L460	42	L459 and estradiol	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	OFF	2017/04/17 13:10
L461	152	L459 and transdermal	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	OFF	2017/04/17 13:10
L462	186	Kanios.in. and David.in.	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	OFF	2017/04/17 13:10
L463	40	L462 NOT L459	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	OFF	2017/04/17 13:10
L464	0	(11/245097).APP.	USPAT; USOCR	OR	OFF	2017/04/17 13:10
L465	715	L452 and ("dipropylene glycol" oleyl)	USPAT; USOCR	OR	OFF	2017/04/17 13:10
L466	132	L454 and ("dipropylene glycol" oleyl)	USPAT; USOCR	OR	OFF	2017/04/17 13:10
L467	15844	estradiol and transdermal	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	OFF	2017/04/17 13:10
L468	5484	L467 and ("surface area" flux)	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	OFF	2017/04/17 13:10
L469	921	L468 and acrylic and silicone and (PVP polyvinyl pyrrolidone)	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	OFF	2017/04/17 13:10
L470	35	L469 and estradiol.ab.	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	OFF	2017/04/17 13:10
L471	263	L469 and transdermal.ab.	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	OFF	2017/04/17 13:10
L472	51	L469 and (estradiol NEAR flux)	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	OFF	2017/04/17 13:10
L473	90	L467 and (estradiol NEAR flux)	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	OFF	2017/04/17 13:10
L474	259	MANTELLE.in. and JUAN.in.	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	OFF	2017/04/17 13:10
L475	42	L474 and estradiol	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	OFF	2017/04/17 13:10
L476	152	L474 and transdermal	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	OFF	2017/04/17 13:10
L477	186	Kanios.in. and David.in.	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	OFF	2017/04/17 13:10
L478	40	L477 NOT L474	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	OFF	2017/04/17 13:10
L479	0	(11/245097).APP.	USPAT; USOCR	OR	OFF	2017/04/17 13:10

L480	715	L467 and ("dipropylene glycol" oleyl)	USPAT; USOCR	OR	OFF	2017/04/17 13:10
L481	132	L469 and ("dipropylene glycol" oleyl)	USPAT; USOCR	OR	OFF	2017/04/17 13:10
L482	2	"6638528".pn.	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	OFF	2017/04/17 13:10
L483	4	"4624665".pn.	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	OFF	2017/04/17 13:10
L484	3	"20090041831".pn.	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	OFF	2017/04/17 13:10
L485	15844	estradiol and transdermal	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	OFF	2017/04/17 13:10
L486	5484	L485 and ("surface area" flux)	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	OFF	2017/04/17 13:10
L487	921	L486 and acrylic and silicone and (PVP polyvinyl pyrrolidone)	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	OFF	2017/04/17 13:10
L488	35	L487 and estradiol.ab.	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	OFF	2017/04/17 13:10
L489	263	L487 and transdermal.ab.	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	OFF	2017/04/17 13:10
L490	51	L487 and (estradiol NEAR flux)	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	OFF	2017/04/17 13:10
L491	90	L485 and (estradiol NEAR flux)	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	OFF	2017/04/17 13:10
L492	259	MANTELLE.in. and JUAN.in.	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	OFF	2017/04/17 13:10
L493	42	L492 and estradiol	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	OFF	2017/04/17 13:10
L494	152	L492 and transdermal	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	OFF	2017/04/17 13:10
L495	186	Kanios.in. and David.in.	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	OFF	2017/04/17 13:10
L496	40	L495 NOT L492	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	OFF	2017/04/17 13:10
L497	0	(11/245097).APP.	USPAT; USOCR	OR	OFF	2017/04/17 13:10
L498	715	L485 and ("dipropylene glycol" oleyl)	USPAT; USOCR	OR	OFF	2017/04/17 13:10
L499	132	L487 and ("dipropylene glycol" oleyl)	USPAT; USOCR	OR	OFF	2017/04/17 13:10
L500	15844	estradiol and transdermal	US-PGPUB; USPAT;	OR	OFF	2017/04/17

			USOCR; FPRS; EPO; JPO; DERWENT			13:10
L501	5484	L500 and ("surface area" flux)	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	OFF	2017/04/17 13:10
L502	921	L501 and acrylic and silicone and (PVP polyvinyl pyrrolidone)	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	OFF	2017/04/17 13:10
L503	35	L502 and estradiol.ab.	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	OFF	2017/04/17 13:10
L504	263	L502 and transdermal.ab.	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	OFF	2017/04/17 13:10
L505	51	L502 and (estradiol NEAR flux)	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	OFF	2017/04/17 13:10
L506	90	L500 and (estradiol NEAR flux)	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	OFF	2017/04/17 13:10
L507	259	MANTELLE.in. and JUAN.in.	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	OFF	2017/04/17 13:10
L508	42	L507 and estradiol	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	OFF	2017/04/17 13:10
L509	152	L507 and transdermal	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	OFF	2017/04/17 13:10
L510	186	Kanios.in. and David.in.	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	OFF	2017/04/17 13:10
L511	40	L510 NOT L507	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	OFF	2017/04/17 13:10
L512	0	(11/245097).APP.	USPAT; USOCR	OR	OFF	2017/04/17 13:10
L513	715	L500 and ("dipropylene glycol" oleyl)	USPAT; USOCR	OR	OFF	2017/04/17 13:10
L514	132	L502 and ("dipropylene glycol" oleyl)	USPAT; USOCR	OR	OFF	2017/04/17 13:10
L515	1255486	(monolith$2 estradiol transdermal adhesive coat weight flux).clm.	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	OFF	2017/04/17 13:10
L516	3958	A61K9/7069.cpc.	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	OFF	2017/04/17 13:10
L517	16828	A61K31/565.cpc.	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	OFF	2017/04/17 13:10
L518	422	L516 and L517	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	OFF	2017/04/17 13:10
L519	47	L518 and flux	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	OFF	2017/04/17 13:10

4/ 17/ 2017 1:22:43 PM
C:\ Users\ mjavier\ Documents\ EAST\ Workspaces\ 14024985.wsp

Issue Classification	Application/Control No.	Applicant(s)/Patent Under Reexamination
	14024985	MANTELLE, JUAN
	Examiner	**Art Unit**
	MELISSA JAVIER	1611

CPC						
Symbol					**Type**	**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					**Type**	**Set**	**Ranking**	**Version**
			/					
			/					

(Assistant Examiner)	(Date)	**Total Claims Allowed:** 14	
/MELISSA FISHER/ Primary Examiner.Art Unit 1611	04/17/2017	O.G. Print Claim(s)	O.G. Print Figure
(Primary Examiner)	(Date)	1	None

Issue Classification	Application/Control No.	Applicant(s)/Patent Under Reexamination
	14024985	MANTELLE, JUAN
	Examiner	**Art Unit**
	MELISSA JAVIER	1611

US ORIGINAL CLASSIFICATION		INTERNATIONAL CLASSIFICATION										
CLASS	SUBCLASS	CLAIMED					NON-CLAIMED					
		A	6	1	K	31 / 565 (2006.01.01)						
CROSS REFERENCE(S)		A	6	1	K	9 / 70 (2006.01.01)						
CLASS	SUBCLASS (ONE SUBCLASS PER BLOCK)											

		Total Claims Allowed:	
(Assistant Examiner)	(Date)	14	
/MELISSA FISHER/ Primary Examiner.Art Unit 1611	04/17/2017	O.G. Print Claim(s)	O.G. Print Figure
(Primary Examiner)	(Date)	1	None

Issue Classification	Application/Control No.	Applicant(s)/Patent Under Reexamination
	14024985	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	Original
1	1		17												
2	2		18												
3	3		19												
4	4		20												
5	5	10	21												
6	6	11	22												
7	7	12	23												
8	8	13	24												
9	9	14	25												
	10														
	11														
	12														
	13														
	14														
	15														
	16														

(Assistant Examiner)	(Date)	**Total Claims Allowed:** 14	
/MELISSA FISHER/ Primary Examiner.Art Unit 1611	04/17/2017	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.:	14/024,985
Appl. Filing Date:	9/12/2013
Examiner:	Melissa L. Fisher
Art Unit:	1611
Confirmation Number:	7031

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		Previously Paid For		Extra Claims Present		Rate		Fee Totals
RCE Fee 1.17(e):							$1,700.00	=	$1,700.00
							0		
Total Claims:	15	-	20	=	0	x	$80.00	=	$0.00
Independents	1	-	3	=	0	x	$420.00	=	$0.00
First presentation of any Multiple Dependent Claims:						+	$780.00	=	$0.00
CLAIMS FEE 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

Appl. No.: 14/024,985

Filing Date: September 12, 2013

Examiner: Javier

Art Unit: 1611

Confirmation Number: 7031

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 reflected in the listing of claims which begins on page 2.

Remarks/Arguments begin on page 5 of this document.

Please amend the application as follows:

Amendments to the Claims:

This listing of claims will replace all prior versions, and listings, of claims in the application:

Listing of Claims:

1. (Previously Presented) 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/cm^2 and includes greater than 0.156 mg/cm^2 estradiol, and the system achieves an estradiol flux of from about 0.0125 to about 0.05 $mg/cm^2/day$, based on the active surface area.

2. (Previously Presented) The transdermal drug delivery system of claim 1, wherein the adhesive polymer matrix comprises a polymer blend comprising an acrylic adhesive, a silicone adhesive, and soluble PVP.

3. (Previously Presented) The transdermal drug delivery system of claim 1, 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.

4. (Original) The transdermal drug delivery system of claim 3, wherein the penetration enhancer comprises oleyl alchol.

5. (Original) The transdermal drug delivery system of claim 3, wherein the penetration enhancer comprises dipropylene glycol.

6. (Original) The transdermal drug delivery system of claim 3, wherein the penetration enhancer comprises oleyl alcohol and dipropylene glycol.

7. (Original) The transdermal drug delivery system of claim 3, 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.

8. (Previously Presented) The transdermal drug delivery system of claim 1, 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.

9. (Previously Presented) The transdermal drug delivery system of claim 1, 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.

Claims 10-20 (Canceled)

21. (Previously Presented) The transdermal drug delivery system of claim 1, wherein the system achieves an estradiol flux of about 0.0125 mg/cm^2/day, based on the active surface area.

22. (Previously Presented) The transdermal drug delivery system of claim 1, wherein the system achieves an estradiol flux of about 0.0133 mg/cm^2/day, based on the active surface area.

23. (Previously Presented) The transdermal drug delivery system of claim 1, wherein the system achieves an estradiol flux of about 0.015 mg/cm^2/day, based on the active surface area.

24. (Previously Presented) The transdermal drug delivery system of claim 1, wherein the system achieves an estradiol flux of about 0.0167 mg/cm^2/day, based on the active surface area.

25. (Previously Presented) The transdermal drug delivery system of claim 1, wherein the system achieves an estradiol flux of about 0.0175 mg/cm^2/day, based on the active surface area.

26. (New) The transdermal drug delivery system of claim 1, 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 1-9 and 21-25 was mailed April 26, 2017.

Claim 26 is 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 1-9 and 21-26 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:	14024985
Filing Date:	12-Sep-2013
Title of Invention:	TRANSDERMAL ESTROGEN DEVICE AND DELIVERY
First Named Inventor/Applicant Name:	Juan Mantelle
Filer:	Courtenay C. Brinckerhoff
Attorney Docket Number:	041457-1016

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($)
Miscellaneous:				
RCE- 2ND AND SUBSEQUENT REQUEST	1820	1	1700	1700
		Total in USD ($)		**1700**

Electronic Acknowledgement Receipt

EFS ID:	29406834
Application Number:	14024985
International Application Number:	
Confirmation Number:	7031
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:	041457-1016
Receipt Date:	06-JUN-2017
Filing Date:	12-SEP-2013
Time Stamp:	12:46:24
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	060617INTEFSW12465100
Deposit Account	
Authorized User	
The Director of the USPTO is hereby authorized to charge indicated fees and credit any overpayment as follows:	

File Listing:

Document Number	Document Description	File Name	File Size(Bytes)/ Message Digest	Multi Part /.zip	Pages (if appl.)
1	Request for Continued Examination (RCE)	RCE.pdf	102172 3da374833353b7928de9621aa0b2e774dc62738b	no	3
Warnings:					
This is not a USPTO supplied RCE SB30 form.					
Information:					
2	Amendment Submitted/Entered with Filing of CPA/RCE	amendment.pdf	105720 152db8670311ae5e7d06fbd6a1ae19fe5f6f22a6	no	5
Warnings:					
Information:					
3	Fee Worksheet (SB06)	fee-info.pdf	30589 7ab9b89a3f8c5c5fe052bc328c0d2eae1e887611	no	2
Warnings:					
Information:					
		Total Files Size (in bytes):	238481		

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.

PTO/SB/06 (09-11)
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.

PATENT APPLICATION FEE DETERMINATION RECORD Substitute for Form PTO-875	Application or Docket Number 14/024,985	Filing Date 09/12/2013	☒ To be Mailed

ENTITY: ☒ LARGE ☐ SMALL ☐ MICRO

APPLICATION AS FILED – PART I

	(Column 1)	(Column 2)		
FOR	NUMBER FILED	NUMBER EXTRA	RATE ($)	FEE ($)
☐ 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 FEE (37 CFR 1.16(o), (p), or (q))	N/A	N/A	N/A	
TOTAL CLAIMS (37 CFR 1.16(i))	minus 20 =	*	X $ =	
INDEPENDENT CLAIMS (37 CFR 1.16(h))	minus 3 =	*	X $ =	
☐ APPLICATION SIZE FEE (37 CFR 1.16(s))	If the specification and drawings exceed 100 sheets of paper, the application size fee due is $310 ($155 for small entity) for each additional 50 sheets or fraction thereof. See 35 U.S.C. 41(a)(1)(G) and 37 CFR 1.16(s).			
☐ MULTIPLE DEPENDENT CLAIM PRESENT (37 CFR 1.16(j))				
* If the difference in column 1 is less than zero, enter "0" in column 2.			TOTAL	

APPLICATION AS AMENDED – PART II

		(Column 1)		(Column 2)	(Column 3)		
AMENDMENT	06/06/2017	CLAIMS REMAINING AFTER AMENDMENT		HIGHEST NUMBER PREVIOUSLY PAID FOR	PRESENT EXTRA	RATE ($)	ADDITIONAL FEE ($)
	Total (37 CFR 1.16(i))	* 15	Minus	** 20	= 0	X $80 =	0
	Independent (37 CFR 1.16(h))	* 1	Minus	***4	= 0	X $420 =	0
	☐ Application Size Fee (37 CFR 1.16(s))						
	☐ FIRST PRESENTATION OF MULTIPLE DEPENDENT CLAIM (37 CFR 1.16(j))						
						TOTAL ADD'L FEE	0

		(Column 1)		(Column 2)	(Column 3)		
AMENDMENT		CLAIMS REMAINING AFTER AMENDMENT		HIGHEST NUMBER PREVIOUSLY PAID FOR	PRESENT EXTRA	RATE ($)	ADDITIONAL FEE ($)
	Total (37 CFR 1.16(i))	*	Minus	**	=	X $ =	
	Independent (37 CFR 1.16(h))	*	Minus	***	=	X $ =	
	☐ Application Size Fee (37 CFR 1.16(s))						
	☐ FIRST PRESENTATION OF MULTIPLE DEPENDENT CLAIM (37 CFR 1.16(j))						
						TOTAL ADD'L FEE	

* If the entry in column 1 is less than the entry in column 2, write "0" in column 3.
** If the "Highest Number Previously Paid For" IN THIS SPACE is less than 20, enter "20".
*** If the "Highest Number Previously Paid For" IN THIS SPACE is less than 3, enter "3".
The "Highest Number Previously Paid For" (Total or Independent) is the highest number found in the appropriate box in column 1.

LIE
LISA THOMAS

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1611	

NOTIFICATION DATE	DELIVERY MODE
06/14/2017	ELECTRONIC

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	Application No.	Applicant(s)	
	14/024,985	MANTELLE, JUAN	
	Examiner	Art Unit	
	Melissa Fisher	1611	

All participants (applicant, applicant's representative, PTO personnel):

(1) *Melissa Fisher*.

(2) *Courtenay Brinckerhoff*.

(3) *Richard Guy*.

(4) _____.

Date of Interview: *08 June 2017*.

Type: ☐ Telephonic ☐ Video Conference
☒ Personal [copy given to: ☐ applicant ☐ applicant's representative]

Exhibit shown or demonstration conducted: ☐ Yes ☐ No.
If Yes, brief description: _____.

Issues Discussed ☐101 ☐112 ☐102 ☐103 ☒Others
(For each of the checked box(es) above, please describe below the issue and detailed description of the discussion)

Claim(s) discussed: _____.

Identification of prior art discussed: *None*.

Substance of Interview
(For each issue discussed, provide a detailed description and indicate if agreement was reached. Some topics may include: identification or clarification of a reference or a portion thereof, claim interpretation, proposed amendments, arguments of any applied references etc...)

Discussed the attached agenda.

Specifically, Applicant's representative and Dr. Guy explained how the included data supported the unexpected results that increasing the coat weight of the drug-containing adhesive layer resulted in an increased flux per unit area, and permitted the development of smaller transdermal drug delivery systems that achieve comparable daily dosages. .

Applicant recordation instructions: The formal written reply to the last Office action must include the substance of the interview. (See MPEP section 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 thirty 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 interview

Examiner recordation instructions: Examiners must summarize 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 general thrust of each argument or issue discussed, a general indication of any other pertinent matters discussed regarding patentability and the general 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	

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
7) 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/cm^2 and includes greater than 0.156 mg/cm^2 estradiol, and that the transdermal drug delivery system achieves an estradiol flux of from about 0.0125 to about 0.05 $g/cm^2/day$, 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/cm^2 estradiol, and that the transdermal drug delivery achieves an estradiol flux of from about 0.0125 to about 0.05 $g/cm^2/day$, based on the active surface area.

[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)

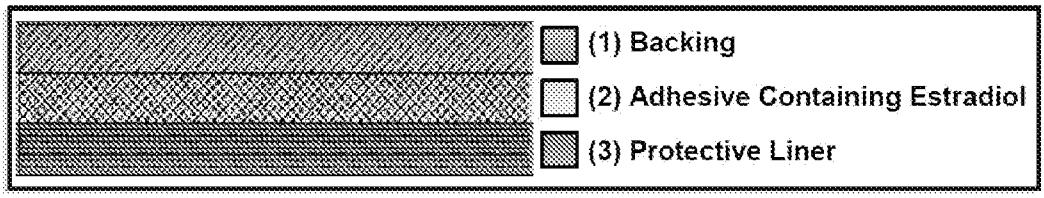
Introduction of Expert

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

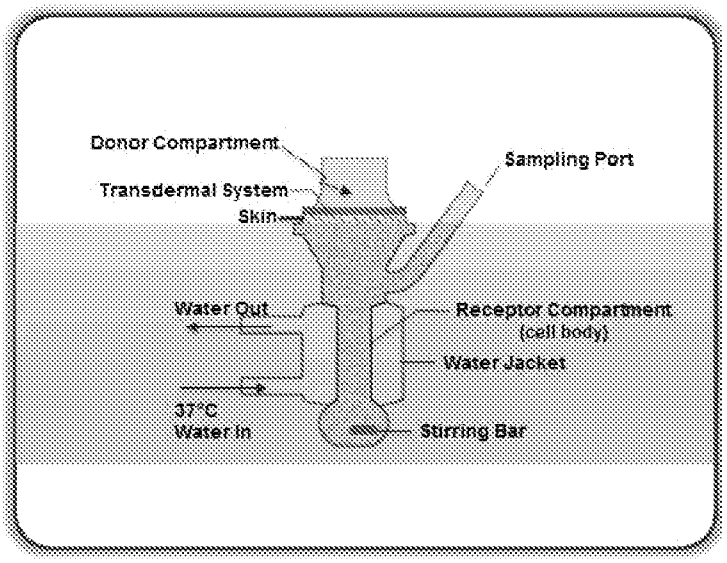
- over 30 years' research experience in the field of topical and transdermal drug delivery, including the study of drug absorption into and through the skin
- Bachelor of Arts in chemistry from Oxford University (UK) (1977)
- Master of Arts in chemistry from Oxford University (1980)
- Ph.D. in pharmaceutical 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.

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:

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

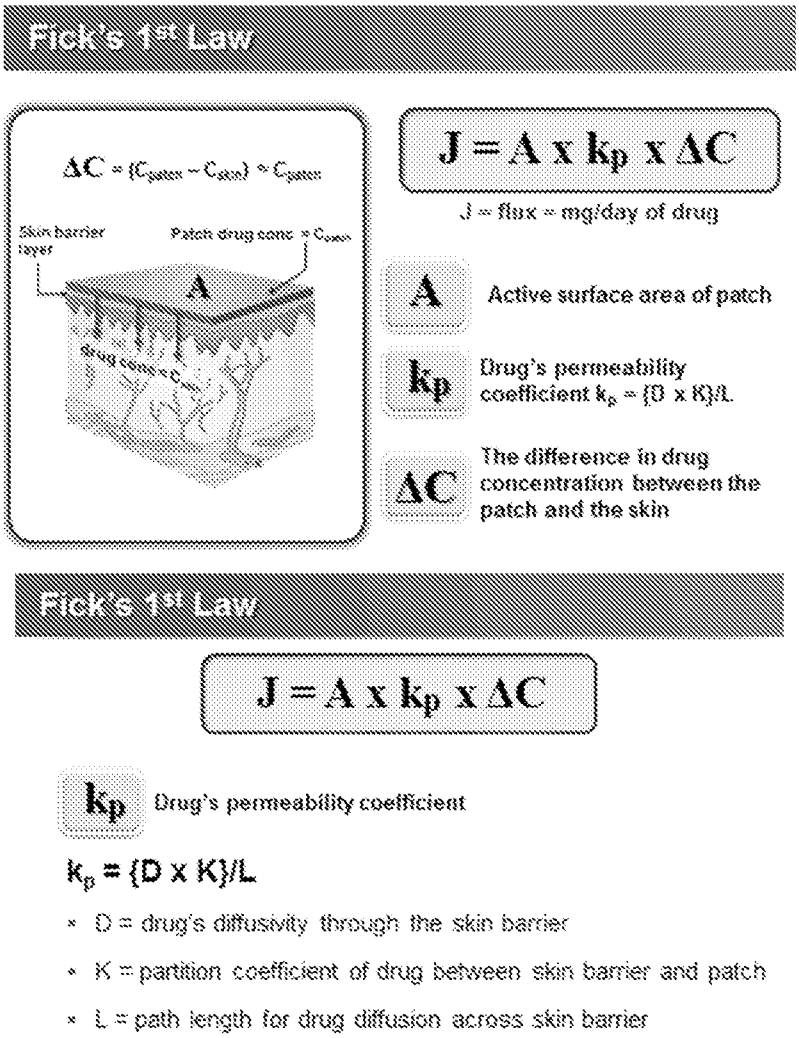
In this formula:

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 $k_p = \{D \times K\}/L$, 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.
- 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.

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

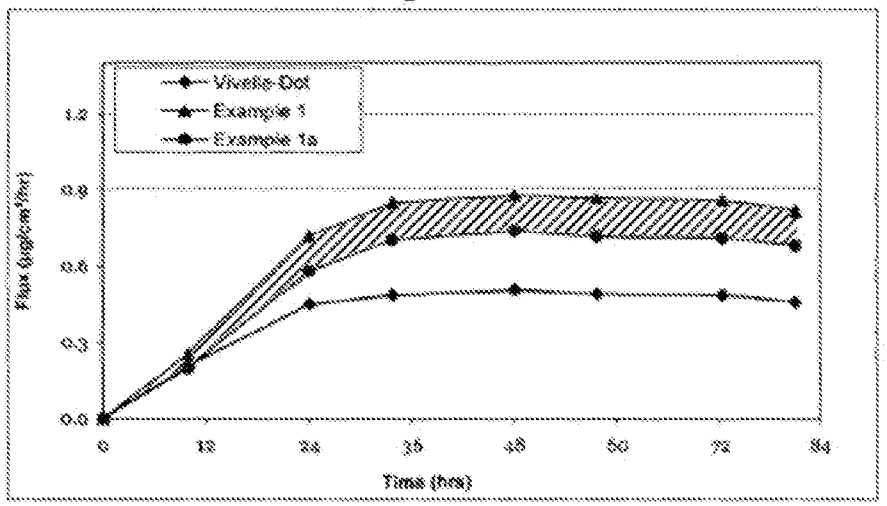
The specification illustrates this surprising and unexpected effect in Example 1, which describes an *in vitro* flux study conducted to assess the flux of estradiol from different systems. Figure 1 reports the flux of drug across the skin for the systems tested in Example 1.

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)	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/cm^2 (Example 1a, ●) and 15 mg/cm^2 (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.

Figure 1

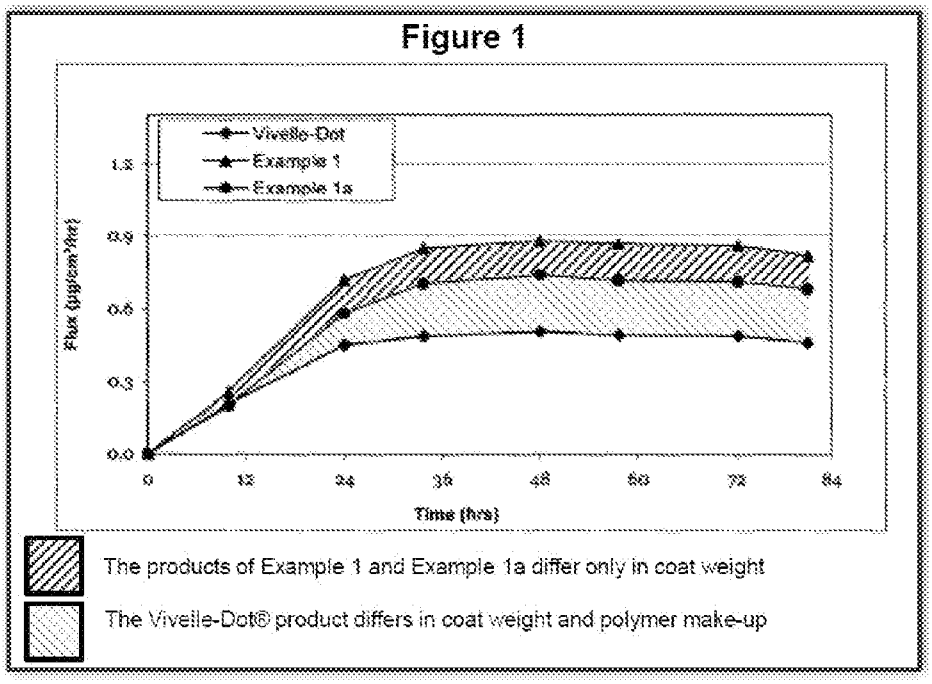


The only difference between Example 1 and Example 1a is the coat weight of the polymer matrix

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/cm^2 estradiol and has a polymer matrix coat weight of 10 mg/cm^2. *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

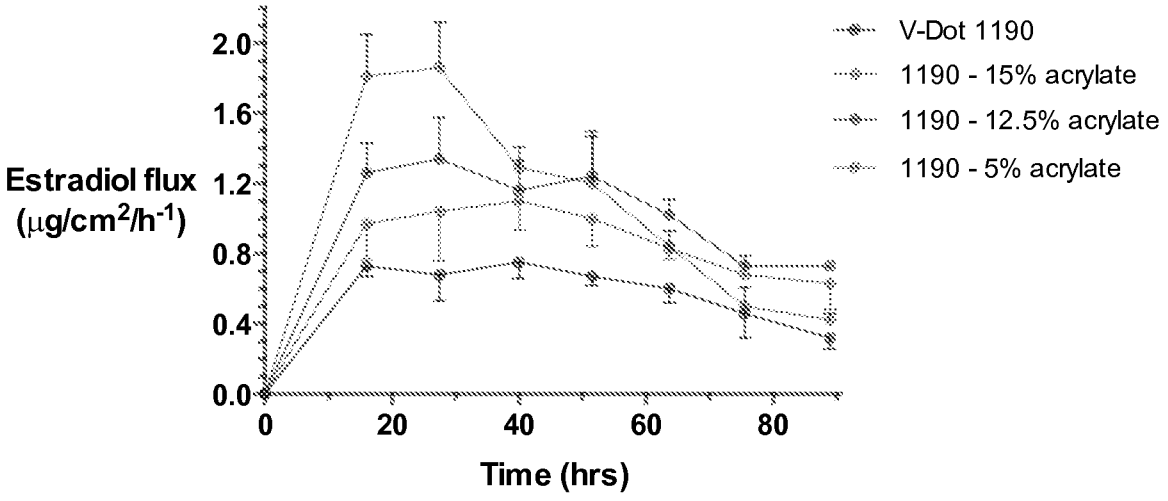
As noted above, it was known in the art that the relative amounts of acrylic adhesive and silicone adhesive used in an estradiol polymer matrix can impact the flux of estradiol. This is described in the '976 Patent, which explains that this is because estradiol's solubility in acrylic adhesives differs 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/cm^2) 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 (% by weight)	5% Acrylic	10% Acrylic	12.5% Acrylic	15% Acrylic	17.5% Acrylic
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

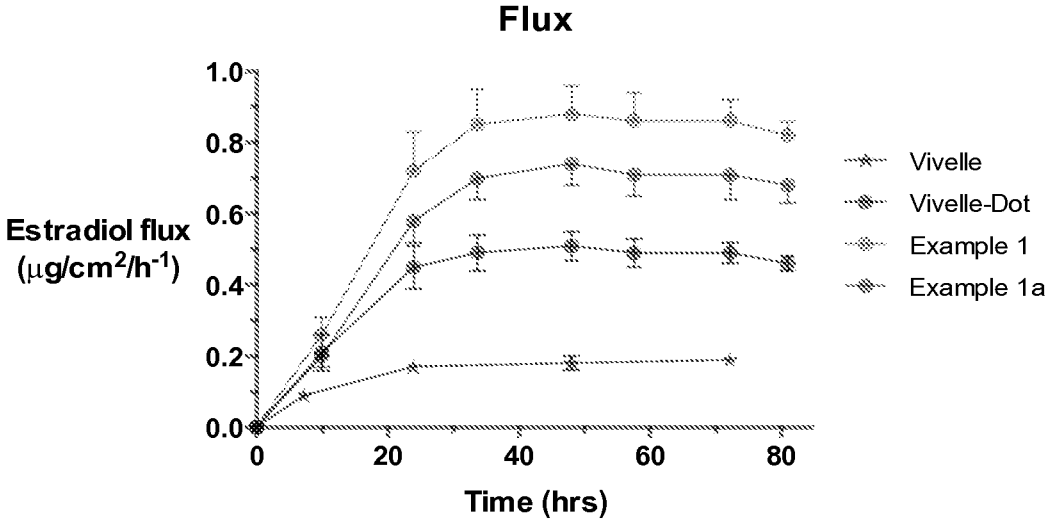
A representative sample of the data from this Flux Study are shown in the figure below. The results show that initial flux increased as the relative amount of acrylic polymer decreased but the initially higher flux from the 5% acrylic composition was not sustained:

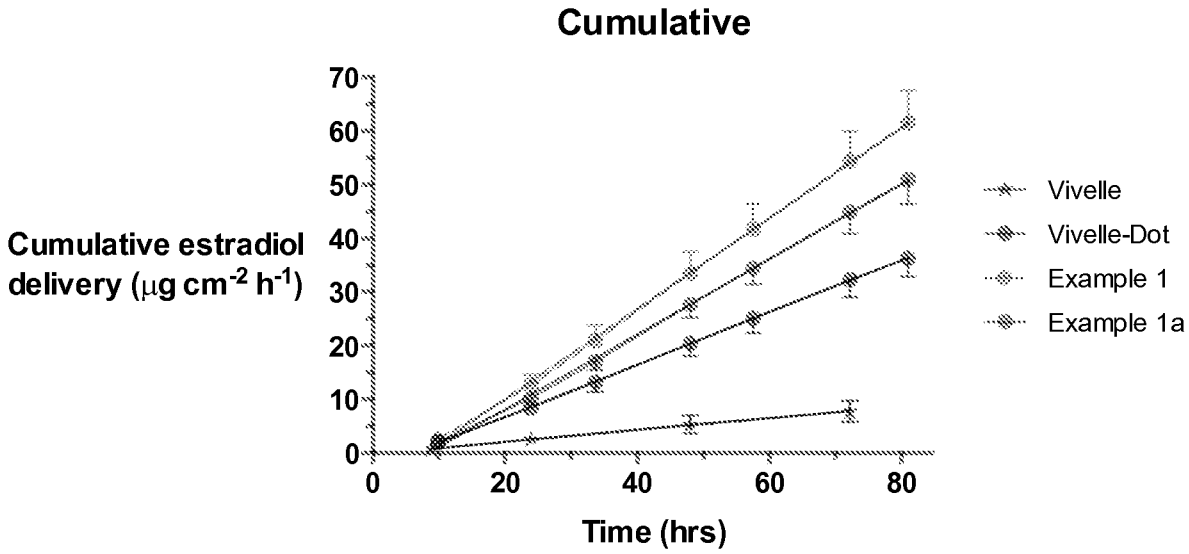


EXPERIMENTAL DATA – IMPACT OF COAT WEIGHT ON FLUX

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/cm^2 and 15 mg/cm^2. 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.



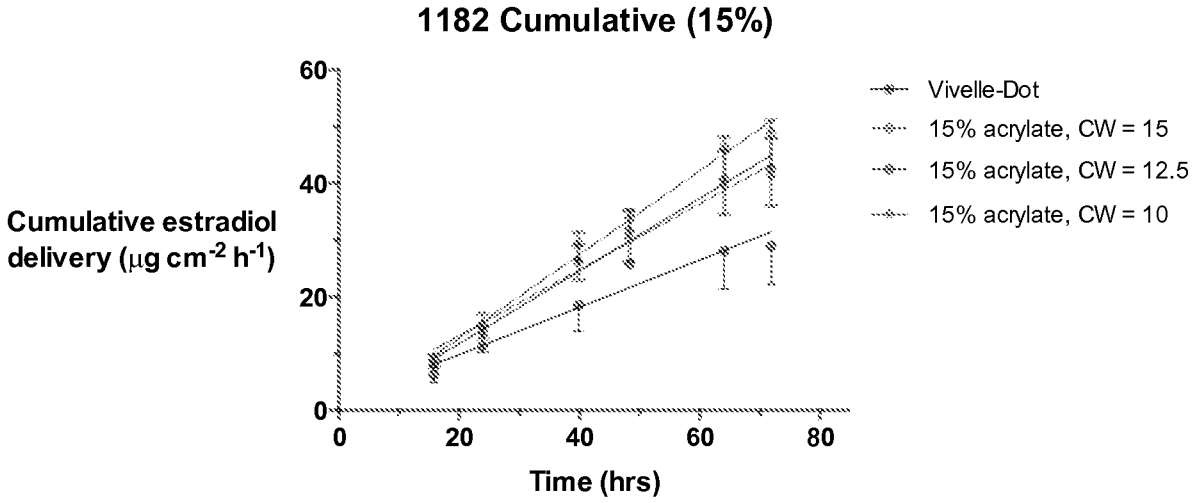


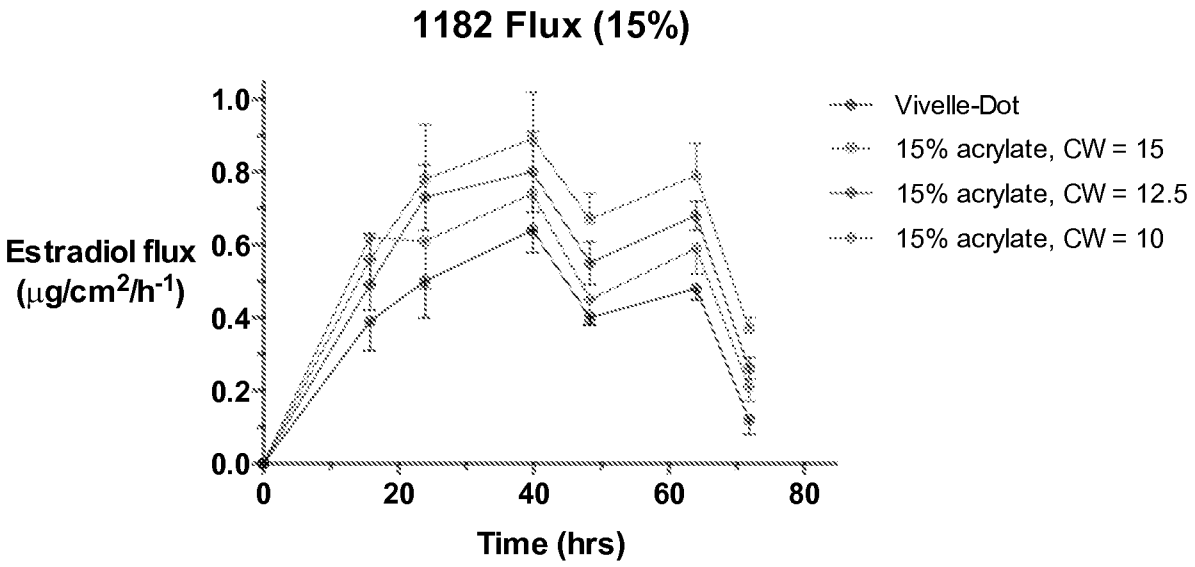
Flux Study 1182 conducted by Noven tested four different formulations at three different target coat weights and used a Vivelle-Dot® system as an internal control. The four formulations differed in the relative amounts of acrylic adhesive and silicone adhesive, as follows:

Component (% by weight)	10% Acrylic	15% Acrylic	17.5% Acrylic	20% Acrylic
Acrylic Adhesive	10	15	17.5	20
Silicon Adhesive	66.9	61.9	59.4*	56.9
Dipropylene Glycol	8	8	8	8
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.

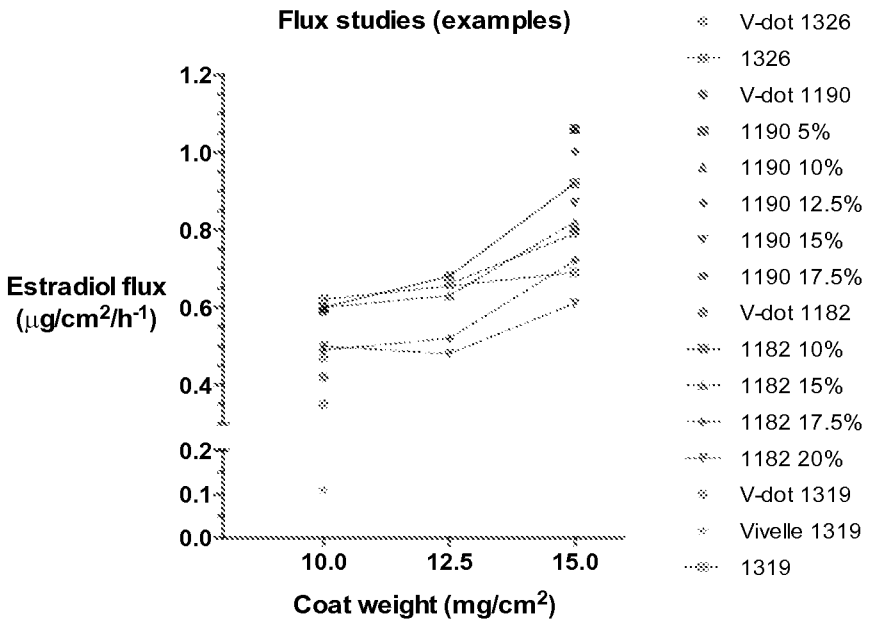
The different target coat weights assessed were 10 mg/cm^2, 12.5 mg/cm^2 and 15 mg/cm^2. The overall results show that increasing coat weight from 10 mg/cm^2 to 15 mg/cm^2 surprisingly and unexpectedly increased flux. For illustration, results for the composition with 15% acrylic polymer at a coat weight of 10 mg/cm^2, 12.5 mg/cm^2, and 15 mg/cm^2 (◉) 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:

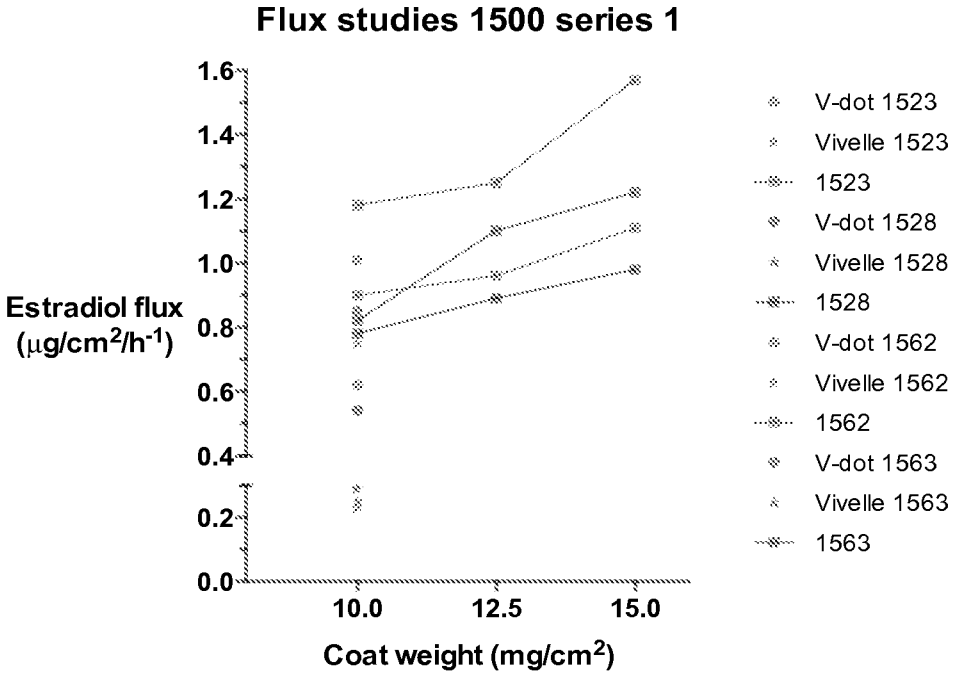


Flux Studies 1523, 1528, 1562 and 1563 assessed other formulations at different target coat weights, as outlined in the following table.

Flux Study	Formulation Components (% by weight)						Coat Wt. (mg/cm^2)	Drug Flux ($\mu g/cm^2 \cdot h$)
	Acrylate	Silicone	DPG	OAlc	PVP	Estradiol		
1523	10	69.4	8	6	5	1.6	15	1.57
	10	69.4	8	6	5	1.6	12.5	1.25
	10	69.4	8	6	5	1.6	10	1.18
	Control (flux): Vivelle-Dot® (1.01 $\mu g/cm^2 \cdot h$)							
1528	10	69.4	8	6	5	1.6	15	0.98
	10	69.4	8	6	5	1.6	12.5	0.89
	10	69.4	8	6	5	1.6	10	0.78
	Control (flux): Vivelle-Dot® (0.54 $\mu g/cm^2 \cdot h$)							
1562 (Form. 1)	10	69.4	8	6	5	1.6	15	1.11
	10	69.4	8	6	5	1.6	12.5	0.96
	10	69.4	8	6	5	1.6	10	0.90

Flux Study	Formulation Components (% by weight)						Coat Wt. (mg/cm^2)	Drug Flux ($\mu g/cm^2 \cdot h$)
	Acrylate	Silicone	DPG	OAlc	PVP	Estradiol		
	Control (flux): Vivelle-Dot® (0.62 $\mu g/cm^2 \cdot h$)							
1563 (Form. 1)	10	69.4	8	6	5	1.6	15	1.22
	10	69.4	8	6	5	1.6	12.5	1.10
	10	69.4	8	6	5	1.6	10	0.82
	Control (flux): Vivelle-Dot® (0.85 $\mu g/cm^2 \cdot h$)							

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/cm^2 and 15 mg/cm^2 using both Vivelle and Vivelle-Dot® as internal controls.

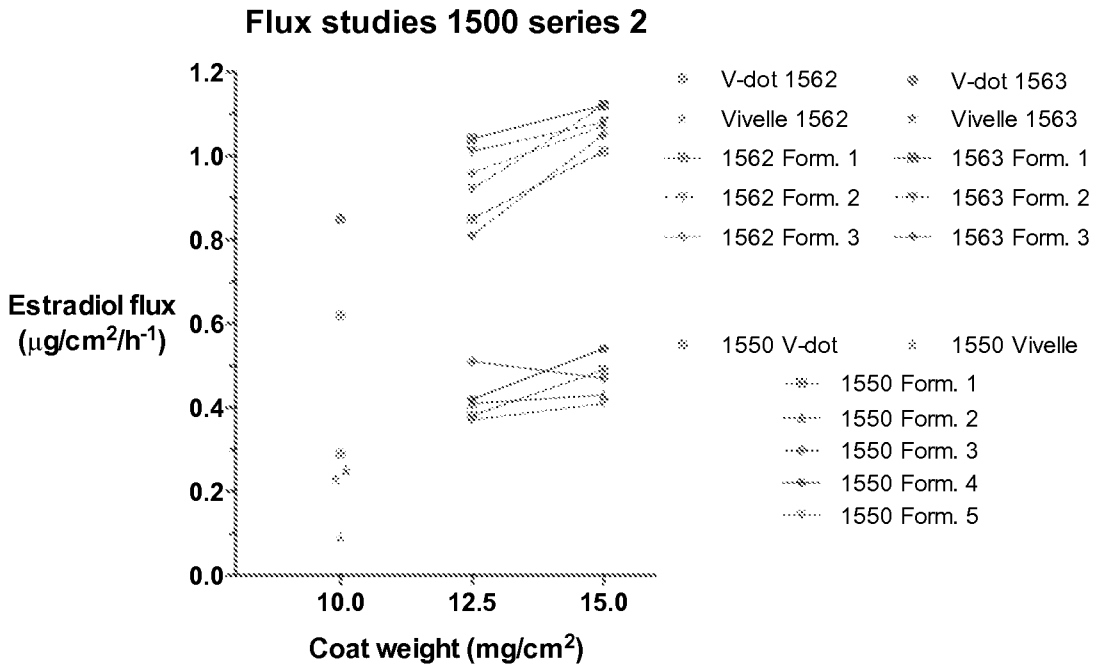
Flux Study	Formulation Components (% by weight)						Coat Wt. (mg/cm^2)	Drug Flux (µg/cm^2•h)
	Acrylate	Silicone	DPG	OAlc	PVP	Estradiol		
1562 (Form. 1)	10	69.4	8	6	5	1.6	15	1.01
	10	69.4	8	6	5	1.6	12.5	0.85
1562 (Form. 2)	7	72.6	8	6	5	1.4	15	1.12
	7	72.6	8	6	5	1.4	12.5	0.92
1562 (Form. 3)	7	74.6	8	6	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 (Form. 1)	10	69.4	8	6	5	1.6	15	1.12
	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 Control (flux): Vivelle-Dot® (0.85 µg/cm^2•h)								

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

Formulation	Formulation Components (% by weight)						Coat Wt. (mg/cm^2)	Drug Flux (µg/cm^2•h)
	Acrylate	Silicone	DPG	OAlc	PVP	Estradiol		
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

Formulation	Formulation Components (% by weight)						Coat Wt. (mg/cm^2)	Drug Flux ($\mu g/cm^2 \cdot h$)
	Acrylate	Silicone	DPG	OAlc	PVP	Estradiol		
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	0.37
Control (flux): Vivelle-Dot® (0.29 $\mu g/cm^2 \cdot h$)								

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:



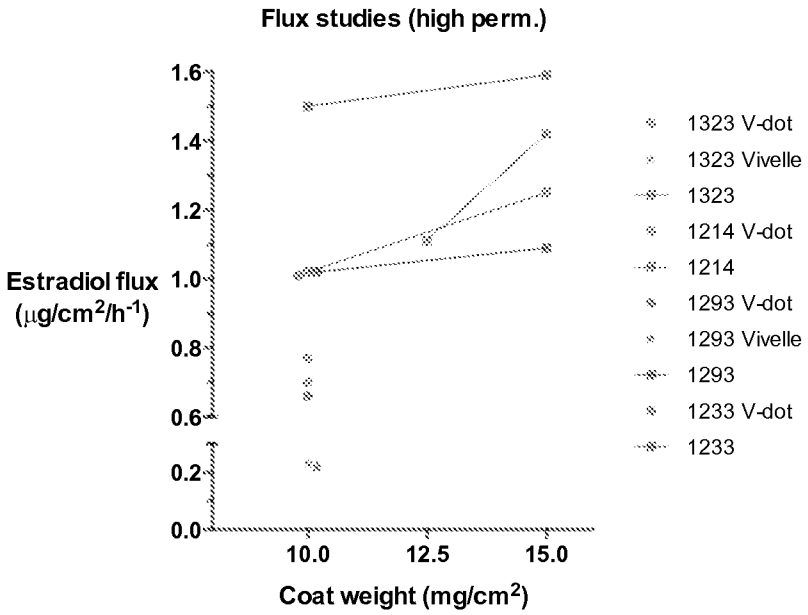
EXPERIMENTAL DATA – IMPACT OF SKIN PERMEABILITY ON FLUX

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/cm^2 and 15 mg/cm^2 (and used Vivelle-Dot® and Vivelle as internal controls).

Study #	Formulation Components (% by weight)						Coat Wt. (mg/cm^2)	Drug Flux (µg/cm^2•h)
	Acrylate	Silicone	DPG	OAlc	PVP	Estradiol		
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): Vivelle-Dot® (0.77 µg/cm^2•h)								
Control (flux): Vivelle® (0.23 µg/cm^2•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 (flux): Vivelle-Dot® (0.7 µg/cm^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): Vivelle-Dot® (0.66 µg/cm^2•h)								
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 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 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).

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/cm^2 and includes greater than 0.156 mg/cm^2 estradiol, and the system achieves an estradiol flux of from about 0.0125 to about 0.05 $g/cm^2/day$, 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/cm^2 and includes greater than 0.156 mg/cm^2 estradiol, wherein the system achieves an estradiol flux of from about 0.0125 to about 0.05 $mg/cm^2/day$, 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/cm^2 and includes greater than 0.156 mg/cm^2 estradiol, and the system achieves an estradiol flux of from about 0.0125 to about 0.05 mg/cm^2/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/cm^2 estradiol and achieves an estradiol flux of from about 0.0125 to about 0.0167 mg/cm^2/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/cm^2 estradiol, achieves an estradiol flux of from about 0.0125 to about 0.0167 mg/cm^2/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/cm^2 estradiol and achieves an estradiol flux of from about 0.0125 to about 0.05 mg/cm^2/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 mg/cm^2 estradiol and achieves an estradiol flux of from about 0.0125 to about 0.05 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.: 14/024,985

Filing Date: September 12, 2013

Examiner: Javier

Art Unit: 1611

Confirmation Number: 7031

SUPPLEMENTAL RESPONSE

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

Commissioner:

This paper is filed with a Request for Prioritized Examination (Track I), 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/Arguments begin on page 4 of this document.

Listing of Claims:

1. (Previously Presented) 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/cm^2 and includes greater than 0.156 mg/cm^2 estradiol, and the system achieves an estradiol flux of from about 0.0125 to about 0.05 $mg/cm^2/day$, based on the active surface area.

2. (Previously Presented) The transdermal drug delivery system of claim 1, wherein the adhesive polymer matrix comprises a polymer blend comprising an acrylic adhesive, a silicone adhesive, and soluble PVP.

3. (Previously Presented) The transdermal drug delivery system of claim 1, 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.

4. (Original) The transdermal drug delivery system of claim 3, wherein the penetration enhancer comprises oleyl alchol.

5. (Original) The transdermal drug delivery system of claim 3, wherein the penetration enhancer comprises dipropylene glycol.

6. (Original) The transdermal drug delivery system of claim 3, wherein the penetration enhancer comprises oleyl alcohol and dipropylene glycol.

7. (Original) The transdermal drug delivery system of claim 3, 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.

8. (Previously Presented) The transdermal drug delivery system of claim 1, 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.

9. (Previously Presented) The transdermal drug delivery system of claim 1, 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.

Claims 10-20 (Canceled)

21. (Previously Presented) The transdermal drug delivery system of claim 1, wherein the system achieves an estradiol flux of about 0.0125 $mg/cm^2/day$, based on the active surface area.

22. (Previously Presented) The transdermal drug delivery system of claim 1, wherein the system achieves an estradiol flux of about 0.0133 $mg/cm^2/day$, based on the active surface area.

23. (Previously Presented) The transdermal drug delivery system of claim 1, wherein the system achieves an estradiol flux of about 0.015 $mg/cm^2/day$, based on the active surface area.

24. (Previously Presented) The transdermal drug delivery system of claim 1, wherein the system achieves an estradiol flux of about 0.0167 $mg/cm^2/day$, based on the active surface area.

25. (Previously Presented) The transdermal drug delivery system of claim 1, wherein the system achieves an estradiol flux of about 0.0175 $mg/cm^2/day$, based on the active surface area.

26. (Previously Presented) The transdermal drug delivery system of claim 1, 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 1-9 and 21-25 was mailed April 26, 2017. Claim 26 was presented in the response filed June 6, 2017. No claims are amended, added or canceled herein. Thus, claims 1-9 and 21-26 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/

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

Substitute for form 1449/PTO				Complete if Known	
INFORMATION DISCLOSURE STATEMENT BY APPLICANT				**Application Number**	14/024985
Date Submitted: June 15, 2017				**Filing Date**	9/12/2013
				First Named Inventor	Juan Mantelle
(use as many sheets as necessary)				Art Unit	1611
				Examiner Name	Melissa L. Fisher
Sheet	1	of	1	Attorney Docket Number	041457-1016

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	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[6]
	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 03/23/2017 in application number 13/553,972 (US 2013/0156815)	
	A3	Office Action issued on 06/15/2017 in application number 14/870,574 (US 2016/0015655)	

Examiner Signature		Date Considered	

4848-1103-8538.1

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.

11. 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.

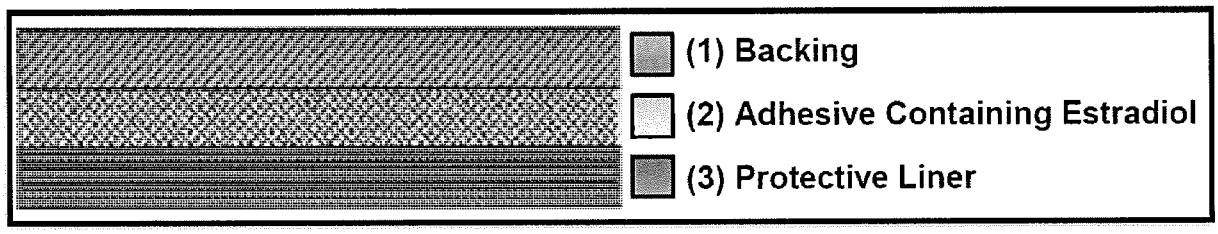
II. THE PENDING CLAIMS

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/cm^2, includes greater than 0.156 mg/cm^2 estradiol, and achieves an estradiol flux of from about 0.0125 to about 0.05 $mg/cm^2/day$, 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/cm^2 estradiol and achieves an estradiol flux of from about 0.0125 to about 0.05 $mg/cm^2/day$, 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.



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 µg/hour) from a transdermal patch across the skin:

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

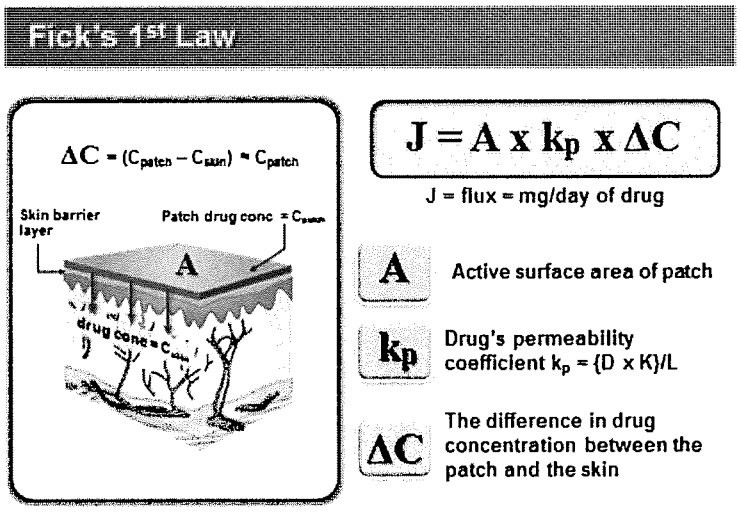
In this formula:

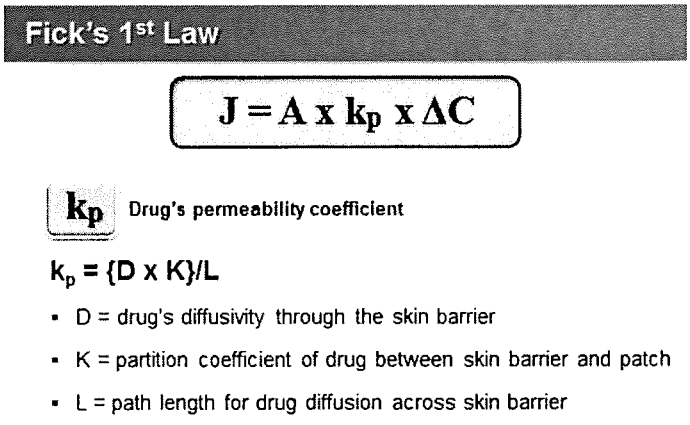
A is the active surface area of the patch.

k_p is the drug's permeability coefficient across the skin, and can be defined as $k_p = \{D \times K\}/L$, 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:





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].

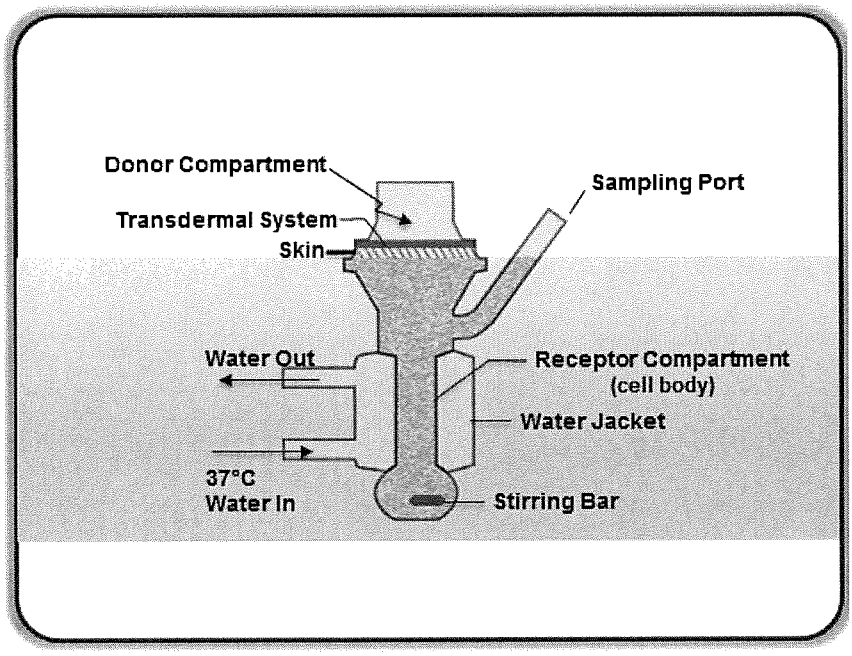
21. As stated in paragraph [0015] in the specification:

> 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.

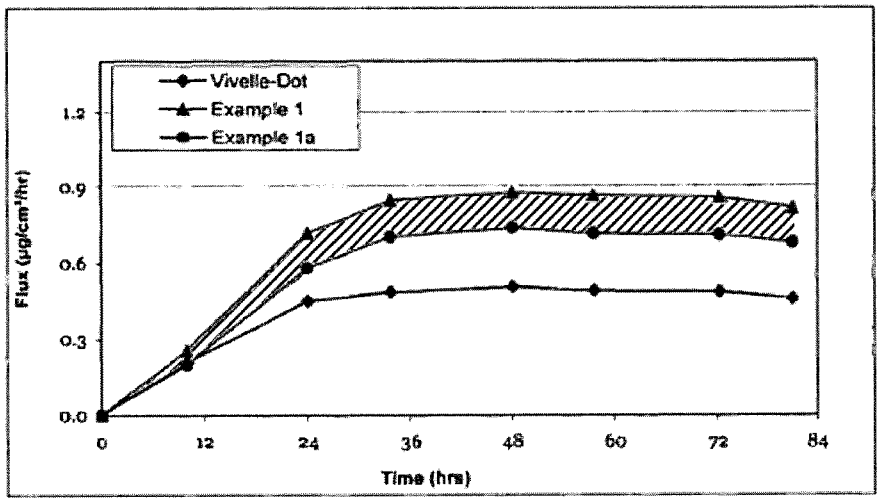
(hours) Average Time	(mcg/cm2) Average Cum.	(mcg/cm2) Cum. Stdev	(mcg/cm2 hr) Average Flux	(mcg/cm2 hr) Flux Stdev
0.00	0.00	0.00	0.00	0.00
9.92	2.55	0.49	0.26	0.05
23.95	12.64	1.99	0.72	0.11
33.65	20.85	2.91	0.85	0.10
48.03	33.45	4.10	0.88	0.08
57.58	41.70	4.81	0.86	0.08
72.20	54.23	5.71	0.86	0.06
81.02	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/cm^2 (Example 1a, ●) and 15 mg/cm^2 (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.

Figure 1



The only difference between Example 1 and Example 1a is the coat weight of the polymer matrix

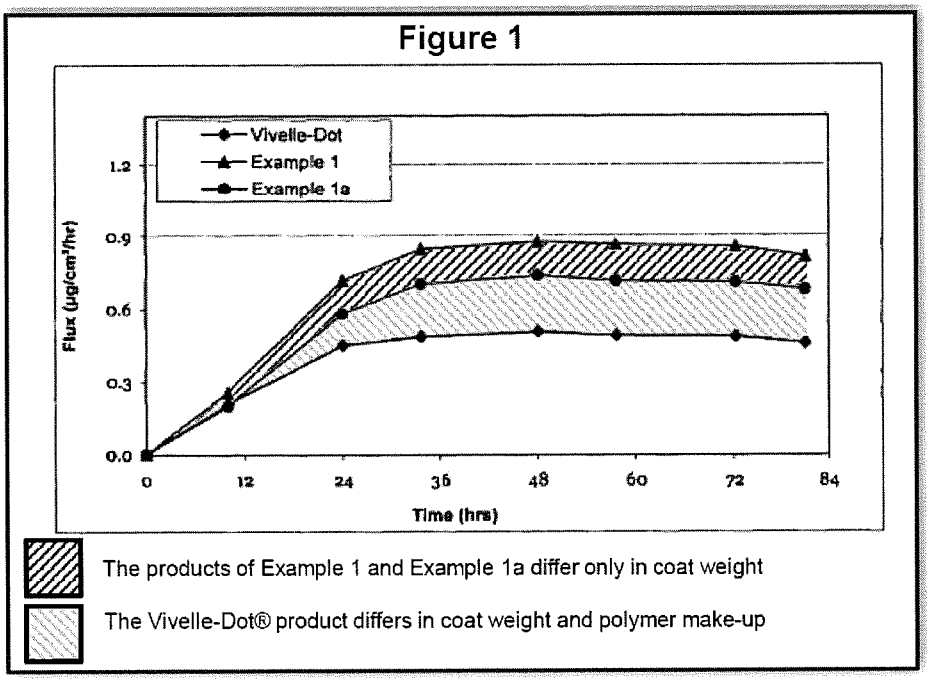
The only experimental variable different between Example 1a and Example 1 is the coat weight of the polymer matrix. The difference in flux reported in Figure 1 between Example 1a and Example 1 can only be attributed, therefore, to the difference in coat weight, which is a surprising and unexpected result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

24. 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/cm^2 estradiol and has a polymer matrix coat weight of 10 mg/cm^2. *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.

25. 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.

Figure 1



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

26. 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:

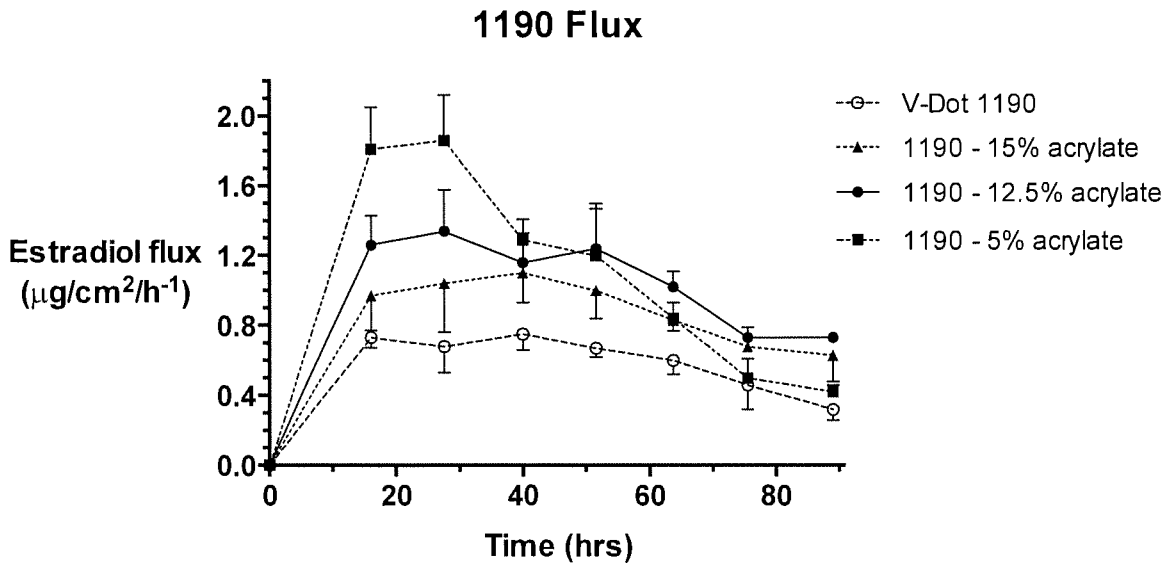
> As shown, varying the silicone to acrylic psa ratio from 56.9:20 to 61.9:15 to 66.9:10 resulted in an average flux rate increase … with the additional effect of having altered the initial burst effect and subsequent sustenance of the pseudo-zero-order delivery profile. As can be seen in Figure 2, higher 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/cm^2) 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 (% by weight)	5% Acrylic	10% Acrylic	12.5% Acrylic	15% Acrylic	17.5% Acrylic
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

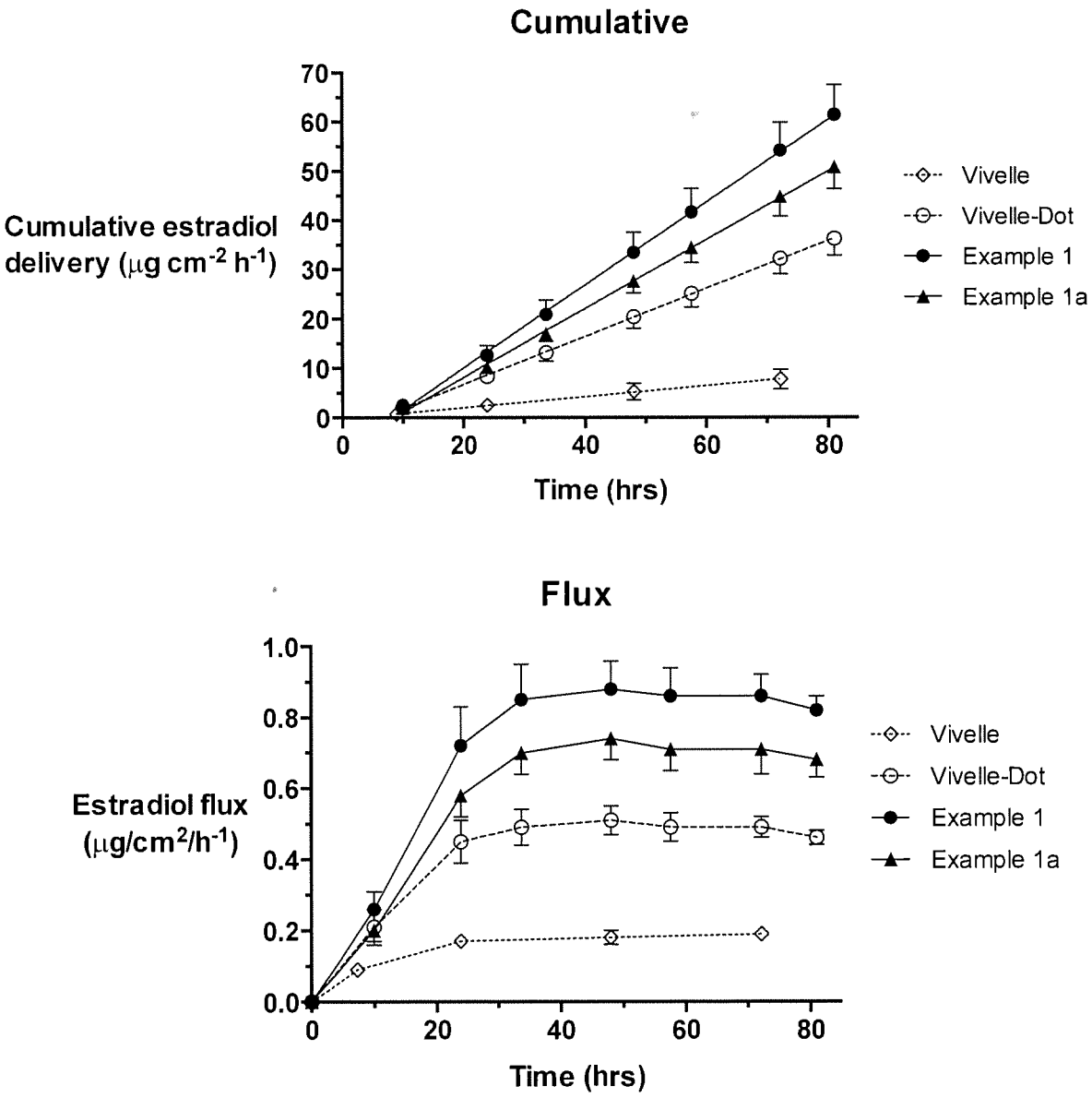
A representative sample of the data from this Flux Study are shown in the figure below. The results (reported as the average of 5 replicates) show that initial flux increased as the relative amount of acrylic polymer decreased but the initially higher flux from the 5% acrylic composition was not sustained:



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/cm^2 and 15 mg/cm^2. 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.

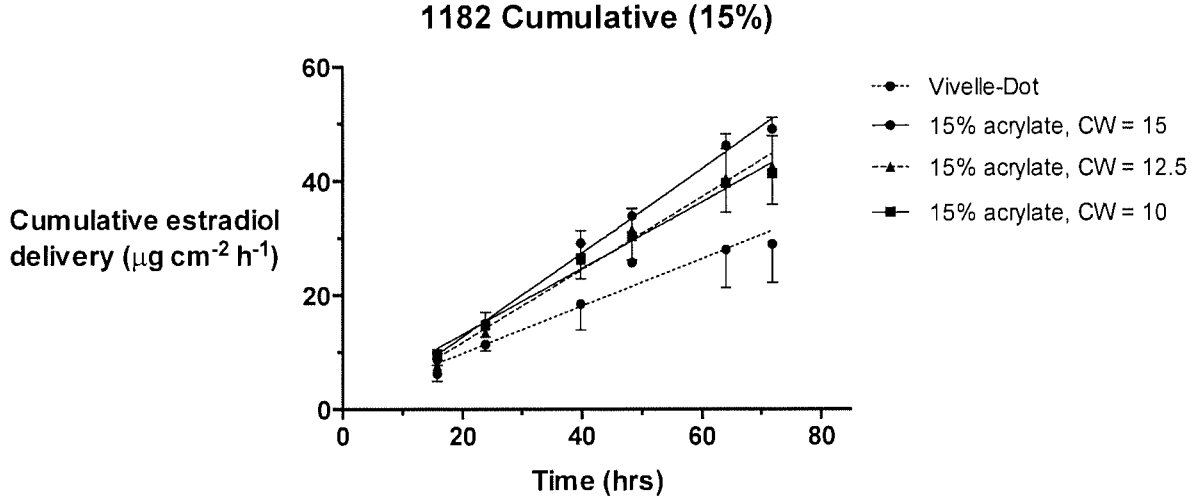


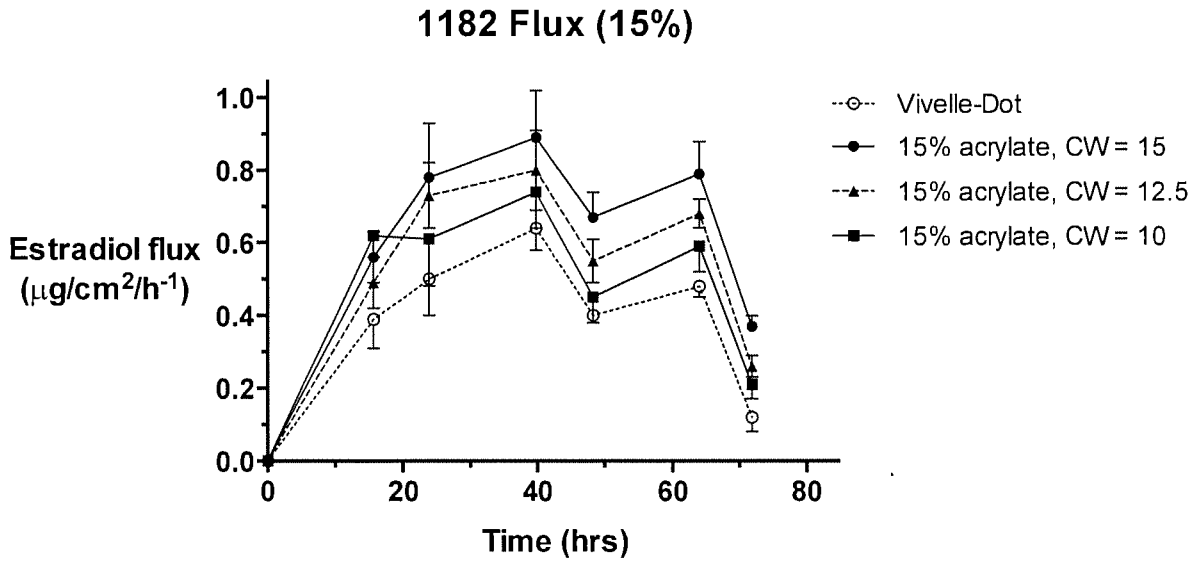
30. Flux Study 1182 conducted by Noven tested four different formulations at three different target coat weights and used a Vivelle-Dot® system as an internal control. The four formulations differed in the relative amounts of acrylic adhesive and silicone adhesive, as follows:

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

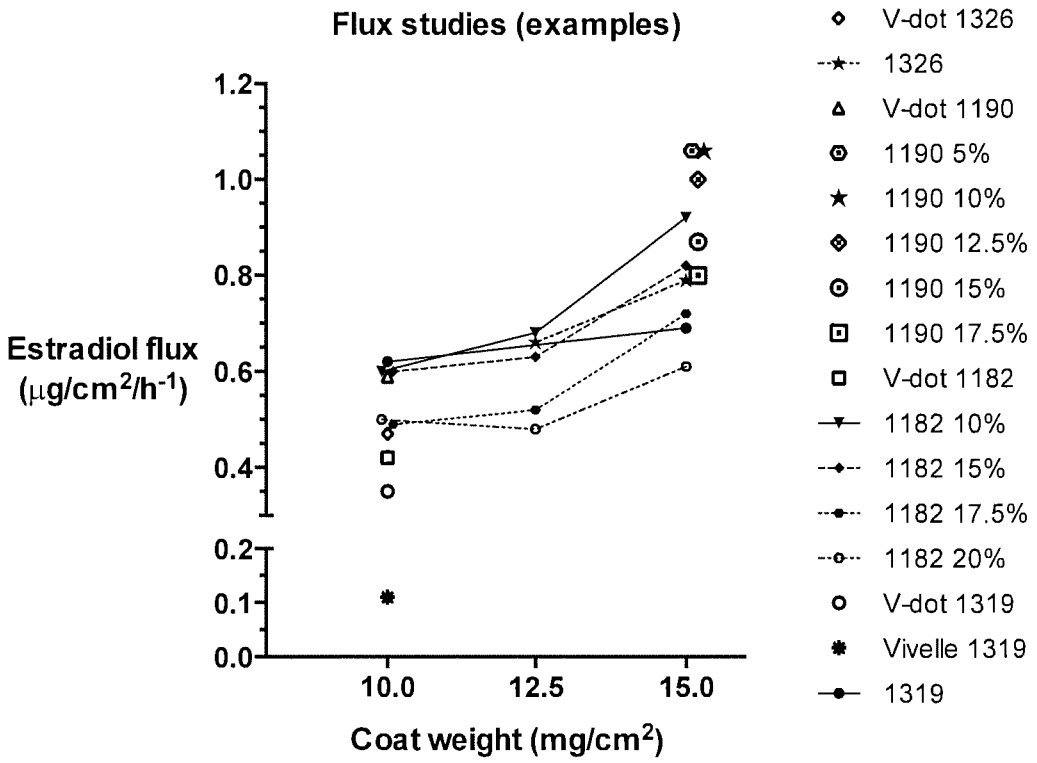
*Reported as 59.9%, but likely used 59.4% Silicone Adhesive.

The different target coat weights assessed were 10 mg/cm^2, 12.5 mg/cm^2 and 15 mg/cm^2. The overall results show that increasing coat weight from 10 mg/cm^2 to 15 mg/cm^2 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/cm^2, 12.5 mg/cm^2, and 15 mg/cm^2 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 μg/cm^2/hr):



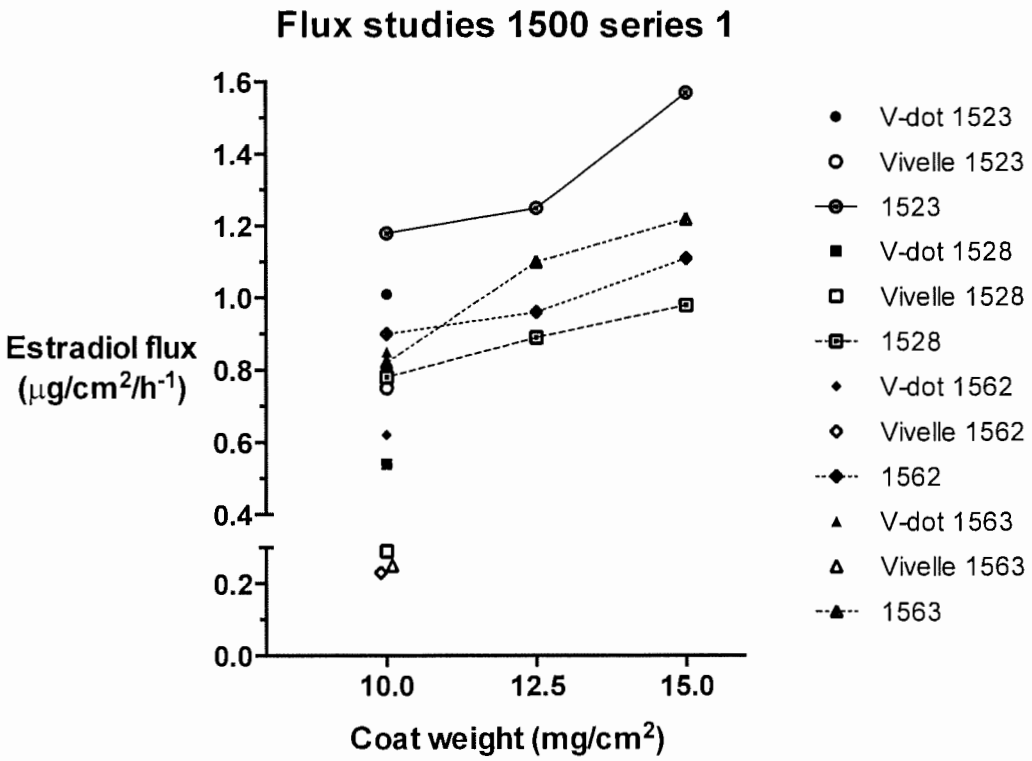
32. Collectively, the results from Flux Study 1190 and Flux Study 1182 indicate that while the relative amounts of acrylic adhesive and silicone adhesive impact the flux of estradiol—as was known in the art—the coat weight of the polymer matrix also impacts flux—which was not known in the art, and indeed 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	Formulation Components (% by weight)						Coat Wt. (mg/cm^2)	Drug Flux ($\mu g/cm^2 \cdot h$)
	Acrylate	Silicone	DPG	OAlc	PVP	Estradiol		
1523	10	69.4	8	6	5	1.6	15	1.57
	10	69.4	8	6	5	1.6	12.5	1.25
	10	69.4	8	6	5	1.6	10	1.18
	Control (flux): Vivelle-Dot® (1.01 $\mu g/cm^2 \cdot h$)							

Flux Study	Formulation Components (% by weight)						Coat Wt. (mg/cm^2)	Drug Flux ($\mu g/cm^2 \cdot h$)
	Acrylate	Silicone	DPG	OAlc	PVP	Estradiol		
1528	10	69.4	8	6	5	1.6	15	0.98
	10	69.4	8	6	5	1.6	12.5	0.89
	10	69.4	8	6	5	1.6	10	0.78
	Control (flux): Vivelle-Dot® (0.54 $\mu g/cm^2 \cdot h$)							
1562 (Form. 1)	10	69.4	8	6	5	1.6	15	1.11
	10	69.4	8	6	5	1.6	12.5	0.96
	10	69.4	8	6	5	1.6	10	0.90
	Control (flux): Vivelle-Dot® (0.62 $\mu g/cm^2 \cdot h$)							
1563 (Form. 1)	10	69.4	8	6	5	1.6	15	1.22
	10	69.4	8	6	5	1.6	12.5	1.10
	10	69.4	8	6	5	1.6	10	0.82
	Control (flux): Vivelle-Dot® (0.85 $\mu g/cm^2 \cdot h$)							

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/cm^2 and 15 mg/cm^2 using both Vivelle and Vivelle-Dot® as internal controls.

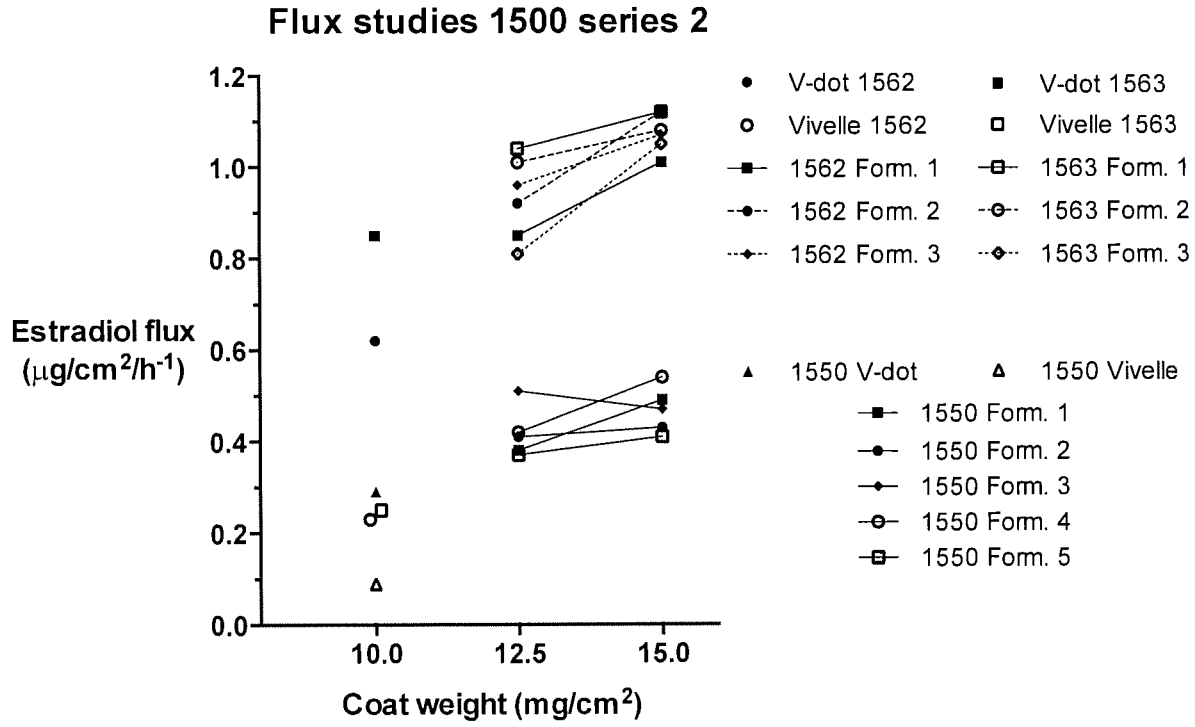
Flux Study	Formulation Components (% by weight)						Coat Wt. (mg/cm^2)	Drug Flux (μg/cm^2•h)
	Acrylate	Silicone	DPG	OAlc	PVP	Estradiol		
1562 (Form. 1)	10	69.4	8	6	5	1.6	15	1.01
	10	69.4	8	6	5	1.6	12.5	0.85
1562 (Form. 2)	7	72.6	8	6	5	1.4	15	1.12
	7	72.6	8	6	5	1.4	12.5	0.92
1562 (Form. 3)	7	74.6	8	6	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	Formulation Components (% by weight)						Coat Wt. (mg/cm^2)	Drug Flux ($\mu g/cm^2 \cdot h$)
	Acrylate	Silicone	DPG	OAlc	PVP	Estradiol		
(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 Control (flux): Vivelle-Dot® (0.85 $\mu g/cm^2 \cdot h$)								

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

Formulation	Formulation Components (% by weight)						Coat Wt. (mg/cm^2)	Drug Flux ($\mu g/cm^2 \cdot h$)
	Acrylate	Silicone	DPG	OAlc	PVP	Estradiol		
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
	10	73.4	6	6	3	1.6	12.5	0.37
Control (flux): Vivelle-Dot® (0.29 $\mu g/cm^2 \cdot h$)								

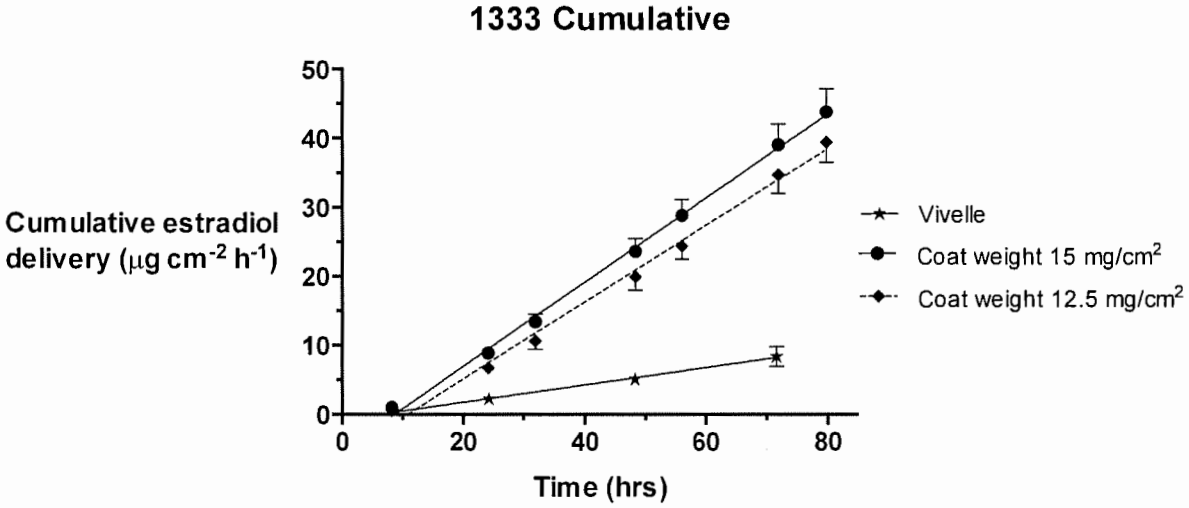
37. The estimated estradiol fluxes from 1562 and 1563 (second series) (reported as the average of 3 replicates; some values are slightly displaced along the x-axis to facilitate visualization of the data points) and 1550 are illustrated below (reported as the average of 4 replicates), and again show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

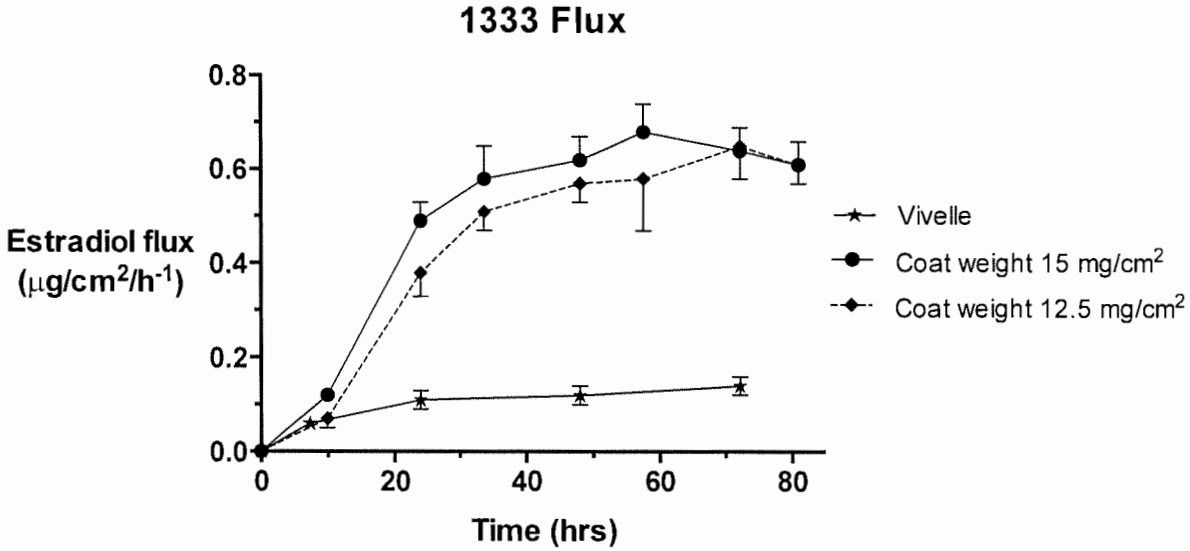


38. Although the results for Flux Study 1550 - Formulation 3 show a higher flux for the lower coat weight, that does not change my opinion that the totality of the data show the surprising and unexpected result that increasing coat weight increases flux. Indeed, Formulation 3 of Flux Study 1550 is the 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/cm^2 and 15 mg/cm^2 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/cm^2 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.





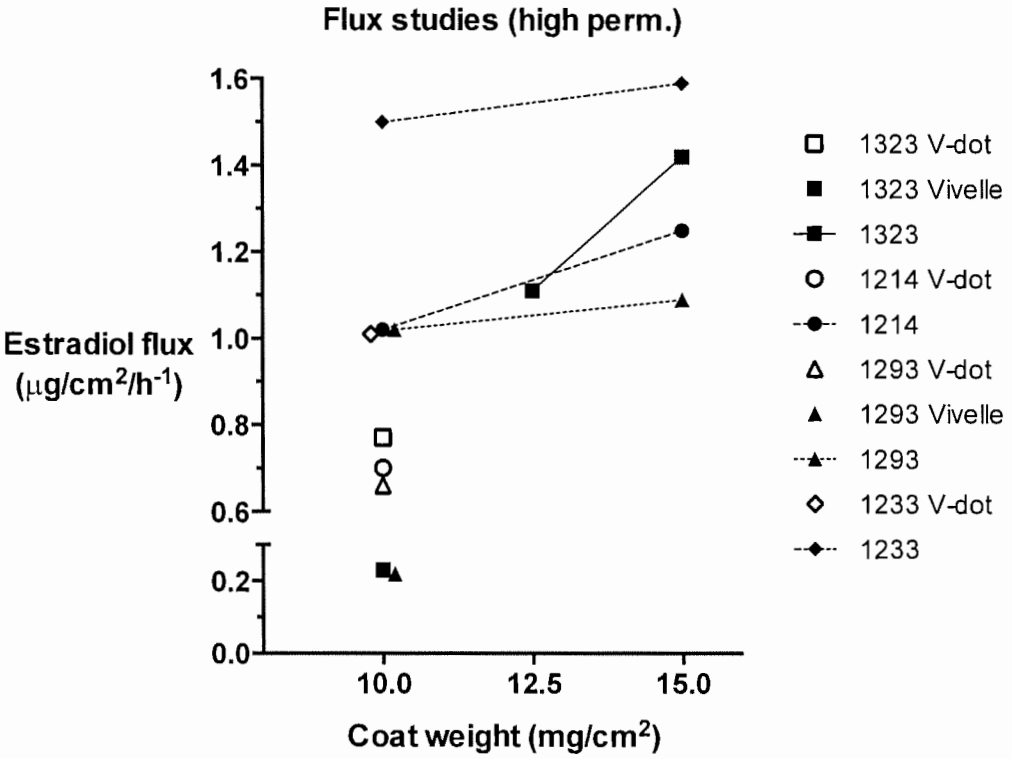
VII. EXPERIMENTAL DATA – IMPACT OF SKIN PERMEABILITY ON FLUX

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/cm^2 and 15 mg/cm^2 (and used Vivelle-Dot® and Vivelle as internal controls).

Study #	Formulation Components (% by weight)						Coat Wt. (mg/cm^2)	Drug Flux ($\mu g/cm^2 \cdot h$)
	Acrylate	Silicone	DPG	OAlc	PVP	Estradiol		
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): Vivelle-Dot® (0.77 $\mu g/cm^2 \cdot h$)								
Control (flux): Vivelle® (0.23 $\mu g/cm^2 \cdot h$)								
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 (flux): Vivelle-Dot® (0.7 $\mu g/cm^2 \cdot h$)								
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): Vivelle-Dot® (0.66 $\mu g/cm^2 \cdot h$)								
Control (flux): Vivelle® (0.22 $\mu g/cm^2 \cdot h$)								
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 $\mu g/cm^2 \cdot h$)								

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 sustain 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

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Current Position & Address:

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Adjunct Professor
University of California, San Francisco
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

2001-04	Professeur 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
1988	Young Investigator Award (1st recipient), Controlled Release Society
	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 co-direction 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).

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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 h-index 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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Research Awards, Fellowships and Extramural Grants (since 1994)

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 *In Vivo* and *In Vitro* 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 Iontophoretic 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 6th 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 *Versus* 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

1998-2000 Novartis Pharma, Inc. (Switzerland), SFr 105,000: Supersaturation as a Method to Improve Topical Bioavailability of Lipophilic Drugs

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

	Electrorepulsion *Versus* Electroosmosis
1999-2001	Galderma (France), SFr410,000: Topical Dermatological Drug Product Bioavailability and Bioequivalence *in vivo*
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), € 26,955: Skin Penetration Enhancement with Naturally-Occuring Oils
	Abbott Laboratories (USA), € 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: Iontophoresis 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.

2000 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 *In Vivo* 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, *In Vivo*: 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: *In vitro* 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 *in vivo* - Effect of Vehicle
Current position: Professor, University of Kentucky, USA

1995- Gilles Touraille, Pharm.D.: Postgraduate Research Pharmacist: Assessment of Dermal Exposure *in vivo* - 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; pI 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 Therapy 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: *In vivo-in vitro* correlations for topical bioavailability
	Mohammed Zaher Shehab, Ph.D.: Postdoctoral Scientist: *In vivo-in vitro* 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: *In vivo-in vitro* 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
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	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
2017-	Member, Editorial Advisory Board, International Journal of Pharmaceutics

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

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

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)

2006 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)

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)

2009 Bilateral Collaboration on Education and Research. UKIERI Awards Symposium. New Delhi, India (March 23)

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)

2011 Optimising Topical Formulations to Deliver Actives into the Skin: Mechanisms and Methodologies. L'Oréal. Aulnay-sous-Bois, France (March 4)

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 Microscpy. 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)

2013 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. 20ème 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. 28ème seminaire de 3ème 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)

2014 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)

2016 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. 11ème 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

2)

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 Patent Application Fee Transmittal

Application Number:	14024985
Filing Date:	12-Sep-2013
Title of Invention:	TRANSDERMAL ESTROGEN DEVICE AND DELIVERY
First Named Inventor/Applicant Name:	Juan Mantelle
Filer:	Courtenay C. Brinckerhoff/Christine Arthur
Attorney Docket Number:	041457-1016

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:				
PROCESSING FEE, EXCEPT PROV. APPLS.	1830	1	140	140
Petition:				
Patent-Appeals-and-Interference:				
Post-Allowance-and-Post-Issuance:				

Description	Fee Code	Quantity	Amount	Sub-Total in USD($)
Extension-of-Time:				
Miscellaneous:				
			Total in USD ($)	**140**

Electronic Acknowledgement Receipt

EFS ID:	29507226
Application Number:	14024985
International Application Number:	
Confirmation Number:	7031
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:	041457-1016
Receipt Date:	15-JUN-2017
Filing Date:	12-SEP-2013
Time Stamp:	13:06:54
Application Type:	Utility under 35 USC 111(a)

Payment information:

Submitted with Payment	yes
Payment Type	CARD
Payment was successfully received in RAM	$140
RAM confirmation Number	061517INTEFSW13074000
Deposit Account	
Authorized User	

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

File Listing:

Document Number	Document Description	File Name	File Size(Bytes)/ Message Digest	Multi Part /.zip	Pages (if appl.)
1		responsetrack1ids.pdf	355038 c2ba1571e9815a91365c19d5ce76f620dfca411a	yes	8

Multipart Description/PDF files in .zip description

Document Description	Start	End
Supplemental Response or Supplemental Amendment	1	4
TrackOne Request	5	5
Transmittal Letter	6	7
Information Disclosure Statement (IDS) Form (SB08)	8	8

Warnings:					
Information:					
2	Affidavit-traversing rejectns or objectns rule 132	132decl.pdf	1433115 3c300e42c8f93b0dbb8bb1fc32a56382060fa97d	no	29
Warnings:					
Information:					
3	Affidavit-traversing rejectns or objectns rule 132	cv.pdf	555354 b99b4d401fad2d4686fd049074e007ee4fd0604d	no	78
Warnings:					
Information:					
4	Non Patent Literature	mantelle.pdf	1759342 f9fd1666860cbf1d3ed3d9261a1e18ccf23ba4b7	no	3
Warnings:					
Information:					

5	Non Patent Literature	a2.pdf	401705 67e021de357efcf55eabb2f3935453b9f0f2e55c	no	7
Warnings:					
Information:					
6	Non Patent Literature	a3.pdf	698742 653b8bde58a14de9794057a9a1dc6bcd91794f7a	no	17
Warnings:					
Information:					
7	Fee Worksheet (SB06)	fee-info.pdf	30714 e64aefa989efe0becaedd6e01938111b84f347e7	no	2
Warnings:					
Information:					
			Total Files Size (in bytes):	5234010	

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.

Doc Code: TRACK1.REQ
Document Description: TrackOne Request

PTO/AIA/424 (04-14)

CERTIFICATION AND REQUEST FOR PRIORITIZED EXAMINATION UNDER 37 CFR 1.102(e) (Page 1 of 1)

First Named Inventor:	Juan Mantelle	Nonprovisional Application Number (if known):	14/024985
Title of Invention:	Transdermal Estrogen Device and Delivery		

APPLICANT HEREBY CERTIFIES THE FOLLOWING AND REQUESTS PRIORITIZED EXAMINATION FOR THE ABOVE-IDENTIFIED APPLICATION.

1. The processing fee set forth in 37 CFR 1.17(i)(1) and the prioritized examination fee set forth in 37 CFR 1.17(c) have been filed with the request. The publication fee requirement is met because that fee, set forth in 37 CFR 1.18(d), is currently $0. The basic filing fee, search fee, and examination fee are filed with the request or have been already been paid. I understand that any required excess claims fees or application size fee must be paid for the application.

2. I understand that the application may not contain, or be amended to contain, more than four independent claims, more than thirty total claims, or any multiple dependent claims, and that any request for an extension of time will cause an outstanding Track I request to be dismissed.

3. The applicable box is checked below:

I. ☐ Original Application (Track One) - Prioritized Examination under § 1.102(e)(1)

i. (a) The application is an original nonprovisional utility application filed under 35 U.S.C. 111(a). This certification and request is being filed with the utility application via EFS-Web.

---OR---

(b) The application is an original nonprovisional plant application filed under 35 U.S.C. 111(a). This certification and request is being filed with the plant application in paper.

ii. An executed inventor's oath or declaration under 37 CFR 1.63 or 37 CFR 1.64 for each inventor, **or** the application data sheet meeting the conditions specified in 37 CFR 1.53(f)(3)(i) is filed with the application.

II. ☑ Request for Continued Examination - Prioritized Examination under § 1.102(e)(2)

i. A request for continued examination has been filed with, or prior to, this form.
ii. If the application is a utility application, this certification and request is being filed via EFS-Web.
iii. The application is an original nonprovisional utility application filed under 35 U.S.C. 111(a), or is a national stage entry under 35 U.S.C. 371.
iv. This certification and request is being filed prior to the mailing of a first Office action responsive to the request for continued examination.
v. No prior request for continued examination has been granted prioritized examination status under 37 CFR 1.102(e)(2).

Signature Courtenay C Brinckerhoff	Date June 15, 2017
Name (Print/Typed) Courtenay C. Brinckerhoff	Practitioner Registration Number 37,288

Note: *This form must be signed in accordance with 37 CFR 1.33. See 37 CFR 1.4(d) for signature requirements and certifications. Submit multiple forms if more than one signature is required.**

☑ *Total of 1 forms are submitted.

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

First Inventor Name:	Juan Mantelle
Title:	Transdermal Estrogen Device and Delivery
Application No.:	14/024985
Filing Date:	9/12/2013
Examiner:	Melissa L. Fisher
Art Unit:	1611
Confirmation No.:	7031

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.

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.

Document A2 is an Office Action which issued in the parent application, and Document A3 is an Office Action which issued in the child application.

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

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

PTO/SB/06 (09-11)
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.

PATENT APPLICATION FEE DETERMINATION RECORD Substitute for Form PTO-875	Application or Docket Number 14/024,985	Filing Date 09/12/2013	☐ To be Mailed

ENTITY: ☒ LARGE ☐ SMALL ☐ MICRO

APPLICATION AS FILED – PART I

	(Column 1)	(Column 2)		
FOR	NUMBER FILED	NUMBER EXTRA	RATE ($)	FEE ($)
☐ 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 FEE (37 CFR 1.16(o), (p), or (q))	N/A	N/A	N/A	
TOTAL CLAIMS (37 CFR 1.16(i))	minus 20 =	*	X $ =	
INDEPENDENT CLAIMS (37 CFR 1.16(h))	minus 3 =	*	X $ =	
☐ APPLICATION SIZE FEE (37 CFR 1.16(s))	If the specification and drawings exceed 100 sheets of paper, the application size fee due is $310 ($155 for small entity) for each additional 50 sheets or fraction thereof. See 35 U.S.C. 41(a)(1)(G) and 37 CFR 1.16(s).			
☐ MULTIPLE DEPENDENT CLAIM PRESENT (37 CFR 1.16(j))				
* If the difference in column 1 is less than zero, enter "0" in column 2.			TOTAL	

APPLICATION AS AMENDED – PART II

		(Column 1)		(Column 2)	(Column 3)		
AMENDMENT	06/15/2017	CLAIMS REMAINING AFTER AMENDMENT		HIGHEST NUMBER PREVIOUSLY PAID FOR	PRESENT EXTRA	RATE ($)	ADDITIONAL FEE ($)
	Total (37 CFR 1.16(i))	* 15	Minus	** 20	= 0	X $80 =	0
	Independent (37 CFR 1.16(h))	* 1	Minus	***4	= 0	X $420 =	0
	☐ Application Size Fee (37 CFR 1.16(s))						
	☐ FIRST PRESENTATION OF MULTIPLE DEPENDENT CLAIM (37 CFR 1.16(j))						
						TOTAL ADD'L FEE	0

		(Column 1)		(Column 2)	(Column 3)		
AMENDMENT		CLAIMS REMAINING AFTER AMENDMENT		HIGHEST NUMBER PREVIOUSLY PAID FOR	PRESENT EXTRA	RATE ($)	ADDITIONAL FEE ($)
	Total (37 CFR 1.16(i))	*	Minus	**	=	X $ =	
	Independent (37 CFR 1.16(h))	*	Minus	***	=	X $ =	
	☐ Application Size Fee (37 CFR 1.16(s))						
	☐ FIRST PRESENTATION OF MULTIPLE DEPENDENT CLAIM (37 CFR 1.16(j))						
						TOTAL ADD'L FEE	

* If the entry in column 1 is less than the entry in column 2, write "0" in column 3.
** If the "Highest Number Previously Paid For" IN THIS SPACE is less than 20, enter "20".
*** If the "Highest Number Previously Paid For" IN THIS SPACE is less than 3, enter "3".
The "Highest Number Previously Paid For" (Total or Independent) is the highest number found in the appropriate box in column 1.

LIE
MARISSA BLYTHER

UNITED STATES PATENT AND TRADEMARK OFFICE

Commissioner for Patents
United States Patent and Trademark Office
P.O. Box 1450
Alexandria, VA 22313-1450
www.uspto.gov

MAILED
JUN 23 2017
OFFICE OF PETITIONS

Foley & Lardner LLP
3000 K STREET N.W.
SUITE 600
WASHINGTON DC 20007-5109

Doc Code: TRACK1.GRANT

Decision Granting Request for Prioritized Examination (Track I or After RCE)	Application No.: 14/024,985

The requisite $4000.00 Prioritized Examination Fee (Fee Code 1817) has been charge to Deposit Account No. 19-0741, pursuant to the deposit account authorization that accompanied the present Request. Payment of these fees are required for acceptance of an application into the Prioritized Examination, Track 1, Program.

1. THE REQUEST FILED June 15, 2017 IS **GRANTED.**

The above-identified application has met the requirements for prioritized examination

A. ☐ for an original nonprovisional application (Track I).
B. ☒ for an application undergoing continued examination (RCE).

2. **The above-identified application will undergo prioritized examination.** The application will be accorded special status throughout its entire course of prosecution until one of the following occurs:

A. filing a **petition for extension of time** to extend the time period for filing a reply;
B. filing an **amendment to amend the application to contain more than four independent claims, more than thirty total claims**, or a multiple dependent claim;
C. filing a **request for continued examination**;
D. filing a notice of appeal;
E. filing a request for suspension of action;
F. mailing of a notice of allowance;
G. mailing of a final Office action;
H. completion of examination as defined in 37 CFR 41.102; or
I. abandonment of the application.

Telephone inquiries with regard to this decision should be directed to Brian W. Brown at 571-272-5338.

/Brian W. Brown/
[*Signature*]

Petitions Examiner, Office of Petitions
(Title)

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

NOTICE OF ALLOWANCE AND FEE(S) DUE

22428 7590 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.
14/024,985	09/12/2013	Juan Mantelle	041457-1016	7031

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. THIS 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 fees.

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**
Commissioner for Patents
P.O. Box 1450
Alexandria, Virginia 22313-1450
or Fax (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.

CURRENT CORRESPONDENCE ADDRESS (Note: Use Block 1 for any change of address)

22428 7590 06/27/2017
Foley & Lardner LLP
3000 K STREET N.W.
SUITE 600
WASHINGTON, DC 20007-5109

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, must have its own certificate of mailing or transmission.

Certificate of Mailing or Transmission
I hereby certify that this Fee(s) Transmittal is being deposited with the United States Postal Service with sufficient postage for first class mail in an envelope addressed to the Mail Stop ISSUE FEE address above, or being facsimile transmitted to the USPTO (571) 273-2885, on the date indicated below.

(Depositor's name)
(Signature)
(Date)

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
14/024,985	09/12/2013	Juan Mantelle	041457-1016	7031

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

EXAMINER	ART UNIT	CLASS-SUBCLASS
FISHER, MELISSA L	1611	424-487000

1. Change of correspondence address or indication of "Fee Address" (37 CFR 1.363).
- ❑ Change of correspondence address (or Change of Correspondence Address form PTO/SB/122) attached.
- ❑ "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.**

2. For printing on the patent front page, list
(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 2 registered patent attorneys or agents. If no name is listed, no name will be printed.
1 _____
2 _____
3 _____

3. ASSIGNEE NAME AND RESIDENCE DATA TO BE PRINTED ON THE PATENT (print or type)

PLEASE NOTE: Unless an assignee is identified below, no assignee data will appear on the patent. If an assignee is identified below, the document has been filed for recordation as set forth in 37 CFR 3.11. Completion of this form is NOT a substitute for filing an assignment.

(A) NAME OF ASSIGNEE (B) RESIDENCE: (CITY and STATE OR COUNTRY)

Please check the appropriate assignee category or categories (will not be printed on the patent) : ❑ Individual ❑ Corporation or other private group entity ❑ Government

4a. The following fee(s) are submitted:
- ❑ Issue Fee
- ❑ Publication Fee (No small entity discount permitted)
- ❑ Advance Order - # of Copies _____

4b. Payment of Fee(s): **(Please first reapply any previously paid issue fee shown above)**
- ❑ A check is enclosed.
- ❑ 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 overpayment, to Deposit Account Number _____ (enclose an extra copy of this form).

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 PTO/SB/15A and 15B), issue fee payment in the micro entity amount will not be accepted at the risk of application abandonment.
- ❑ Applicant asserting 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.
- ❑ 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 micro entity status, as applicable.

NOTE: This form must be signed in accordance with 37 CFR 1.31 and 1.33. See 37 CFR 1.4 for signature requirements and certifications.

Authorized Signature _____ Date _____

Typed or printed name _____ Registration No. _____

PTOL-85 Part B (10-13) Approved for use through 10/31/2013. OMB 0651-0033 U.S. Patent and Trademark Office; U.S. DEPARTMENT OF COMMERCE

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.
14/024,985	09/12/2013	Juan Mantelle	041457-1016	7031

22428 7590 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

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. 14/024,985	Applicant(s) MANTELLE, JUAN	
	Examiner Melissa Fisher	Art Unit 1611	AIA (First Inventor to File) Status No

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

All claims being allowable, PROSECUTION ON THE MERITS IS (OR REMAINS) CLOSED in this application. If not included herewith (or previously mailed), a Notice of Allowance (PTOL-85) or other appropriate communication will be mailed in due course. **THIS NOTICE OF ALLOWABILITY 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.

1. ☒ This communication is responsive to *6/15/2017*.
   ☐ A declaration(s)/affidavit(s) under **37 CFR 1.130(b)** was/were filed on_____.
2. ☐ An election was made by the applicant in response to a restriction requirement set forth during the interview on _____; the restriction requirement and election have been incorporated into this action.
3. ☒ The allowed claim(s) is/are *1-9 and 21-26*. 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:
   1. ☐ Certified copies of the priority documents have been received.
   2. ☐ Certified copies of the priority documents have been received in Application No. _____ .
   3. ☐ Copies of the certified copies of the priority documents have 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 communication to file a reply complying with the requirements noted below. Failure to timely comply will result in ABANDONMENT of this application.
THIS THREE-MONTH PERIOD IS NOT EXTENDABLE.

5. ☐ CORRECTED DRAWINGS (as "replacement sheets") must be submitted.
   ☐ including changes required by the attached Examiner's Amendment / Comment or in the Office action of Paper No./Mail Date _____.

   Identifying indicia such as the application number (see 37 CFR 1.84(c)) should be written on the drawings in the front (not the back) of each sheet. Replacement sheet(s) should be labeled as such in the header according to 37 CFR 1.121(d).
6. ☐ DEPOSIT OF and/or INFORMATION about the deposit of BIOLOGICAL MATERIAL must be submitted. Note the attached Examiner's comment regarding REQUIREMENT FOR THE DEPOSIT OF BIOLOGICAL MATERIAL.

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 _____ .
5. ☒ Examiner's Amendment/Comment
6. ☐ Examiner's Statement of Reasons for Allowance
7. ☐ Other _____.

/Melissa Fisher/
Primary Examiner, Art Unit 1611

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 6/15/2017 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

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.

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

Issue Classification	Application/Control No.	Applicant(s)/Patent Under Reexamination
	14024985	MANTELLE, JUAN
	Examiner	**Art Unit**
	MELISSA JAVIER	1611

CPC						
Symbol					**Type**	**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					**Type**	**Set**	**Ranking**	**Version**
			/					
			/					

		Total Claims Allowed:	
(Assistant Examiner)	(Date)	15	
/MELISSA FISHER/ Primary Examiner.Art Unit 1611	06/22/2017	O.G. Print Claim(s)	O.G. Print Figure
(Primary Examiner)	(Date)	1	None

Issue Classification	Application/Control No.	Applicant(s)/Patent Under Reexamination
	14024985	MANTELLE, JUAN
	Examiner	**Art Unit**
	MELISSA JAVIER	1611

US ORIGINAL CLASSIFICATION		INTERNATIONAL CLASSIFICATION												
CLASS	SUBCLASS	CLAIMED					NON-CLAIMED							
		A	6	1	K	31 / 565 (2006.01.01)								
CROSS REFERENCE(S)		A	6	1	K	9 / 70 (2006.01.01)								
CLASS	SUBCLASS (ONE SUBCLASS PER BLOCK)													

(Assistant Examiner)	(Date)	Total Claims Allowed: 15	
/MELISSA FISHER/ Primary Examiner.Art Unit 1611	06/22/2017	O.G. Print Claim(s)	O.G. Print Figure
(Primary Examiner)	(Date)	1	None

Issue Classification	Application/Control No.	Applicant(s)/Patent Under Reexamination
	14024985	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	Original
1	1		17												
2	2		18												
3	3		19												
4	4		20												
5	5	10	21												
6	6	11	22												
7	7	12	23												
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9	9	14	25												
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	11														
	12														
	13														
	14														
	15														
	16														

		Total Claims Allowed:	
(Assistant Examiner)	(Date)	15	
/MELISSA FISHER/ Primary Examiner.Art Unit 1611	06/22/2017	O.G. Print Claim(s)	O.G. Print Figure
(Primary Examiner)	(Date)	1	None

UNITED STATES PATENT AND TRADEMARK OFFICE

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United States Patent and Trademark Office
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P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

BIB DATA SHEET

CONFIRMATION NO. 7031

SERIAL NUMBER	FILING or 371(c) DATE RULE	CLASS	GROUP ART UNIT	ATTORNEY DOCKET NO.
14/024,985	09/12/2013	424	1611	041457-1016

APPLICANTS
NOVEN PHARMACEUTICALS, INC., Miami, FL;

INVENTORS
Juan Mantelle, Miami, FL;

**** CONTINUING DATA ***************************
This application is a CON of 13/553,972 07/20/2012
which is a CON of 12/216,811 07/10/2008 PAT 8231906

**** FOREIGN APPLICATIONS ***************************

**** IF REQUIRED, FOREIGN FILING LICENSE GRANTED ****
09/26/2013

Foreign Priority claimed ☐ Yes ☑ No 35 USC 119(a-d) conditions met ☐ Yes ☑ No Verified and Acknowledged /MELISSA L JAVIER/ Examiner's Signature	☐ Met after Allowance Initials	STATE OR COUNTRY	SHEETS DRAWINGS	TOTAL CLAIMS	INDEPENDENT CLAIMS
		FL	1	11	2

ADDRESS

Foley & Lardner LLP
3000 K STREET N.W.
SUITE 600
WASHINGTON, DC 20007-5109
UNITED STATES

TITLE

TRANSDERMAL ESTROGEN DEVICE AND DELIVERY

FILING FEE RECEIVED		
1740	FEES: Authority has been given in Paper No._____ to charge/credit DEPOSIT ACCOUNT No._____ for following:	☐ All Fees ☐ 1.16 Fees (Filing) ☐ 1.17 Fees (Processing Ext. of time) ☐ 1.18 Fees (Issue) ☐ Other _____ ☐ Credit

EAST Search History

EAST Search History (Prior Art)

Ref #	Hits	Search Query	DBs	Default Operator	Plurals	Time Stamp
L1	3998	A61K9/7069.cpc.	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	OFF	2017/06/22 17:52
L2	16956	A61K31/565.cpc.	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	OFF	2017/06/22 17:52
L3	425	L1 and L2	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	OFF	2017/06/22 17:52
L4	48	L3 and flux	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	OFF	2017/06/22 17:52
L5	16100	estradiol and transdermal	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	OFF	2017/06/22 17:54
L6	5556	L5 and ("surface area" flux)	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	OFF	2017/06/22 17:54
L7	937	L6 and acrylic and silicone and (PVP polyvinyl pyrrolidone)	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	OFF	2017/06/22 17:54
L8	51	L7 and (estradiol NEAR flux)	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	OFF	2017/06/22 17:54
L9	188	Kanios.in. and David.in.	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	OFF	2017/06/22 17:54
L10	727	L5 and ("dipropylene glycol" oleyl)	USPAT; USOCR	OR	OFF	2017/06/22 17:55
L11	135	L7 and ("dipropylene glycol" oleyl)	USPAT; USOCR	OR	OFF	2017/06/22 17:55
L12	16100	estradiol and transdermal	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	OFF	2017/06/22 17:55
L13	5556	L12 and ("surface area" flux)	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	OFF	2017/06/22 17:55
L14	937	L13 and acrylic and silicone and (PVP polyvinyl pyrrolidone)	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	OFF	2017/06/22 17:55

6/22/2017 5:56:13 PM
C:\Users\mjavier\Documents\EAST\Workspaces\14024985.wsp

Search Notes	Application/Control No.	Applicant(s)/Patent Under Reexamination
	14024985	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)	5/14/2015	MJ
Inventor search in EAST	5/14/2015	MJ
Google Scholar search (keywords used: monolithic transdermal estradiol flux)	5/14/2015	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	9/9/2016	MJ
Updated Google Scholar search	9/9/2016	MJ
A61K9/7069.cpc. and flux	9/9/2016	MJ
A61K31/565.cpc. and flux	9/9/2016	MJ
Updated EAST search	12/22/2016	MJ
Updated Google Scholar search	12/22/2016	MJ
A61K9/7069.cpc. and flux	12/22/2016	MJ
A61K31/565.cpc. and flux	12/22/2016	MJ
Updated EAST search	4/17/2017	MF
Updated Google Scholar search	4/17/2017	MF
Updated EAST search	6/22/2017	MF

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

SEARCH NOTES		
Search Notes	**Date**	**Examiner**
Updated Google Scholar search	6/22/2017	MF

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 adhesive coat weight flux).clm.	9/9/2016	MJ
	(monolith$2 estradiol transdermal adhesive coat weight flux).clm.	12/22/2016	MJ
	(monolith$2 estradiol transdermal adhesive coat weight flux).clm.	4/17/2017	MF
	(monolith$2 estradiol transdermal adhesive coat weight flux).clm.	6/22/2017	MF

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

PTO/SB/08 (modified)

Substitute for form 1449/PTO				Complete if Known	
INFORMATION DISCLOSURE STATEMENT BY APPLICANT				**Application Number**	14/024985
Date Submitted: June 15, 2017				**Filing Date**	9/12/2013
				First Named Inventor	Juan Mantelle
(use as many sheets as necessary)				Art Unit	1611
				Examiner Name	Melissa L. Fisher
Sheet	1	of	1	Attorney Docket Number	041457-1016

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	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[6]
	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 03/23/2017 in application number 13/553,972 (US 2013/0156815)	
	A3	Office Action issued on 06/15/2017 in application number 14/870,574 (US 2016/0015655)	

Examiner Signature	/Melissa L Fisher/	Date Considered	06/22/2017

4848-1103-8538.1

ALL REFERENCES CONSIDERED EXCEPT WHERE LINED THROUGH. /M.L.F./

PART B - FEE(S) TRANSMITTAL

Complete and send this form, together with applicable fee(s), to: Mail **Mail Stop ISSUE FEE**
Commissioner for Patents
P.O. Box 1450
Alexandria, Virginia 22313-1450
or Fax (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.

CURRENT CORRESPONDENCE ADDRESS (Note: Use Block 1 for any change of address)

22428 7590 06/27/2017

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

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, must have its own certificate of mailing or transmission.

Certificate of Mailing or Transmission

I hereby certify that this Fee(s) Transmittal is being deposited with the United States Postal Service with sufficient postage for first class mail in an envelope addressed to the Mail Stop ISSUE FEE address above, or being facsimile transmitted to the USPTO (571) 273-2885, on the date indicated below.

(Depositor's name)
(Signature)
(Date)

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
14/024,985	09/12/2013	Juan Mantelle	041457-1016	7031

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

EXAMINER	ART UNIT	CLASS-SUBCLASS
FISHER, MELISSA L	1611	424-487000

1. Change of correspondence address or indication of "Fee Address" (37 CFR 1.363).
- ☐ Change of correspondence address (or Change of Correspondence Address form PTO/SB/122) attached.
- ☐ "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.**

2. For printing on the patent front page, list
(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 2 registered patent attorneys or agents. If no name is listed, no name will be printed.

1 Foley & Lardner LLP
2
3

3. ASSIGNEE NAME AND RESIDENCE DATA TO BE PRINTED ON THE PATENT (print or type)

PLEASE NOTE: Unless an assignee is identified below, no assignee data will appear on the patent. If an assignee is identified below, the document has been filed for recordation as set forth in 37 CFR 3.11. Completion of this form is NOT a substitute for filing an assignment.

(A) NAME OF ASSIGNEE: Noven Pharmaceuticals, Inc.

(B) RESIDENCE: (CITY and STATE OR COUNTRY): Miami, FLORIDA

Please check the appropriate assignee category or categories (will not be printed on the patent) : ☐ Individual ☒ Corporation or other private group entity ☐ Government

4a. The following fee(s) are submitted:
- ☒ Issue Fee
- ☐ Publication Fee (No small entity discount permitted)
- ☐ Advance Order - # of Copies _____

4b. Payment of Fee(s): **(Please first reapply any previously paid issue fee shown above)**
- ☐ A check is enclosed.
- ☒ 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 overpayment, to Deposit Account Number 19-0741 (enclose an extra copy of this form).

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 PTO/SB/15A and 15B), issue fee payment in the micro entity amount will not be accepted at the risk of application abandonment.
- ☐ Applicant asserting 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.
- ☐ 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 micro entity status, as applicable.

NOTE: This form must be signed in accordance with 37 CFR 1.31 and 1.33. See 37 CFR 1.4 for signature requirements and certifications.

Authorized Signature Courtenay C. Brinckerhoff Date June 27, 2017

Typed or printed name Courtenay C. Brinckerhoff Registration No. 37,288

PTOL-85 Part B (10-13) Approved for use through 10/31/2013. OMB 0651-0033 U.S. Patent and Trademark Office; U.S. DEPARTMENT OF COMMERCE

Electronic Patent Application Fee Transmittal

Application Number:	14024985
Filing Date:	12-Sep-2013
Title of Invention:	TRANSDERMAL ESTROGEN DEVICE AND DELIVERY
First Named Inventor/Applicant Name:	Juan Mantelle
Filer:	Courtenay C. Brinckerhoff
Attorney Docket Number:	041457-1016

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($)
Extension-of-Time:				
Miscellaneous:				
			Total in USD ($)	**960**

Electronic Acknowledgement Receipt

EFS ID:	29623707
Application Number:	14024985
International Application Number:	
Confirmation Number:	7031
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:	041457-1016
Receipt Date:	27-JUN-2017
Filing Date:	12-SEP-2013
Time Stamp:	17:34:14
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	062817INTEFSW17345600
Deposit Account	190741
Authorized User	Katie Newcomb

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

37 CFR 1.16 (National application filing, search, and examination fees)

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.)
1	Issue Fee Payment (PTO-85B)	1016_IF.pdf	71345 0a3ca541ccd1c033b9c7ffbd57fdb1b2c3d19caa	no	1
Warnings:					
Information:					
2	Fee Worksheet (SB06)	fee-info.pdf	30781 1abb165082b147f4d7e0ec26cd012ae35e8d247b	no	2
Warnings:					
Information:					
		Total Files Size (in bytes):	102126		

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.

PTO/SB/08 (09-06)
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

INFORMATION DISCLOSURE STATEMENT BY APPLICANT

Date Submitted: April 7, 2014

(use as many sheets as necessary)

Sheet 1 of 4

Complete if Known	
Application Number	14/024,985
Filing Date	09/12/2013
First Named Inventor	Juan Mantelle
Art Unit	1615
Examiner Name	Unassigned
Attorney Docket Number	041457-1016

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
	A1	2013/0156815	06/20/2013	MANTELLE	
	A2	8,231,906	07/31/2012	MANTELLE	
	A3	8,343,538	~~04/13/2006~~	KANIOS ET AL. January 1, 2013	
	A4	5,446,070	08/29/1995	MANTELLE	
	A5	4,915,950	04/1990	MIRANDA ET AL.	
	A6	6,562,363	05/13/2003	MANTELLE ET AL.	
	A7	6,221,383	04/24/2001	MIRANDA ET AL.	
	A8	6,235,306	05/22/2001	MIRANDA ET AL.	
	A9	2005/0169977 A1	08/04/2005	KANIOS	
	A10	2005/0129749 A1	06/16/2005	STRAUSS	
	A11	2006/0240087 A1	10/26/2006	HOUZE ET AL.	
	A12	2006/0233870 A1	10/19/2006	HOUZE ET AL.	
	A13	4,994,278	02/19/1991	SABOLTSKY ET AL.	
	A14	4,494,278	2/19/1991	SABLOTSKY ET AL.	
	A15	5,300,291	4/5/1994	SABLOTSKY ET AL.	
	A16	5,958,446	9/28/1999	MIRANDA ET AL.	
	A17	5,474,783	12/12/1995	MIRANDA ET AL.	
	A18	4,814,168	3/21/1989	SABLOTSKY ET AL.	
	A19	4,994,267	2/19/1991	SABLOTSKY	
	A20	~~5,565,286~~ 5,656,286	8/12/1997	MIRANDA ET AL.	
	A21	6,024,976	2/15/2000	MIRANDA ET AL.	
	A22	6,337,086	1/8/2002	KANIOS ET AL.	
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Change(s) applied to document, /N.B.H./ 11/2/2015

Examiner Signature		Date Considered	

*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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4852-6538-3706 ALL REFERENCES CONSIDERED EXCEPT WHERE LINED THROUGH. /M.J./

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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.

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