POSTER SESSION

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Development of a Platform for Peptide Stability Assessment on Solid Substrates

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Transdermal drug delivery systems utilizing microneedles offer a minimally invasive route of administration for peptide formulations typically administered parenterally. In addition, microneedles could offer a way to overcome common challenges associated with peptide solution formulations, including poor chemical and physical stability even under refridgerated conditions. Drug-coated microneedles penetrate the tough epidermis and deposit drug within the skin, typically using water soluble formulations that dissolve off the microneedles into the dermal layer. Key areas of interest involving coated microneedles include understanding the coating process, evaluating solid state stability of the coated formulation, and examining the compatibility of microneedle surfaces and peptide formulations. Here, we will present the development of a platform experimental design to investigate peptide stability on solid substrates. The goal of this study aims to establish a screening tool for new compounds in early stages of development in order to evaluate the compatibility of a typical microneedle surface with different peptide formulations. To evaluate surface/formulation compatibility, peptide formulations were deposited onto metal disc surfaces and stored under various conditions to assess chemical stability of coated formulations in comparison to corresponding solution formulations. A number of variables were tested, including solid substrate material, surface treatment, choice of excipients, and peptide sequence to evaluate peptide stability in the solid state. Overall, these studies reveal the complexity and wide array of challenges associated with performing robust compatibility experiments for peptides dried on surfaces.

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Confronting Contamination: Analytical Case Studies

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Contaminant identification is of great concern to the pharmaceutical and medical device industry. Therefore, it is critical to understand and find a potential contaminant's origin quickly. Two contaminant identification case studies will be presented. The use of multiple analytical techniques is paramount to determining a contaminant's identity. These case studies include analytical techniques such as Fourier Transform Infrared Spectroscopy (FT-IR), Scanning Electron Microscopy Energy Dispersive X Ray Spectroscopy (SEM/EDS), and Gas Chromatography Mass Spectrometry (GC/MS). The first case study is a contaminant identification of a brown material present on a pharmaceutical tablet. This brown material was the source of a potential field recall of an entire lot of a drug product. After isolation and rush analysis, the contaminant was identified, it clearly came from an external source at the consumer

end and a field recall was unnecessary for the product. The second case study presented is material isolated during the cleaning validation of medical grade tubing. The yellow material observed was analyzed by FTIR and SEM/EDS in order to determine the bulk chemical identification. The material was determined to be consistent with polymeric material of the bulk tubing material that was causing issues to downstream processes. After identification, the material was quantified using Gel Permeation Chromatography (GPC). This allows the client to be able to monitor the cleaning procedure.

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Investigation and Mitigation of Discoloration in Pediatric Powder-for-Suspension Formulations

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Oral suspension formulations are well-suited for pediatric patients that are too young or otherwise unable to swallow tablets or capsules and also benefit from flexible dosage amounts. Multi-dose suspension products typically contain a thickening agent to maintain API particles in suspension, a preservative to inhibit microbial growth, and a pH modifier to achieve an appropriate pH. Prototype powder-for-suspension formulations containing xanthan gum as thickener, potassium sorbate as preservative, and citric acid as acidulant, were found to exhibit discoloration during stability studies. **Objective:** Quantitate the discoloration of these formulations, understand the root cause and mitigate the discoloration risk. **Methods:** The underlying cause was explored by testing excipient compatibility and identifying a signature degradation product. Color assessment by reflectance spectrophotometry and UV-visible absorbance was applied to facilitate comparison of different formulations. **Results:** Excipient compatibility experiments identified discoloration in mixtures of xanthan gum and citric acid. Xanthan gum can be hydrolyzed into its constituent sugars, and these are known to further degrade into reactive compounds including 5-hydroxymethylfurfural, which was identified in discolored formulations. Reflectance colorimetry was found to be effective for measuring discoloration and was used to evaluate several possible alternatives to citric acid. **Implications:** Discoloration was attributed to xanthan gum hydrolysis with subsequent tautomerization and dehydration reactions, catalyzed by citric acid. The use of an alternative acidulant reduces but does not eliminate the discoloration, and refrigeration is ultimately a more effective mitigation strategy. These are important considerations for any formulation that contains xanthan gum and acidifier, irrespective of the API.

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Cutting Edge Concepts in Pharmaceutical analysis: AQbD a way to achieve robust methods through its lifecycle

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Method robustness and reliability are the major concerns when developing methods in Pharmaceutical Analysis. In order to address these concerns, it is becoming a trend in the pharmaceutical industry the introduction of some new concepts during the analytical method development and its lifecycle [1]. Here we present how to combine these cutting edge concepts during analytical method development, as part of a workflow model for drug substance analysis by liquid chromatography. As an outcome, a structured and

scientific based approach, known as Analytical QbD (**AQbD**), is obtained. This approach encompasses several steps, such as: setting pre-defined objectives or Analytical Target Profile (**ATP**); selection of an appropriate technology; prior-knowledge collection through a risk assessment process where potential sources of variability affecting method performance are identified, then method understanding is explored via design-of-experiments (DoEs) using factors from the risk assessment stage. This AQbD methodology ends up with ATP verification and a risk mitigation phase, where all sources of variability are reduced and controlled through a formal definition of a method control strategy over lifecycle, Analytical Control Strategy (**ACS**). The overall workflow **Lifecycle Management** contains as key enablers Risk Management (**RM**) and Knowledge Management (**KM**), that ensure a method is fit for its intended purpose over the entire lifecycle of the method.

[1] C. Burgess, P.D. Curry, J. Ermer, G.S. Gratzl, J.P. Hammond, J. Herrmann, et al., Stimuli article: Proposed New USP General Chapter : The Analytical Procedure Lifecycle 1220, Pharmacopeial Forum 43(1). (2017).

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Integration of Fully Automated Dissolution in New Product Development of Solid Dosage Pharmaceutical Products

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While pharmaceutical drug release can be measured *in-vivo* by testing for the active ingredient in blood plasma, this approach is significantly limited by obvious impracticalities. *In-vitro* drug dissolution is used as a practical and effective alternative. However, *in-vitro* drug dissolution can be a time and labor intensive process for pharmaceutical companies, often being a rate-limiting factor for development in analytical laboratories. A fully automated dissolution system was implemented and proven to significantly reduce analyst effort, improve efficiency, and accelerate productivity. Multiple dissolution parameters and candidate formulae can be screened rapidly to determine viability, thus improving development cycle time in the analytical laboratory.