

Microneedle, Transdermal & Intradermal Drug Delivery Systems 2019

Advanced Design, Development & Delivery of Skin-Mediated Therapies and Vaccines
September 18–19, Metro Meeting Centers, Boston, MA

Featuring Lessons Learned & Case Studies From Industry Experts



Audra Stinchcomb
University of Maryland



Mikolaj Milewski
Merck



Lisa Dick
3M



Ryan Donnelly
Queens College



Nicky Bertolo
Latch Medical



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Donald Kellerman
Zosano Pharma



Ajay Banga
Mercer University



Harvinder Gill
Texas Tech



Jasmine Musakhanian
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Leandro Santos
Incyte Corporation



Gyorgy Vas
Intertek



Michael Schrader
Vaxess Technologies



Michael Ruberto
Material Needs



Courtney Jarrahan
Path



Tanima Sinha
Dept. of Health & Human Services

And Comprehensive Coverage On:

- Next Generation MN Systems: Delivering High Drug Doses Transdermally Using Microarray Patches
- In Vitro Permeation Testing in Dermal Drug Discovery and Development
- Overcoming Unique Challenges Facing Skin Delivery Systems
- Delivering Therapeutic Peptides—A Case Study Using a Solid Microstructured TD System
- Latest Advances in Microneedle Drug and Vaccine Delivery
- Optimizing Dissolving Microneedles & Coated Microneedles for Drug Delivery
- Improving Formulation Design in Dermal/Transdermal Drug Delivery
- Mechanisms of Dermal and Transdermal Absorption of Drugs
- Regulatory and Experimental Considerations for Extractable and Leachable Analysis of TDD Systems
- Exploring the Therapeutic Potential of Cannabinoid Medicines Via Skin Delivery
- And 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:



Wednesday, September 18, 2019

8:15 *Complimentary Breakfast & Chairperson's Welcome and Opening Remarks*



Michael Eakins, President, Eakins & Associates

Key Challenges and Opportunities in Non-Invasive Skin Delivery

8:45 *Overcoming Unique Challenges facing Skin Delivery Systems*



Dr. Ajay Banga, Chair & Professor of Pharmaceutical Sciences, Mercer University

Unique challenges facing non-invasive delivery of lipophilic and hydrophilic drugs into skin will be discussed. These challenges and potential solutions will be presented by way of examples from our research and will include discussion of delivery of an extremely lipophilic drug past epidermis into dermis, and requirements of drug loading vs. drug crystallization in pressure sensitive adhesives to design 7-day transdermal patches. Adapting in vitro permeation testing in Franz cells to accommodate delivery technologies such as iontophoresis, conducting in vitro microdialysis, and addressing practical issues of rubbing, spreadability, lateral diffusion of drugs in skin, and considerations relating to size and isoelectric point of polypeptide drugs vs. skin pH will also be discussed.

9:25 *Role of Drug, Excipient, and Formulation Design in Dermal/Transdermal Delivery*



Jasmine Musakhanian, Scientific & Marketing Director, Gattefossé USA

With the few and far between trailblazing successes in transdermal products, the prospects of drug delivery across the skin in a non-invasive manner may appear unattainable for most API. Fortunately, the prospects are changing, given the huge body of work in recent years that have improved understanding of the skin physiology and the potential pathways for overcoming its barrier properties.

Also, progress has been made in the evaluation and characterization methods for assessing the suitability of one or another permeation enhancer relative to the drug at hand. Combined, these advances enable a retrospective analysis of the past publications under a new light, arriving therefore at guiding principles in formulation design which were not possible before. This presentation highlights the implications of drug solubilization vs dispersion in the vehicle; selection of vehicle type(s);

and possible synergies between excipients to drive molecules' diffusion, partitioning, penetration, and permeation. Providing examples and case studies, this presentation explores the interpolations between the skin barrier properties, drug chemistry, and the excipient/solubilizer choices that could help modulate the delivery of different types of molecules.

10:05 *Exhibit Viewing & Networking Coffee Break*

Critical Issues—IVPT: Its Role in Drug Discovery & Development

10:40 *In Vitro Permeation Testing in Dermal Drug Discovery and Development*



Leandro Santos, Associate Director, Clinical Sciences, Incyte Corporation

In vitro permeation testing (IVPT) has been used in the evaluation of semi-solid formulations, transdermal and microneedle patches for over forty years and, while different apparatuses are available, the underlying concept is the same: a test article is applied on top of a biological membrane/appendage (e.g. skin, nail), which interfaces with donor (occluded or non-occluded) and receptor compartments; the latter is where the receiving fluid (buffer) is present and can follow a static or flow-through configuration.

Considered a low-throughput technique, IVPT has some limitations in a discovery environment where multiple compounds and prototype formulations must be quickly screened during lead generation/optimization and drug development. Such barriers can be overcome by in silico prioritization/selection of compounds, as well as improved bioanalytical and automation workflows. Additionally, IVPT data should always be put into context of other in vitro or in vivo models that can complement pharmacokinetic results with pharmacodynamic endpoints, yielding to early PK/PD correlations as a de-risking development strategy. This presentation aims at discussing IVPT workflows used in dermal drug discovery across different topical dosage forms, and approaches on how to properly contextualize such results.

11:20 *Experience Over 12 Months with Repeated Application of a Microneedle System in Phase III Trial*



Donald Kellerman, Vice President, Clinical Development, Zosano Pharmaceuticals

Zosano Pharma recently completed a 12-month, phase III safety study of Qtrypta – zolmitriptan delivered intracutaneously via microneedles. We will present select safety results, specifically pertaining to application site findings after repeated administration.

12:00 *Complimentary Networking Lunch*

Technology Spotlight—The Present & Future of Microneedle Drug Delivery

1:05

Coated Microneedles: The Technology, its Current Status and Future Potential



Dr. Harvinder Gill, Assoc. Professor and Whitacre Endowed Chair of Science & Engineering, Texas Tech University

Coated microneedles can be used to deliver therapeutics through the skin. The focus of this talk is to provide an overview of the microneedle coating technology, where it stands now, and what lies ahead. Primary design considerations for developing microneedle coatings will be presented, and different coating methods that have been developed to make coatings on microneedles will be discussed along with their pros and cons. Some case illustrations will be presented to highlight both the current status and potential products that may emerge in the recent future based on the coated microneedle technology.

1:40

Optimizing the Coating of a Novel Interlocking Microneedle Patch for Transdermal Drug Delivery Applications



Dr. Nicky Bertollo, CEO, Latch Medical (Co-Authors: Manita Dangol, Amy Ni Chuinneagain, Eoin O’Cearbhaill)

Microneedle-facilitated transdermal drug delivery offers substantial potential benefits including painlessness, patient compliance and controlled release. Particularly, solid metallic microneedles are of interest due to their biocompatibility and high mechanical strength. Coating these metallic microneedles allows delivery of drugs in solid, dry and stable state thus abolishing the need for cold chain storage, especially desirable for protein drugs and vaccines. Conventionally, microneedles are designed to perpendicularly insert into skin and fabricated predominantly utilizing micro-molding and lithographic techniques. However, only 10–30% of the microneedle length routinely penetrates the skin, a factor that is often masked by local tissue deformation. Consequently, payload deliver is often highly variable.

Exploiting a novel insertion mechanism, we have developed a two-component microneedle system, with angled microneedles that are designed to interdigitate in the tissue once the components are clicked together. This interlocking microneedle patch (IMP) offers full near full-microneedle-length penetration and robust adhesion to skin without damaging the tissue and which can be removed by reversing the clicking mechanism. Here, we report a new drug delivery system compatible with IMPs, in which drug is coated using a controlled dripping method. Key technical benefits of this system offer enhanced drug dosing and loading high molecular weight protein drugs. The goal of the present work is to assess the technical feasibility of a coated IMP drug delivery system.

Laser sintered SLS 3D printing (MLabs, Germany) was used for the fabrication of stainless steel (316L) IMPs. The printed microneedles were electropolished at 2.5 A for 90 sec (Esma E972, USA). Fluorescein isothiocyanate (FITC) was used as a model dye. A coating formulation containing Carboxymethyl Cellulose (CMC) and Poloxamer 188 (Sigma Aldrich, Ireland) was coated using a controlled droplet dripping method in which optimized volume of the formulation was dropped manually onto each MN and dried at RT overnight. The uniformity in coating was visually confirmed using Fluorescence Microscopy (Olympus, USA). The coated IMP was applied to porcine skin to confirm penetration of the coated IMP in an ex vivo model.

Both interdigitating components of the interlocking microneedle patch were coated with controlled dripping method resulting into a uniform coating of each MNs from shaft to the tip. A rapid dissolution of FITC was observed within 5 min. Application of IMP manually onto the porcine allowed the penetration and diffusion of FITC into the skin.

The successful coating of a model dye onto IMPs and diffusion into the skin demonstrates the potential of utilizing this platform for transdermal drug delivery purposes.

2:15

Delivering High Drug Doses Transdermally Using Microarray Patches



Dr. Ryan Donnelly, Chair in Pharmaceutical Technology, Queen’s University Belfast

This presentation describes production of unique microneedle array patches prepared from cross-linked poly(methylvinylether-co-maleic acid) which contain no drug themselves. Instead, they rapidly take up skin interstitial fluid upon skin insertion to form continuous, unblockable, hydrogel conduits from attached patch-type drug reservoirs to the dermal microcirculation. Importantly, such microneedles, which can be fabricated in a wide range of patch sizes and microneedle geometries, can be easily sterilised, resist hole closure while in place and are removed completely intact from the skin. Delivery of macromolecules is no longer limited to what can be loaded into the microneedles themselves and transdermal drug delivery is now controlled by the crosslink density of the hydrogel system rather than the stratum corneum, while electrically-modulated delivery and the potential for minimally-invasive extraction of skin interstitial fluid for monitoring purposes are also unique features. This technology has the potential to overcome the limitations of conventional microneedle designs and greatly increase the range of type of drug deliverable transdermally, with ensuing benefits for industry, healthcare providers and, ultimately, patients. A second important technology to be described here is high dose dissolving microneedles, used to deliver long-acting nanoparticles into the viable skin layers for sustained administration of clinically-relevant doses over weeks or months. This technology has clear utility in prevention and treatment of HIV, contraception and management of schizophrenia, amongst several other indications.

2:55 *Exhibit Viewing & Networking Coffee Break*

3:20 **Solid Microstructured Transdermal System for delivery of a therapeutic peptide and preclinical pharmacokinetics**



Lisa Dick, Lab Manager & Technology Leader, 3M Drug Delivery Systems & Mikolaj Milewski, Principal Scientist, Merck

The skin has long been recognized as a target for local and systemic drug delivery. The transdermal route of drug administration is, however, limited by the substantial barrier properties of the skin. Physiologically beneficial protection that the skin provides against xenobiotic permeation is a drawback from the perspective of transdermal transport of therapeutic agents. One of the technologies that enables temporary breach of the skin barrier and effective drug delivery is microneedles (MN).

This talk discusses how two companies collaborated to progress the development of a peptide drug product which had physical and chemical stability challenges as a solution formulation. Here we report development of a MN array (solid Microstructured Transdermal System, sMST), a peptide formulation coating on the tips of the MN, and preclinical pharmacokinetic assessment in Yucatan minipigs. In vivo delivery from peptide coated sMST was accompanied by a transient, self-resolving skin irritation, and yielded high absolute bioavailability reaching 88% and 74% for two coated sMST formulations as compared to a 75% for a subcutaneous injection. Also, the stability of the peptide was substantially improved when coated on the sMST system with minimal degradation recorded at room temperature versus a liquid-state subcutaneous formulation. The present work highlighted that microneedles can offer a viable alternative delivery option for a peptide therapeutic with improved stability and excellent delivery efficiency.

4:00 **Efficient Delivery of an Encapsulated Pharmaceutical Using Dissolving Microneedles**



Dr. Hyungil Jung, Professor, Yonsei University & CEO Juvic, Inc.

Dissolving microneedles (DMNs) are tiny needles capable of delivering medicines in a minimally invasive manner. The dissolution time required for DMNs, based on their backbone polymer generally takes up to 2 hours. Additionally, by adjusting the backbone polymer it would be possible to achieve a fast or sustained release

functionalities. Traditionally, DMNs were fabricated over patches for application over the skin. The DMN patches and stiffness properties of skin however, prevents DMNs from complete skin insertion, highly reducing the delivery efficiency of encapsulated compounds.

To improve delivery efficiency of encapsulated medicines, "Microlancer", a micro-pillar based DMN applicator was developed. Microlancer is a patchless, self-administered DMN delivery system capable of inserting drug-loaded DMNs without the involvement of a patch in a minimally invasive manner. Investigations showed that Microlancer is capable of achieving a delivery efficiency of $97 \pm 2\%$ regardless of skin type or hairiness. This system was tested using valproic acid (VPA) which is an FDA-approved anticonvulsant drug that has been shown to effectively stimulate hair follicle (HF) regrowth. Our studies showed that VPA encapsulated DMNs could efficiently deliver encapsulated compounds and stimulate hair follicles with higher efficiency than topical application.

In addition, by designing novel shapes of DMNs, we could develop microstructures capable of penetrating the skin for improved delivery efficiency. Data showed that by changing the morphology of DMN, we could achieve a complete skin inserting without utilizing any applicator. Overall, achievement of a highly efficient delivery has become possible via our newly developed dissolving microneedle delivery systems.

4:30 **Roundtable Discussion—What Next? Expanding Therapeutic Applications Through Microneedle Technology**

Moderator:

Harvinder Gill, Texas Tech University

Panelists:

- Nicky Bertollo, UC Dublin
- Lisa Dick, 3M
- Ryan Donnelly, Queen's University, Belfast
- Hyungil Jung, Yonsei University
- Mikolaj Milewski, Merck

Discussants:

The Audience

5:05 *End of Day One*

Thursday, September 19, 2019

8:15

Complimentary Breakfast

**Drug Development Spotlight—
Preclinical & Clinical Case Studies in
Microneedle Drug & Vaccine Delivery**

8:30

**Improved Influenza Vaccination Through
Infection Mimicry Using Silk Microneedles**



**Michael Shrader, CEO, Vaxess Technologies
(Co-Authors: Kathryn M. Kosuda, Jordan A. Stinson, and Archana V. Boopathy)**

Recent studies have shown that modulating the kinetics of antigen presentation to mimic those of a natural infection can drive more potent immune responses. To achieve sustained vaccine delivery, we have developed a microneedle patch composed of silk tips encapsulating antigen, and a dissolving base layer. Upon application, silk microneedle tips are implanted in the dermis and slowly deliver antigen over one to two weeks, with release kinetics tuned by the degree of crystallinity in the silk biopolymer matrix. Using this infection mimicry approach enabled by the MIMIX microneedle platform, Vaxess is developing an improved, more broadly protective influenza vaccine that is shelf-stable and easily administered.

The use of silk fibroin, a low-cost biomaterial from the silkworm *Bombyx mori*, represents a unique approach to developing microneedles. Previous studies have shown silk fibroin's ability to encapsulate and stabilize a number of biomacromolecules in dried formats, making the material a strong candidate for use as a drug delivery vehicle. Silk fibroin possesses superior mechanical strength to other biomaterials, while offering controllable processing under aqueous conditions and tunable biodegradability which enables controlled release ranging from a few hours to over one month.

Vaxess has leveraged the properties of silk fibroin in the microneedle format for tunable vaccine delivery. Antigen release from silk microneedles can be extended compared to the equivalent injection in mice and modulated by silk formulation and processing. Application of influenza vaccine loaded silk microneedles was studied in BALB/c mice. Sustained release of vaccine over one week led to robust and significant improvement in humoral responses, measured by serum IgG and hemagglutination inhibition (HAI) titers. Compared to an equivalent dose delivered by intramuscular injection, MIMIX delivery of influenza vaccine resulted in higher HAI responses and improved seroconversion up to 6 months post-immunization. Sustained release led to increased plasma cells and HAI titers against both vaccine and drifted influenza viruses, suggesting stronger and broader protection. MIMIX immunization also resulted in increased T-cell responses which have been shown to influence the rate of virus clearance upon infection. Taken together, these results support the development of a more efficacious and broadly protective influenza vaccine using sustained release silk microneedles.

9:10

**Vaccination with 1/6th Standard Dose of a
Split Inactivated Influenza Vaccine Using
the Nanopatch™ Induces Comparable
Immune Responses to Conventional Full-Dose
Intramuscular Injection—Results From A Phase I
Randomized Controlled Clinical Trial**



David Hoey, CEO & Director, Vaxxas (Co-Authors: Angus H. Forster, Katey Witham, Alexandra C. I. Depelsenaire, Margaret Veitch, James W Wells, Adam Wheatley, Melinda Pryor, Jason Licklitter, Barbara Francis, Steve Rockman, Jesse Bodle, Julian Hickling, Germain J. P. Fernando)

The Nanopatch is a high-density micro-array patch (MAP) for vaccine delivery into the skin. MAPs have the potential to be a safer, more acceptable, easier to use and more cost-effective method for the administration of vaccines. We have conducted a placebo-controlled, randomized, partially blinded phase I trial (ACTRN 12618000112268) using the Nanopatch to deliver a monovalent influenza vaccine. This is the first clinical evaluation of the vaccine dose-sparing potential of a MAP.

Nanopatches were coated with a split inactivated influenza virus vaccine (A/Singapore/GP1908/2015 [H1N1]) (A/Sing). Healthy volunteers were vaccinated with doses of 15, 10, 5, or 2.5 µg of A/Sing haemagglutinin (HA) via Nanopatches applied to the volar forearm (FA), or 15 µg HA via Nanopatches applied to the upper arm (UA). Control groups received uncoated Nanopatches applied to the FA ('placebo control') or commercially available Afluria® quadrivalent influenza vaccine (QIV) containing A/Singapore/GP1908/2015 [H1N1] HA (15 µg/dose). Serological, mucosal and cellular immune responses were assessed pre- and post-vaccination. Skin biopsies were taken from a subset of volunteers before and three days after Nanopatch application and analysed by flow-cytometry and immunofluorescence to compare the influx and migration of cells from the application site of vaccine-coated and uncoated Nanopatches.

The A/Sing vaccine coated onto Nanopatches was stable when stored at 40°C for at least 12 months. Nanopatch vaccination was safe and well-tolerated; any AEs were mild or moderate. 2.5 µg HA administered by Nanopatch induced haemagglutination inhibition (HAI) and microneutralization (MN) titres that were not significantly different to those induced by 15 µg HA injected IM. Nanopatch delivery of 15 µg (FA and UA) and 10 µg (FA) HA resulted in a faster increase in HAI responses than IM injection, with 83%, 95% and 90% subjects respectively seroconverting at day 8, compared with 68% for the IM QIV group. The results from a panel of exploratory assays (antibody-dependent cellular cytotoxicity, CD4+ T cell cytokine production, memory B cell activation, and recognition of non-vaccine strains) indicated that overall, Nanopatch delivery induced a range of responses that were similar or potentially superior to those seen with IM injection of QIV.

Vaccination using the Nanopatch and a thermostable formulation of influenza vaccine that can be stored outside

the cold-chain, was safe and well-tolerated and resulted in immune responses that were equivalent to or enhanced compared with IM injection. Using the Nanopatch, a 2.5 µg dose (1/6 of the standard dose), induced HAI and MN titres equivalent to those seen with 15 µg HA injected IM.

9:50

Exhibit Viewing & Networking Coffee Break

10:15

PATH Microarray Patch Center of Excellence



Courtney Jarrahan, Portfolio Leader, Packaging & Delivery Technologies, PATH

PATH's Microarray Patch (MAP) Center of Excellence is a four-year initiative to mobilize efforts to accelerate the development of MAPs for critical vaccines and essential medicines and ensure that the MAP delivery technology platform can maximize its impact by meeting global public health needs. The Center of Excellence is collaborating with global stakeholders and partners to rapidly identify critical public health applications, develop well-informed target product profiles, perform technical development, advance manufacturing processes, and clarify regulatory pathways for MAPs, with the aim of maximizing the potential of this innovative delivery technology platform. We have developed a framework to prioritize vaccines and drugs for MAP delivery and are conducting studies to gather user and stakeholder perspectives. To better define the regulatory pathway for MAPs, the Center of Excellence is leading an effort to develop the foundation for future pharmacopeial test methods for the technology class in partnership with regulatory agencies, public health organizations, academia, and industry. We are also evaluating manufacturing readiness and the feasibility of manufacturing MAP products at large scale.

Key learning objectives from the PATH Microarray Patch Center of Excellence session:

- Global health priorities for MAPs for use in low-resource settings.
- Factors that will determine the potential for MAPs to improve access and delivery of vaccines and essential medicines.
- Goals and progress in regulatory pathway definition for MAPs.
- MAP manufacturing challenges and readiness.
- How the Center of Excellence is engaging with MAP technology developers and industry.

10:55

Roundtable Discussion—What Next? Lessons Learned from Preclinical Through Clinical Phase Trials

Moderator: TBA

Panelists:

- David Hoey, Vaxxas
- Pete Schmidt, Zosano
- Michael Schrader, Vaxess

Discussants:

The Audience

11:25

Predicting the Heat Effect on Drug Absorption from Transdermal Patches, Semisolids, and Solutions: In Vitro Permeation Testing to Human Studies



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

Abstract Coming Soon

12:05

Complimentary Networking Lunch

Regulatory Spotlight—Meeting FDA & USP Safety & Quality Requirements for Transdermal Patches/Systems

1:10

Alternative Strategies of Vaccine Administration for Improved Pandemic Influenza Preparedness Capabilities



Tanima Sinha, MSc, MScPH, Lead Interdisciplinary Scientist, Biomedical Advanced Research and Development Authority (BARDA), Assistant Secretary for Preparedness and Response, Department of Health and Human Services, US Government, Washington, DC

Within the United States Government (USG), the Biomedical Advanced Research and Development Authority (BARDA), part of the Health and Human Services, Office of the Assistant Secretary for Preparedness and Response, was established to aid in preparing our nation from chemical, biological, radiological, and nuclear (CBRN) threats, as well as from pandemic influenza (PI) and emerging infectious diseases (EID).

Prevention of disease, caused by seasonal and novel influenza strains of pandemic potential, continues to be a public health challenge. Traditional parenteral vaccinations are the primary medical intervention for prevention of infections with these viruses. In an effort to improve preparedness capabilities and satisfy the 2017 Pandemic Influenza Plan (PIP) calling for the first doses of vaccines to be available at 12 weeks, (<https://www.cdc.gov/flu/pandemic-resources/pdf/pan-flu-report-2017v2.pdf>), the ASPR/BARDA is gathering information from developers for alternative routes of administration for seasonal and pandemic/pre-pandemic influenza vaccines. Technologies/mechanisms can include, but are not limited to, micro-needles, patches and/or other needle-free options, and devices not requiring specialized medical training. These approaches may possibly reduce the required number of doses and/or reduce or eliminate the need for an adjuvant, as is typically the case for a novel virus in a naïve population.

The use of alternative routes of administration to deliver vaccine could simplify the response to a pandemic by, for example, eliminating cold chain shipping and storage requirements or reducing the need for vials, needles and syringes and, as a result, reducing medical waste. Additional benefits could result in increased immunization up-

take and improved dissemination of influenza vaccine to remote areas in both domestic and international settings.

The Influenza and Emerging Infectious Diseases Division (IEIDD) of BARDA is seeking information regarding ways an interested contractor could assist the ASPR/BARDA with development of alternative routes and regimens of influenza vaccine administration for seasonal and pandemic influenza.

1:50 Extractables and Leachables Assessments for Transdermal Patches



Dr. Michael A. Ruberto,
Material Needs Consulting

Transdermal patches can be complex systems consisting of films constructed from various types of polymers that are bound together with tie layers or adhesives. The pouches that are used to package and protect these patches often have a similar multilaminate construction. Evaluating the leachables risk for transdermal patches can, therefore, be a difficult task given all of the potential sources of leachables. Ensuring that the multilaminate pouches are compliant with USP <661.1> and <661.2> can also be an issue. The use of a transdermal patch is unique compared to many other types of drug products and/or their delivery systems, since the transdermal patches are typically worn on the body for several hours or even days. They can see various temperatures conditions and even be worn during exercising where they can be extracted by sweat under elevated temperatures. Designing a leachables testing study plan that takes this type of an application into account is essential to meet FDA expectations. In general, the FDA expectations for an appropriate extractables and leachables risk assessment for transdermal patches can be quite varied depending on the type of patch, its materials of construction, typical use, and packaging. They are considered to be higher risk drug products, but best practices for their testing have not yet been developed by the Product Quality Research Institute (PQRI). This presentation will focus on actual strategies that have proven to be successful in meeting the challenges described above for transdermal patches and their packaging systems.

2:30 *Exhibit Viewing & Networking Coffee Break*

2:45 Extractable and Leachable Testing for Transdermal Drug Delivery Systems



Dr. Gyorgy Vas, Intertek Pharmaceutical Services, Trace Organic Analytical Group
(Co-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 or even eliminate 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 non-intentionally "delivered" with the same route of administration.

The extractable testing of transdermal systems is straightforward, does not require "out of box" thinking. In contrary 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. Few examples also will be provided for mitigating FDA deficiency letters related to transdermal delivery systems.

Drug Discovery Spotlight—Unlocking the Potential of Cannabinoids Via the Skin

3:25

An Overview of the Therapeutic Potential of Cannabinoid Medicines Applied On The Skin



Dr. Theo Kapanadze,
Chief Scientific Officer, Diteba

Due to its wide variety of medical benefits, cannabinoids are used to treat a number of common conditions, including chronic pain, inflammation, seizures, insomnia, spasms, multiple sclerosis, and mental disorders such as anxiety and depression. As the topical products, medical cannabinoids could be directly applied to certain areas of the body as an effective means of relieving pain and soreness, reducing inflammation, and soothing inflammatory skin conditions such as psoriasis, dermatitis, and eczema

For each pathology, it remains to be determined what type of cannabinoid and what route of administration are the most suitable to maximize the beneficial effects of each preparation and minimize the incidence of undesirable reactions.

Due to low bioavailability of oral cannabinoids formulations, alternative routes of drug administration, including mucosal or sublingual dosing, vaporization of product and inhalation, and rectal administration, have been developed to improve the amount of delivered cannabinoids. The transcutaneous is another alternative route of cannabinoid exposure that avoids first-pass metabolism and improves bioavailability. Also, transdermal delivery of cannabinoids is hoped to reduce negative side effects seen with inhalation or oral dosing products.

The main aim of our study was to evaluate In Vitro percutaneous absorption profiles of major (THC/CBD) alone, and in combination with minor cannabinoids onto and through human ex vivo skin dosing with varieties of exclusively developed topical formulations. Specifically, we aimed to compare and evaluate (24/48hrs) In Vitro absorption profiles of the selected cannabinoids in enhance

of In Vivo bioavailability. We also expected that the THC induced changes might be more pronounced after oral administration because of the expected presence of the potent psychoactive metabolite 11-OH-THC that could not be formed at all through the skin permeation. Finally, since THC and CBD are chemically related compounds, it has been reported that under certain (acidic) conditions, CBD can be cyclised to THC in vitro. More recently the important question has been raised as to whether CBD can also be converted to THC in vivo. Therefore our aim was to ascertain whether permeation CBD through the skin could result in the presence of THC and if so, this could potentially mediate therapeutic effects.

The collected samples analyzed on contents of cannabinoids by UPLC-MS/MS. In addition, the identification of minor cannabinoids and metabolites was achieved by means of UPLC-QToF. In vitro skin absorption, kinetic parameters obtained from both finite and infinite dose model have been calculated and assessed for characterization of topical formulations.

4:00

Translation of a Novel Microneedle from Bench to Pilot; and Under GMP: A Case Study



Ahmad Ghoniem, Ph.D., Business Developer & Scientist, Tessa Labtec, GmbH

Tessa Labtec, a globally acting CDMO in the field of planar dosage forms, is working with several pharmaceutical partners to bring dermal/transdermal patches and oral thin films from idea to market. By now development of a typical matrix patch is an industry classic. However, translating novel microneedle technologies from bench to pilot requires the work of all typical stakeholders (formulators, chemists, . . . etc), as well as regulatory and process considerations and—above all—a lot of various engineering disciplines.

In this case study, you will hear about the challenges and outcomes of one of our scientific projects: bringing a novel microneedle patch that has been developed in a lab scale to a commercial scale.

4:30

Close of Program

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PharmaEd Resources does not offer refunds. However, if you cannot attend after registering, we are happy to apply your registration fee to another PharmaEd Resources event, or transfer your registration to a colleague. Notice of cancellation must be received at least 5 days prior to the event.