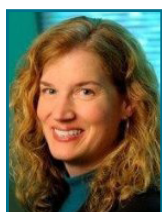


5th Annual Transdermal & Intradermal Drug Delivery Systems 2018

Advanced Design, Development & Delivery
of Skin-Mediated Therapies and Vaccines

September 6–7, 2018, Racquet Club of Philadelphia, PA

Featured Speakers Include:



Audra Stinchcomb
University of Maryland



Bobby Singh
Corium



Lisa Dick
3M



Ajay Banga
Mercer University



Narasimha Murthy
University of Miss.



Conor O'Mahoney
Tyndall National Institute

With Comprehensive Coverage On:

- Product Development and Quality Control Expectations with Respect to Transdermal and Topical Systems
- Meeting USP <661.2> Specifications for Transdermal Packaging Systems--a Case Study
- Dermal Penetration Enhancers – Key Formulation Considerations
- Clinical PKPD Aspects of Transdermal Delivery
- Semisolids to Patches to Delivery Technologies: Unique IVPT Challenges As We Adapt the Franz Cell
- Smart Microsystems for Transdermal Delivery & Diagnostics
- Latest Advances in Microneedle Drug and Vaccine Delivery
- Mechanisms of Dermal and Transdermal Absorption of Drugs
- Resolving Regulatory Compliance Issues for TDD & IDD Systems
- Regulatory and Experimental Considerations for Extractable and Leachable Analysis of Microneedle Patches: A Case Study
- And much more!

The growing interest in alternative routes of drug administration has experts predicting that the market for transdermal and intradermal drug delivery systems will exceed \$30 billion in 2020. The industry is on the threshold of bringing into commercial production a new generation of transformative TDD and IDD therapies and delivery systems. That is why you cannot afford to miss this two-day intensive conference. Pharma Ed brings together leading researchers in the field to share the most recent advances in the design, formulation, and delivery of skin-mediated therapies and vaccines.

With Representation From:



Thursday, September 6, 2018

8:00 *Complimentary Breakfast & Chairperson's Welcome and Opening Remarks*

Spotlight on IVPT—Key Challenges and Opportunities

8:30 **Semisolids To Patches To Delivery Technologies: Unique IVPT Challenges as we Adapt the Franz Cell**
Dr. Ajay Banga, Chair & Professor of Pharmaceutical Sciences, Mercer University

In vitro permeation testing (IVPT) in Franz diffusion cells typically involves study of drug transport into and across skin from dermatological formulations. Experimental design considerations include type of skin (or membrane), spread ability of formulation, occlusion, and sink conditions in receptor chamber, to name just a few. As we adapt the Franz cells for other uses, additional considerations and challenges need to be considered. For example, rubbing a formulation may be difficult and a spray dosage form may be hard to apply. With a transdermal patch, exposed vs. total surface area needs to be considered and the patch may not remove easily from epidermis for assay of skin. Delivery technologies or in vitro microdialysis bring additional unique challenges. When using microneedles, it may be advisable to use dermatomed skin rather than epidermis. Iontophoresis may need a larger infinite volume placed in donor chamber in some cases. These and other challenges will be discussed.

9:10 **Microstructural Characterization and In Vitro Permeation Testing of Topical Products**
S. Narasimha Murthy Ph.D., Professor of Pharmaceutics and Drug Delivery, University of Mississippi; Scientific Advisor, Topical Products Testing LLC

The topical products that are compositionally similar could differ in terms of arrangement of matter depending on the process variables. The generic products are generally required to match the reference product (RLD) with respect to all the quality attributes to be able to match the performance attributes of the RLD. In Vitro Permeation Studies (IVPT) is a great tool for testing the bioavailability/bioequivalence of topical products. In this presentation, some of the microstructural characteristics, case studies and development of an IVPT protocol for testing topical products will be discussed.

9:50 **Maximizing Your Chances of Success in Topical Product Development**
Dr. Jon Lenn Ph.D., Senior Vice President for US Operations, MedPharm

Topical product development presents a suite of challenges. This presentation will highlight key considerations in:

- API design and selection
- Importance of preformulation and baseline understanding
- Formulation selection; the drug, the patient, the disease, & the market
- Performance testing models for formulation optimization and selection
- In vivo models – how relevant are they?

10:30 *Networking Coffee Break*

10:55 **Dermal Penetration Enhancers – Key Formulation Considerations**
Jasmine Musakhanian, Scientific & Marketing Director, Gattefossé USA

The growing interest in percutaneous absorption is a reflection of a growing need for alternative routes of administration to facilitate delivery of challenging molecules that suffer from poor oral bioavailability. Assisting the passage of a molecule to or across the skin however comes with its own unique set of challenges, especially if the objective is to deliver the drug in a safe and non-invasive manner. This presentation explores the role of penetration and permeation enhancing excipients in modulating the delivery of different types of molecules. Providing examples and case studies, the presentation highlights the key issues; implications of drug solubilization vs. dispersion in the vehicle; selection of vehicle type(s); and possible synergies between select combinations of excipients to drive molecules' diffusion, partitioning, penetration, and permeation.

Regulatory Spotlight—Meeting USP Guidelines for Transdermal Packaging

11:35 **Meeting USP <661.2> Specifications for Transdermal Packaging Systems—a Case Study**
Dr. Michael Ruberto, Material Needs Consulting; Lars Christensen, Technical Director, Danapak Flexibles A/S

Abstract Coming Soon

12:15 *Complimentary Networking Lunch*

Spotlight on Microneedle Delivery Systems—The Current State of Clinical Trials

1:25 **Clinical PKPD Aspects of Transdermal Delivery**
Dr. Bobby Singh, Ph.D., Chief Technology Officer, Corium International

Abstract Coming Soon

2:05 **Recent Advancements in Intradermal Delivery of Biopharmaceuticals**
Lisa Dick, Ph.D., Lab Manager & Technology Leader, 3M Drug Delivery Systems

Abstract Coming Soon

Research Spotlight—Dissolving Microneedles

2:45

Dissolving Microneedles for Pharmaceutical Drug Delivery

Dr. Hyungil Jung, Professor, Yonsei University; CEO, Juvic Inc., South Korea

Dissolving microneedles are referred to micro-scale needles that are capable of delivering pharmaceutical compounds, proteins and other large biomolecules into the skin in a minimally invasive manner. These microneedles depending on their matrix backbone structure may take from seconds to hours to dissolve, providing fast or sustained release functionalities. Based on recent researches, achievement of a highly efficient delivery has become possible via dissolving microneedles and it is expected that microneedles would replace the widely used hypodermic needles in the near future. Also dissolving microneedles have various potentials, the activity of encapsulated compounds can be significantly reduced during fabrication process. Therefore, we have evaluated and optimized dissolving microneedle fabrication factors by which activity of encapsulated compounds including lysozyme, exendin-4, etc. can be highly maintained throughout the fabrication process. We have also developed dissolving microneedles capable of delivering valproic acid that showed a higher efficiency compared with topical application. Overall, our focus is on developing new methods to overcome the limitations of traditional microneedle systems through novel technologies.

3:25

Afternoon Networking & Coffee Break

3:50

Vaccination Using Dissolving Microneedle Patches

Dr. Yasmine Gomaa, Research Scientist, School of Chemical & Biomolecular Engineering, Georgia Tech

There is arguably no single preventive health intervention more cost-effective than immunization. It currently prevents between 2-3 million deaths every year. An additional 1.5 million deaths could be avoided, however, if global vaccination coverage is improved. Currently, almost all recommended vaccinations are administered by injection which is a major setback especially in developing countries lacking the required infrastructure, resources in addition to the pain and phobia associated with the injection. This urges the need for advanced technologies that can ease logistics, reduce the cost of vaccinations and improve acceptability. Dissolving Microneedle (DMN) patches are a novel skin delivery technology for vaccines that has been developed throughout the past years. When applied to skin, the needles penetrate the skin layers and dissolve releasing the vaccine cargo. This technology offers numerous advantages over the traditional needle and syringe used to administer vaccines. Being a small single dose unit that fully dis-

solve after insertion would increase the vaccination safety and reduce transportation and waste costs. With the proper vaccine formulation in the DMN patch, the need for a cold chain of storage and transportation can be alleviated which constitute a large sector in the vaccination campaigns costs. Furthermore, administration of DMN patches is simple, requires minimal training and painless.

Our lab has recently published the first-in-man study on influenza DMN patches showing well tolerance, robust immune response and superior acceptability of the DMN patch compared to the conventional influenza vaccination with needle and syringe. With advances in the microneedle vaccine delivery technology, vaccination coverage and disease eradication are expected to increase.

4:30

End of Day One

Friday, September 7, 2018

8:00

Complimentary Breakfast

Research Spotlight—Immunotherapies & Smart Microsystems

8:30

Cutaneous Peanut Allergen Immunotherapy using Coated Microneedles

Dr. Harvinder Gill, Associate Prof., Texas Tech University

Peanut allergy is a life-threatening condition. About 1% of the US population (~3 million people) has peanut allergies, and there is no FDA-approved treatment. Strict avoidance, and a peanut-free diet is the only option available to manage peanut allergies. We have recently hypothesized that microneedles (MNs) can be used to deliver peanut allergen into the skin for cutaneous peanut immunotherapy. In this presentation, in vivo efficacy data from the use of MNs coated with peanut allergen in a mouse model of peanut sensitization will be shared. Balb/c mice were first sensitized to peanut allergen. They were then treated with multiple doses of peanut allergen delivered into their skin using coated MNs. Peanut IgG (total IgG, IgG1, and IgG2a) and IgE levels were measured. Efficacy of treatment was evaluated by challenging the mice orally with peanut proteins. Anaphylactic score, serum mast cell protease 1 (MCPT-1) and serum histamine levels were quantified after oral challenge. IgE levels were also monitored. It was found that MNs treatment induced significantly higher IgG antibodies without any significant increase in IgE levels as compared to untreated mice (naïve mice). Significantly lower anaphylactic score, MCPT-1, and histamine levels in serum were observed in MN-treated mice after the mice were orally challenged with peanut proteins, as compared to untreated mice (sensitized but untreated). The data of this study shows that MN-based cutaneous allergen immunotherapy is able to offer protection against

oral peanut challenge, and overall it is an exciting new technology that has potential to treat food allergies.

9:10 Smart Microsystems for Transdermal Delivery & Diagnostics

Conor O'Mahony, Senior Scientist, Tyndall National Institute

It is striking that expensive and frequently prescribed drugs are still provided in rather basic delivery devices (i.e. conventional syringes or pen injectors) that incorporate no diagnostic capability and that provide little or no feedback regarding patient compliance.

In response to these limitations, Micro Transdermal Interface Platforms (MicroTIPs) will merge microneedle technologies with wearable and flexible electronics to form intelligent, patch-like systems, capable of independently diagnosing physiological conditions and autonomously delivering relevant therapeutic doses, while simultaneously relaying information to clinical supervisors using wireless protocols. As well as microneedle arrays for transdermal delivery, biopotential monitoring and interstitial diagnostics, other ancillary subsystems for ultraprecise fluidic control, data analysis, power management, system validation, and wireless radio management are required. All of these must be integrated and packaged in a flexible and unobtrusive form factor.

This presentation identifies areas where new and emerging microneedle technologies and electronics could be used in such platforms, and summarizes recent progress at Tyndall towards various aspects of MicroTIPs technology.

9:50 *Networking Coffee Break*

10:15 Update on a Long-Term Safety Trial Using a Microneedle System

Peter Schmidt, Senior Director, Medical Affairs, Zosano Pharma

Zosano Pharma has been conducting a long-term (12 month) safety trial of its ADAM zolmitriptan microneedle system. The primary purpose of the trial is to quantify the skin safety/tolerability of the ADAM system in subjects treating at least 2 migraines per month. As of September 2018, we will have treated over 250 subjects in this trial. We will present an overview of skin tolerability seen to date.

10:55 In Vitro - In Vivo Correlation (IVIVC) of Transdermal Nicotine, Fentanyl, Lidocaine, and Diclofenac in Healthy Human Volunteers

Audra Stinchcomb, Ph.D., Chief Scientific Officer and Founder of F6 Pharma Inc.; Professor, University of Maryland

We have determined drug concentrations in healthy human volunteers by pharmacokinetic and skin (tape) stripping analyses. This data was then compared for its

correlation with carefully harmonized in vitro skin permeation tests. The effect of transient heat application on the absorption rates in vitro and in humans was also evaluated. The IVIVC from this large harmonized dataset will be discussed.

11:35 Dermaject® Intradermal Injection Device Enables Reproducible And Standardized Intradermal Injections In Ex Vivo Skin

Markus Clemenz, Managing Director, Verapido

Dermaject® intradermal injection device is a novel, CE marked and convenient device for intradermal injections into the top layer of the skin (intradermal / intracutaneous route). This best in class device features a newly developed and patented cannula insertion mechanism, mimicking the Mantoux injection method, combined with microneedle technology. A special mechanism was developed to protect against needlestick injuries. The design is compact and intended for single use in humans. Intradermal injections with dermaject® in ex vivo human skin were located superficially and showed a low variance of the distance to the skin surface, thus demonstrating reproducibility and standardization for intradermal injection depth. Therefore dermaject® is a highly relevant solution for all parenteral substances injected via the intradermal route.

12:15 *Complimentary Networking Lunch*

Extractables & Leachables Testing for TDDS—What You Need to Know

1:15 Extractable and Leachable Testing for Transdermal Drug Delivery Systems: How to Resolve FDA Deficiency Situations Related to Those Issues

Gyorgy Vas, Ph.D., Trace Organic Analytical Group, Intertek Pharmaceutical Services (Contributing Authors: Louis Fleck, Howard Carpenter.)

Transdermal drug delivery systems are relatively complex pharmaceutical products. The formulation contains multiple excipients and in addition a dermal contact adhesive. The performance of the delivery systems depends on the quality of the dermal adhesive and the formulation, which delivers the drug on a pre-determined rate.

The dermal delivery route is getting more and more popular, since the effect of the delivered drug can be localized, which may reduce the systemic side effects. However since the formulation has extended contact time, besides the drug is being delivered excipients, degradation products and packaging related components can also be "delivered" with the same route of administration.

The extractable testing of transdermal systems are straightforward, does not requires "out of box" thinking. The leachables testing requires more complex approaches, as the regulatory expectation is to test the finished

products with biologically relevant extraction media. The presentation will focus on different test approaches, to present options for leachable testing, how to evaluate the actual leachables and validate analytical methods what are requires non-routine extraction methods and as well detection capability down to ppb level.

The complex formulation combined with the low level testing requirement are very challenging analytical task. Component identification, analytical method development and validation are not as simple as for the components present at a ppm level or above. The presentation will also presenting case studies and solutions for non-conformance situations related to TDS systems.

1:50

Regulatory and Experimental Considerations for Extractable and Leachable Analysis of Microneedle Patches: A Case Study

Dr. Xiao Jia, Analyst, EKG Labs

In recent months, microneedle patches have been making headlines for their potential future as a drug delivery platform. Microneedle patches currently find their widest application as cosmetic delivery devices, and their developers are not required to seek approval from the FDA. Due to the lack of regulatory requirements, there is little information about the extractable profiles of these devices. Assuming these patches gain traction as a drug delivery platform, the FDA will undoubtedly require extractable evaluation of these devices.

Extractables are substances in a device or product, potentially impacting its safety or efficacy, which can be forced out using certain solvents or stressed conditions. Regulatory bodies often require in-depth analytical investigations into the extractable profile of devices and products in order to get a full profile of the potential hazards associated with a medical product and to ensure patient and consumer safety.

EKG Labs performed an extractable evaluation on two brands of commercially available microneedle patch cosmetic devices. Rodan+Fields's "Redefine Acute Care Skincare for Expression Lines" claims to hold themselves to FDA standards while ARTPE's "Renutrive 3D Microsome Eyepatch" is not sold in the United States but is available to purchase through online retailers. Testing was performed under the general guidance of ISO 10993-12. Patches were extracted at 37°C in both hexane (a nonpolar solvent) and ethanol (a polar solvent) alongside method controls. After extraction times of 24 hours, 48 hours, and 96 hours, sample and control extracts were analyzed via LC/MS and GC/MS. Additional nitric acid digestions were analyzed via ICP/MS. Finally, SEM imaging was performed on the samples.

2:25

Afternoon Networking Break

2:40

Critical Issues—Latest Advances in Semisolid Topical Formulations

Old and New Excipients for Dermal and Transdermal Drug Delivery

Nancy S. Marchant Ph.D., Global Technology Manager, Lubrizol LifeSciences

Delivery of actives to and through the skin for cosmetic and therapeutic applications has been a focus of Lubrizol Corp. for over 50 years. Carbopol® Polymers are used to formulate a wide variety of semisolid applications to increase mucosal retention (buccal, vaginal, and ophthalmic), stabilize suspensions and emulsions, and improve the sensory of topical semisolid formulations. Recently, Lubrizol has focused on our Thermoplastic Polyurethane (TPU) polymers that are used for breathable wound care and implantable medical device applications for use in transdermal drug delivery. We have demonstrated the advantages of TPU via in vitro testing for rapid delivery hydrogel films as well as controlled release mixed matrix drug in adhesive patches. Examples of our polymers and demonstration of efficacy in dermal and transdermal formulation will be presented.

3:20

Topical Dermatological Generic Drug Products: Advances demonstrating In Vitro Bioequivalence (Beyond the in vivo Clinical Endpoint Bioequivalence Study)

Theo Kapanadze D.Sc., Ph.D., Chief Scientific officer, NDI ADRL Inc. dba Diteba

Bioequivalence assessment of locally acting topical dosage forms is challenging. Historically, there were limited options for alternate approaches to clinical endpoint BE studies. Regulatory agencies recognized the need to find more sensitive and efficient surrogate approaches to demonstrate BE for topical dermatological products. US FDA Develops science-based regulatory standards that address product complexities and manufacturing issues, reducing the barrier for new generic drug development and provides new valid and reproducible In Vitro approaches for topical generic product equivalence. In order to meet new regulatory requirements, an In Vitro Release Testing (IVRT) methodology as well as Percutaneous Absorption, using human skin In Vitro permeation (IVPT) model should be appropriately developed and validated. Having an appropriate validated IVRT/IVPT methods is mandatory for topical products development and FDA approval. This presentation is outlines specifics of developing and validating such In Vitro methodologies.

4:00

Close of Program

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