C_{patch} .

The following images illustrate these factors:





 $k_p = \{D \times K\}/L$

- D = drug's diffusivity through the skin barrier
- K = partition coefficient of drug between skin barrier and patch
- · L = path length for drug diffusion across skin barrier

- 18. Fick's 1st law indicates that there are four general ways to increase flux:
 - Increase the active surface area of the patch to cause a proportional change in flux.
 - Increase the drug concentration in the patch until it reaches its limiting solubility.
 - Adjust the formulation to increase K, *e.g.*, cause drug concentration to approach more closely its limiting solubility.
 - Introduce a penetration enhancer into the formulation to increase D and/or alter the value of K.

Nothing in Fick's 1st law indicates or predicts that increasing the coat weight (thickness) of a polymer matrix would increase flux. This is because no factor in Fick's 1st law embodies or includes coat weight.

IV. THE INVENTION

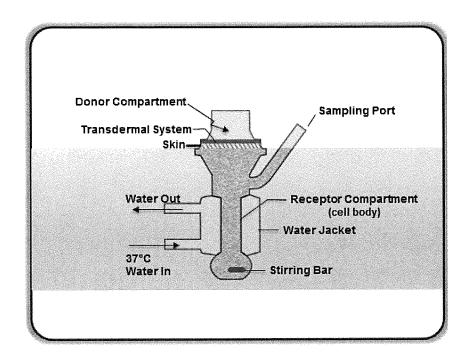
- 19. As set forth in the specification of the pending applications, the subject matter includes transdermal drug delivery systems for the transdermal delivery of estrogen that have a smaller active surface area than the prior art Vivelle-Dot® patches, but achieve daily dosages that are about equal to or greater than the Vivelle-Dot® patches. That is, the subject matter includes transdermal drug delivery systems that achieve daily dosages that are about equal to a Vivelle-Dot® patch, in a smaller size. *See, e.g.*, Specification, at paragraph [0014].
- 20. As stated in the specification, "the Applicant surprisingly discovered that increasing the coat weight of the drug-containing adhesive layer resulted in an increased flux per unit area, and thus permitted the development of smaller transdermal drug delivery systems that achieve comparable daily dosages." Specification, at paragraph [0014].
- 21. As stated in paragraph [0015] in the specification:

This result was surprising because coat weight is typically selected to control the duration of delivery, but is not generally understood to impact delivery rate. Thus, while it is known in the art to increase coat weight to provide delivery over a

longer period of time, it was not known that increasing coat weight could increase delivery rate or flux, and thus permit the development of a smaller system while maintaining daily dosage.

I agree with this statement because, as explained above, nothing in Fick's 1st law indicates or predicts that increasing the coat weight (thickness) of a polymer matrix would increase flux. That is, in accordance with Fick's 1st law, simply increasing the thickness of the patch formulation, i.e., increasing the coat weight, would not increase flux, because coat weight per se would not affect any of the parameters/variables that determine flux according to Fick's 1st law. Thus, a person of ordinary skill in the art would not have thought of coat weight as a parameter to be adjusted to affect the flux of a drug from a transdermal patch. Indeed, the person of ordinary skill in the art would not have viewed coat weight as having any effect on flux and would not have been motivated to consider adjusting coat weight as a flux enhancement method. Rather, coat weight was understood by persons of ordinary skill in the art to affect only the duration over which a certain flux could be maintained. That is, persons of ordinary skill in the art understood that an increase in coat weight would potentially extend the time period over which the patch would achieve a given flux, and so might be adjusted to modify the wear period of a patch. However, neither Fick's 1st law, nor any other principle of transdermal drug delivery known in the art, indicated that increasing the coat weight of the drug-containing polymer matrix would increase flux.

22. The specification illustrates this surprising and unexpected effect in Example 1, which describes an *in vitro* flux study conducted to assess the flux of estradiol from different systems. The image below shows a typical Franz diffusion cell set up used to conduct an *in vitro* flux study.



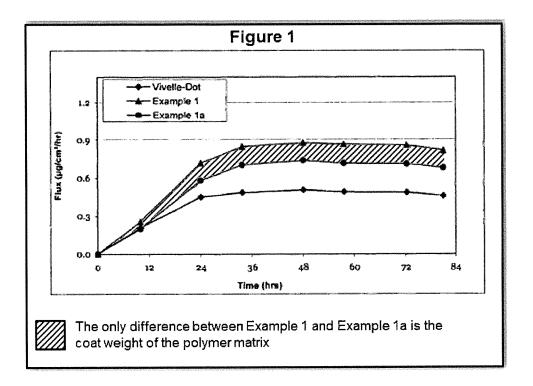
In general, the receptor compartment is filled with a receiver solution that is stirred and held at a constant (typically, physiological) temperature. A transdermal system is placed on a skin sample in the donor compartment, and the contents of the receptor compartment are sampled (withdrawn) periodically and analyzed for drug (for example, estradiol) content. From this information, the cumulative amount of drug delivered over time and the flux of drug across the skin as a function of time is calculated. An illustration of the type of experimental data collected with this approach is shown below for one particular formulation; the results are presented as the average cumulative amounts of drug delivered, and the average drug flux, as a function of time, with the corresponding standard deviations for 4 replicate Franz diffusion cells.

(hours)	(mcg/cm2)	(mcg/cm2)	(mcg/cm2 hr)	(mcg/cm2 hr)
Average Time	Average Cum.	Cum. Stdev	Average Flux	Flux Stdev
0.00	0.00	0.00	0.00	0.00
9.92	2.55	0.49	0.26	0.05
23.95	12.64	1.99	0.72	0.11
33.65	20.85	2.91	0.85	0.10
48.03	33.45	4.10	0.88	0.08
57.58	41.70	4.81	0.86	0.08
72.20	54.23	5.71	0.86	0.06
81.02	61.43	6.07	0.82	0.04

23. Figure 1 reports the flux of drug across the skin for the systems tested in Example 1. Example 1 sets forth the polymer matrix formulation used to prepare Example 1 and Example 1a. As noted in the prosecution history of the '906 Patent, in the Amendment and Reply filed April 20, 2011, the specification as filed had a clerical error in the formulation listed (see below), but the flux data presented in Figure 1 is correct.

	Example 1	Actual Formulation
Silicone (4502)	56.9	66.9
Acrylic (Gelva 788)	20	10
PVP (Kollidon K-30)	7.5	7.5
DPG	8	8
Oleyl Alcohol	6	6
Estradiol	1.6	1.6

As described in the specification, test systems were prepared by applying the polymer matrix to a release liner at two different coat weights: 12.5 mg/cm² (Example 1a, •) and 15 mg/cm² (Example 1, ▲), and estradiol flux was assessed in an *in vitro* flux study. As reported in Figure 1, the system with the higher coat weight exhibited a greater flux.

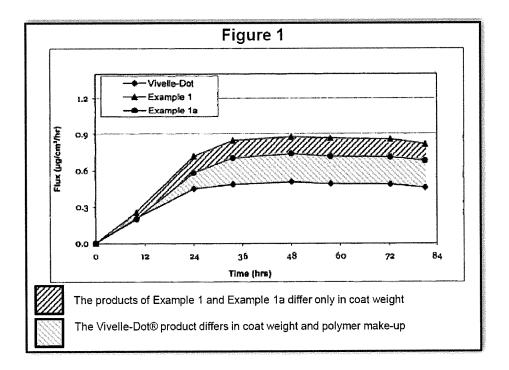


The <u>only</u> experimental variable different between Example 1a and Example 1 is the coat weight of the polymer matrix. The difference in flux reported in Figure 1 between Example 1a and Example 1 can only be attributed, therefore, to the difference in coat weight, which is a surprising and unexpected result that is not predicted by Fick's 1st Law.

Figure 1 also reports results achieved with a Vivelle-Dot® system. As described in the prescribing information, Vivelle-Dot® is a monolithic transdermal drug delivery system for estradiol with a polymer matrix layer that includes estradiol as the only drug, acrylic adhesive, silicone adhesive, oleyl alcohol, povidone, and dipropylene glycol. The specification states that each Vivelle-Dot® patch includes 0.156 mg/cm² estradiol and has a polymer matrix coat weight of 10 mg/cm². See, e.g., Specification at paragraph [0013]; [0074]. Although Vivelle-Dot® includes the same polymer matrix components of the Example 1 formulation, I have been informed that the Vivelle-Dot® formulation includes different amounts of some components, including different relative amounts of acrylic adhesive and silicone adhesive, with a greater relative amount of acrylic adhesive. That is, the formulation of Examples 1 and 1a have less acrylic adhesive and more silicone adhesive than the Vivelle-Dot® formulation. I have been

informed that the precise formulation of Vivelle-Dot® is confidential, proprietary information of a third party that Noven is contractually obligated to maintain confidential.

I understand from prior art such as U.S. Patent No. 6,024,976 (the "'976 Patent") and Mantelle, et al., Effect of Silicone/Acrylic PSA Blends on Skin Permeation, 26 Proc. Internat'l Symp. Controlled Release of Bioactive Materials 5123, 415-16 (Revised July 1999) ("Mantelle Article"), and from Juan A. Mantelle, "Dot Matrix® Technology," in Modified Release Drug Delivery Technology (2nd ed. 2008) 405-14 ("Mantelle Chapter"), and the experimental data presented below, that the difference in relative amounts of acrylic adhesive and silicone adhesive between the formulation of Examples 1 and 1a and the Vivelle-Dot® formulation contributes to the difference in flux seen in Figure 1 between Vivelle-Dot® and Example 1 and Example 1a.



I cannot quantify the relative contributions of coat weight and polymer composition to the differences in flux observed between the Vivelle-Dot® system and Examples 1 and 1a systems. However, based on the difference in flux between the Example 1 and 1a systems (which, as explained above, can only be due to the difference in coat weight), and in view of other experimental data discussed below, it is my opinion that the difference in coat weight is

contributing to the difference in flux between the Vivelle-Dot® system and the Example 1 and 1a systems.

V. EXPERIMENTAL DATA – IMPACT OF POLYMER MAKE-UP ON FLUX

As noted above, I understand from prior art such as the '976 Patent and the Mantelle Article that the relative amounts of acrylic adhesive and silicone adhesive used in an estradiol polymer matrix can impact the flux of estradiol. As described in the '976 Patent, this is because estradiol's solubility in acrylic adhesives differs from that in silicone adhesives. The potential effect of the relative amounts of acrylic adhesive and silicone adhesive is illustrated in Examples 10-13 and Figure 6 of the '976 patent, which reports:

FIG. 6 shows estradiol flux progressively increased with increased silicone polymer content during the first 22 hours of delivery, but was affected to a much lesser degree during the remainder of the study (22 to 99 hours). Thus, significant adjustment of the estradiol delivery rate during the initial phase of delivery was accomplished, with minor effects on the later delivery phase, by modulating the polysiloxane to polyacrylate polymer ratio. FIG. 6 also illustrates that the delivery characteristics over time can be adjusted by the appropriate choice of polymers and respective weight ratios. For example, the formulation of Example 10 delivers drug at approximately the same rate over time whereas the formulation of Example 13 delivers more quickly in the early phase than the latter.

A similar effect is reported in the Mantelle Article, which states:

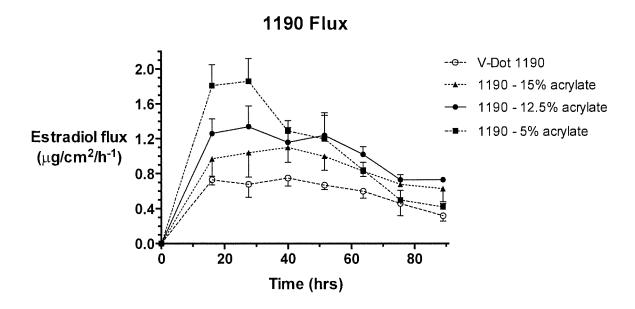
As shown, varying the silicone to acrylic psa ratio from 56.9:20 to 61.9:15 to 66.9:10 resulted in an average flux rate increase ... with the additional effect of having altered the initial burst effect and subsequent sustenance of the pseudo-zero-order delivery profile. As can be seen in Figure 2, higher silicone to acrylic psa ratios resulted in a shift of the permeation profile from a pseudo-zero-order to a first order delivery system incapable of sustaining the targeted 84 hour delivery.

Thus, it was known in the art that the relative amounts of acrylic adhesive and silicone adhesive in an estradiol polymer matrix can impact estradiol flux, and that increasing the relative amount of silicone polymer generally increased the flux but may alter the drug delivery profile such that the increased flux is not sustained.

27. This effect is shown by the results for Flux Study 1190 conducted by Noven. Flux Study 1190 tested five different formulations at the same target coat weight (15 mg/cm²) and used a Vivelle-Dot® system (♦) as an internal control. The five formulations differed in the relative amounts of acrylic adhesive and silicone adhesive, as follows:

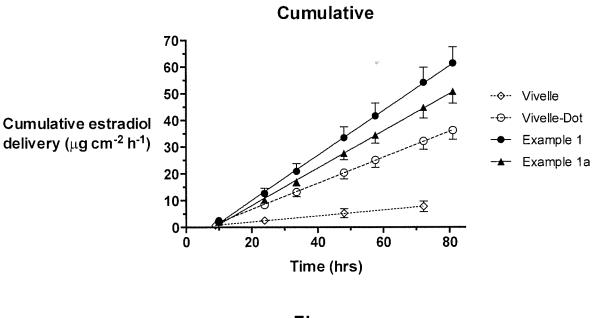
Component	5% Acrylic	10% Acrylic	12.5% Acrylic	15% Acrylic	17.5% Acrylic
(% by weight)					
Acrylic Adhesive	5	10	12.5	15	17.5
Silicon Adhesive	71.9	66.9	64.5	61.9	59.4
Dipropylene Glycol	8	8	8	8	8
Oleyl Alcohol	6	6	6	6	6
PVP	7.5	7.5	7.5	7.5	7.5
Estradiol	1.6	1.6	1.6	1.6	1.6

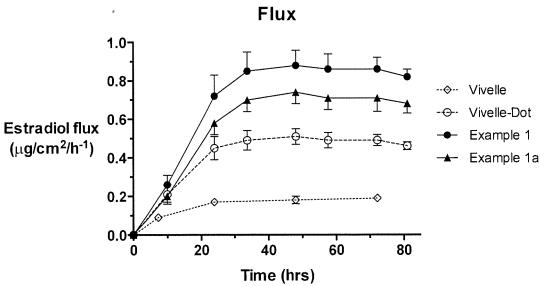
A representative sample of the data from this Flux Study are shown in the figure below. The results (reported as the average of 5 replicates) show that initial flux increased as the relative amount of acrylic polymer decreased but the initially higher flux from the 5% acrylic composition was not sustained:



VI. EXPERIMENTAL DATA – IMPACT OF COAT WEIGHT ON FLUX

- 28. As noted above, while it was known in the art that the relative amounts of acrylic adhesive and silicone adhesive in an estradiol polymer matrix can impact estradiol flux, it was not known or expected that the coat weight of the polymer matrix would impact flux, but Noven conducted a number of other flux studies that showed this effect with monolithic transdermal drug delivery systems for estradiol as described in the pending applications.
- 29. Flux Study 1326 is the flux study reported in Example 1 of the pending applications. As discussed above, the same formulation (1.6 % estradiol, 10% acrylic adhesive, 66.9% silicone adhesive, 6% oleyl alcohol, 7.5% povidone, and 8% dipropylene glycol) was tested at coat weights of 12.5 mg/cm² and 15 mg/cm². Both Vivelle® and Vivelle-Dot® were used as internal controls. As noted above, the results (see below) (reported as the average of 4 replicates) show that the increase in the coat weight of the polymer matrix from Example 1a to Example 1 resulted in an increased flux of estradiol.



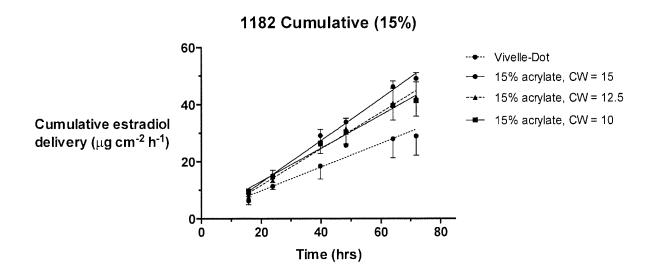


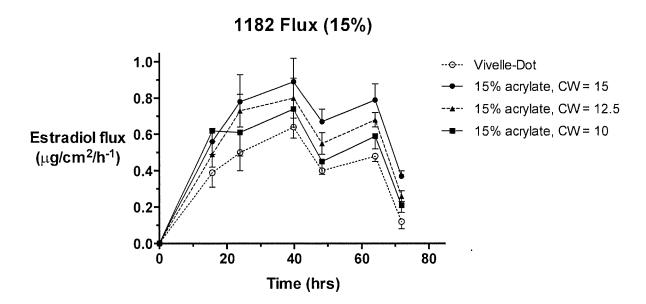
30. Flux Study 1182 conducted by Noven tested four different formulations at three different target coat weights and used a Vivelle-Dot® system as an internal control. The four formulations differed in the relative amounts of acrylic adhesive and silicone adhesive, as follows:

Component	10% Acrylic	15% Acrylic	17.5% Acrylic	20% Acrylic
(% by weight)				
Acrylic	10	15	17.5	20
Adhesive				
Silicon	66.9	61.9	59.4*	56.9
Adhesive				
Dipropylene	8	8	8	8
Glycol				
Oleyl Alcohol	6	6	6	6
PVP	7.5	7.5	7.5	7.5
Estradiol	1.6	1.6	1.6	1.6

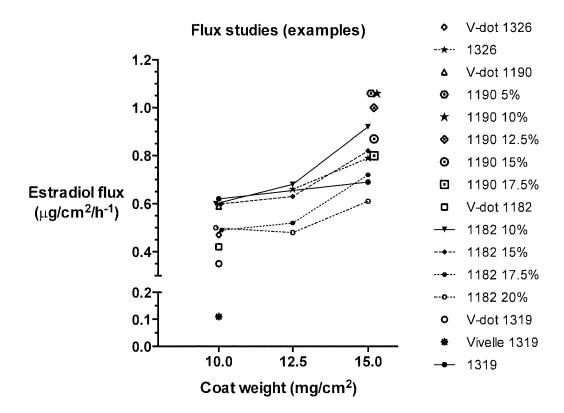
^{*}Reported as 59.9%, but likely used 59.4% Silicone Adhesive.

The different target coat weights assessed were 10 mg/cm², 12.5 mg/cm² and 15 mg/cm². The overall results show that increasing coat weight from 10 mg/cm² to 15 mg/cm² surprisingly and unexpectedly increased flux. For illustration, results (reported as the average of 4 replicates) for the composition with 15% acrylic polymer at a coat weight of 10 mg/cm², 12.5 mg/cm², and 15 mg/cm² are set forth below (Vivelle-Dot® was used as an internal control).





31. The estimated estradiol fluxes from Flux Studies 1190 and 1182 (reported as the average of 5 and 4 replicates, respectively) are shown below (some values are slightly displaced along the x-axis to facilitate visualization of each data point; for example, the estimated flux for 1182 10% at a coat weight of 10 mg/cm^2 is plotted at 9.9 on the x-axis and the estimated flux for 1182 15% at a coat weight of 10 mg/cm^2 is plotted at 10.1 on the x-axis, because they both had an estimated flux of $0.6 \text{ µg/cm}^2/\text{hr}$):

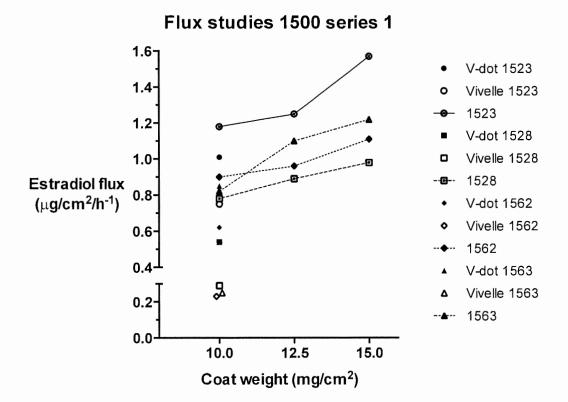


- 32. Collectively, the results from Flux Study 1190 and Flux Study 1182 indicate that while the relative amounts of acrylic adhesive and silicone adhesive impact the flux of estradiol—as was known in the art—the coat weight of the polymer matrix also impacts flux—which was not known in the art, and indeed was a surprising and unexpected result not predicted by Fick's 1st law of diffusion.
- 33. Flux Studies 1523, 1528, 1562 and 1563 assessed other formulations at different target coat weights, as outlined in the following table.

Flux Study	For	nulation C	Coat Wt.	Drug Flux				
	Acrylate	Silicone	DPG	OAlc	PVP	Estradiol	(mg/cm ²)	$(\mu g/cm^2 \cdot h)$
	10	69.4	8	6	5	1.6	15	1.57
	10	69.4	8	6	5	1.6	12.5	1.25
1523	10	69.4	8	6	5	1.6	10	1.18
	Control (flux): Vivelle-Dot® (1.01 μg/cm ² •h)							

Elem Cande	Forn	nulation Co	Coat Wt.	Drug Flux							
Flux Study	Acrylate	Silicone	DPG	OAlc	PVP	Estradiol	(mg/cm ²)	(µg/cm ² •h)			
	10	69.4	8	6	5	1.6	15	0.98			
	10	69.4	8	6	5	1.6	12.5	0.89			
1528	10	69.4	8	6	5	1.6	10	0.78			
	Control (flux): Vivelle-Dot® (0.54 μg/cm ² •h)										
	10	60.4	0			1.6	1.5	1 1 1			
	10	69.4	8	6	5	1.6	15	1.11			
1562	10	69.4	8	6	5	1.6	12.5	0.96			
(Form. 1)	10	69.4	8	6	5	1.6	10	0.90			
(1 01111. 1)	Control (flux): Vivelle-Dot® (0.62 μg/cm ² •h)										
	10	69.4	8	6	5	1.6	15	1.22			
					5			1.10			
1563 (Form. 1)	10	69.4	8	6		1.6	12.5				
	10	69.4	8	6	5	1.6	10	0.82			
(1 01111. 1)	Control (flux): Vivelle-Dot® (0.85 µg/cm ² •h)										

34. The estimated estradiol fluxes from Flux Studies 1523, 1528, 1562, and 1563 are illustrated below (reported as the average of 3 or 4 replicates; some values are again slightly displaced along the x-axis to facilitate visualization of the data points), and again show the surprising and unexpected impact of polymer matrix coat weight on flux:



35. Flux Studies 1562 and 1563 were repeated with different formulations at coat weights of 12.5 mg/cm² and 15 mg/cm² using both Vivelle and Vivelle-Dot® as internal controls.

E1 C4	Forn	nulation Co	Coat Wt.	Drug Flux				
Flux Study	Acrylate	Silicone	DPG	OAlc	PVP	Estradiol	(mg/cm ²)	(µg/cm ² •h)
1562	10	69.4	8	6	5	1.6	15	1.01
(Form. 1)	10	69.4	8	6	5	1.6	12.5	0.85
1562 (Form. 2)	7	72.6	8	6	5	1.4	15	1.12
	7	72.6	8	6	5	1.4	12.5	0.92
1562 (Form. 3)	7	74.6	8	6	3	1.4	15	1.07
	7	74.6	8	6	3	1.4	12.5	0.96
1562 Control (flux): Vivelle-Dot® (0.62 μg/cm ² •h)								
1563	10	69.4	8	6	5	1.6	15	1.12

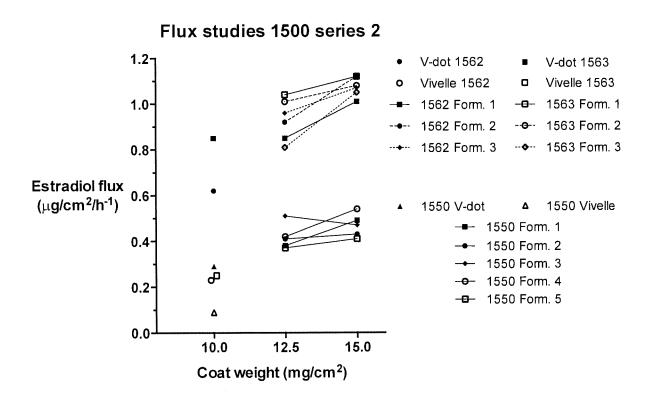
Flux Study	Form	nulation Co	Coat Wt.	Drug Flux					
	Acrylate	Silicone	DPG	OAlc	PVP	Estradiol	(mg/cm ²)	(µg/cm ² •h)	
(Form. 1)	10	69.4	8	6	5	1.6	12.5	1.04	
1563 (Form. 2)	7	72.6	8	6	5	1.4	15	1.08	
	7	72.6	8	6	5	1.4	12.5	1.01	
								i i	
1563 (Form. 3)	7	74.6	8	6	3	1.4	15	1.05	
	7	74.6	8	6	3	1.4	12.5	0.81	
1563 Control (flux): Vivelle-Dot® (0.85 μg/cm ² •h)									

36. Flux Study 1550 assessed other formulations at different target coat weights, as outlined in the following table.

Formulation	Formulati	on Compo	Coat Wt.	Drug Flux				
	Acrylate	Silicone	DPG	OAlc	PVP	Estradiol	(mg/cm ²)	$(\mu g/cm^2 \cdot h)$
Form. 1	10	71.6	8	6	3	1.4	15	0.49
	10	71.6	8	6	3	1.4	12.5	0.38
Form. 2	10	69.4	8	6	5	1.6	15	0.43
	10	69.4	8	6	5	1.6	12.5	0.41
Form. 3	7	72.6	8	6	5	1.4	15	0.47
	7	72.6	8	6	5	1.4	12.5	0.51
Form. 4	7	74.6	8	6	3	1.4	15	0.54
	7	74.6	8	6	3	1.4	12.5	0.42
Form. 5	10	73.4	6	6	3	1.6	15	0.41
rom. 3	10	73.4	6	6	3	1.6	12.5	0.41
Control (flux):	Vivelle-D	ot® (0.29	μg/cm²	•h)				

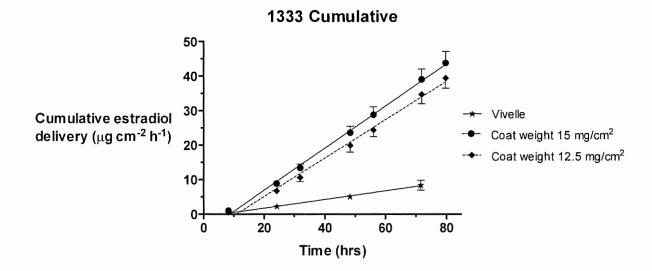
22

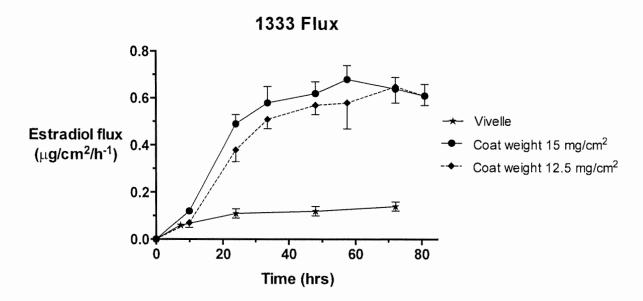
37. The estimated estradiol fluxes from 1562 and 1563 (second series) (reported as the average of 3 replicates; some values are slightly displaced along the x-axis to facilitate visualization of the data points) and 1550 are illustrated below (reported as the average of 4 replicates), and again show the surprising and unexpected impact of polymer matrix coat weight on flux:



- 38. Although the results for Flux Study 1550 Formulation 3 show a higher flux for the lower coat weight, that does not change my opinion that the totality of the data show the surprising and unexpected result that increasing coat weight increases flux. Indeed, Formulation 3 of Flux Study 1550 is the same formulation as Formulation 2 of Flux Study 1562 and Formulation 2 of Flux Study 1563 and, in both of those flux studies, this formulation exhibited a higher flux at the higher coat weight.
- 39. I also reviewed Flux Study 1333, which assessed the flux of a formulation having the same components as the Example 1 formulation at a target coat weight of 12.5 mg/cm² and 15 mg/cm² and used a Vivelle® system as an internal control. Although the researcher, who

oversaw this study, prepared the graphs shown below (reporting the average of 4 replicates), which indicate that increasing coat weight increased flux, the experimental data reported by the technician correlate the 12.5 mg/cm² sample with the higher flux results. I understand that the researcher, who oversaw this study, believes that the technician switched or mislabeled the samples. However, regardless of whether this set of flux results are reported correctly, they do not change my opinion that the totality of the data, when viewed in its entirety, consistently show the surprising and unexpected result that increasing coat weight increases flux. Indeed, as shown above, several other studies using the same formulations show that the higher coat weight was correlated with greater flux.



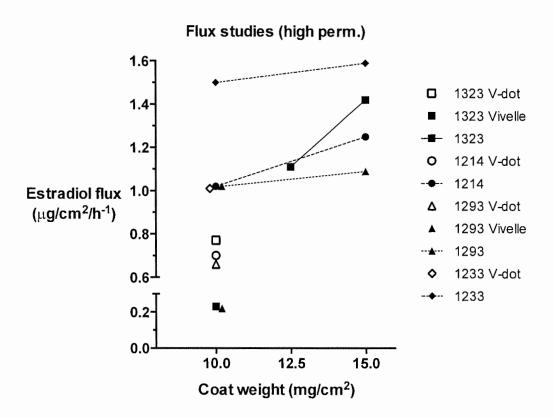


VII. EXPERIMENTAL DATA – IMPACT OF SKIN PERMEABILITY ON FLUX

- 40. Since drug flux is a measure of the rate at which drug passes through the skin, the permeability of the skin sample used in a flux study can impact the results. The permeability of human skin varies from person to person and region of skin to region of skin. I understand that Noven accounted for this variability by using internal controls, such as Vivelle®-Dot or Vivelle®, since it was very familiar with the flux of these FDA-approved systems which were developed at Noven .
- 41. The impact of skin permeability on flux and the usefulness of an internal control in this context is illustrated in Flux Studies 1214, 1233, and 1293, which assessed the flux of formulations having the same components as the Example 1 formulation at target coat weights of 10 mg/cm² and 15 mg/cm² (and used Vivelle-Dot® and Vivelle as internal controls).

Ctuder#	For	rmulation (Compo	nents (%	Coat Wt.	Drug Flux				
Study #	Acrylate	Silicone	DPG	OAlc	PVP	Estradiol	(mg/cm ²)	(µg/cm ² •h)		
1323	10	66.9	8	6	7.5	1.6	15	1.42		
	10	66.9	8	6	7.5	1.6	12.5	1.11		
Control (1	Control (flux): Vivelle-Dot® (0.77 μg/cm ² •h)									
Control (1	flux): Vivel	le® (0.23 j	ıg/cm²•	h)						
1214	10	66.9	8	6	7.5	1.6	15	1.25		
	10	66.9	8	6	7.5	1.6	10	1.02		
Control (1	flux): Vivel	le-Dot® (0).7 μg/c	m²•h)						
1293	10	66.9	8	6	7.5	1.6	15	1.09		
	10	66.9	8	6	7.5	1.6	10	1.02		
Control (Control (flux): Vivelle-Dot® (0.66 μg/cm ² •h)									
Control (1	Control (flux): Vivelle® (0.22 μg/cm ² •h)									
1233	10	66.9	8	6	7.5	1.6	15	1.59		
	10	66.9	8	6	7.5	1.6	10	1.50		
Control (flux): Vivelle-Dot® (1.01 μg/cm ² •h)										

The cumulative flux results (reported as the average of 4 or 5 replicates; some values are once more slightly displaced along the x-axis to facilitate visualization of each data point) are illustrated below:



42. In these studies, the estradiol flux from Vivelle-Dot® was higher than usual, indicating that the donor skin had a higher permeability than usual. While the product label and the patient information leaflet indicate that the estradiol transdermal flux from the Vivelle®-Dot system is nominally 0.4 μg cm⁻² h⁻¹, the values observed in these flux studies were 1.5 to 2.5-fold higher. The high fluxes seen from the test formulations are therefore completely consistent with that from the Vivelle®-Dot control (and reinforce the clear benefit of including this system as an internal check in experiments such as these).

VIII. NO PRIOR ART SUGGESTS THAT COAT WEIGHT WOULD IMPACT FLUX

43. As I noted above, a person of ordinary skill in the art would not have thought of coat weight as a parameter to be adjusted to affect the flux of a drug from a transdermal patch. In this

regard, I confirm that none of the prior art references cited by the Patent Office Examiner during examination of the pending applications suggests that increasing coat weight would increase flux. Rather, to the extent any of the prior art cited by the Patent Office Examiner discusses coat weight, the references simply provide ranges of typical coat weights. Indeed, prior to the teachings of the specification, the coat weight (thickness) of the polymer matrix was understood to be relevant to the patch's ability to <u>sustain</u> desired flux over time. Thus, while the person of ordinary skill in the art would have expected an increase in coat weight to extend the period that the patch could sustain a given flux (*i.e.*, the number of days for which a patch would deliver the target daily dose), he or she would not have expected an increase in coat weight to increase flux (*i.e.*, the daily dose). Rather, the prior art shows that the most predictable way to obtain a greater flux of drug across the skin from a transdermal patch is to increase its size, since there is a direct relationship between flux and active surface area in Fick's 1st law of diffusion. This is seen, for example, in the different strengths of Vivelle-Dot®, which differ only in active surface area.

44.

45. Thus, the prior art does not teach or suggest that coat weight is a parameter to be adjusted to affect the rate of drug flux.

However, the pending applications describe this surprising and unexpected result and demonstrate it in Example 1. Moreover, the additional experimental data discussed above provide further support for the surprising and unexpected effect.

* * *

46. I further 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 false statements may jeopardize the validity of the application or any patent resulting therefrom.

June 13, 2017

Date Richard H. Guy

Richard H. GUY - Curriculum Vitae

Richard Guy received an M.A. in Chemistry from Oxford University, and his Ph.D. in Pharmaceutical Chemistry from the University of London in 1980. He then joined the faculty of the University of California, San Francisco (UCSF), where he was Assistant (1980-87), Associate (1987-1991) and finally Full Professor (1991-1996) of Biopharmaceutical Sciences & Pharmaceutical Chemistry. From 1987 until 1996, Dr. Guy was Vice-Chair of the Department of Biopharmaceutical Sciences at UCSF. During the next 8 years, Dr. Guy was Scientific Director of the *Centre interuniversitaire de recherche et d'enseignement* (Universities of Geneva and Lyon), and Professor of Biopharmacy in the Faculty of Sciences at the University of Geneva. In 2004, he assumed his present position as Professor of Pharmaceutical Sciences at the University of Bath and was Head of the Department of Pharmacy & Pharmacology at Bath from 2006 to 2008. He has also fulfilled the broader role of University Research Advisor. He remains an Adjunct Professor of Bioengineering and Therapeutic Sciences at UCSF.

Dr. Guy's principal achievements have been made in the areas of skin barrier function characterization, transdermal drug delivery, enhancement of percutaneous absorption, iontophoresis, noninvasive biosensing of blood glucose and other analytes, and the prediction and assessment of skin penetration and topical bioavailability. In total, Dr. Guy has published over 350 peer-reviewed articles and over 70 book chapters. He has co-authored one book and co-edited 7 others. He is also co-inventor of 12 patents. His research is presently supported by the U.S. Food & Drug Administration and the pharmaceutical and personal care industries. Current h-index (Scopus) is 67, with over 15,000 citations to Dr. Guy's publications.

Specific ongoing projects include: the development and validation of *in vitro-in vivo* correlations for the assessment of topical drug product bioequivalence; investigation of polymeric film-forming systems as sustained release platforms for topical drugs; determination of the disposition of drug and formulation excipients (including nanoparticles) post-application to the skin and nail using coherent Raman scattering and confocal microscopy; and derivation and evaluation of predictive models of percutaneous penetration for pharmaceutical and cosmetic 'actives', and for potentially toxic chemicals, which contact the skin.

Dr. Guy was an Associate Editor of the Journal of Pharmaceutical Sciences (2002-07) and currently serves on the editorial advisory boards of Diabetes Technology and Therapeutics, the European Journal of Pharmaceutical Sciences, Skin Pharmacology & Physiology, and the European Journal of Pharmaceutics and Biopharmaceutics. He was President of the Controlled Release Society (CRS) in 2000-01, and has served as a member of the Academy of Pharmaceutical Sciences (GB) board. Dr. Guy serves as a consultant and scientific advisor to several companies in the pharmaceutical, cosmetic and biotechnology industries.

Dr. Guy is an elected Fellow of the Royal Society of Chemistry (1988), the American Association of Pharmaceutical Scientists (1990), the American Association for the Advancement of Science (1992), the Academy of Pharmaceutical Sciences, Great Britain (2007) and the Controlled Release Society (CRS) College of Fellows (2010). He was the first recipient of the CRS Young Investigator Award in 1988, when he also won the British Pharmaceutical Conference Science Award. Dr. Guy was awarded, for his work in "reverse iontophoresis" and noninvasive glucose monitoring, the Prix Applications Médicales de l'Electricité, 1997 by the Institut Electricité Santé, Paris, France. In April 2000, Dr. Guy received the APV Research Award for Outstanding Achievements in the Pharmaceutical Sciences and, in 2007, he won the "Prix Pharmapeptides" from the Universities of Geneva and Lyon. In 2010, Dr. Guy became a Fellow of The School of Pharmacy (now the UCL School of Pharmacy), University of London, in recognition of "his distinguished contribution to the pharmaceutical sciences", and he received the CRS Founders Award in 2013. The Maurice-Marie Janot Award from the Association Pharmacie Galénique Industrielle (APGI) followed in 2016 for his "original and innovative papers in the domain of pharmaceutics, biopharmaceutics and pharmaceutical technology", the same year that he was awarded the degree of Doctor of Science from Oxford University.

Curriculum Vitae - Richard H. Guy

Date of Birth: November 27, 1954 **Nationality:** British

Current Position & Address:

Professor of Pharmaceutical Sciences Adjunct Professor

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University of Bath

Department of Bioengineering & Therapeutic Sciences

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Education (Undergraduate, Graduate, Postgraduate, Fellowships)

1977 B.A., Chemistry (First Class)

Oxford University, Oxford, England

1980 M.A., Chemistry

Oxford University, Oxford, England

1977-80 Ph.D., Pharmaceutical Chemistry

University of London, London, England

2016 D.Sc., Medical Sciences Division

Oxford University, Oxford, England

Specialty; Subspecialty

Chemistry; Physical Pharmaceutical Chemistry

Academic and Professional Positions Held

1978-80 Teaching Fellow

School of Pharmacy, University of London, London, England

1980-87 Assistant Professor

Departments of Biopharmaceutical Sciences and Pharmaceutical Chemistry, School of Pharmacy, University of California, San Francisco, California

1982-96 Research Associate

Department of Dermatology, School of Medicine University of California, San Francisco, California

1986-2000 Honorary Professor

The Welsh School of Pharmacy, Cardiff University, Cardiff, Wales

1987-91 Associate Professor

Departments of Biopharmaceutical Sciences and Pharmaceutical Chemistry, School of Pharmacy, University of California, San Francisco, California

1987-96 Member

Bioengineering Graduate Group, School of Medicine

University of California, San Francisco; and

College of Engineering, University of California - Berkeley, California

Vice-Chairman

Department of Biopharmaceutical Sciences, School of Pharmacy

University of California, San Francisco, California

1989 Academic Visitor (sabbatical)

Department of Chemistry

Imperial College of Science, Technology & Medicine, University of London

London, England

Chercheur (sabbatical)

Centre International de Recherches Dermatologiques

Sophia Antipolis, Valbonne, France

1991-96 Professor

Departments of Biopharmaceutical Sciences and Pharmaceutical Chemistry,

School of Pharmacy, University of California, San Francisco, California

1994-95 Visiting Professor (sabbatical)

Faculté de Pharmacie de Châtenay-Malabry, Université de Paris-Sud, France

1995 Visiting Professor (sabbatical)

Facultad de Farmacia, Departamento de Farmacología, Farmacia y Tecnología

Farmacéutica, Universidade de Santiago de Compostela, Spain

1996-2001 Adjunct Professor [Professeur Associé]

Faculté des Sciences, Université de Genève, Genève, Switzerland

1996 -2001 Directeur Scientifique

Centre interuniversitaire de recherche et d'enseignement, "Pharmapeptides" Universités de Genève et Lyon, Campus Universitaire, Archamps, France

1996- Adjunct Professor

Department of Bioengineering and Therapeutic Sciences,

School of Pharmacy, University of California, San Francisco, California

1997-98 Professeur Invité

Faculté de Pharmacie, Université Claude Bernard, Lyon, France

2001-03 Directeur

Ecole romande de pharmacie, Universités de Genève et Lausanne

Genève, Lausanne, Switzerland

Professeur 2001-04

Faculté des Sciences, Université de Genève, Genève, Switzerland

Directeur

Centre interuniversitaire de recherche et d'enseignement, "Pharmapeptides" Universités de Genève et Lyon, Campus Universitaire, Archamps, France

Visiting Professor

University of Greenwich, England

2004-**Professor of Pharmaceutical Sciences**

University of Bath, Department of Pharmacy & Pharmacology

Bath, England

2006-08 Head, Department of Pharmacy & Pharmacology

University of Bath, Bath, England

2008-10 University Research Adviser

University of Bath, Bath, England

2015 Academic Visitor (sabbatical)

Physical & Theoretical Chemistry Laboratory, Department of Chemistry

Oxford University

Honors and Awards

1984 Pennwalt Award for the "Best Pharmaceutical Paper," Controlled Release Society. San Francisco, California

1984-87 Special Emphasis Research Career Award, National Institute of Occupational Safety and Health,

"Cutaneous Toxicity: Predictive Pathways"

1987 Walter F. Enz Lecturer, Department of Pharmaceutical Chemistry, University of Kansas.

Lawrence, Kansas

4th Annual Minnetonka Lectureship in Pharmaceutics, College of Pharmacy, University of

Minnesota. Minneapolis, Minnesota

Young Investigator Award (1st recipient), Controlled Release Society 1988

British Pharmaceutical Conference Science Award

Elected Fellow of the Royal Society of Chemistry

1990 Elected Fellow of the American Association of Pharmaceutical Scientists

Lecturer in the University of Medicine & Dentistry of New Jersey Distinguished Lecture Series

in Biomaterials and Biomedical Devices, Rutgers University. Piscataway, New Jersey

1992 Elected Fellow of the American Association for the Advancement of Science 1993 Visiting Eminent Scholar Series in Drug Delivery, University of Florida, Gainesville, Florida 1997 Recipient, Prix Applications Médicales de l'Electricité, 1997, Electricité de France, Institut Electricité Santé, Paris, France 1999 Lauréat du Concours "Création d'enterprise de technologies innovantes", Ministère de l'Education Nationale, de la Recherche et de la Technologie, France 2000 Recipient, APV (International Association for Pharmaceutical Technology) Research Award for Outstanding Achievements in the Pharmaceutical Sciences 2005 APGI (Association de Pharmacie Galénique Industrielle) Sanofi-Aventis Young Investigator Award to Anke Sieg, Ph.D., former doctoral student, for her thesis performed under the codirection of Dr. M.B. Delgado-Charro & Prof. R.H. Guy 2006 Research cited in The Better World Report. "Technology Transfer Stories: 25 Innovations that Changed the World". 2006 edition. http://www.autm.net/documents/AUTM_BWR.pdf. 'Tiny monitor gives diabetics frequent, automatic readings', ch. 6, pp. 55-58. The first non-invasive continuous monitoring device, pioneered at the University of California, San Francisco, helps patients better manage diabetes. 2007 Elected Fellow of the Academy of Pharmaceutical Sciences, Great Britain (APSGB). Prix Pharmapeptides, Universities of Geneva and Lyon. 2010 Elected to the College of Fellows of the Controlled Release Society Elected Fellow of The School of Pharmacy, University of London (now the UCL School of Pharmacy), in recognition of "his distinguished contribution to the pharmaceutical sciences" 2013 Founders Award, Controlled Release Society 2014 Award from the Royal Pharmaceutical Society of Great Britain to the RPSGB Pharmaceutical Science Expert Advisory Panel (RHG is a member) in recognition of its contribution to promoting the pharmaceutical sciences 2016 D.Sc., Medical Sciences Division, Oxford University, Oxford, England Maurice-Marie Janot Award from the Association de Pharmacie Galénique Industrielle (APGI) for original and innovative research in pharmaceutics, biopharmaceutics and pharmaceutical technology.

Description of Current Research Program

Research focuses on skin barrier function characterization, transdermal drug delivery, enhancement of percutaneous absorption, iontophoresis, noninvasive biosensing, and the prediction and assessment of skin penetration and topical bioavailability. Specific ongoing projects include: measurement of the skin's biomechanical properties at the nanoscale using atomic force microscopy; the potential of polymeric film-forming systems as sustained release platforms for topical drugs; determination of the disposition of drug and formulation excipients (including nanoparticles) post-application to the skin and to

the nail using coherent Raman scattering and confocal microscopy; the impact of laser, microneedle and other poration technologies on drug delivery into and through skin and nail; examination of a graphene-based biosensor for noninvasive, transdermal glucose monitoring; development of *in vitro – in vivo* correlations with which to assess the bio(in)equivalence of topical drug products; and derivation and evaluation of predictive models of percutaneous penetration for pharmaceutical and cosmetic 'actives', and for potentially toxic chemicals, which come into contact with skin.

PUBLICATIONS

Journal Articles

- (1) The Estimation of Diffusion Coefficients Using the Rotating Diffusion Cell. R.H. Guy and R. Fleming. *Int. J. Pharmaceut.* **3**, 143-149 (1979).
- (2) A Novel Method to Study the Permeability of a Phospholipid Barrier. R.H. Guy and R. Fleming. *J. Chem. Soc., Chem. Commun.*, 729-730 (1979).
- (3) Long-Time Solution of the Equations Describing the Flow of ²²Na⁺ in a Finite Composite System Containing a Synthetic Phospholipid-Protein Membrane: Calculation of Permeability Coefficient. R.H. Guy and R. Fleming. *Int. J. Pharmaceut.* **4**, 241-248 (1980).
- (4) A Theoretical Description Relating Skin Penetration to the Thickness of the Applied Medicament. R.H. Guy, and J. Hadgraft. *Int. J. Pharmaceut.* **6**, 321-332 (1980).
- (5) Diffusion Coefficient Determination Using a Filter-Paper Diaphragm Cell Technique. A.D. Cadman, R. Fleming, and R.H. Guy. *J. Pharm. Pharmacol.* **33**, 121-123 (1981).
- (6) Capillary Diffusion and Interfacial Kinetics. R.H. Guy and J. Hadgraft. *J. Colloid Interface Sci.* **80**, 386-392 (1981).
- (7) Interfacial Transport of Salicylic Acid. R.H. Guy and J. Hadgraft. *J. Colloid Interface Sci.* **81**, 69-74 (1981).
- (8) Calculations of Drug Release Rates From Cylinders. R.H. Guy and J. Hadgraft. *Int. J. Pharmaceut.* **8**, 159-165 (1981).
- (9) Transport Across a Phospholipid Barrier. R.H. Guy and R. Fleming. *J. Colloid Interface Sci.* **83**, 130-137 (1981).
- (10) A Theoretical Comparison of Release Rates of Drugs Into Sink and Non-Sink Conditions. R.H. Guy and J. Hadgraft. *J. Pharm. Sci.* **70**, 1243-1245 (1981).
- (11) Diffusion of Lysozyme Chloride in Water and Aqueous Potassium Chloride Solutions. A.D. Cadman, R. Fleming, and R.H. Guy. *Biophys. J.* **37**, 569-574 (1982).
- (12) Kinetics of Solute Transfer Across Aqueous Phase- Liquid Hydrocarbon Interfaces. R.H. Guy, T.R. Aquino, and D.H. Honda. *J. Phys. Chem.* **86**, 280-283 (1982).
- (13) The Influence of Urea on the Kinetics of Interfacial Transfer. R.H. Guy, D.H. Honda, and T.R. Aquino. J. Colloid Interface Sci. 87, 107-114 (1982).
- (14) Rapid Radial Transport of Methyl Nicotinate in the Dermis. R.H. Guy and H.I. Maibach. *Arch. Dermatol. Res.* **273**, 91-95 (1982).
- (15) A Pharmacokinetic Model for Percutaneous Absorption. R.H. Guy, J. Hadgraft, and H.I. Maibach. *Int. J. Pharmaceut.* **11**, 119-129 (1982).
- (16) Percutaneous Metabolism with Saturable Enzyme Kinetics. R.H. Guy and J.Hadgraft. *Int. J. Pharmaceut.* **11**, 187-197 (1982).

- (17) Calculations of Drug Release Rates from Spherical Particles. R.H. Guy, J. Hadgraft, I. W. Kellaway, and M. J. Taylor. *Int. J. Pharmaceut.* **11**, 199-207 (1982).
- (18) Solute Transfer Across Liquid-Liquid Interfaces. Kinetic and Thermodynamic Evaluation. R.H. Guy, T.R. Aquino III, and D.H. Honda. *J. Phys. Chem.* **86**, 2861-2866 (1982).
- (19) Release of Non-Electrolytes from Liposomes. R.H. Guy, J. Hadgraft, M.J. Taylor, and I.W. Kellaway. *J. Pharm. Pharmacol.* **35**, 12-14 (1983).
- (20) Solute Transfer Across Liquid-Liquid Interfaces. R.H. Guy. Ann. N.Y. Acad. Sci. 404, 194-197 (1983).
- (21) Kinetics and Thermodynamics of Interfacial Transfer. R. Fleming, R.H. Guy and J. Hadgraft. *J. Pharm. Sci.* **72**, 142-145 (1982).
- (22) Malathion Percutaneous Absorption Following Repeated Administration To Man. R.C. Wester, H.I. Maibach, D.A.W. Bucks, and R.H. Guy. *Toxicol. Appl. Pharmacol.* **68**, 116-119 (1983).
- (23) Interfacial Transfer Kinetics of ²²Na+ Across a Synthetic Phospholipid-Protein Membrane. R. Fleming, R.H. Guy, and J. Hadgraft. *J. Colloid Interface Sci.* **94**, 54-59 (1983).
- (24) Noninvasive Assessment of Local Nicotinate Pharmacodynamics by Photoplethysmography. E. Tur, R.H. Guy, M. Tur, and H.I. Maibach. *J. Invest. Dermatol.* **80**, 499-503 (1983).
- (25) A Physicochemical Interpretation of the Pharmacokinetics of Percutaneous Absorption. R.H. Guy and J. Hadgraft. *J. Pharmacokin. Biopharm.* **11**, 189-203 (1983).
- (26) Percutaneous Absorption: Transport in the Dermis. W.J. Albery, R.H. Guy, and J. Hadgraft. *Int. J. Pharmaceut.* **15**, 125-148 (1983).
- (27) Noninvasive Assessments of the Percutaneous Absorption of Methyl Nicotinate in Humans. R.H. Guy, R.C. Wester, E. Tur, and H.I. Maibach. *J. Pharm. Sci.* **72**, 1077-1079 (1983).
- (28) Drug Delivery to Local Subcutaneous Structures Following Topical Administration. R.H. Guy and H.I. Maibach. *J. Pharm. Sci.* **72**, 1375-1380 (1983).
- (29) Percutaneous Absorption: Multidose Pharmacokinetics. R.H. Guy, J. Hadgraft, H.I. Maibach. *Int. J. Pharmaceut.* **17**, 23-28 (1983).
- (30) Preliminary Skin Blood Flow Measurements Appear Unsuccessful for Assessing Topical Corticosteroid Effect. M. Amantea, E. Tur, H.I. Maibach, and R.H. Guy. *Arch. Dermatol. Res.* **275**, 419-420 (1983).
- (31) Basal Perfusion of the Cutaneous Microcirculation: Measurements as a Function of Anatomic Position. E. Tur, M. Tur, H.I. Maibach, and R.H. Guy. *J. Invest. Dermatol.* **81**, 441-446 (1983).
- (32) Correction Factors for Determining Body Exposure From Forearm Percutaneous Absorption. R.H. Guy and H.I. Maibach. *J. Appl. Toxicol.* **4**, 26-28 (1984).
- (33) Pharmacodynamic Measurements of Methyl Nicotinate Percutaneous Absorption. R.H. Guy, E. Tur, B. Bugatto, C. Gaebel, L.B. Sheiner, and H.I. Maibach. *Pharmaceut. Res.* **1**, 76-81 (1984).
- (34) A Theoretical Description of the Effects of Volatility and Substantivity on Percutaneous Absorption. R.H. Guy and J. Hadgraft. *Int. J. Pharmaceut.* **18**, 139-147 (1984).

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Publication metrics

A citation analysis of Dr. Guy's career-to-date peer-reviewed outputs (>370 in total as of 11-2016) shows that they have been cited over 15,000 occasions (average citations per article ~35) and that his Scopus hindex is 67.

In an editorial in *Pharmaceutical Research*, which is the official journal of the American Association of Pharmaceutical Scientists, marking the occasion of its 25th Anniversary at the end of 2008. (*Lee, VHL. Shaping the transformation of pharmaceutical science. Pharm Res 25, 2707-2712, 2009*), it was noted that Dr. Guy had co-authored more papers (72) than anyone else in *Pharmaceutical Research*, and that one of these publications was the fourth most cited in the journal (390 citations at the end of 2008, currently 689).

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- (79) Imaging Drug Delivery to Skin with Coherent Raman Scattering Microscopy. N.A. Belsey, L.R. Contreras-Rojas and R.H. Guy. Chapter in *Noninvasive Diagnostic Techniques in Clinical Dermatology*, pp. 225-231. Edited by E. Berardesca, H.I. Maibach and K.P. Wilhelm, Springer, Berlin, Germany, 2014.
- (80) Pharmacology of the Skin: Principles of Topical Drug Delivery. R.H. Guy. Chapter 13 in *Rook's Textbook of Dermatology, 9th Edition*. ISBN: 978-1-118-44119-0. Edited by C.E.M. Griffiths, J. Barker, R.J.G. Chalmers, T.O. Bleiker and D. Creamer, Wiley-Blackwell, Ltd., Chichester, U.K., 2016.

1994-96	U.S. Environmental Protection Agency, \$183,074 TDC: Estimating the Absorbed Dose from Dermal Exposure to Environmental Pollutants: Development of Guidelines for Acquisition, Interpretation and Use of <i>In Vivo</i> and <i>In Vitro</i> Data (Co-Investigator; A.L. Bunge, Principal Investigator)
1994-98	U.S. Air Force, 94NL023, \$433,293 TDC: Prediction and Assessment of Dermal Exposure
1994-98	National Institutes of Health, 1-R01-ES06825, \$1,029,303 TDC: Dermal Absorption from Soils: Evaluation and Prediction (Co-Investigator; A.L. Bunge, Principal Investigator)
1995-98	National Institutes of Health, 1-R01-DA-09292, \$95,658 TDC: Neonatal Skin: Barrier Function and Drug Delivery
	U.S. Environmental Protection Agency, \$245,268 TDC: Structure-Activity Relationships for Predicting Pesticide Dermal Absorption from Multimedia (Co-Investigator; A.L. Bunge, Principal Investigator)
1997-99	U.S. Air Force, 94NL023, \$647,814 TDC: Dermal Absorption of Chemicals from Evaporating Vehicle Mixtures (Co-Investigator; A.L. Bunge, Principal Investigator)
1998-01	Fonds national suisse de la recherche scientifique, SFr 180,000: Mechanisms of lontophoretic Drug Delivery Across Skin
1999-02	Programme Commun de Recherche en Génie Biomédical 1999-2002, SFr 374,000: Bioengineering for Transdermal Therapy and Diagnosis
2000-02	Fonds national suisse de la recherche scientifique, SFr 126,000: Prevention of Intravascular Device-Related Infections: Electrically-Mediated Skin Antisepsis [A. Naik, principal investigator]
2000-03	Fonds national suisse de la recherche scientifique, SFr 260,000: Reverse Iontophoresis: Noninvasive Drug Monitoring via the Skin [M.B. Delgado-Charro, principal investigator]
2003-04	U.S. Army Medical Research Acquisition Activity, \$231,380: Skin Bioengineering – Noninvasive Transdermal Monitoring
	U.S. Food & Drug Administration, \$12,000: Dermatopharmacokinetics – Improvement of Methodology for Assessing Bioequivalence of Topical Dermatological Drug Products [A.L. Bunge, principal investigator; total budget \$100,000]
2003-08	U.S. National Institutes of Health, 1-R01-EB-001420, \$675,000 TDC: Skin Bioengineering – Noninvasive Transdermal Monitoring
2005-08	Parkinson's Disease Society, UK, £105,781 TDC: Optimizing the Pharmacological Treatment of Parkinson's Disease via Transdermal Iontophoresis [M.B. Delgado-Charro, principal investigator]
2005-09	European Commission 6 th Framework, NMP3-CT-2005-011844, €244,952 TDC:

	Nanostructured Waterborne Polymer Films with Outstanding Properties [J.M. Asua, Program Director]	
2009-10	Department of the Environment, Food and Rural Affairs (Defra), PS2616, £91,800 FEC: Skin Uptake and Penetration of Pesticides	
2009-11	Medical Research Council, G0802728, £242,172 FEC: Transdermal delivery of a Buprenorphine/Naltrexone Combination for the Treatment of Drug Abuse [S.M. Husbands, principal investigator]	
2013-15	National Institute for Health Research (NIHR), £333,787 (Bath share £9,772): Choice of moisturiser in eczema treatment (COMET)	
2013-18	U.S. Department of Health & Human Services; Food & Drug Administration, 1-U01-FD-004947-01, \$2,499,989 (Bath share £434,779): Bioequivalence of topical drug products: in vitro - in vivo correlations [A.L. Stinchcomb, U. of Maryland, principal investigator]	
2015-16	MRC Confidence-in-Concepts Scheme: £67,057 (100% FEC): "The 'Glucose Pathfinder': Noninvasive, transdermal, path-selective and highly specific glucose monitoring on a graphene platform" [A. Ilie, principal investigator]	
2015-18	Sir Halley Stewart Trust: £50,000: New method for glucose monitoring in diabetics [A. Ilie, principal investigator]	
2016-19	The Leo Foundation: DKK 3,564,000 (£309,514): Development and validation of physiologically-based pharmacokinetic model for dermal absorption [M.B. Delgado-Charro, principal investigator]	
Participation in Other Sponsored Research Activity (since 1994)		
1994-95	Becton Dickinson Transdermal Systems (USA), \$35,000 TDC: Iontophoresis and the pH Profile of the Skin	
1995-96	Becton Dickinson Transdermal Systems (USA), \$35,000 TDC: Peptide Iontophoresis: Electrorepulsion <i>Versus</i> Electroosmosis	
1997-98	Tilderm Systems (France), SFr67,000: Electroosmosis and Skin Impedance	
	Electricité de France, Institut Electricité Santé, FF300,000: Nouvelle Méthode non invasive de diagnostique et de suivi thérapeutique par ionophorèse inverse (ICI)	
	Cygnus, Inc. (USA), \$55,482: Ultrasound-Enhanced Transport Across the Skin: Effect of Frequency?	
1997-99	Novartis Pharma, Inc. (Switzerland), SFr215,250: Topical Drug Bioavailability: Evaluation and Optimisation	

Novartis Pharma, Inc. (Switzerland), SFr 105,000: Supersaturation as a Method to Improve

Becton Dickinson Transdermal Systems (USA), \$150,000 TDC: Peptide Iontophoresis:

Topical Bioavailability of Lipophilic Drugs

1998-2000

	Electrorepulsion Versus Electroosmosis
4000 0004	
1999-2001	Galderma (France), SFr410,000: Topical Dermatological Drug Product Bioavailability and Bioequivalence <i>in vivo</i>
2001-2002	Hisamitsu Pharmaceutical Co. Ltd. (Japan), SFr 70,000: Mechanisms of Iontophoresis
	Pierre-Fabre, Institut de Recherche (France), FF 120,000: L'Eau dans la Peau
	L'Oréal (France), SFr 121,000: Skin Absorption Databases
2001-2005	Leo Pharmaceutical Products, Inc. (Denmark), SFr 375,015: The Rational Design of Dermatological Products
2002	Power Paper (Israel), € 42,500: Iontophoresis of Cosmeceuticals
2002-2003	DPC Products, Inc. (USA), \leqslant 26,955: Skin Penetration Enhancement with Naturally-Occuring Oils
	Abbott Laboratories (USA), \in 57,504: Transdermal Development of Mavik - Options and Strategies
2002-2005	Servier, Institut des recherches internationals (France), SFr 105,000: Development of a Transdermal 'Spray Patch' for the Systemic Administration of Testosterone
	Bracco Research S.A. (Switzerland), SFr 172,269: Sonoporation
2003	L'Oréal (France), € 14,600: Iontophoresis of Vitamin C
2003-2004	Novozymes A/S (Denmark), € 68,170: Hyaluronic Acid: Skin Penetration and Hydration
2003-2005	L'Oréal (France), \$ 150,150: Skin Absorption Database Project
	Vyteris, Inc. (USA), SFr 463,000 "Vyteris Europe"
2003-2006	Vyteris, Inc. (USA), \$ 147,000: Iontophoretic Drug Delivery: Increasing the Odds
2004	L'Oréal (France), € 15,000: Iontophoresis of Vitamin C
	L'Oréal (France), € 15,000: Skin Uptake of Nanoparticles
	Proctor & Gamble (UK), € 9,000: Reverse Iontophoresis and Skin Health
2005-2006	Vyteris, Inc. (USA), £26,500: Iontophoretic Drug Delivery: Increasing the Odds
	Ascend Therapeutics (USA), £37,170: Feasibility study for transdermal delivery of a group of related compounds
	Galderma Research & Development (France), £27,000: Iontophoretic Delivery of Amorolfine across the Nail
2006-2010	York Pharma/BBSRC Case Award, £67,500: Bioavailability of Topically Applied Drugs for the Treatment of Atopic Eczema and Other Related Diseases
2007-2008	EyeGate Pharmaceuticals, Inc. (USA), £36,791: Ocular Iontophoresis

	GlaxoSmithKline (USA), £15,000: Dermatopharmacokinetics of Docosanol ex vivo
2009-2010	Zealand Pharma (Denmark), £33,691: In vitro Assessment of Transdermal Peptide Delivery
2010	LSC, Inc. (USA), £25,066 TDC: Dermal delivery of an "active" from hydroxysomes.
2010-2013	Leo Pharma A/S (Denmark), £73,577 TDC: Dermal Controlled Release. 3-year PhD studentship.
	Leo Pharma A/S (Denmark), £232,011 TDC: Imaging drug disposition and pharmacokinetics in skin by stimulated Raman scattering microscopy. 2-year postdoctoral fellowship.
2011	Exchange Supplies, Ltd. (U.K.), £23,051 TDC: Alternative buffers: Identifying suitable alternatives or additives to citric and ascorbic acid as a harm reduction tool to reduce the risks associated with illicit heroin and crack cocaine injections. [J. Scott, principal investigator]
	Grünenthal GmbH (Germany), £12,999 TDC: Iontophoresis of tapentadol hydrochloride.
	L'Oréal (France), £13,851 TDC: lontophoresis and electrical enhancement in the cosmetic and skin-care fields: a review.
	L'Oréal (France), £8.015 TDC: Iontophoresis and cosmetics [UnivMed].
2011-12	Orexo AB (Sweden), £140,708 TDC: Orexo facilities and partial secondment agreement.
2012-13	Orexo AB (Sweden), £140,708 TDC: Orexo facilities and partial secondment agreement.
2012-15	GlaxoSmithKline Research & Development (USA), £192,573 TDC: Examining formulation effects on drug-vehicle skin penetration enhancement.
2013	Reckitt Benkiser (U.K.) £38,110: Ibuprofen delivery across the skin.
2013-17	Syngenta Ltd./BBSRC Case Award, £123,520 TDC: Quantification of dermal absorption from pesticide residues from treated plant surfaces.
2014	Unilever, £16,344: S12 Delivery into and through mammalian skin.
2015	Benanova, Inc., £10,503: Skin penetration and distribution of polymeric nanoparticle formulations.

Other Creative Activities and Accomplishments

- 1992 U.S. Patent # 5,115,805, "Ultrasound-Enhanced Delivery of Materials Into and Through the Skin." D. Bommannan, H. Okuyama, R.H. Guy, P. Stauffer, and G.L. Flynn
- 1993 U.S. Patent # 5,231,975, "Ultrasound-Enhanced Delivery of Materials Into and Through the Skin." D. Bommannan, H. Okuyama, R.H. Guy, P. Stauffer, and G.L. Flynn
- 1994 U.S. Patent # 5,279,543, "Device for Iontophoretic Non-Invasive Sampling or Delivery of Substances." P. Glikfeld, C. Cullander, R.S. Hinz, and R.H. Guy
- 1994 U.S. Patent # 5,323,769, "Ultrasound-Enhanced Delivery of Materials Into and Through the Skin." D. Bommannan, H. Okuyama, R.H. Guy, P. Stauffer, and G.L. Flynn
- 1994 U.S. Patent # 5,362,307, "Method for the Iontophoretic Non-Invasive Determination of the In Vivo Concentration Level of and Inorganic or Organic Substance." R.H. Guy, G. Rao, P. Glikfeld, C. Cullander and R.S. Hinz
- 1997 U.S. Patent # 5,636,632, "Ultrasound-Enhanced Sampling of Materials Through the Skin". D. Bommannan, H. Okuyama, R.H. Guy, P. Stauffer, and G.L. Flynn
- 1998 U.S. Patent # 5,730,714, "Method for the Iontophoretic Non-Invasive Determination of the In Vivo Concentration Level of Glucose." R.H. Guy, G. Rao, P. Glikfeld, C. Cullander and R.S. Hinz
- 1999 U.S. Patent # 5,911,223, "Introduction of Modifying Agents into Skin by Electroporation". J.C. Weaver, T.E. Zewert, U. Pliquett, R.Vanbever, M.R. Prausnitz, T. Chen, C. Cullander, R. Guy and R.S. Langer.
- Spanish 'Patente de Invención' #009602541, "Procedimiento de control por iontoforesis del paso a través de membranas de sustancias incluidas en microemulsiones". G. Iglesias Vilas, M.B. Delgado Charro, J. Blanco Mendéz, M.A. López Quintela and R.H. Guy.
- 2001/2 Patent Application EP1401532 (WO03000340), "Method for Noninvasively Determining the Relative Levels of Two Substances Present in a Biological System". M.B. Delgado-Charro and R.H. Guy.
- 2003 European Patent EP 673622B1, "Device for Iontophoretic Non-Invasive Sampling or Delivery of Substances." P. Glikfeld, C. Cullander, R.S. Hinz, and R.H. Guy
- 2003 U.S. Patent # 6,542,765 B1, "Method for the Iontophoretic Non-Invasive Determination of the In Vivo Concentration Level of and Inorganic or Organic Substance." R.H. Guy, G. Rao, P. Glikfeld, C. Cullander and R.S. Hinz
- 2004 U.S. Patent # 6,714,815 B2, "Method for the Iontophoretic Non-Invasive Determination of the In Vivo Concentration Level of and Inorganic or Organic Substance." R.H. Guy, G. Rao, P. Glikfeld, C. Cullander and R.S. Hinz
- 2009 U.S. Patent # 7,555,337 B2, "Method for Non-Invasively Determining the Relative Levels of Two Biological Substances." R.H. Guy and M.B. Delgado-Charro
- 2009 Canadian Patent # CA 2450965, "Method for Non-Invasively Determining the Relative Levels of Two Biological Substances." R.H. Guy and M.B. Delgado-Charro

- 2009 Patent application WO/2009/065787, "Use of Amorolfine for Treating a Nail Disease by Iontophoresis." R.H. Guy and M.B. Delgado-Charro
- 2010 U.S. Patent # 7,693,573 B2, "Method for Non-Invasively Determining the Relative Levels of Two Biological Substances." R.H. Guy and M.B. Delgado-Charro
- 2012 European Patent 1401532, "Device for Non-Invasively Determining the Relative Levels of Two Substances Present in a Biological System." R.H. Guy and M.B. Delgado-Charro
- 2014 European Patent Application WO2014012652 (A1), "Electric-field Assisted Administration of Tapentadol." I. Friedrich, M. Mikyna, S. Gedat and R.H. Guy
- 2016 GB Patent Application 1607265.4, "Multiplexed Transdermal Extraction and Detection Devices for Non-Invasive Monitoring of Substances and Methods of Use." A. Ilie, F. Dougmene, B. Dupont, R.H. Guy, L.Lupani, F. Merken and R.M. Tyrrell
- Note: Italicised patents were initially licensed to Cygnus, Inc. (and are now licensed to Johnson & Johnson), and comprise integral intellectual property associated with a U.S. Food & Drug Administration and CE-mark approved device (the GlucoWatch® Biographer) for noninvasive glucose monitoring.

Graduated Ph.D. Students

1983-89	Daniel A.W. Bucks, Pharmaceutical Chemistry, University of California, San Francisco Thesis: "Prediction of Percutaneous Absorption" Current position: Dow Chemical, California, USA
1984-89	Victoria Knepp, Pharmaceutical Chemistry, University of California, San Francisco Thesis: "Controlled Drug Release from a Novel Liposomal Delivery System"
	Kathleen V. Roskos, Pharmaceutical Chemistry, University of California, San Francisco Thesis: "The Effect of Skin Aging on the Percutaneous Penetration of Chemicals Through Human Skin" Current position: Nektar, Inc., California, USA
1987-90	D. Bommannan, Bioengineering, University of California, San Francisco - University of California, Berkeley Thesis: "Enhancement of Transdermal Drug Delivery: Mechanisms and Methodologies" Current position: MaxVal California, USA
1991-96	Norris G. Turner, Pharmaceutical Chemistry, University of California, San Francisco Thesis: "Mechanisms of Iontophoretic Drug Delivery" Current position: Purdue Pharma, Connecticut, USA
1992-97	Lourdes Nonato, Bioengineering, University of California, San Francisco - University of California, Berkeley Thesis: "Evolution of Skin Barrier Function in Premature Neonates"
1994-96	Fabrice Pirot, Faculté de Médicine et de Pharmacie de Besançon, Université de Franche- Comté Thesis: "Analyse, Mesure et Prédiction de la Diffusion dans le Stratum Corneum Humain" Current position: Université Claude-Bernard Lyon 1
1996-2000	Ingo Alberti, Pharmaceutical Sciences, University of Geneva Thesis: "Local Bioavailability of Topical Dermatological Formulations <i>In Vivo</i> in Man" Current position: University of Geneva, Switzerland
1997-2000	Katrin Moser, Pharmaceutical Sciences, University of Geneva Thesis: "Supersaturation for the Enhanced Dermal Delivery of Lipophilic Drugs"
	Diego Marro, Pharmaceutical Sciences, University of Geneva Thesis: "Electromigration and Electroosmosis Contributions to iontophoretic Drug Delivery" Current position: Pharmacist-Manager, Huesca, Spain
1997-2001	Catherine Curdy, Pharmaceutical Sciences, University of Geneva Thesis: "Fonction Barrière du Stratum Corneum, chez l'Homme, <i>In Vivo</i> : Ionophorèse versus Diffusion Passive" Current position: Novartis Consumer Health, Nyon, Switzerland
	Gilles Touraille, Faculté de Pharmacie de Châtenay-Malabry, Université Paris XI Thesis: "Modalités d'Absorption Percutanée à Partir de Terre Contaminée par une Substance Chimique" [co-advisor: Prof. Jean-Paul Marty] Current position: EMEA, London, UK
1998-2001	Nabila Sekkat, Pharmaceutical Sciences, University of Geneva Thesis: "A Model for Neonatal Skin: Barrier Function and Drug Delivery"

Current position: Novartis, Basel, Switzerland

1998-2002 Gustavo Merino, Pharmaceutical Sciences, University of Geneva

Thesis: "Mechanisms of Ultrasound-Enhanced Skin Penetration" Current position: Carrefour Parapharmacie, Rennes, France

2000-2003 Rocio Alvarez-Román, Pharmaceutical Sciences, University of Geneva

Thesis: "Evaluation of Nanoparticle-Based Vehicles for (Trans)dermal Drug Delivery"

Current position: Universidad Nacional Autónoma de México, Mexico

2000-2004 Benoît Leboulanger, Pharmaceutical Sciences, University of Geneva

Thesis: "Evaluation de l'Ionophorèse Inversée comme Méthode Non-invasive pour le

Monitoring Thérapeutique"

Current position: Novartis, Basel, Switzerland

Anke Sieg, Pharmaceutical Sciences, University of Geneva

Thesis: "The Internal Standard Concept for Non-Invasive Glucose Monitoring Using Reverse

Iontophoresis"

Current position: Dow Corning, Belgium

2000-2005 Yannic Schuetz, Pharmaceutical Sciences, University of Geneva

Thesis: "Administration Transdermique des Peptides par Ionophorèse: Impact des Propriétés

Moléculaires sur les Mécanismes de Transport et Applications Thérapeutiques"

Current position: Triskel Integrated Services, Geneva, Switzerland

Isabel Diaz del Consuelo, Pharmaceutical Sciences, University of Geneva

Thesis: " Evaluation de la Muqueuse Oesophagienne de Porc comme Modèle pour l'Etude in

vitro de la Perméabilité Buccale "

Current position: Ipsen, SA, Barcelona, Spain

Nada Abla, Pharmaceutical Sciences, University of Geneva

Thesis: "Administration Transdermique par Ionophorèse: Effet de la Barrière Cutanée et Impact

des Propriétés Physico-chimiques des Peptides sur leur Transport"

Current position: Ferring SA, Lausanne, Switzerland

Blaise Mudry, Pharmaceutical Sciences, University of Geneva

Thesis: "Prediction and Optimization of Iontophoretic Transport Across the Skin"

Current position: Ferring SA, Lausanne, Switzerland

Christophe Herkenne, Pharmaceutical Sciences, University of Geneva

Thesis: "Evaluation and Optimization of Topical Drug Bioavailability"

Current position: DebioPharm, Martigny, Switzerland

2001-2005 Sophie Mehier-Humbert, Pharmaceutical Sciences, University of Geneva

Thesis: "Mechanistic Investigation of Microbubble-Mediated Sonoporation for Intracellular

Gene Delivery"

Current position: CEO, Cerma SA, Archamps, France (biotech start-up)

Marie-Laure Leichtnam, Pharmaceutical Sciences, University of Geneva

Thesis: "Mise au Point d'un Spray pour l'Administration Transdermique de Testostérone à Visée

Systémique"

2003-2006 Sandra Wiedersberg, Faculty of Science, University of Bath

Thesis: "Dermatopharmacokinetics and Pharmacodynamics of Topical Glucocorticoids"

Current position: Research Scientist, LTS Lohmann Therapie-Systeme AG

2003-2007 Valentine Wascotte, Faculté de Pharmacie, Université catholique de Louvain, Belgium

Thesis:

Current position: Research Scientist, GSK, Belgium

2004-2007 Jean-Philippe Sylvestre

Thesis: "Applications of Iontophoresis in Sports Medicine"

Current position: University of Montreal, Canada

2005-2008 Xiao Wu

Thesis: "Characterisation and evaluation of novel nanoparticulate formulations for application

to the skin"

Current position: Eli Lilly & Co., Indianapolis, IN, U.S.A.

2005-2009 Lisa Russell

Thesis: "Dermatopharmacokinetics: an approach to evaluate topical bioavailability"

Current position: Consultant Pharmacist, Nottingham PCT

Asma Djabri

Thesis: "Iontophoresis in paediatric medicine: noninvasive drug delivery and monitoring

applications"

Current position: Pharmacist

2006-2010 Manda Tsang

Thesis: "Formulation and delivery of topically applied drugs for the treatment of atopic eczema

and other related diseases"

Current position:

2008-2011 Quan Yang

Thesis: "Application of Biophysics and Bioengineering to the Assessment of Skin Barrier

Function"

Current position: MHRA, London, UK

2008-2013 Premrutai Thitilertdecha

Thesis: "Formulation optimization for the topical delivery of active agents in traditional

medicines"

Current position: Centre for Thai Traditional Medicine, Faculty of Medicine, Siriraj Hospital,

Mahidol University, Bangkok, Thailand

2010-2014 Kit Frederiksen

Thesis: "In situ polymeric film-forming systems for sustained topical delivery"

Current position: Novo Nordisk, Denmark

2011-2014 Hazel Garvie-Cook

Thesis: "Micro- and nano-scale assessment of novel (trans)dermal drug delivery strategies"

Current position: Postdoctoral Research Associate, University of Bath

Wing Chiu

Thesis: "Mechanism and optimisation of drug delivery into and through the nail"

Current position: Postdoctoral Research Associate, University of Bath

Professional Research Personnel, Postgraduate Personnel, and Postdoctoral Fellows

University of California, San Francisco

1982-83	Ethel Tur, M.D., Visiting Research Associate in Dermatology: Non-invasive monitoring of percutaneous absorption Current position: Ichilov Medical Center, Tel Aviv, Israel Michael Amantea, B.S., President's Undergraduate Fellow: The influence of alcohol at a model biomembrane interface Current position: UCSD School of Pharmacy, California, USA
1982–2001	Robert Hinz, Ph.D., Research Associate: Interfacial transport: Kinetics and perturbation
1983	Veronique Drouard, M.Pharm., Visiting Postgraduate Research Pharmacist: UV erythema Current position: Givaudan, Paris, France Charles Ryll, Pharm.D., M.S. Graduate Student: Pharmaceutical Chemistry
1983-84	Sharif Elamir, M.D., Visiting Research Associate in Dermatology: Quantification of irritation Larry Schall, M.D., Research Associate in Dermatology: Blood flow to the skin monitored by laser Doppler velocimetry
1983-89	Daniel A.W. Bucks, Graduate Student: Pharmaceutical Chemistry Current position: Dow Chemical, California, USA
1984	Eva M. Carlström, Postgraduate Research Chemist: <i>In vitro</i> skin penetration Current position: AstraZeneca, Sweden
1984-85	John M. Stevenson, B.S., Postgraduate Research Biologist: Skin irritancy studies Bruce A. Firestone, Graduate Student: Pharmaceutical Chemistry Current position: Allergan, California, USA
1984-88	Kathleen V. Roskos, Graduate Student: Pharmaceutical Chemistry Current position: Nektar, Inc., California, USA
1984-89	Victoria M. Knepp, Graduate Student: Pharmaceutical Chemistry Current position: Alza Corp., California, USA
1985	Kamaljit Ryatt, M.D., Visiting Lecturer in Dermatology: Skin blood flow Current position: Dermatologist, England
1985-86	GianCarlo Santus, Ph.D., Visiting Scientist (Sabbatical): Transdermal drug delivery and cutaneous metabolism Current position: NiCox, Sophia Antipolis, France Diana Villaflor, M.D., Visiting Postdoctoral Research Chemist: The influence of aging on the barrier function of skin
1985-	Cynthia Lorence, B.S., Research Associate: Percutaneous absorption of organic compounds in vitro

1985-89	Joy Houk, M.S., Graduate Student: Pharmaceutical Chemistry
1986-88	Geoffrey Ridout, Ph.D., Postdoctoral Research Chemist: Models for percutaneous absorption Katherine L. Kendrick, Ph.D., Postdoctoral Research Chemist: Interfacial transfer kinetics Peretz Glikfeld, Dip. Chem. Eng., Postdoctoral Research Chemical Engineer: Transdermal drug delivery by iontophoresis Current position: Israel Institute for Biological Research, Ness-Ziona, Israel
1987-88	C. Hodson, B.A., Research Associate: In vitro skin absorption
1987-90	D. Bommannan, M.S., Graduate Student: Bioengineering Current position: CEO, Maxval Group, California, USA Christopher Cullander, Ph.D., Postdoctoral Research Biophysicist: Electrical properties of skin Current position: University of California – San Francisco, USA
1987-89	Takashi Kai, M.S., Postgraduate Research Chemist: Percutaneous penetration enhancement Current position: Nippon Shokubai Co. Ltd., Japan Vivien Mak, Ph.D., Postdoctoral Research Chemist: Spectroscopic investigations of skin barrier function Current position: Independent consultant
1988-90	Naruhito Higo, B.S., Postgraduate Research Chemist: Transdermal drug delivery and cutaneous metabolism Current position: Hisamitsu Pharmaceutical Co. Ltd, Tsukuba, Japan Philip G. Green, Ph.D., Postdoctoral Research Chemist: Iontophoretic delivery of peptides across the skin Current position: Merck Bioventures, New Jersey, USA
1989-90	Daniel A.W. Bucks, Ph.D.: Assistant Research Chemist: Percutaneous absorption Current position: Dow Chemical, California, USA Hirohito Okuyama, M.S.: Postgraduate Research Chemist: Effects of ultrasound on transdermal drug delivery Current position: Boehringer Ingelheim, Narita, Japan
1990-92	Carol L. Gay, Ph.D.: Postdoctoral Research Chemist: Enhancement of Transdermal Delivery Current position: GlaxoSmithKiline Consumer Health, Weybridge, England
1990-93	Girish Rao, Ph.D.: Postdoctoral Research Chemist: Transdermal Sampling of Blood Glucose by Iontophoresis Current position: Unilever, India
1990-94	Christopher Cullander, Ph.D.: Assistant Research Biophysicist: Electrophysiological and Microscopic Evaluations of Skin Barrier Function Current position: Adjunct Associate Professor, University of California – San Francisco

1990-96 Jurij J. Hostynek, Ph.D.: Visiting Scientist: Prediction of Risk Following Dermal Exposure to Toxic Chemicals Current position: Research scientist, University of California, San Francisco 1991-92 Jens Brange, M.Sc.: Visiting Professor of Pharmacy: Iontophoretic Delivery of Insulin Analogs Across the Skin Liselotte Langkjaer, M.Sc.: Visiting Assistant Professor of Pharmacy: Iontophoretic Delivery of Insulin Analogs Across the Skin Current position: Novo Nordisk, Bagsværd, Denmark Ronald van der Geest, B.S.: Postgraduate Research Student: Transdermal Delivery of Oligonucleotides Current position: Tibotec-Virco Co., VA, Belgium 1991-93 Aeri Kim, Ph.D.: Postdoctoral Research Chemist: Iontophoretic Delivery of Insulin Analogs Across the Skin Current position: LG, Inc., Korea Rhonda Brand, Ph.D.: Postdoctoral Research Bioengineer: Biophysical Analysis of the Effect of Iontophoresis on Skin Barrier Function Current position: NorthWestern University, Illinois, USA M. Begoña Delgado Charro, Ph.D.: Visiting Assistant Professor: Iontophoretic Delivery of **LHRH Analogs and Antagonists** Current position: University of Bath, UK, Senior Lecturer in Pharmaceutical Sciences Seaung Oh, Ph.D.: Postdoctoral Research Chemist: Skin Impedance, Electroporation, and Transdermal Drug Delivery Current position: Sookmyung Women's University, Seoul, Korea 1991-94 Aarti Naik, Ph.D.: Postdoctoral Research Chemist: IR Spectroscopic Investigations of Skin **Barrier Function** Current position: Triskel SA, Geneva, Switzerland 1991-96 Norris Turner, Pharm.D.: Graduate Student: Pharmaceutical Chemistry Current position: Pfizer, Connecticut, USA 1992-93 Frédérique Hueber, Ph.D.: Postdoctoral Research Chemist: Iontophoresis of Oligonucleotides Current position: L'Oréal Research, Paris, France Amalia Rodriguez-Bayon, Ph.D.: Postdoctoral Research Chemist: Iontophoretic Delivery of LHRH Analogs and Antagonists. Current position: Associate Professor, Complutense University, Madrid, Spain Karine Buffard, B.S.: Postgraduate Research Student: Measurement of Skin Permeability In Vivo 1992-94 Elena Aspe-Carranza, M.S.: Postgraduate Research Student: Transdermal Delivery of an **Antiviral Drug** 1992-97 Lourdes Nonato, M.S.: Graduate Student: Bioengineering

1994	Patrizia Santi, Ph.D.: Visiting Assistant Professor of Pharmacy: Mechanisms of Iontophoretic Transport Current position: Professor, University of Parma, Italy	
1994-96	Jouni Hirvonen, Ph.D.: Postdoctoral Research Chemist: Noninvasive Biological Monitoring via the Skin Current position: Professor and Dean, University of Helsinki, Finland	
1994-96	Yogeshvar Kalia, Ph.D.: Postdoctoral Research Chemist: Theoretical and Experimental Modeling of Iontophoretic Drug Delivery Current position: Associate Professor, University of Geneva, Switzerland Fabrice Pirot, Pharm.D.: Postgraduate Research Pharmacist: Assessment of Dermal Exposure in vivo Current position: Associate Professsor, Université Claude-Bernard Lyon 1	
1995-96	Audra Stinchcomb, Ph.D.: Postgraduate Research Chemist: Chemical Absorption Across Human Skin <i>in vivo</i> - Effect of Vehicle Current position: Professor, University of Kentucky, USA	
1995-	Gilles Touraille, Pharm.D.: Postgraduate Research Pharmacist: Assessment of Dermal Exposure <i>in vivo</i> - Vehicle Effects Current position: EMEA, London, U.K.	
1996	Monica Rodríguez-Fernandez: Postgraduate Research Student: Isoelectric Point of the Skin	
University of Geneva - Centre Interuniversitaire de Recherche et d'Enseignement, Archamps		
1996	Virginia Merino-Sanjuan, Ph.D.: Visiting Professor: Reverse Iontophoresis Current position: Associate Professor, University of Valencia, Spain	
1996, 1999	Alicia Lopéz, Ph.D. Visiting Postdoctoral Fellow: Reverse Iontophoresis; pl of Skin Current position: Associate Professor, University Cardenal Herrera, Valencia, Spain	
1996-2000	Ingo Alberti, Dip. Pharm.: Doctorant: Evaluation and Optimisation of Topical Drug Bioavailability Current position: Swiss Medical Authority, Basel, Switzerland	
1996-2001	Yogeshvar Kalia, Ph.D.: Maître Assistant: Theoretical and Experimental Modeling of Iontophoretic Drug Delivery Current position: Associate Professor, University of Geneva, Switzerland	
1996-2003	M. Begoña Delgado-Charro, Ph.D.: Maître Assistante: Iontophoresis, Sonophoresis and Novel Topical Formulations Current position: Senior Lecturer in Pharmaceutical Sciences, University of Bath, UK	
1996-2004	Aarti Naik, Ph.D. Visiting Postdoctoral Fellow, Maître Assistante: Mechanism and Enhancement of Transdermal Drug Delivery Current position: Triskel, SA, Geneva, Switzerland	

1997 Asteria Luzardo-Alvarez, Dip. Pharm.: Visiting Graduate Student: Iontophoresis and Isoelectric Point of Skin Current position: University of Santiago de Compostela, Spain Antonella Casiraghi, Pharm.D.: Visiting Graduate Student: Infrared spectroscopy and Skin Current position: University of Milan, Italy 1997-2000 Diego Marro, Dip. Pharm.: Doctorant: Electrorepulsion and Electroosmosis in the **Iontophoretic Delivery of Peptides** Current position: Visiting Professor, University Cardenal Herrera, Valencia, Spain Katrin Moser, Dip. Pharm.: Doctorante: Supersaturation and Topical Drug Delivery Current position: MIT, Boston, USA 1997-2001 Catherine Curdy, Dipl. Pharm.: Doctorante: Skin Barrier Function Current position: Novatris Consumer Health, Nyon, Switzerland Gilles Touraille, Pharm. D.: Doctorant: Skin Penetration of Toxic Compounds Following Exposure to Contaminated Soil Current position: EMEA, London 1998-2000 Renata F.V. Lopez, Dipl. Pharm.: Visiting Graduate Student: Iontophoresis and Photodynamic Current position: Professor, University of São Paulo, Ribeirão Preto, Brazil 1998-2001 Nabila Sekkat, Dipl. Pharm.: Doctorante: A Model for Neonatal Skin Barrier Function Current position: Ferring, Lausanne, Switzerland 1998-2002 Gustavo Merino, Dipl. Pharm.: Doctorant: Ultrasound-Enhanced Transport Across the Skin Current position: Carrefour pharmacie, France 1999 Monica Dias, Ph.D.: Visiting Postdoctoral Scientist: Infrared spectroscopy and Skin Current position: EMEA, London, England 2000 Nathalie Dujardin, Pharm.D.: Visiting Graduate Student: Electroporation of the Skin Peretz Glikfeld, Dipl. Chem. Eng.: Visiting Scientist: Drug Delivery to the Nail Current position: Israel Institute for Biological Research, Ness-Ziona, Israel 2000-01 Hirotoshi Adachi, Ph.D.: Visiting Postdoctoral Scientist: Prevention of Intravascular Device-Related Infections - Electrically-Mediated Skin Antisepsis Current position: Hisamitsu Pharmaceutical Co. Ltd, San Diego, CA 2000-04 Rocio Alvarez-Román, Pharm.D.: Doctorante: Particulate Formulations for Topical Drug Delivery to the Skin Current position: Associate Professor, Universidad Autónoma de Nuevo León, Mexico Benoît Leboulanger, M.S.: Doctorant: Noninvasive Therapeutic Drug Monitoring by Reverse Iontophoresis Current position: Novartis, Basel, Switzerland Anke Sieg, Pharm.D.: Doctorante: Noninvasive Glucose Monitoring by Reverse Iontophoresis

Current position: Dow-Corning, Brussels, Belgium

2000-05 Yannic Schütz, Dipl. Pharm.: Doctorante: Iontophoretic Delivery of peptides Across the Skin

Current position: DebioPharm, Martigny, Switzerland

Nada Abla, Dipl. Pharm.: Doctorante: Structure-Activity Relationships for peptide

Iontophoresis

Current position: Merck Serono, Geneva, Switzerland

2001-05 Christophe Herkenne, Dipl. Pharm.: Doctorant: Rational Design of Topical Formulations

Current position: DebioPharm, Martigny, Switzerland

Blaise Mudry, Dipl. Pharm.: Doctorant: Structure-Transport Relationships for Iontophoretic

Drug Delivery Across the Skin

Current position: Ferring, Lausanne, Switzerland

Sophie Mehier, M.S.: Doctorante: Sonoporation – Ultrasound-Mediated Gene Delivery

Current position: Managing Director, Cerma, SA, Archamps, France

Isabel Diaz, Pharm.D.: Doctorante: Transmucosal Drug Delivery

Current position: Ipsen SA, Barcelona, Spain

Marie-Laure Leichtnam, M.S.: Doctorante: Development of a Transdermal 'Spray Patch' for

the Systemic Administration of Testosterone

2002-04 Emmanuelle Sublet, M.S.: Staff Research Associate: Topical and Transdermal Drug Delivery

Current position: Staff Research Associate, University of Geneva

Danielle Masuelle, M.S.: Staff Research Associate: Topical and Transdermal Drug Delivery

Current position: Staff Research Associate, University of Geneva

Yves Jacques, Ph.D.: Senior Scientist: Transmucosal Drug Delivery

Current position: Independent consultant

2002 Valentine Wascotte, B.S.: Visiting Erasmus Student: Novel Formulations for Application in

Reverse Iontophoresis

Current position: GSK, Belgium

Nuria Uson, M.S.: Visiting Graduate Student: Microemulsions as Topical Vehicles

Current position: CSIC, Barcelona, Spain

2003-04 M. Begoña Delgado-Charro, Ph.D.: Collaboratrice Scientifique: Reverse Iontophoresis and

Prediction of Skin Permeability

Current position: Senior Lecturer in Pharmaceutical Sciences, University of Bath, UK

Susan Nixon, Pharm.D.: Doctorante: Noninvasive Monitoring of Lactate by Reverse

Iontophoresis

Current position: Novartis Consumer Health, Nyon, Switzerland

2004 Rocio Alvarez-Román, Ph.D.: Postdoctoral Scientist: Particulate Formulations for Topical

Drug Delivery to the Skin

Current position: Associate Professor, Universidad Autónoma de Nuevo León, Mexico

University of Bath, Department of Pharmacy & Pharmacology

2004-06	Sandra Weidersberg, Pharm.D.: Ph.D. student: Dermatopharmacokinetics of Topical Steroids Current position: Lohmann LTS, Neuwid, Germany
	Sara Nicoli, Ph.D.: Visiting Scientist: Evaluation of Topical Drug Bioavailability in the Skin Current position: Associate Professor, University of Parma, Italy
2004-07	Jean-Philippe Sylvestre, M.S.: Ph.D. student: Applications of Iontophoresis in Sports Medicine Current position: Postdoctoral scientist, University of Montreal, Canada
2005-08	Xiao Wu, M.Pharm.: Ph.D. student: Interactions of Nanoparticles with Skin Current position: Postdoctoral scientist, University of Kentucky, U.S.A.
2005-09	Lisa Russell, M.Pharm.: Ph.D. student: Dermatopharmacokinetics Current position: Pharmacist, Bristol PCT
	Asma Djabri, M.Pharm.: Ph.D. student: Applications of Iontophoresis in Pediatrics Current position: Pharmacist
2006-07	Camille Bouissou, Ph.D.: Postdoctoral Scientist: Reverse Iontophoresis as a Tool to Characterize "Skin Health".
2006-08	Sevgi Gungor, Ph.D.: Visiting Scientist: Transdermal Delivery of Anti-Cancer Drugs Current position: Associate Professor, Istanbul University, Turkey
2006-10	Manda Tsang, B.Sc.: Ph.D. student: Bioavailability of Topically Applied Drugs for Eczema
2006-16	Sarah Cordery, B.Sc.: Research Associate: Skin Research; Ph.D. student: Transdermal Treatment of Drug Abuse
2008-11	Quan Yang, M.Pharm.: Ph.D. student: Application of Biophysics and Bioengineering to the Assessment of Skin Barrier Function
2008-13	Premrutai Thitilertdecha, B.Sc.: Ph.D. student: Topical delivery of active agents in traditional medicines
2009-10	Christopher Campbell, Ph.D.: Postdoctoral Scientist: Disposition of nanoparticles on the skin Ian Benzeval, Ph.D.: Postdoctoral Scientist: Drug delivery to the nail
	Natalie Belsey, Ph.D.: Postdoctoral Scientist: Skin uptake and penetration of pesticides
2010-12	Natalie Belsey, Ph.D.: Postdoctoral Scientist: Imaging drug disposition and pharmacokinetics in skin by stimulated Raman scattering microscopy.
2009-	Luis Rodrigo Contreras-Rojas, M.Pharm.: Ph.D. student: Disposition of nanoparticles on the skin

2010-14	Kit Frederiksen, M.Sc.: Ph.D. student: Controlled drug delivery to the skin.
2011-14	Hazel Garvie-Cook, M.Phys.: Ph.D. student: Atomic Force Microscopy Investigations of the Nanomechanical Properties of Skin and Nail
	Wing Sin Chiu, M.Pharm.: Ph.D. student: Drug Delivery to the Skin and Nail
2011-15	Bertrand Dupont, M.Eng.: Ph.D. student: Novel Applications of Graphene-Based Biosensors to the Skin
	Duygu Celebi, M.Chem.: Ph.D. student: Novel, sustainable gel materials for topical drug delivery
2013-14	Leila Leal, Ph.D.: Visiting Professor: In vivo-in vitro correlations for topical bioavailability
2013-	James Clarke, B.Sc.: Ph.D. student: Quantification of dermal absorption from pesticide residues from treated plant surfaces
	Simon Vanstone, M.Phys.: Ph.D. student: Atomic Force Microscopy Investigations of the Nanomechanical Properties of Skin and Nail
2014-15	Hazel Garvie-Cook, Ph.D.: Postdoctoral Scientist: Imaging drug disposition and pharmacokinetics in skin.
	Wing Sin Chiu, Ph.D.: Postdoctoral Scientist: <i>In vivo-in vitro</i> correlations for topical bioavailability
	Mohammed Zaher Shehab, Ph.D.: Postdoctoral Scientist: <i>In vivo-in vitro</i> correlations for topical bioavailability
2014-	M. Alice Naciel Tabosa, Pharm.D.: Ph.D. student: Development and validation of a pharmacokinetic model for dermal absorption
2015-	Magdalena Hoppel, Pharm.D., Ph.D.: Postdoctoral Scientist: Development and validation of a pharmacokinetic model for dermal absorption
	Andrea Pensado-Lopez, Pharm.D., Ph.D.: Postdoctoral Scientist: <i>In vivo-in vitro</i> correlations for topical bioavailability
	Luca Lupani, Pharm.D.: Ph.D. student: Novel Applications of Graphene-Based Biosensors to the Skin
	Floriant Doungmene, Ph.D.: Postdoctoral Scientists: Novel Applications of Graphene-Based Biosensors to the Skin

Doctoral Dissertation Committees

1982-84	Ming-Zong Lai, Pharmaceutical Chemistry, University of California - San Francisco
1986-88	Kathleen V. Roskos, Pharmaceutical Chemistry, University of California - San Francisco
1986-89	Victoria M. Knepp, Pharmaceutical Chemistry, University of California - San Francisco Daniel A.W. Bucks, Pharmaceutical Chemistry, University of California - San Francisco
1988-90	Aeri Kim, Pharmaceutical Chemistry, University of California - San Francisco Seaung Oh, Pharmaceutical Chemistry, University of California - San Francisco D. Bommannan, Bioengineering, University of California - San Francisco - , University of California - Berkeley
1989-92	José M. Cornejo-Bravo, Pharmaceutical Sciences, University of California - San Francisco
1991-94	Marcello Gutierrez, Pharmaceutical Chemistry, University of California - San Francisco Murali Ramanathan, Bioengineering, University of California - San Francisco, University of California - Berkeley
1992	Tamie Minami, Pharmaceutical Sciences, University of Sydney, Australia
1993	Nagahiro Yoshida, Pharmaceutical Sciences, University of Queensland, Australia
1993-95	Sarah Noonberg, Bioengineering, University of California - San Francisco, University of California - Berkeley
1994	Uwe Rohr, Habilitationsschrift, Pharmaceutical Technology, Rheinische Friedrich-Wilhelms- Universität, Bonn, Germany
	Lucas Ferreira, Groupe de Formation Doctorale Biologie et Pharmacologie Cutanées, Université de Paris-Sud, Châtenay-Malabry, France
1995	Malua de Carvalho Bouton, Diplôme de Doctorat, L'Université Claude Bernard-Lyon 1, Lyon, France
	Fernando Guerra Domínguez, Facultad de Farmacía, Universidad de La Laguna, Tenerife, Spain
1996	Vikram K. Ramanathan, Pharmaceutical Chemistry, University of California - San Francisco Norris G. Turner, Pharmaceutical Chemistry, University of California - San Francisco Bernard Neau, Groupe de Formation Doctorale Biologie et Pharmacologie Cutanées, Université de Paris-Sud, Châtenay-Malabry, France Abdou E. Said, Faculté de Médicine et de Pharmacie de Besançon, Université de Franche-Comté
	Fabrice Pirot, Faculté de Médicine et de Pharmacie de Besançon, Université de Franche- Comté
	Christain Surber, Ph.D., Faculty of Medicine, University of Basel, Switzerland (Habilitation)

1997 Gabriela Marginean-Lazar, Groupe de Formation Doctorale Biologie et Pharmacologie Cutanées, Université de Paris-Sud, Châtenay-Malabry, France Anne Jadoul, Université catholique de Louvain, Ecole de Pharmacie, Unité de Pharmacie Galénique, Industrielle et Officinale Claudia Witschi, Université de Genève, Faculté des Sciences, Section de Pharmacie Sophie Chesnoy, Groupe de Formation Doctorale Pharmacotechnie et Biopharmacie, Université de Paris-Sud, Châtenay-Malabry, France Adriana Ganem-Quintanar, Université de Genève, Faculté des Sciences, Section de Pharmacie Jacques Bailly, Groupe de Formation Doctorale Biologie et Pharmacologie Cutanées, Université de Paris-Sud, Châtenay-Malabry, France 1998 Peter Boderke, Swiss Federal Institute of Technology, Zürich (ETH-Z) Ronald van der Geest, Leiden University, The Netherlands 1999 Laure Brinon, Groupe de Formation Doctorale Pharmacotechnie et Biopharmacie, Université de Paris-Sud, Châtenay-Malabry, France 2000 Gwénaëlle Potard, Groupe de Formation Doctorale Pharmacologie Expérimentale et Clinique, Université de Paris-Sud, Châtenay-Malabry, France Nicole Wyttenbach, Swiss Federal Institute of Technology, Zürich (ETH-Z) Ingo Alberti, Université de Genève, Faculté des Sciences, Section de Pharmacie Katrin Moser, Université de Genève, Faculté des Sciences, Section de Pharmacie Diego Marro, Université de Genève, Faculté des Sciences, Section de Pharmacie Claudia Valenta, Ph.D., University of Vienna, Austria (Habilitation) Alain Boucaud, Université de Tours, France 2001 Pascale Clement, Groupe de Formation Doctorale Pharmacologie Expérimentale et Clinique, Université de Paris-Sud, Châtenay-Malabry, France Véronique Gobry, Swiss Federal Institute of Technology, Lausanne (EPFL) Catherine Curdy, Université de Genève, Faculté des Sciences, Section de Pharmacie Nabila Sekkat, Université de Genève, Faculté des Sciences, Section de Pharmacie Gilles Touraille, Groupe de Formation Doctorale Pharmacologie Expérimentale et Clinique, Université de Paris-Sud, Châtenay-Malabry, France 2002 Nathalie Dujardin, Faculty of Medicine, Université catholique de Louvain, Belgium Christain Tran, Faculty of Pharmacy, Université Claude-Bernard – Lyon 1, France Ignacio de Miguel Clave, Université Paul Sabatier de Toulouse, France Gustavo Merino, Université de Genève, Faculté des Sciences, Section de Pharmacie Sandrine Geinoz, Université de Lausanne, Faculté des Sciences 2003 Rocio Alvarez-Román, Université de Genève, Faculté des Sciences, Section de Pharmacie Anne-Rose Denet, Faculty of Medicine, Université catholique de Louvain, Belgium 2004 Benoît Leboulanger, Université de Genève, Faculté des Sciences, Section de Pharmacie

	Nuria Usón Sanchiz, Universitat de Barcelona, Spain
	Anke Sieg, Université de Genève, Faculté des Sciences, Section de Pharmacie
	Fabienne Jeanneret, Université de Genève, Faculté des Sciences, Section de Pharmacie
	Brigette Traversa, Victoria College of Pharmacy, Monash University, Australia
2005	Laïla Boulmedarat, Ecole doctorale 'Innovation thérapeutique: du fondamental a l'appliqué' Université de Paris-Sud, Châtenay-Malabry, France
	Yannic Schuetz, Université de Genève, Faculté des Sciences, Section de Pharmacie
	Sophie Mehier-Humbert, Université de Genève, Faculté des Sciences, Section de Pharmacie Nada Abla, Université de Genève, Faculté des Sciences, Section de Pharmacie
	Marie-Laure Leichtnam, Université de Genève, Faculté des Sciences, Section de Pharmacie Isabel Diaz de Consuelo, Université de Genève, Faculté des Sciences, Section de Pharmacie
	Blaise Mudry, Université de Genève, Faculté des Sciences, Section de Pharmacie
	Christophe Herkenne, Université de Genève, Faculté des Sciences, Section de Pharmacie
	Yingxin Cui, London South Bank University
	Rebecca Watkinson, University of Greenwich
	Rebecca watkinson, oniversity of dicentificing
2006	Paul Prentice, University of Dundee
	Delphine Soury, Ecole doctorale 'Innovation thérapeutique: du fondamental a l'appliqué', Université de Paris-Sud, Châtenay-Malabry, France
	Giorgio Ottoviani, Faculté des sciences, Université de Genève, Switzerland
2007	Valentine Wascotte, Université catholique de Louvain, Brussels, Belgium
	Andrés Femenía Font, Universidad CEU Cardenal Herrera, Valencia, Spain
2008	Corinne Eenschooten, Danish Technical University, Lyngby, Denmark
	Virginie Vallet, Faculty of Pharmacy, Université Claude-Bernard – Lyon 1, France
2009	Yanjun Zhao, King's College, London
2010	Kent Wooi Ng, Cardiff University, Cardiff
	Oliver Ackaert, Leiden University, Leiden, The Netherlands
	Carine Jacques, Université Paul Sabatier – Toulouse III, Toulouse, France
2011	Harshal Kubavat, University of Bath
	Marina Krämer, University of Bath
	Marta Jorge Cabral Machado, University of London
2014	Xueqin Chen, Ecole Centrale, Marseille, France
	Vikas Hegde, University of Dundee
2015	
2015	Martin Rowland, University of Bath
	Clemence Chenevas-Paule, University of Sunderland

Masters Examinations or Theses Committees

1984	Chairman, Masters Degree Committee, Charles Ryll, Pharmaceutical Chemistry
1993	Masters Degree Committee, Karine Buffard, Pharmacy, Université de Paris-sud
1997	Docteur en Pharmacie Degree Committee, Gilles Touraille, Pharmacy, Université de Paris-sud

UNIVERSITY AND PUBLIC SERVICE

University Service

1998-2004	Faculty search committees, University of Geneva
2001-2003	Director, Ecole romande de pharmacie, Universities of Geneva and Lausanne
2004-2006	Executive Committee, Department of Pharmacy & Pharmacology, University of Bath Research Committee, Department of Pharmacy & Pharmacology, University of Bath
2004-	Professorial promotion/appointment committees, University of Bath
2006-2008	Executive Committee, Faculty of Sciences, University of Bath Head of Department of Pharmacy & Pharmacology, University of Bath
2005-2009	External examiner, The Welsh School of Pharmacy, Cardiff University
2006-2008	Board of Studies, Faculty of Sciences, University of Bath Biosciences Services Management Committee, University of Bath Chair, Strategy Committee, Department of Pharmacy & Pharmacology, University of Bath Chair, Operating Committee, Department of Pharmacy & Pharmacology, University of Bath Chair, Safety Committee, Department of Pharmacy & Pharmacology, University of Bath Chair, ETG Committee, Department of Pharmacy & Pharmacology, University of Bath Chair, Board of Studies, M.Pharm. degree, Department of Pharmacy & Pharmacology, University of Bath Chair, Board of Studies, M.Pharmacol. and B.Pharmacol. degrees, Department of Pharmacy & Pharmacology, University of Bath
2008-11	University of Bath Research Committee
2008-10	University Research Students Committee, University of Bath Chair, University of Bath Research Information Group University Research Advisor, University of Bath
2009-10	Chair, Research Information Advisory Group, University of Bath
2009-	University of Bath Senate
2010-12	Chair, Research Staff Working Group, University of Bath Impact Sub-Group, REF 2014, Unversity of Bath
2010-13	Chair, Research Committee, Department of Pharmacy & Pharmacology, University of Bath Research Committee, Faculty of Science, University of Bath Unit of Assessment Leader, REF 2014, University of Bath
2011-12	Academic Staff Development Steering Committee, University of Bath
2013-	Disciplinary Committee of Senate, University of Bath
2014	Academic Staff Appeal Committee, University of Bath

2015	Member, External Assessment Panel, B.Sc. programme in Cosmetic Science, University of Sunderland
2015-16	Member, "Partridge Group", responsible for new M.Pharm. curriculum development and GPhC reaccreditation, Department of Pharmacy & Pharmacology, University of Bath.
2016-	Metrics in Research Assessment and Management Working Group, University of Bath

Service to Educational, Governmental, and Other Agencies		
1998-	Referee, Engineering and Physical Sciences Research Council, U.K.	
2002	External Referee, Upjohn Research Award, University of Michigan, Ann Arbor, Michigan	
	External Reviewer, Foundation for Research & Development, South Africa	
	Reviewer, American Diabetes Association	
2004-	External Reviewer, Biotechnology and Biological Sciences Research Council, U.K.	
	Referee, Medical Research Council, U.K.	
	Referee, Science Foundation Ireland	
	External Reviewer, U.S. National Institutes of Health	
	Expert Reviewer, Cosmetics, Toiletries and Fragrance Association, New York, USA	
2005-6	Member, Expert Group on the application of the Threshold of Toxicological Concern (TTC) to the safety evaluation of cosmetic ingredients and end products, COLIPA (The European Cosmetic, Toiletry and Perfumery Association), Brussels, Belgium	
	Member, Scientific Committee on Consumer Products, Working Group on 'Nanotechnology', European Commission, Health & Consumer Protection Directorate-General, Brussels, Belgium.	
2006	External Reviewer, Foundation for Research & Development, South Africa	
	Referee, Israel Science Foundation	
2007	Contributor to European Commission, Health & Consumer Protection Directorate-General, Scientific Committee on Consumer Products "Opinion on Safety of Nanomaterials in Cosmetic Products", adopted December 18, 2007. http://ec.europa.eu/health/ph-risk/committees/04-sccp/docs/sccp_o_123.pdf	
2009	Expert, European Medicines Evaluation Agency, London, U.K.	
	Panel member, Research Councils for Health and Natural Sciences and Engineering of the Academy of Finland	
	Expert, Federal Trade Commission, Washington, DC, USA	
	Reviewer, Diabetes U.K.	

2010	Expert witness on behalf of the Minister for Health & Ageing, Australia (Therapeutic Goods Administration), Administrative Appeals Tribunal, Sydney
	External Reviewer, National Research Foundation, South Africa
	External Assessor for the internal review of the University of Nottingham's School of Pharmacy
2010-	Member, Expert Advisory Panel for Pharmaceutical Science, Royal Pharmaceutical Society of Great Britain
2011	Member, The Danish Council for Independent Research, Danish Agency for Science, Technology & Innovation, Medical Bio-Pharma grants review panel
	External Reviewer, British Skin Foundation
	External Reviewer, SPARKS
	External Reviewer, Wellcome Trust
2012	External Panel Member, Appointment committee for the Norbrook Chair in Pharmaceutical Sciences, University of Ulster
	External Assessor, Chair in Pharmaceutical Sciences, Welsh School of Pharmacy, Cardiff University
	External Member, Professors interview panel, University of the Arts London
	External Reviewer, ETH Zurich Research Commission
2013-14	Assessor for the REF Sub-panel 3: Allied Health Professions, Dentistry, Nursing and Pharmacy.
2013	External Reviewer, National Institute of Health Research
2014	External Reviewer, Czech Research Foundation
	External Reviewer (Stage 1 panel), Science Foundation Ireland
	Panel Member, International Life Sciences Research Announcement (ILSRA) Physiology, Monitoring and Pharmacology, NASA (Washington, D.C., USA)
2015	External Reviewer, Hadwen Trust
	External Reviewer, Queen's University, Belfast, MRC Confidence-in-Concepts grant applications
	External Reviewer, National Research, Development and Innovation Office, Hungary
2015-16	Panel Member, NC3Rs CRACK-IT Challenge Review Panel – Metaboderm, Wellcome Trust, U.K.

PROFESSIONAL ACTIVITIES

Service to Scholarly and Professional Societies (since 1994)

1994	Co-Director (with Professeur Jean-Paul Marty), "Administration Transdermique de Médicaments," a 3-day course covering all aspects of the transdermal administration of drugs. Marne la Vallée, France
	Co-Chairman (with Professeur Jean-Paul Marty), 21st International Symposium on Controlled Release of Bioactive Materials, Controlled Release Society. Nice, France
1994-95	Member, Organizing Committee, "Prediction of Percutaneous Penetration: Methods, Measurements, Modeling." International Conference. Montpellier, France
1994-97	Member, Electorate Nominating Committee, AAAS Section on Pharmaceutical Sciences. American Academy for the Advancement of Science. Washington, DC
1998-2001	Vice-President, President-Elect and President, Controlled Release Society, Deerfield, Illinois
2002-2006	Member, Høst-Madsen Award Committee, Fédération internationale de pharmacie (F.I.P.), The Hague, Netherlands
2003	Discussion Leader, Gordon Research Conference on 'Barrier function of mammalian skin', Roger Williams University, Rhode Island, USA
2003-	Member, Executive Committee, Skin Forum
2005	Discussion Leader, Gordon Research Conference on 'Barrier function of mammalian skin', Mount Holyoke College, Massachusetts, USA
2008	Co-Chair, Lohmann LTS Academy Symposium on "Unmet Needs in Transdermal Drug Delivery", Königswinter, Germany
2009	Debate Leader, Gordon Research Conference on 'Barrier function of mammalian skin', Waterville Valley, New Hampshire, USA
2011	Discussion Leader, Gordon Research Conference on 'Barrier function of mammalian skin', Waterville Valley, New Hampshire, USA
	Conference Scientific Chair, Academy of Pharmaceutical Sciences, Great Britain, PharmSci 2011, Nottingham, UK
2011-	Member of, now Advisor to, the Board of the Academy of Pharmaceutical Sciences, Great Britain
	Member, Expert Working Group on the 'evaluation of oral-to-dermal extrapolation', European Commission Project 'Integrated In Silico Models for the Prediction of Human repeated Dose Toxicity of COSMetics to Optimise Safety' (COSMOS).
2014	Co-author, "New Medicines, Better Medicines, Better Use of Medicines", a guide to the science underpinning pharmaceutical practice, Royal Pharmaceutical Society, London, May 2014.

Service to Scholarly and Professional Journals		
1981 –	Referee, International Journal of Pharmaceutics Referee, Journal of Physical Chemistry Referee, Canadian Journal of Chemical Engineering	
1982 –	Referee, Journal of Pharmaceutical Sciences	
1983 –	Referee, Journal of Investigative Dermatology Referee, Pharmaceutical Research	
1984 –	Referee, Journal of Controlled Release Referee, Journal of Pharmacokinetics and Biopharmaceutics Referee, Chemical Reviews	
1985 –	Referee, Archives of Dermatology Referee, Microvascular Research Referee, Life Sciences	
1986 –	Referee, Science	
1986 –	Referee, Journal of the American Chemical Society Referee, Mathematical Biosciences	
1987 –	Referee, S. African Journal of Science Referee, Drug Design and Delivery Referee, Skin Pharmacology	
1987-2008	Member, Editorial Advisory Board, Skin Pharmacology	
1988 –	Referee, Plastic and Reconstructive Surgery Referee, Toxicology and Applied Pharmacology Referee, Industrial and Chemical Engineering Research	
1990 –	Referee, Diabetes Care Referee, Chest	
1992-2003	Member, Editorial Advisory Board, Advanced Drug Delivery Reviews Referee, American Institute of Chemical Engineers Journal Referee, Toxicology and Applied Pharmacology	
1993–4	Member, Editorial Advisory Board, Pharmaceutical Research	
1993 –	Referee, European Journal of Pharmaceutical Sciences Referee, Journal of Pharmacology and Experimental Therapeutics Referee, European Journal of Pharmaceutics and Biopharmaceutics Referee, Journal of Drug Targeting Referee, Bioorganic & Medicinal Chemistry	

1994 –	Referee, Journal of Exposure Analysis and Environmental Epidemiology
1995 –	Referee, S.T.P. Pharma Sciences (Editions de Santé)
1996 –	Member, Editorial Advisory Board, European Journal of Pharmaceutics and Biopharmaceutics
1997-2000	Member, Editorial Advisory Board, Journal of Controlled Release
1997-2003	Member, Editorial Advisory Board, Journal of Pharmacy & Pharmacology
2000-16	Member, Editorial Advisory Board, Diabetes, Technology & Therapeutics Referee, Diabetes, Technology & Therapeutics
2001-02	Member, Editorial Advisory Board, Drug Discovery Today
2002-07	Associate Editor, Journal of Pharmaceutical Sciences Referee, Photochemistry & Photobiology
2003-	Referee, Bioelectrochemistry Referee, Nature Reviews, Drug Discovery
2003-	Member, Editorial Advisory Board, European Journal of Pharmaceutical Sciences
2004-	Referee, Sensors and Actuators, B Referee, Environmental Science & Technology
2005-	Referee, Journal of Drug Delivery Science & Technology Referee, Nature Reviews Immunology Referee, Skin Pharmacology & Physiology
2006-	Referee, Pharm. Biochem. Behaviour Referee, Proceedings of the National Academy of Sciences, USA Referee, Journal of Medicinal Chemistry Referee, Expert Opinion in Drug Delivery Referee, American Journal of Drug Delivery
2008-	Member, Editorial Advisory Board, Skin Pharmacology & Physiology Member, Editorial Advisory Board, Journal of Pharmaceutical Sciences Referee, Journal of Pharmacokinetics and Pharmacodynamics Referee, Biophysical Journal
2009-	Referee, Nature Nanotechnology Referee, Journal of Drug Targeting
2010-	Referee, Toxicology Letters Referee, ACS Nano

2011-Referee, Molecular Pharmaceutics Referee, AAPS J. Referee, Nanomedicine 2012-Referee, International Journal of Cosmetic Science 2014-Referee, Chemical Research in Toxicology Referee, PLoS One 2015-Referee, Nature Protocols Referee, Environmental Science & Technology Referee, Lab on a Chip Referee, Annals of Otology, Rhinology & Laryngology 2016-Referee, Clinical Pharmacokinetics Referee, J. Appl. Toxicol. Referee, J. Exposure Sci. Environ. Epidemiol. Referee, Nature Nanotechnology

Consultant or Service as a Professional Expert (since 1994; active in green)

2017-

1994-5	Co-Founder and Member, Board of Directors, De Novo, Inc., Menlo Park, California Member, Scientific Advisory Board, De Novo, Inc., Menlo Park, California
1994-9	Consultant, Becton Dickinson Transdermal Systems, Franklin Lakes, New Jersey: Iontophoresis and Formulation Member, Scientific Advisory Board, Advanced Polymer Systems, Redwood City, California
1994-2001	Consultant, Unilever Research, Port Sunlight, England: Skin/hair care
1995-6	Consultant, Tilderm Systems, Laboratoires Fournier, Chenôve, France: Iontophoresis Member, Scientific Advisory Board, Advanced Therapies Inc., Novato, California
1996	Consultant, Searle, Skokie, Illinois: Transdermal drug delivery Consultant, Zyma SA, Nyon, Switzerland: Topical and transdermal drug delivery
1996-9	Consultant, Novo Nordisk, Denmark: Iontophoresis and drug delivery Consultant, Novartis, Basel, Switzerland: Optimization of topical drug delivery
1996-8	Member, Scientific Advisory Board, EKOS LLC, Seattle, Washington Consultant, Cellegy, Inc., Foster City, California: Topical drug delivery
1997-8	Consultant, CIRD-Galderma, Sophia Antipolis, France: Topical drug delivery Consultant, Institut de Recherche Pierre Fabre, Castanet Tolosan, France

Member, Editorial Advisory Board, International Journal of Pharmaceutics

1997-8	Member, Scientific Advisory Board, Biovector, Toulouse, France
1998-9	Member, Scientific Advisory Board, Cellegy, Inc., Foster City, California
1999-2000	Consultant, éthymed, Paris, France Consultant, Innothera, Paris, France
1999-2002	Consultant, Pacific Corporation, Seoul, Korea
2001-2013	Consultant, L'Oréal, Paris, France
2001-2003	Member, Scientific Advisory Board, LSC, Inc., Burlingame, California
2001-2004	Consultant, OM Pharma, Geneva, Switzerland
2001-2006	Member, Scientific Advisory Board, Vyteris, Inc., Fair Lawn, New Jersey
2002-2007	Member, Scientific Advisory Board, TransPharma, Inc., Israel
2002-2004	Consultant, GSK Consumer Health, Weybridge, England Consultant, Abbott Laboratories, Abbott Park, Illinois
2003	Consultant, Laboratoires Besins
2003-2004	Consultant, Galderma SA, Sophia Antipolis, France
2004-2005	Consultant, Shire Pharmaceuticals, PLC, Basingstoke, UK
2004-2006	Consultant; Member, Scientific Advisory Board, PowerPaper, Inc., Israel Consultant, Firmenich, SA, Geneva, Switzerland
2005	Consultant, Amgen, Inc., Cambridge, UK
2005-2009	Consultant, York Pharma, Sheffield, UK
2005-2010	Member, Scientific Advisory Board, Acrux, Ltd., Melbourne, Australia
2006	Member, Scientific Advisory Board, Connetics, Inc., Palo Alto, CA, USA
2006-2008	Consultant, Shire Pharmaceuticals, PLC, Basingstoke, UK
2006-2010	Member, Scientific Advisory Board, DBV Technologies, Paris, France
2006-2013	Member, Scientific Advisory Board, EyeGate Pharmaceuticals, Inc., Waltham, MA, USA
2007	Consultant, GSK, Parsippany, NJ, USA Consultant, Unilever, Trumbull, CT, USA
2007-2008	Consultant, Altea Therapeutics, Atlanta, GA, USA

	Consultant, Pharmakodex, Chippenham, U.K.
2008-2011	Member, Scientific Advisory Board, Vyteris, Inc., Fair Lawn, New Jersey, USA Chair, Scientific Advisory Board, Altea Therapeutics, Atlanta, GA, USA
2008	Consultant, Acclarent, Inc., Palo Alto, CA, USA Consultant, Serentis, Ltd., Cambridge, U.K. Consultant, TPG Partners, Fort Worth, TX, USA Consultant, Rader, Fishman & Grauer PLLC, Bloomfield Hills, Michigan, USA
2008-09	Consultant, OBJ, Ltd., Leederville, WA, Australia
2009	Consultant, Bristol Myers Squibb, Moreton, Wirral, U.K.
2009-2010	Consultant, Therapeutic Goods Administration, Canberra, Australia
2009-	Consultant, PMIC, Anthony, France
2010-	Consultant, Grunenthal GmbH, Germany Consultant, Leo Pharma A/S, Denmark
1997	Consultant, Novartis Pharma, Basel, Switzerland Consultant, Isdin S.A., Spain
2011-	Consultant, Nemaura Pharma, Loughborough, U.K.
2012	Consultant, Genentech, South San Francisco, CA, USA Consultant, GSK Consumer Health, Parsippany, NJ, USA Consultant, Sanofi Recherche, Montpellier, France
2012-	Consultant, Delenex AG, Zurich, Switzerland
2013-	Consultant, Dermira, Inc., Redwood City, CA, USA Consultant, Nitto Denko Technical Corporation, Oceanside, CA, USA
2013-14	Chair, Expert Panel Meeting on Topical Ketoprofen, Hisamitsu Pharmaceutical Co., Ltd., Japan
2014-	Consultant, GSK Consumer Health, Singapore Consultant, Medivation, Inc., San Francisco, CA, USA Consultant, Mundipharma Research Ltd., Cambridge, U.K.
2016-	Member, Scientific Advisory Board, Almirall S.A., Barcelona, Spain Member, Scientific Advisory Board, Pierre-Fabre, Toulouse, France

Consultant, L'Oréal, Paris, France

Invited Lectures and Seminars (since 2005)

2005

Mechanisms of Iontophoretic and Sonophoretic Drug Delivery Across the Skin. United Kingdom and Ireland Controlled Release Society, 11th Annual Symposium, Aston University, Birmingham, UK (January 6)

Recent Advances in Transdermal Administration. Plenary Lecture. VII Congreso de la Sociedad Española de Farmacia Industrial y Galénica. Salamanca, Spain (February 8)

Science Meets the Skin: Delivering Drugs Legally. Inaugural lecture. University of Bath, Bath, UK (February 23)

Physical Delivery Methods: Iontophoresis and Beyond. Skin Science and Advances in Aesthetic Therapies Symposium, 39th Annual Conference of the Australian Society of Cosmetic Chemists. Brisbane, Australia (March 16)

Following Substances Into (and Through) the Skin by Tape-Stripping. 39th Annual Conference of the Australian Society of Cosmetic Chemists. Brisbane, Australia (March 17)

Biophysical Techniques in Skin Research: Infrared (IR) Spectroscopy. 39th Annual Conference of the Australian Society of Cosmetic Chemists. Brisbane, Australia (March 20)

Following Substances Into (and Through) the Skin by Tape-Stripping. Acrux, Inc. Melbourne, Australia (March 22)

(Trans)dermal Technologies. Hud och Läkemedel («Skin and Drugs»), University of Göteborg, Gothenburg, Sweden (May 18)

Method Development and Modeling to Characterize Penetration, Absorption, Dose, and Local Effects Resulting from Dermal Exposures. Plenary lecture, Occupational and Environmental Exposures of the Skin to Chemicals, Karolinska Institute, Stockholm, Sweden (June 12)

Closing the Loop: Noninvasive Drug Delivery and Clinical Monitoring via the Skin. Invited Lecture, 32nd Annual Meeting & Exposition of the Controlled Release Society, Miami Beach, Florida, USA (June 20)

Novel Transdermal Technologies to Control, Manipulate and Optimize Drug Input Across the Skin. Sanofi-Aventis, Paris, France (June 28)

Dermatopharmacokinetics: Opportunities and Limitations for Assessment of Topical Bioavailability. Invited speaker, 6th Annual Meeting of Skin Forum, University College, Winchester, UK (June 30)

(Trans)Dermal Technologies for Delivery and Diagnosis. Proctor & Gamble, Egham, UK (July 10)

Dermatopharmacokinetics: Opportunities and Limitations for Assessment of Topical Bioavailability. York Pharma, Sheffield, UK (July 12)

Latest Developments in Iontophoresis. PowerPaper Scientific Advisory Board meeting, Paris, France (September 2)

Dermatopharmacokinetics: A Tool for Determining Bioequivalence between Topical Formulations. Invited speaker, "Biointernational 2005: Towards Resolution of Complex BE Issues", Royal Pharmaceutical Society, London, UK (October 24)

Measurement and Prediction of the Rate and Extent of Drug Delivery into and through the Skin. Invited speaker, 2nd EUFEPS Conference on "Optimizing Drug Delivery and Formulation", Versailles, France (November 23)

Penetration of Molecules and Particles (?) into and through the Skin. Nanotoxicology Symposium: Toxicology and Technology of Nanoparticles. Centre for Xenobiotic and Environmental Risk Research, University of Zurich, Zurich, Switzerland (January 11)

Drug Delivery into and through the Skin: Quantification, Enhancement and Optimization. Connetics Visiting Lecture Series, Palo Alto, CA, USA (April 19)

Novel Transdermal Technologies to Control, Manipulate and Optimize Drug Input across the Skin. L'Oréal Research, Aulnay-sous-Bois, France (May 22)

Novel Transdermal Technologies to Control, Manipulate and Optimize Drug Input across the Skin. Galderma Research & Development, Sophia Antipolis, France (July 10)

Drug Delivery into and through the Skin: Quantification, Enhancement and Optimization. Galderma Research & Development, Sophia Antipolis, France (July 11)

Science Meets the Skin: Delivering Drugs Legally. U3A, Warminster (July 19)

Transdermal Science and Technology in the New Millenium. Invited speaker, Teikoku Seiyaku Reception, 33rd Annual Meeting & Exposition of the Controlled Release Society, Vienna, Austria (July 23)

Closing the Loop: Noninvasive Drug Delivery and Clinical Chemistry via the Skin. Invited speaker, British Pharmaceutical Conference, Manchester, UK (September 6)

Estimating the Percutaneous Absorption of Fragrance Materials. Expert panel meeting of the Research Institute of Fragrance Materials, Berlin, Germany (September 11)

Topical Bioavailability: Stripping and Science. Invited speaker, 2nd APGI Symposium: Skin & Formulation. Versailles, France (October 10)

Chemical Enhancement of Transdermal Drug Delivery. Corium, Inc. Redwood City, CA, USA (October 23)

Novel Transdermal Technologies to Control, Manipulate and Optimize Drug Input across the Skin. Connetics, Inc., Palo Alto, CA, USA (October 24)

Topical Bioavailability: Quantification and Optimization. Invited speaker, 2nd International Meeting of the Society for Skin Pharmacology and Physiology: *Skin Physiology: Irritation and Penetration Pathways*. Rome, Italy (November 6)

Electrotransport Across the Skin: Physical Chemistry, Bioengineering and Clinical Application. Physical & Theoretical Chemistry Laboratory, Department of Chemistry, Oxford University, Oxford (November 13)

2006

2007

Closing the Loop: Noninvasive Drug Delivery and Clinical Monitoring via the Skin. The Strathclyde Institute of Pharmacy & Biomedical Sciences, University of Strathclyde, Galsgow, Scotland (January 30)

Skin Barrier Function: Biophysics, Models and Measurements. Conopco, Inc., (Unilever), Trumbull, CT, USA (March 15)

Iontophoresis: Basic Principles and Potential Applications. Eyegate Pharmaceuticals, Waltham, MA, USA (March 16)

Topical Bioavailability: Stripping and Science. Invited speaker, 8th Skin Forum, London (April 4)

Opportunities and Limitations for Assessment of Topical Bioavailability. Chulalongkorn University, Faculty of Pharmaceutical Sciences, Bangkok, Thailand (May 14)

Electrotransport Across the Skin: Physical Chemistry, Bioengineering and Clinical Application. Chulalongkorn University, Faculty of Pharmaceutical Sciences, Bangkok, Thailand (May 14)

Transdermal Science and Technology in the New Millenium. Altea Therapeutics, Atlanta, GA, USA (June 14)

Drug Delivery: Hits, Hype and Hope for the 21st Century. Dept. of Pharmacy & Pharmacology, Centenary Science Day Celebration, University of Bath (July 5)

Assessment of Topical Drug Delivery and Bioavailability. Invited speaker. Gordon Research Conference on "Barrier Function of Mammalian Skin", Newport, RI, USA (August 6)

New Technologies in the Evolution of Transdermal Drug Delivery. Plenary speaker. 5th International Postgraduate Research Symposium on Pharmaceutics. Istanbul, Turkey (September 14)

New Aspects of Cutaneous Drug Penetration. Invited speaker. World Congress of Dermatology, Buenos Aires, Argentina (October 4)

Predicting the Rate and Extent of Chemical Absorption into and through the Skin. Invited speaker. American College of Toxicology, 28th Annual Meeting, Charlotte, NC, USA (November 13)

Transdermal Drug Delivery: Principles, Practice and Promise. Hisamitsu Pharmaceutical Co., Ltd., 160th Anniversary Symposium. Plenary speaker. Tokyo, Japan (December 1)

Assessment of Topical Drug Delivery and Bioavailability. Hisamitsu Pharmaceutical Co., Ltd., Tosu, Kyushu, Japan (December 3)

2008

Iontophoresis, Electroporation and Other Techniques to Overcome the Skin's Barrier. L'Oréal (Cosmétique Active), Asnières, Paris, France (January 9)

Electrotransport Across the Skin: Physical Chemistry, Bioengineering and Clinical Application. Plenary speaker, "Perspectives in Percutaneous Penetration", 11th International Conference, La Grande Motte, France (March 26)

Dermatopharmacokinetics. Invited speaker, "Perspectives in Percutaneous Penetration", 11th International Conference, La Grande Motte, France (March 27)

Topical Drug Bioavailability: Dermatopharmacokinetics. Invited speaker, "Topical and Transdermal Drugs – Challenges and Opportunities", Swedish Academy of Pharmaceutical Sciences, Stockholm, Sweden (April 23)

Dermatopharmacokinetics: Assessment of Topical Drug Bioavailability. Galderma S.A., Sophia Antipolis, France (June 16)

Topical Drug Bioavailability and Dermatopharmacokinetics. Invited speaker, 4th Skin Focus Meeting, Cardiff (June 18)

Topical Drug Bioavailability and Dermatopharmacokinetics. Invited speaker, L'Oréal Research, Aulnay-sous-Bois, France (October 13)

Iontophoretic Drug Delivery. Invited speaker. Lohmann LTS Academy Symposium on "Unmet Needs in Transdermal Drug Delivery", Königswinter, Germany (October 16)

Disposition of Nanoparticles Contacting the Skin. 1st International Conference on Dermatotoxicology, Vaals, The Netherlands (October 25)

Bioengineering and the Skin: Transdermal technologies for Drug Delivery and Clinical Monitoring. Department of Chemical Engineering, University of Cambridge, Cambridge (November 26)

Bilateral Collaboration on Education and Research. UKIERI Awards Symposium. New Delhi, India (March 23)

2009

Assessment of Topical Bioavailability. Invited speaker. Annual meeting of the British Society for Investigative Dermatology, Royal Agricultural College, Cirencester (March 30)

Transdermal Drug Delivery for Children. Invited speaker. Pharmaceutical Translational Research Conference. Medicines for Children Research Network. The School of Pharmacy, University of London, London (April 2)

Transdermal Drug Delivery. Invited speaker. 5th GPA/UKCPA Joint Annual National Conference. Leicester (May 16)

Transdermal Delivery Techniques. Invited speaker. Joint Conference in Medical Sciences 2009. Mahidol-Chulalongkorn Universities. Bangkok, Thailand (June 23)

Bioavailability of Actives Applied Topically to the Skin. Invited speaker. Joint Conference in Medical Sciences 2009. Mahidol-Chulalongkorn Universities. Bangkok, Thailand (June 23)

Non-Invasive Monitoring Across the Skin. Bath Biosensor Network, 1st Bath Interdisciplinary Meeting on Biosensors. Bath (September 23)

The Stratum Corneum as a Pharmacokinetic Compartment. Invited speaker. "StratumCorneum VI", International Society of Stratum Corneum Research. Boston, MA, USA (October 1)

Disposition of Nanoparticles Contacting the Skin: a Reality Check... Invited speaker.

Dermatopharmaceutics Focus Group Meeting, Annual Meeting of the American Association of Pharmaceutical Scientists. Los Angeles, CA, USA (November 11)

Microdialysis and Stratum Corneum Tape-Stripping for Dermatopharmacokinetics. Invited speaker. Annual Meeting of the American Association of Pharmaceutical Scientists. Los Angeles, CA, USA (November 11)

Fonction Barrière de la Peau. Les Matinees Scientifiques de Cosmétique Active. L'Oréal. Asnières-sur-Seine, France (December 4)

Research Study Options in the U.K. and at the University of Bath. Ph.D. Workshop China 2009. Beijing, China (December 12)

2010 Transdermal Drug Delivery. Department of Bioengineering & Therapeutic Sciences, University of California – San Francisco, San Francisco, CA, USA (January 25)

Optimising Topical Formulations for Drug Delivery into the Skin: Mechanisms and Methodologies. Leo Pharma A/S, Ballerup, Denmark (March 4)

Transdermal Drug Delivery Technologies. School of Pharmacy, Queen's University Belfast. Belfast, N. Ireland (March 10)

Topical Bioavailablity and Formulation Optimisation. Invited speaker. 8th International Conference & Workshop on Biological Barriers. Saarland University, Saarbrücken, Germany (March 29)

Dermatopharmacokinetics: Assessment of Topical Drug Bioavailability. Leiden-Amsterdam Centre for Drug Research. Leiden University, Leiden, The Netherlands (April 28)

Dermatopharmacokinetics: Clinical Perspectives. University of Valencia. Valencia, Spain (June 1)

Predicting the Rate and Extent of Chemical Absorption Into and Through the Skin. Dermal Exposure Working Group, International Life Sciences Institute (ILSI) Research Foundation & U.S. Environmental Protection Agency, Washington, DC, USA (June 21)

Probing Drug Delivery to the Skin Using Stimulated Raman Scattering Microscopy. Invited speaker. 7th Annual Coherent Raman Microscopy Workshop, Harvard University, Cambridge, MA, USA (June 25)

Les Systèmes Iontophorétiques. L'Oréal. Asnières-sur-Seine, France (July 12)

Bioavailability Issues in Dermal Delivery – In Vivo Methods. Invited speaker. Academy of Pharmaceutical Sciences G.B., UK PharmSci 2010, University of Nottingham (September 1)

Optimising Topical Formulations to Deliver Actives into the Skin: Mechanisms and Methodologies. Unilever. Trumbull, CT, USA (December 14)

Skin – "That Unfakeable Young Surface". Invited speaker. Festschrift for Prof. Jonathan Hadgraft. The School of Pharmacy, University of London (December 16)

Optimising Topical Formulations to Deliver Actives into the Skin: Mechanisms and Methodologies. L'Oréal. Aulnay-sous-Bois, France (March 4)

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Measuring Drug Permeation and Penetration into and through Skin Using Coherent Raman Microscopy. Invited speaker. Skin Forum 12th Annual Meeting (with APV). Frankfurt, Germany (March 29)

Imaging Drug Delivery to Skin with Stimulated Raman Scattering Microscopy. Invited speaker. 39th Interpharm Research Conference. Brockenhurst, UK (May 13)

Transdermal Technology for Drug Delivery. Invited speaker. 3rd PharmSciFair. Prague, Czech Republic (June 15)

Measuring Drug Permeation and Penetration into and through Skin Using Coherent Raman Microscopy. Invited speaker. CARS Explorer Symposium: Optical Solutions to Biomedical Problems. Marseille, France (June 20)

Imaging Drug Delivery to Skin with Stimulated Raman Scattering Microscopy. Leo Pharma A/S, Ballerup, Denmark (June 23)

Electrotransport Across the Skin – Delivery and Sampling. Invited speaker. Skin Trailblazer, 2nd Workshop. Boston, MA, USA (August 7)

Is There a Future for (Transdermal) Drug Delivery? Conference Scientific Chair's Address. PharmSci 2011, Academy of Pharmaceutical Sciences, Great Britain. Nottingham (August 31)

Imaging Drug Delivery to Skin Using Coherent Raman Scattering Microscopy. Invited speaker. PharmSci 2011, Academy of Pharmaceutical Sciences, Great Britain. Nottingham (August 31)

Predicting the Rate and Extent of Chemical Absorption through the Skin. International Life Sciences Institute (ILSI), COSMOS expert group 2, Brussels, Belgium (September 13)

Formulation Chemistry and (Trans)Dermal Drug Delivery. [in French] D.Young & Co., London (September 27)

Is There a Future for Transdermal Drug Delivery? Invited speaker. LTS Academy 8th Symposium "New Horizons in Drug Delivery: 35 years on". Bonn, Germany (September 29)

A Tiered Approach to Dermal Exposure Assessment for Anti-Microbial Pesticides. Speaker. Society for Risk Analysis 2011 Annual Meeting, Charleston, SC, USA (December 6)

A Tiered Approach to Dermal Exposure Assessment for Anti-Microbial Pesticides. U.S. Environmental Protection Agency, Crystal City, VA, USA (December 8)

1998 Predicting the Flux of Cosmetic Ingredients across the Skin. International Life Sciences Institute (ILSI), COSMOS expert group 2, Brussels, Belgium (March 19)

Transdermal Drug Delivery from Gels. Invited speaker, "Perspectives in Percutaneous Penetration", 13th International Conference, La Grande Motte, France (April 12)

Skin Biophysics and Transdermal Technologies for Drug Delivery and Clinical Monitoring. Department of Physics, University of Exeter, Exeter (April 23)

Imaging Drug Delivery to Skin Using Coherent Raman Scattering Microscopy. Invited speaker. Workshop on Applications of Coherent Raman Scattering Microscopy. University of Exeter, Exeter (April 23).

Disposition of Nanomaterials Applied to the Skin: Assessment and Imaging. Invited speaker. International Meeting: The Fundamental Pillars of Nanotechnology for the Cosmetic Industry. São Paulo, Brazil (May 18)

Delivering Actives into the Skin: Separating Fact from Fiction. Invited speaker. 5th Society of Cosmetic Scientists Annual Scientific Symposium, "Cosmetic Science: The Good, The Bad and The Beautiful", Trinity College, Dublin, Ireland (May 31)

Administration transdermique des médicaments: la technologie de pointe. [in French] Invited speaker. Académie galénique Michel Lanquetin: Sciences pharmaceutiques. Monte Carlo, Monaco (June 1)

Dermatopharmacokinetics: Assessing Bioavailability of Topically Applied "Actives". L'Oréal Research, Aulnay-sous-Bois, France (June 6)

Delivery of Ketoprofen from a Topical Patch Product: a Benefit/Risk Analysis. Invited speaker. 11th Congress of The European Society of Contact Dermatitis. Malmö, Sweden (June 13)

Improving the Bioavailability of Topically and Transdermally Administered Drugs. Invited speaker. 39th Annual Meeting of the Controlled Release Society. Quebec City, Canada (July 17)

Transdermal Drug Delivery - Past, Present and Future: Basic Science, Regulatory Challenges and New Technologies. GlaxoSmithKline Consumer Health. Parsippany, NJ, USA (July 19)

Technologies for Drug Delivery into and through the Skin. Reckitt Benkiser. Hull (July 27)

Noninvasive Sensing of Glucose and Other Analytes Across the Skin. Invited speaker. International Mini-Symposium on Sensing and Drug Delivery Systems. University of Bath (August 6)

Improving the Bioavailability of Topically and Transdermally Administered Drugs. Centre for Dermatology and Genetic Medicine, University of Dundee (October 9)

Transdermal Drug Delivery and Associated Pathology. Invited speaker. 27th Annual Scientific Meeting of the British Society of Toxicological Pathology. Astra Zeneca, Alderley Edge (November 16)

Predicting Chemical Uptake into Skin. Invited speaker. Society for Chemical Industry, Symposium: "Uptake across the leaf cuticle and skin", London (November 22)

Predicting and Measuring Drug Delivery into and through the Skin. Invited speaker. Sanofi-Aventis, Symposium: "Biopharmaceutical aspects of specific administration routes: Ocular, Otic and Cutaneous", Montpellier, France (November 29)

Imaging Drug Delivery to Skin Using Coherent Raman Scattering Microscopy. L'Oréal Research, Aulnay-sous-Bois, France (December 4)

Transdermal Drug Delivery Technology. "Drug Delivery Strategies for Biologics", Knowledge Transfer Network – Healthtech and Medicines, BioCity – Nottingham, (December 13)

Topical and Transdermal Drug Delivery: Rules, Tools and Nanoparticles. National Institute for Pharmaceutical Education & Research, Mohali (Punjab), India (January 21)

Topical and Transdermal Drug Delivery: Rules, Tools and Nanoparticles. Invited speaker. Controlled Release Society Indian Chapter, 13th International Symposium. Mumbai, India (January 22)

Transdermal Drug Delivery. Department of Bioengineering & Therapeutic Sciences, University of California – San Francisco, San Francisco, CA, USA (January 24)

Topical Drug Delivery: Rules, Tools and Nanoparticles. Stiefel, a GSK company. Research Triangle Park, NC, USA (March 14)

Modélisation de la Barrière et du Passage Transcutané. Invited speaker. 20^{ème} Cours francophone de Biologie de la Peau (CoBiP 2013). Lyon, France (March 22)

Predicting and Measuring Drug Delivery into and through the Skin. University of Maryland, School of Pharmacy, Baltimore, MD, USA (May 20)

Dermatopharmacokinetics and Tape Stripping the Stratum Corneum: Origins and Problems. Invited speaker. Topical Drug Bioavailability/Bioequivalence Summit. University of Maryland, School of Pharmacy, Baltimore, MD, USA (May 21)

Decision Framework for Data Needs to Estimate Dermal Exposure. Invited speaker. Webinar - Thresholds of Toxicological Concern: An Example of Integrated Approaches to Testing and Assessment. U.S. Environmental Protection Agency, Washington, DC, USA (June 11)

Topical and Transdermal Drug Delivery: Rules, Tools and Nanoparticles. Invited speaker. Skin Forum 12th Annual Meeting, UCL School of Pharmacy, London (June 26)

Skin – "The Finest Clothing Ever Made". Founders Award address, 40th Annual Meeting of the Controlled Release Society. Honolulu, HI, USA (July 22)

Probing the Skin-Drug Delivery Platform Interface. Invited speaker. Gordon Conference on "Barrier Function of Mammalian Skin". Waterville Valley, NH, USA (August 21)

Predicting and Measuring Drug Delivery into and through the Skin. Invited speaker. 28^{eme} seminaire de 3^{ème} cycle en sciences pharmaceutiques, "Innovation in Medicinal Chemistry". Zermatt, Switzerland (September 11)

Drug Delivery and Targeting to Appendageal Structures in the Skin. Dermira, Inc. Redwood City, CA, USA (October 11)

Predicting, Measuring and Optimising Drug Delivery to the Skin. Invited speaker. 4th Annual Symposium of the Pan Asian Pacific Skin Barrier Research Society. Seoul, Korea (October 15)

Stratum Corneum et Imagerie. Invited speaker. Société Francophone d'Ingénierie et d'Imagerie Cutanée. Paris, France (October 24)

L'Absorption Cutanée – Théorie et Practique. Invited short-course lecturer. L'Oréal Research. Chevilly-Larue, Paris, France (November 5-6)

Dermatopharmacokinetics (DPK): Potential and Limitations of Stratum Corneum Tape-Stripping. Invited speaker. Topical Bioequivalence Symposium. UCL School of Pharmacy. London (December 19)

Optimisation and Quantification of Topical Drug Delivery to the Skin. National Skin Centre, Singapore (March 3)

Optimisation and Quantification of Topical Drug Delivery to the Skin. British High Commission Sponsored Lecturer, Singapore International Conference on Skin Research, Singapore (March 4)

Bioequivalence of Topical Drug Products: Development of *in vitro-in vivo* Correlations. Stiefel, a GSK company. Research Triangle Park, NC, USA (March 28)

Drug Delivery into and through the Skin. Invited speaker. 9th World Congress on Pharmaceutics, Biopharmaceutics and Pharmaceutical Technology. Lisbon, Portugal (April 3)

Nanoparticles and Skin: Unmoveable Objects and Irresistible Barrier. Invited speaker. 5th FIP Pharmaceutical Sciences World Congress. Melbourne, Australia (April 16)

Imaging Drug Delivery to Skin and Nail with Microspectroscopic Techniques. National Physical Laboratory. Teddington, U.K. (May 28)

Topical Bioavailability/Bioequivalence – Product Development and Regulatory Science. Stiefel, a GSK company. Webinar (June 2)

Transdermal Drug Delivery: Assessment and Evaluation of Feasibility. Tesa-Labtec GmbH, Langenfeld, Germany (July 3)

Technology is not Always Enough – a Lesson from Glucose Monitoring. PROSense (Marie-Curie ITN) Workshop on "Clinical perspectives and commercial forces on biosensor devices". University of Bath (September 18)

Predicting, Measuring and Optimising Drug Delivery to the Skin. Pfizer, Inc., Cambridge, MA, USA (October 30)

Applying Advanced Spectroscopic and Imaging Techniques to Optimize Lipid-Based (Trans)dermal Drug Formulations. Invited speaker. American Association of Pharmaceutical Scientists, 2014 Annual Meeting & Exposition. San Diego, CA, USA (November 5)

Imaging the Disposition of Topical Drug Formulations Applied to the Skin. Invited speaker. Gattefossé Formulation Masterclass 2014. St. Priest, Lyon, France (November 24)

2015 Drug Delivery into and through the Skin. Almirall, S.A. Barcelona, Spain (February 9)

Application of Coherent Raman Scattering Microscopy to Topical Product Design and Development. Almirall, S.A. Barcelona, Spain (February 9)

Non-invasive, Reverse Iontophoretic Glucose Monitoring across the Skin. Physical &

Theoretical Chemistry Laboratory, Oxford University, Oxford (March 2)

Transdermal Drug Delivery: a Mature and Evolving Technology. Invited speaker. 1st European Conference on Pharmaceutics: Drug Delivery. Reims, France (April 13)

Imaging Drug Delivery to Skin and Nail with Microspectroscopic Techniques. Institut Fresnel, UMR 7249, Marseille, France (April 15)

Predicting, Measuring and Optimising the Delivery of Actives into the Skin. Unilever Research, Trumbull, CT, USA (April 27)

Imaging Drug Delivery to Skin and Nail with Micro(spectro)scopic Techniques. Oxford Institute of Biomedical Engineering, Oxford University, Oxford (June 2)

Predicting, Measuring and Optimising Drug Delivery to the Skin. Invited speaker. 6th Dermatological Product Development Workshop. Association for Applied Human Pharmacology. London (June 23)

In vivo Skin Stripping Studies to Evaluate Bioequivalence of Topical Drug Products. Invited speaker. FDA workshop: "Bioequivalence Testing of Topical Drug Products". Silver Spring, MD, USA (July 15)

Imaging Drug Delivery to Skin and Nail with Micro(spectro)scopic Techniques. Keynote speaker. Gordon Conference on "Barrier Function of Mammalian Skin". Waterville Valley, NH, USA (August 16)

Assessment and Optimisation of Drug Delivery to the Skin. Invited speaker. 39th Annual Meeting of the Spanish Society of Pharmacology. Valencia, Spain (September 16)

Imaging Drug Delivery to Skin and Nail with Micro(spectro)scopic Techniques. Hisamitsu Pharmaceutical Co. Ltd. Tsukuba, Japan (September 24)

Transdermal Drug Delivery: Scientific Ingenuity *versus* Skin Barrier Function. Keynote speaker. Transdermal Drug Delivery System World Symposium 2015. Tokyo, Japan (September 26)

Imaging Drug Delivery to Skin and Nail with Micro(spectro)scopic Techniques. University of Bath, Department of Pharmacy & Pharmacology, Bath (March 9)

La pénétration des médicaments à travers l'ongle. Invited speaker. 11^{ème} Colloque Francophone Thématique de Biologie Cutanée. Lyon, France (March 16).

Assessing Topical Bioavailability and Bioequivalence. Universidade Federal de Pernambuco, Department of Pharmaceutical Sciences, Recife, Brazil (March 29)

Transdermal Technologies for Drug Delivery and Clinical Monitoring. Universidade Federal de Pernambuco, Centre for Health Sciences, Recife, Brazil (March 30)

I've Got You Under My Skin. Maurice-Marie Janot Award Lecture, 10th World Meeting on Pharmaceutics, Biopharmaceutics and Pharmaceutical Technology, Glasgow (April 4)

Imaging Drug Delivery to Skin and Nail with Micro(spectro)scopic Techniques. Plenary speaker. International Society for Biophysics & Imaging of the Skin, Lisbon, Portugal (June

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Skin Pharmacokinetics: Modelling, Assessment and Manipulation. L'Oréal Research, Aulnay-sous-Bois, France (June 17).

Transdermal Technologies for Drug Delivery and Clinical Monitoring. University of Bath, Centre for Sustainable Chemical Technologies, Bath (July 12)

Drug Delivery to Targets in the Skin and Nail: Measurement and Optimisation. Plenary speaker. 4th Conference on Innovation in Drug Delivery, Antibes, France (September 26)

Optimisation and Evaluation of Topical Drug Bioavailability in the Skin. Pierre-Fabre, R&D Pharma, Toulouse, France (October 3)

Electronic Acknowledgement Receipt					
EFS ID:	29510807				
Application Number:	13553972				
International Application Number:					
Confirmation Number:	3635				
Title of Invention:	TRANSDERMAL ESTROGEN DEVICE AND DELIVERY				
First Named Inventor/Applicant Name:	Juan Mantelle				
Customer Number:	22428				
Filer:	Courtenay C. Brinckerhoff/Christine Arthur				
Filer Authorized By:	Courtenay C. Brinckerhoff				
Attorney Docket Number:	041457-0992				
Receipt Date:	15-JUN-2017				
Filing Date:	20-JUL-2012				
Time Stamp:	15:39:54				
Application Type:	Utility under 35 USC 111(a)				

Payment information:

Submitted with Payment	no
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File Listing:

Document Number	Document Description File Name		File Size(Bytes)/ Message Digest	Multi Part /.zip	Pages (if appl.)	
			316775			
1		responseids.pdf	b875e9534f867dd8965940d91e2479919aa 03308	yes	9	

	Multipart Description/PDF files in .zip description							
	Document Des	scription	Start	E	nd			
	Supplemental Response or Sup	1	ı	6				
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	Information Disclosure Staten	9		9				
Warnings:								
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	Affidavit-traversing rejectns or objectns		1432767					
2	rule 132	132 decl.pdf	a490c7b359349e78ce5cdcc7bab8af5c2bfa ebc4	no	29			
Warnings:	 							
Information:								
			554175					
3	Affidavit-traversing rejectns or objectns rule 132	cv.pdf	51cd3217c2559d0a15d2e03715bf62a9919 0c7ee	no	78			
Warnings:				•				
Information:								
			1759342					
4	Non Patent Literature	mantelle.pdf	f9fd1666860cbf1d3ed3d9261a1e18ccf23b a4b7	no	3			
Warnings:	-							
Information								
			698742					
5	Non Patent Literature	a3.pdf	653b8bde58a14de9794057a9a1dc6bcd91 794f7a	no	17			
Warnings:	-			l				
Information								
			401705					
6	Non Patent Literature	a2.pdf	67e021de357efcf55eabb2f3935453b9f0f2e 55c	no	7			
Warnings:								
Information:								
		Total Files Size (in bytes)	51	63506				

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.

Approved for use through 1/31/2014. OMB 0651-0032

U.S. Patent and Trademark Office; U.S. DEPARTMENT OF COMMERCE

Under the Paperwork Reduction Act of 1995, no persons are required to respond to a collection of information unless it displays a valid OMB control number.

P	PATENT APPLICATION FEE DETERMINATION RECORD Substitute for Form PTO-875					Application	on or Docket Number 3/553,972	Filing Date 07/20/2012	To be Mailed
							ENTITY: 🛛 L	ARGE 🗌 SMA	LL MICRO
				APPLICA	ATION AS FIL	ED – PAI	RTI		
			(Column 1)	(Column 2)				
Ļ	FOR		NUMBER FIL	.ED	NUMBER EXTRA		RATE (\$)	F	EE (\$)
Ш	BASIC FEE (37 CFR 1.16(a), (b),	or (c))	N/A		N/A		N/A		
	SEARCH FEE (37 CFR 1.16(k), (i), (i)	or (m))	N/A		N/A		N/A		
	EXAMINATION FE (37 CFR 1.16(o), (p),		N/A		N/A		N/A		
	TAL CLAIMS CFR 1.16(i))		min	us 20 = *			X \$ =		
IND	EPENDENT CLAIM CFR 1.16(h))	IS	mi	inus 3 = *			X \$ =		
	APPLICATION SIZE (37 CFR 1.16(s))	FEE of fo fra	f paper, the a or small entity	ation and drawing application size f y) for each additi of. See 35 U.S.C	ee due is \$310 (onal 50 sheets o	\$155 or			
	MULTIPLE DEPEN	IDENT CLAIM	PRESENT (3	7 CFR 1.16(j))					
* If t	the difference in colu	umn 1 is less th	han zero, ente	r "0" in column 2.			TOTAL		
		(Column 1)	APPLICAT	ION AS AMEN		ART II		
AMENDMENT	06/15/2017	CLAIMS REMAINING AFTER AMENDMEN		HIGHEST NUMBER PREVIOUSLY PAID FOR	PRESENT EX	TRA	RATE (\$)	ADDITIO	DNAL FEE (\$)
ME	Total (37 CFR 1.16(i))	* 23	Minus	** 26	= 0		x \$80 =		0
EN	Independent (37 CFR 1.16(h))	* 2	Minus	***5	= 0		x \$420 =		0
AM	Application Si	ize Fee (37 CF	R 1.16(s))						
	FIRST PRESEN	NTATION OF MU	ILTIPLE DEPEN	DENT CLAIM (37 CFF	R 1.16(j))				
							TOTAL ADD'L FE		0
		(Column 1)	(Column 2)	(Column 3)			
		CLAIMS REMAININ AFTER AMENDMEN		HIGHEST NUMBER PREVIOUSLY PAID FOR	PRESENT EX	TRA	RATE (\$)	ADDITIO	DNAL FEE (\$)
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ENDMI	Independent (37 CFR 1.16(h))	*	Minus	***	=		X \$ =		
ΪΝ	Application Size Fee (37 CFR 1.16(s))								
AMI	FIRST PRESEN	NTATION OF MU	ILTIPLE DEPEN	DENT CLAIM (37 CFF	R 1.16(j))			<u></u>	
							TOTAL ADD'L FE		
** If	the entry in column the "Highest Numbe If the "Highest Numb "Highest Number P	er Previously P per Previously I	aid For" IN TH Paid For" IN T	IIS SPACE is less HIS SPACE is less	than 20, enter "20' than 3, enter "3".		LIE KIM WATSON appropriate box in colun		

This collection of information is required by 37 CFR 1.16. 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 1.14. 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.



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

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NOTICE OF ALLOWANCE AND FEE(S) DUE

06/27/2017 Foley & Lardner LLP 3000 K STREET N.W. SUITE 600 WASHINGTON, DC 20007-5109

EXAMINER FISHER, MELISSA L ART UNIT PAPER NUMBER 1611

DATE MAILED: 06/27/2017

APPLICATION NO. FILING DATE		FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
13/553,972	07/20/2012	Juan Mantelle	041457-0992	3635

TITLE OF INVENTION: TRANSDERMAL ESTROGEN DEVICE AND DELIVERY

APPLN. TYPE	ENTITY STATUS	ISSUE FEE DUE	PUBLICATION FEE DUE	PREV. PAID ISSUE FEE	TOTAL FEE(S) DUE	DATE DUE
nonprovisional	UNDISCOUNTED	\$960	\$0	\$0	\$960	09/27/2017

THE APPLICATION IDENTIFIED ABOVE HAS BEEN EXAMINED AND IS ALLOWED FOR ISSUANCE AS A PATENT. PROSECUTION ON THE MERITS IS CLOSED. THIS NOTICE OF ALLOWANCE IS NOT A GRANT OF PATENT RIGHTS. THIS APPLICATION IS SUBJECT TO WITHDRAWAL FROM ISSUE AT THE INITIATIVE OF THE OFFICE OR UPON PETITION BY THE APPLICANT. SEE 37 CFR 1.313 AND MPEP 1308.

THE ISSUE FEE AND PUBLICATION FEE (IF REQUIRED) MUST BE PAID WITHIN THREE MONTHS FROM THE MAILING DATE OF THIS NOTICE OR THIS APPLICATION SHALL BE REGARDED AS ABANDONED. STATUTORY PERIOD CANNOT BE EXTENDED. SEE 35 U.S.C. 151. THE ISSUE FEE DUE INDICATED ABOVE DOES NOT REFLECT A CREDIT FOR ANY PREVIOUSLY PAID ISSUE FEE IN THIS APPLICATION. IF AN ISSUE FEE HAS PREVIOUSLY BEEN PAID IN THIS APPLICATION (AS SHOWN ABOVE), THE RETURN OF PART B OF THIS FORM WILL BE CONSIDERED A REQUEST TO REAPPLY THE PREVIOUSLY PAID ISSUE FEE TOWARD THE ISSUE FEE NOW DUE.

HOW TO REPLY TO THIS NOTICE:

I. Review the ENTITY STATUS shown above. If the ENTITY STATUS is shown as SMALL or MICRO, verify whether entitlement to that entity status still applies.

If the ENTITY STATUS is the same as shown above, pay the TOTAL FEE(S) DUE shown above.

If the ENTITY STATUS is changed from that shown above, on PART B - FEE(S) TRANSMITTAL, complete section number 5 titled "Change in Entity Status (from status indicated above)".

For purposes of this notice, small entity fees are 1/2 the amount of undiscounted fees, and micro entity fees are 1/2 the amount of small entity

II. PART B - FEE(S) TRANSMITTAL, or its equivalent, must be completed and returned to the United States Patent and Trademark Office (USPTO) with your ISSUE FEE and PUBLICATION FEE (if required). If you are charging the fee(s) to your deposit account, section "4b" of Part B - Fee(s) Transmittal should be completed and an extra copy of the form should be submitted. If an equivalent of Part B is filed, a request to reapply a previously paid issue fee must be clearly made, and delays in processing may occur due to the difficulty in recognizing the paper as an equivalent of Part B.

III. All communications regarding this application must give the application number. Please direct all communications prior to issuance to Mail Stop ISSUE FEE unless advised to the contrary.

IMPORTANT REMINDER: Utility patents issuing on applications filed on or after Dec. 12, 1980 may require payment of maintenance fees. It is patentee's responsibility to ensure timely payment of maintenance fees when due.

PART B - FEE(S) TRANSMITTAL

Complete and send this form, together with applicable fee(s), to: Mail Mail Stop ISSUE FEE

Mail Stop ISSUE FEE Commissioner for Patents P.O. Box 1450 Alexandria, Virginia 22313-1450

or <u>Fax</u> (571)-273-2885

INSTRUCTIONS: This form should be used for transmitting the ISSUE FEE and PUBLICATION FEE (if required). Blocks 1 through 5 should be completed where appropriate. All further correspondence including the Patent, advance orders and notification of maintenance fees will be mailed to the current correspondence address as indicated unless corrected below or directed otherwise in Block 1, by (a) specifying a new correspondence address; and/or (b) indicating a separate "FEE ADDRESS" for maintenance fee notifications.

maintenance fee notifica	itions.		() -F)8	r	,		(-)	
CURRENT CORRESPOND	ENCE ADDRESS (Note: Use Bl	lock 1 for any change of address)		Fee(s	:) Transmittal Thi	e certif	icate cannot be used f	or domestic mailings of the for any other accompanying nt or formal drawing, must
²²⁴²⁸ Foley & Lardn 3000 K STREE' SUITE 600		7/2017		I here State addre trans	Cerreby certify that this Postal Service wessed to the Mail mitted to the USP	tificate is Fee(vith suf Stop TO (57	e of Mailing or Trans s) Transmittal is being ficient postage for firs ISSUE FEE address 1) 273-2885, on the da	mission g deposited with the United st class mail in an envelope above, or being facsimile tte indicated below.
	N, DC 20007-5109						(Depositor's name)	
								(Signature)
								(Date)
APPLICATION NO.	FILING DATE		FIRST NAMED INVEN	NTOR		ATTO	RNEY DOCKET NO.	CONFIRMATION NO.
13/553,972	07/20/2012		Juan Mantelle				041457-0992	3635
TITLE OF INVENTION	I: TRANSDERMAL EST	TROGEN DEVICE ANI	DELIVERY					
APPLN. TYPE	ENTITY STATUS	ISSUE FEE DUE	PUBLICATION FEE I	DUE	PREV. PAID ISSUE	E FEE	TOTAL FEE(S) DUE	DATE DUE
nonprovisional	UNDISCOUNTED	\$960	\$0		\$0		\$960	09/27/2017
EXAM	IINER	ART UNIT	CLASS-SUBCLASS	s				
FISHER, N	ÆLISSA L	1611	424-487000					
1. Change of correspond	ence address or indicatio	n of "Fee Address" (37	2. For printing on	the pa	tent front page, lis	st.		
CFR 1.363).			(1) The names of	up to	3 registered paten		neys 1	
Address form PTO/S	oondence address (or Cha B/122) attached.	inge of Correspondence	or agents OR, alter (2) The name of a		•	memb	era 2	
"Fee Address" ind PTO/SB/47; Rev 03-0 Number is required.	lication (or "Fee Address 02 or more recent) attach	" Indication form ed. Use of a Customer	(2) The name of a registered attorney 2 registered patent listed, no name wi	y or ag t attor ill be p	gent) and the name neys or agents. If a printed.	es of u no nan	p to ne is 3	
3. ASSIGNEE NAME A	ND RESIDENCE DATA	A TO BE PRINTED ON	THE PATENT (print of	or type	e)			
PLEASE NOTE: Un recordation as set fort	less an assignee is ident ih in 37 CFR 3.11. Com	ified below, no assignee pletion of this form is NO	e data will appear on to OT a substitute for filing	he pa	tent. If an assigne ssignment.	ee is io	lentified below, the de	ocument has been filed for
(A) NAME OF ASSI			(B) RESIDENCE: (C	_	_			
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4a. The following fee(s) Issue Fee	are submitted:	4	Ib. Payment of Fee(s): (A check is enclose		se first reapply an	y prev	iously paid issue fee	shown above)
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	of Copies		The director is he	reby a	authorized to chare	e the r	required fee(s) any def	ficiency, or credits any n extra copy of this form).
			overpayment, to i	Depos	it Account Number	a	(enclose a	rexua copy or this form).
	tus (from status indicate							
Applicant certifying	ng micro entity status. Se	ee 37 CFR 1.29	NOTE: Absent a value fee payment in the m	id cer nicro e	tification of Micro entity amount will	Entity not be	Status (see forms PTC accepted at the risk of	D/SB/15A and 15B), issue application abandonment.
Applicant assertin	g small entity status. See	37 CFR 1.27	NOTE: If the application was previously under micro entity status, checking this box will be taken to be a notification of loss of entitlement to micro entity status.				ing this box will be taken	
Applicant changir	ng to regular undiscounte	d fee status.	NOTE: Checking thi entity status, as appli	is box icable	will be taken to be	e a noti	ification of loss of enti	tlement to small or micro
NOTE: This form must b	oe signed in accordance v	with 37 CFR 1.31 and 1.3	33. See 37 CFR 1.4 for	signa	ture requirements	and cei	tifications.	
Authorized Signature					Date			
Typed or printed nam	ne				Registration N	Го		
Typed or printed name								

Page 2 of 3



UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE United States Patent and Trademark Office Address: COMMISSIONER FOR PATENTS

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DATE MAILED: 06/27/2017

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
13/553,972	07/20/2012	Juan Mantelle	041457-0992	3635
22428 75	90 06/27/2017		EXAM	INER
Foley & Lardner		FISHER, M	IELISSA L	
3000 K STREET N SUITE 600	N.W.		ART UNIT	PAPER NUMBER
WASHINGTON, I	OC 20007-5109	1611		

Determination of Patent Term Adjustment under 35 U.S.C. 154 (b)

(Applications filed on or after May 29, 2000)

The Office has discontinued providing a Patent Term Adjustment (PTA) calculation with the Notice of Allowance.

Section 1(h)(2) of the AIA Technical Corrections Act amended 35 U.S.C. 154(b)(3)(B)(i) to eliminate the requirement that the Office provide a patent term adjustment determination with the notice of allowance. See Revisions to Patent Term Adjustment, 78 Fed. Reg. 19416, 19417 (Apr. 1, 2013). Therefore, the Office is no longer providing an initial patent term adjustment determination with the notice of allowance. The Office will continue to provide a patent term adjustment determination with the Issue Notification Letter that is mailed to applicant approximately three weeks prior to the issue date of the patent, and will include the patent term adjustment on the patent. Any request for reconsideration of the patent term adjustment determination (or reinstatement of patent term adjustment) should follow the process outlined in 37 CFR 1.705.

Any questions regarding the Patent Term Extension or Adjustment determination should be directed to the Office of Patent Legal Administration at (571)-272-7702. Questions relating to issue and publication fee payments should be directed to the Customer Service Center of the Office of Patent Publication at 1-(888)-786-0101 or (571)-272-4200.

OMB Clearance and PRA Burden Statement for PTOL-85 Part B

The Paperwork Reduction Act (PRA) of 1995 requires Federal agencies to obtain Office of Management and Budget approval before requesting most types of information from the public. When OMB approves an agency request to collect information from the public, OMB (i) provides a valid OMB Control Number and expiration date for the agency to display on the instrument that will be used to collect the information and (ii) requires the agency to inform the public about the OMB Control Number's legal significance in accordance with 5 CFR 1320.5(b).

The information collected by PTOL-85 Part B is required by 37 CFR 1.311. 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 1.14. 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, Virginia 22313-1450. DO NOT SEND FEES OR COMPLETED FORMS TO THIS ADDRESS. SEND TO: Commissioner for Patents, P.O. Box 1450, Alexandria, Virginia 22313-1450. Under the Paperwork Reduction Act of 1995, no persons are required to respond to a collection of information unless it displays a valid OMB control number.

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.

Notice of Allowability Application No. 13/553,972 Examiner Melissa Fisher Art Unit 1611 AlA (First Inventor to File) Status No

The MAILING DATE of this communication appears on the All claims being allowable, PROSECUTION ON THE MERITS IS (OR REM herewith (or previously mailed), a Notice of Allowance (PTOL-85) or other a NOTICE OF ALLOWABILITY IS NOT A GRANT OF PATENT RIGHTS. Tof the Office or upon petition by the applicant. See 37 CFR 1.313 and MPE	AINS) CLOSED in this application. If not included appropriate communication will be mailed in due course. THIS his application is subject to withdrawal from issue at the initiative
1. A declaration(s)/affidavit(s) under 37 CFR 1.130(b) was/were filed	d on
2. An election was made by the applicant in response to a restriction recrequirement and election have been incorporated into this action.	uirement set forth during the interview on; the restriction
3. The allowed claim(s) is/are 14.16.17.21-26.28.29 and 31-42. As a rest the Patent Prosecution Highway program at a participating intellection information, please see http://www.uspto.gov/patents/init_events/pph/	al property office for the corresponding application. For more
4. ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S. Certified copies: a) ☐ All b) ☐ Some *c) ☐ None of the: 1. ☐ Certified copies of the priority documents have been received: 2. ☐ Certified copies of the priority documents have been received: 3. ☐ Copies of the certified copies of the priority documents have been received: International Bureau (PCT Rule 17.2(a)). * Certified copies not received: Applicant has THREE MONTHS FROM THE "MAILING DATE" of this connoted below. Failure to timely comply will result in ABANDONMENT of the THIS THREE-MONTH PERIOD IS NOT EXTENDABLE. 5. ☐ CORRECTED DRAWINGS (as "replacement sheets") must be submused including changes required by the attached Examiner's Amending Paper No./Mail Date Identifying indicia such as the application number (see 37 CFR 1.84(c)) show each sheet. Replacement sheet(s) should be labeled as such in the header 6. ☐ DEPOSIT OF and/or INFORMATION about the deposit of BIOLOGIC attached Examiner's comment regarding REQUIREMENT FOR THE Department of the content of BIOLOGIC attached Examiner's comment regarding REQUIREMENT FOR THE Department of the content of BIOLOGIC attached Examiner's comment regarding REQUIREMENT FOR THE Department of the content of BIOLOGIC attached Examiner's comment regarding REQUIREMENT FOR THE Department of BIOLOGIC attached Examiner's comment regarding REQUIREMENT FOR THE Department of the content of BIOLOGIC attached Examiner's comment regarding REQUIREMENT FOR THE Department of the content of t	eived. eived in Application No eived in Application No eave been received in this national stage application from the nmunication to file a reply complying with the requirements is application. itted. hent / Comment or in the Office action of uld be written on the drawings in the front (not the back) of according to 37 CFR 1.121(d). AL MATERIAL must be submitted. Note the
Attachment(s) 1. Notice of References Cited (PTO-892) 2. Information Disclosure Statements (PTO/SB/08), Paper No./Mail Date 3. Examiner's Comment Regarding Requirement for Deposit of Biological Material 4. Interview Summary (PTO-413), Paper No./Mail Date /Melissa Fisher/ Primary Examiner, Art Unit 1611	5. ☑ Examiner's Amendment/Comment 6. ☑ Examiner's Statement of Reasons for Allowance 7. ☐ Other

U.S. Patent and Trademark Office PTOL-37 (Rev. 08-13) 20170622

Notice of Allowability

Part of Paper No./Mail Date

DETAILED ACTION

The present application is being examined under the pre-AIA first to invent provisions.

Continued Examination Under 37 CFR 1.114

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after allowance or after an Office action under *Ex Parte Quayle*, 25 USPQ 74, 453 O.G. 213 (Comm'r Pat. 1935). Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, prosecution in this application has been reopened pursuant to 37 CFR 1.114. Applicant's submission filed on 6/6/2017 has been entered.

Information Disclosure Statement

The Information Disclosure Statement (IDS) filed 6/15/2017 has been considered by the examiner.

The following is an examiner's statement of reasons for allowance:

The prior art does not teach nor reasonably suggest the claimed monolithic transdermal drug delivery system. Additionally, Applicant's arguments of unexpected results based on the coat weight of the polymer to achieve the claimed flux of drug

Art Unit: 1611

delivery are persuasive. Applicant has additionally filed a Declaration on 6/15/2017 providing further support of the unexpected results previously argued.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Melissa Fisher whose telephone number is (571)270-7430. The examiner can normally be reached on Monday-Friday, 8am-5pm.

Examiner interviews are available via telephone, in-person, and video conferencing using a USPTO supplied web-based collaboration tool. To schedule an interview, applicant is encouraged to use the USPTO Automated Interview Request (AIR) at http://www.uspto.gov/interviewpractice.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Bethany Barham can be reached on 571-272-6175. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Application/Control Number: 13/553,972 Page 4

Art Unit: 1611

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Melissa Fisher/ Primary Examiner, Art Unit 1611

PTO/SB/08 (modified)

	Substitute for for	m 1449/PTQ	C	Complete if Known		
	INFORMATION D	ISCLOSURE	Application Number	13/553972		
	STATEMENT BY	APPLICANT	Filing Date	7/20/2012		
	Data Submittadi	luna 15, 2017	First Named Inventor	Juan Mantelle		
Date Submitted: June 15, 2017			Art Unit	1611		
(use as many sheets as necessary)			Examiner Name	Melissa L. Javier		
Sheet	1	of 1	Attorney Docket Number	041457-0992		

U.S. PATENT DOCUMENTS								
Examiner	Cite	Document Number	Publication Date	Name of Patentee or Applicant of	Pages, Columns, Lines, Where Relevant			
Initials*	No. ¹	Number-Kind Code ² (if known)	MM-DD-YYYY	Cited Document	Passages or Relevant Figures Appear			

UNPUBLISHED U.S. PATENT APPLICATION DOCUMENTS										
Examiner Initials*	Cite No. ¹	U.S. Patent Application Document Serial Number-Kind Code ² (if known)	Filing Date of Cited Document MM-DD-YYYY	Name of Patentee or Applicant of Cited Document	Pages, Columns, Lines, Where Relevant Passages or Relevant Figures Appear					

FOREIGN PATENT DOCUMENTS											
Examiner Initials* Cite No.1 Country Code3-Number4- Kind Code5 (if known)		Publication Date MM-DD-YYYY	Name of Patentee or Applicant of Cited Documents	Pages, Columns, Lines, Where Relevant Passages or Relevant Figures Appear	T ⁶						

		NON PATENT LITERATURE DOCUMENTS				
Examiner Initials*	tem (book magazine jolithai segai symposium catalog eic i gale pageis), volume-is:					
	A1	MANTELLE ET AL., "Effect of Silicone/Acrylic PSA Blends on Skin Permation," Procced. Int'l. Symp. Control. Rel. Bioact. Mater., June 20-23, 1999				
	A2	Notice of Allowance issued on 04/26/2017 in application number 14/024,985 (US 2014/0200530)				
	А3	Office Action issued on 06/15/2017 in application number 14/870,574 (US 2016/0015655)				

		D.L.	
Examiner	/Melissa L Fisher/	Date	06/22/2017
Signature	/Merroe m rrener/	Considered	00/22/2021



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

BIB DATA SHEET

CONFIRMATION NO. 3635

SERIAL NUM	BER	FILING or 371(c)		CLASS	l NO.							
13/553,97	2	07/20/2012		424	1611		_ c)41457-0992				
RULE												
APPLICANTS	S											
INVENTORS Juan Man	ntelle, M	iami, FL;										
		\ ************************************		/2008 PAT 82319	906							
** FOREIGN AF	PPLICA	TIONS **********	*****	•								
** IF REQUIRE 07/31/201		EIGN FILING LICENS	E GRA	NTED **								
Foreign Priority claimed Yes No STATE OR SHEETS TOTAL INDEPENDEN												
35 USC 119(a-d) cond	ditions met MELISSA I	7 110114	ter ince	COUNTRY	DRAWINGS	CLAII		CLAIMS				
Acknowledged	Examiner's	Signature Initials		FL	1	16	5	4				
ADDRESS												
Foley & L 3000 K S												
SUITE 60		IN.VV.										
WASHING UNITED S		DC 20007-5109										
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Issue Classification



Application/Control No.	Applicant(s)/Patent Under Reexamination
13553972	MANTELLE, JUAN

Examiner Art Unit

MELISSA JAVIER 1611

СРС				
Symbol			Туре	Version
A61K	9	7 7069	F	2013-01-01
A61K	9	7 7061	I	2013-01-01
A61K	31	7 565	I	2013-01-01
A61K	47	1 10	I	2013-01-01
A61K	47	32	I	2013-01-01
A61K	9	<i>I</i> 0014	I	2013-01-01

CPC Combination Sets										
Symbol	Туре	Set	Ranking	Version						

		Total Claims Allowed: 23			
(Assistant Examiner)	(Date)				
/MELISSA FISHER/ Primary Examiner.Art Unit 1611	06/22/2017	O.G. Print Claim(s)	O.G. Print Figure		
(Primary Examiner)	(Date)	1	None		

U.S. Patent and Trademark Office Part of Paper No. 20170622

Issue Classification

	Application/Control No.	Applicant(s)/Patent Under Reexamination
'	13553972	MANTELLE, JUAN
	Examiner	Art Unit
	MELISSA JAVIER	1611

US ORIGINAL CLASSIFICATION CLASS SUBCLASS					INTERNATIONAL CLASSIFICATION								N		
								С	LAIMED		NON-CLAIMED			LAIMED	
						Α	6	1	К	31 / 565 (2006.01.01)					
	CROSS REFERENCE(S)					A	6	1	K	9 / 70 (2006.01.01)					
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		Total Claims Allowed:			
(Assistant Examiner)	(Date)	2	3		
/MELISSA FISHER/ Primary Examiner.Art Unit 1611	06/22/2017	O.G. Print Claim(s)	O.G. Print Figure		
(Primary Examiner)	(Date)	1	None		

U.S. Patent and Trademark Office Part of Paper No. 20170622

Issue Classification



Application/Control No.	Applicant(s)/Patent Under Reexamination
13553972	MANTELLE, JUAN
Examiner	Art Unit
MELISSA IAVIED	1611

☐ Claims renumbered in the same order as presented by applicant ☐ CPA ☒ T.D.				☐ R.1.47											
Final	Original	Final	Original	Final	Original	Final	Original	Final	Original	Final	Original	Final	Original	Final	Original
	1	17	17	12	33										
	2		18	13	34										
	3		19	14	35										
	4		20	18	36										
	5	2	21	19	37										
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	8	5	24	22	40										
	9	6	25	15	41										
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	15	10	31												
16	16	11	32												

		Total Claims Allowed: 23	
(Assistant Examiner)	(Date)		
/MELISSA FISHER/ Primary Examiner.Art Unit 1611	06/22/2017	O.G. Print Claim(s)	O.G. Print Figure
(Primary Examiner)	(Date)	1	None

U.S. Patent and Trademark Office Part of Paper No. 20170622

Search Notes



Application/Control No.	Applicant(s)/Patent Under Reexamination
13553972	MANTELLE, JUAN
Examiner	Art Unit
MELISSA JAVIER	1611

CPC- SEARCHED		
Symbol	Date	Examiner

CPC COMBINATION SETS - SEARCHED					
Symbol	Date	Examiner			

US CLASSIFICATION SEARCHED					
Class	Subclass	Date	Examiner		

SEARCH NOTES					
Search Notes	Date	Examiner			
EAST search (see attached history)	8/25/2013	MJ			
Inventor search in EAST	8/25/2013	MJ			
Google Scholar search (keywords used: transdermal monolithic estradiol)	8/25/2013	MJ			
Updated EAST search	2/21/2014	MJ			
Updated Google Scholar search	2/21/2014	MJ			
Updated EAST search	4/29/2015	MJ			
Updated Google Scholar search	4/29/2015	MJ			
Updated EAST search	9/28/2015	MJ			
Updated Google Scholar search	9/28/2015	MJ			
Updated EAST search	4/22/2016	MJ			
Updated Google Scholar search	4/22/2016	MJ			
Updated EAST search	8/22/2016	MJ			
Updated Google Scholar search	8/22/2016	MJ			
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Updated EAST search	12/2/2016	MJ			
Updated Google Scholar search	12/2/2016	MJ			
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Updated EAST search	3/18/2017	MJ			
Updated Google Scholar search	3/18/2017	MJ			

/M.F./ Primary Examiner.Art Unit 1611

SEARCH NOTES		
Search Notes	Date	Examiner
Updated EAST search	6/22/2017	MF
Updated Google Scholar search	6/22/2017	MF

INTERFERENCE SEARCH					
US Class/ CPC Symbol	US Subclass / CPC Group	Date	Examiner		
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	(monolith\$2 estradiol transdermal system adhesive coat weight flux).clm.	8/22/2016	MJ		
	(monolith\$2 estradiol transdermal system adhesive coat weight flux).clm.	12/2/2016	MJ		
	(monolith\$2 estradiol transdermal system adhesive coat weight flux).clm.	3/18/2017	MJ		
	(monolith\$2 estradiol transdermal system adhesive coat weight flux).clm.	6/22/2017	MF		

	/M.F./ Primary Examiner.Art Unit 1611
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U.S. Patent and Trademark Office Part of Paper No.: 20170622

EAST Search History

EAST Search History (Prior Art)

Ref #	Hits	Search Query	DBs	Default Operator	Plurals	Time Stamp
L1	16100	estradiol and transdermal	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	OFF	2017/06/22 18:14
L2	5556	L1 and ("surface area" flux)	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	OFF	2017/06/22 18:14
L3	937	L2 and acrylic and silicone and (PVP polyvinyl pyrrolidone)	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	OFF	2017/06/22 18:14
L4	51	L3 and (estradiol NEAR flux)	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	OFF	2017/06/22 18:14
L5	261	MANTELLE.in. and JUAN.in.	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	OFF	2017/06/22 18:15
L6	42	L5 and estradiol	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	OFF	2017/06/22 18:15
L7	154	L5 and transdermal	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	OFF	2017/06/22 18:15
L8	188	Kanios.in. and David.in.	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	OFF	2017/06/22 18:15
L9	727	L1 and ("dipropylene glycol" oleyl)	USPAT; USOCR	OR	OFF	2017/06/22 18:15
L10	16100	estradiol and transdermal	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	OFF	2017/06/22 18:15
L11	5556	L10 and ("surface area" flux)	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	OFF	2017/06/22 18:15
L12	937	L11 and acrylic and silicone and (PVP polyvinyl pyrrolidone)	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	OFF	2017/06/22 18:16
L13	51	L12 and (estradiol NEAR flux)	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	OFF	2017/06/22 18:16

6/22/2017 6:17:06 PM

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PART B - FEE(S) TRANSMITTAL

Complete and send this form, together with applicable fee(s), to: Mail Mail Stop ISSUE FEE

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22428 7590 06/27/2017 Foley & Lardner LLP 3000 K STREET N.W. SUITE 600	I S a t	Cen hereby certify that the tates Postal Service we ddressed to the Mai ransmitted to the USP	rtificate of Mailing or Transuls Fee(s) Transmittal is bein with sufficient postage for fir I Stop ISSUE FEE address TO (571) 273-2885, on the d	smission g deposited with the United st class mail in an envelope above, or being facsimile ate indicated below.	
WASHINGTON, DC 20007-5109				(Depositor's name)	
, , , , , , , , , , , , , , , , , , , ,				(Signature)	
				(Date)	
APPLICATION NO. FILING DATE	FIRST NAMED INVENT	OR	ATTORNEY DOCKET NO.	CONFIRMATION NO.	
13/553,972 07/20/2012	Juan Mantelle		041457-0992	3635	
TITLE OF INVENTION: TRANSDERMAL ESTROGEN DEVICE	AND DELIVERY				
APPLN. TYPE ENTITY STATUS ISSUE FEE DU	E PUBLICATION FEE DU	E PREV. PAID ISSU	E FEE TOTAL FEE(S) DUE	DATE DUE	
nonprovisional UNDISCOUNTED \$960	\$0	\$0	\$960	09/27/2017	
EXAMINER ART UNIT	CLASS-SUBCLASS				
FISHER, MELISSA L 1611	424-487000				
 Change of correspondence address or indication of "Fee Address" CFR 1.363). 		e patent front page, li	. FOIEV	& Lardner LLP	
☐ Change of correspondence address (or Change of Corresponde Address form PTO/SB/122) attached.	ence (1) The names of up or agents OR, altern	o to 3 registered pater atively,	nt attorneys 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1	C Laranor LL	
The Address indication (or "Fee Address" Indication form PTO/SB/47; Rev 03-02 or more recent) attached. Use of a Custon Number is required.	registered attorney of 2 registered patent a	(2) The name of a single firm (having as a member a registered attorney or agent) and the names of up to 2 registered patent attorneys or agents. If no name is listed, no name will be printed.			
3. ASSIGNEE NAME AND RESIDENCE DATA TO BE PRINTED					
PLEASE NOTE: Unless an assignce is identified below, no ass recordation as set forth in 37 CFR 3.11. Completion of this form	= = = = = = = = = = = = = = = = = = =		ee is identified below, the c	ocument has been filed for	
(A) NAME OF ASSIGNEE	(B) RESIDENCE: (CI				
Noven Pharmaceuticals, Inc.	Miami, FLC	RIDA	•		
Please check the appropriate assignee category or categories (will no	t be printed on the patent):	☐ Individual 🛛 Co	orporation or other private gr	oup entity Government	
4a. The following fee(s) are submitted:			ny previously paid issue fee		
Issue Fee	A check is enclose		ay providenty parameter	5115 WH 225 (C)	
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5. Change in Entity Status (from status indicated above)					
☐ Applicant certifying micro entity status. See 37 CFR 1.29	NOTE: Absent a valid	certification of Micro	Entity Status (see forms PT not be accepted at the risk of	O/SB/15A and 15B), issue	
☐ Applicant asserting small entity status. See 37 CFR 1.27	• •	on was previously un	der micro entity status, check	**	
☐ Applicant changing to regular undiscounted fee status.		oox will be taken to b	e a notification of loss of ent	itlement to small or micro	
NOTE: This form must be signed in accordance with 37 CFR 1.31 ar			and certifications.		

Page 2 of 3

Authorized Signature Couly & Brichall H

Typed or printed name Courtenay C. Brinckerhoff

Date Jone 27, 2017

Registration No.

37,288

Electronic Patent Application Fee Transmittal								
Application Number:	13	553972						
Filing Date:	20-Jul-2012							
Title of Invention:	TRANSDERMAL ESTROGEN DEVICE AND DELIVERY							
First Named Inventor/Applicant Name:	Juan Mantelle							
Filer:	Courtenay C. Brinckerhoff							
Attorney Docket Number:	04	1457-0992						
Filed as Large Entity								
Filing Fees for Utility under 35 USC 111(a)								
Description		Fee Code	Quantity	Amount	Sub-Total in USD(\$)			
Basic Filing:								
Pages:								
Claims:								
Miscellaneous-Filing:								
Petition:								
Patent-Appeals-and-Interference:								
Post-Allowance-and-Post-Issuance:								
UTILITY APPL ISSUE FEE		1501	1	960	960			

Description	Fee Code	Quantity	Amount	Sub-Total in USD(\$)
Extension-of-Time:				
Miscellaneous:				
	Tot	al in USD	(\$)	960

Electronic Acknowledgement Receipt				
EFS ID:	29621910			
Application Number:	13553972			
International Application Number:				
Confirmation Number:	3635			
Title of Invention:	TRANSDERMAL ESTROGEN DEVICE AND DELIVERY			
First Named Inventor/Applicant Name:	Juan Mantelle			
Customer Number:	22428			
Filer:	Courtenay C. Brinckerhoff/Katie Newcomb			
Filer Authorized By:	Courtenay C. Brinckerhoff			
Attorney Docket Number:	041457-0992			
Receipt Date:	27-JUN-2017			
Filing Date:	20-JUL-2012			
Time Stamp:	16:03:26			
Application Type:	Utility under 35 USC 111(a)			

Payment information:

Submitted with Payment	yes
Payment Type	CARD
Payment was successfully received in RAM	\$960
RAM confirmation Number	062817INTEFSW16055600
Deposit Account	190741
Authorized User	Katie Newcomb

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37 CFR 1.16 (National application filing, search, and examination fees)

37 CFR 1.17 (Patent application and reexamination processing fees)

File Listing	g:				
Document Number	Document Description	File Name	File Size(Bytes)/ Message Digest	Multi Part /.zip	Pages (if appl.)
1	lssue Fee Payment (PTO-85B)	0992_IF.pdf	72204 3f9c076ec59853bd4ea896d5e354a47e41f2 bc2d	no	1
Warnings:					
Information:					
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New Applications Under 35 U.S.C. 111

37 CFR 1.21 (Miscellaneous fees and charges)

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

Fee Worksheet (SB06)

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.

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no

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Approved for use through 03/31/2007. OMB 0651-0031

U.S. Patent and Trademark Office: U.S. DEPARTMENT OF COMMERCE

Under the Paperwork Reduction Act of 1995, no persons are required to respond to a collection of information unless it contains a valid OMB control number.

	Substitute for form 1449/PTO			C	omplete if Known
	INFORMATION	DISC	LOSURE	Application Number	13/553,972
STATEMENT BY APPLICANT				Filing Date	07/20/2012
Date Submitted: February 28, 2013			ny 29. 2012	First Named Inventor	Juan Mantelle
			y 20, 2013	Art Unit	1615
	(use as many sheets as necessary)			Examiner Name	Unassigned
Sheet	1	of	4	Attorney Docket Number	041457-0992

				U.S. PATENT DO	CUMENTS	
е	xamin r nitials*	Cite No.1	Document Number Number-Kind Code ² (if known)	Publication Date MM-DD-YYYY	Name of Patentee or Applicant of Cited Document	Pages, Columns, Lines, Where Relevant Passages or Relevant Figures Appear
Accordance.	***************************************	A1	8,231,906	07/31/2012	MANTELLE	1 iguies rippea.
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<u> </u>	~	A38	5,762,952	06/09/1998	BARNHART ET AL.	
		A39	4,591,622	05/27/1986	BLIZZARD ET AL.	

Examiner	Date	
Signature	Considered	
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*EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609. Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant. 1 Applicant's unique citation designation number (optional). 2 See Kinds Codes of USPTO Patent Documents at www.uspto.gov or MPEP 901.04. 3 Enter Office that issued the document, by the two-letter code (WIPO Standard ST.3). 4 For Japanese patent documents, the indication of the year of the reign of the Emperor must precede the serial number of the patent document. 5 Kind of document by the appropriate symbols as indicated on the document under WIPO Standard ST.16 if possible. 6 Applicant is to place a check mark here if English language Translation is attached.

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APPLICATION NO.	ISSUE DATE	PATENT NO.	ATTORNEY DOCKET NO.	CONFIRMATION NO.
13/553,972	08/15/2017	9730900	041457-0992	3635

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Foley & Lardner LLP 3000 K STREET N.W. SUITE 600 WASHINGTON, DC 20007-5109

ISSUE NOTIFICATION

The projected patent number and issue date are specified above.

Determination of Patent Term Adjustment under 35 U.S.C. 154 (b)

(application filed on or after May 29, 2000)

The Patent Term Adjustment is 0 day(s). Any patent to issue from the above-identified application will include an indication of the adjustment on the front page.

If a Continued Prosecution Application (CPA) was filed in the above-identified application, the filing date that determines Patent Term Adjustment is the filing date of the most recent CPA.

Applicant will be able to obtain more detailed information by accessing the Patent Application Information Retrieval (PAIR) WEB site (http://pair.uspto.gov).

Any questions regarding the Patent Term Extension or Adjustment determination should be directed to the Office of Patent Legal Administration at (571)-272-7702. Questions relating to issue and publication fee payments should be directed to the Application Assistance Unit (AAU) of the Office of Data Management (ODM) at (571)-272-4200.

APPLICANT(s) (Please see PAIR WEB site http://pair.uspto.gov for additional applicants):

Juan Mantelle, Miami, FL;

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