PQRI 2020 Webinar Series

Excipient Considerations for Parenteral Drug Development

Moderator: David Schoneker, Black Diamond Regulatory Consulting, LLC
Presenters: Janeen Skutnik-Wilkinson, Biogen
Thomas Tice, Ph.D., Evonik Corporation
I. Welcome and Overview of Webinar
   Moderator: David Schoneker, Black Diamond Regulatory Consulting, LLC

II. Excipients for Parenterals
   Janeen Skutnik-Wilkinson, Biogen

III. Lactide/Glycolide Parenteral Excipients for Successful Drug Delivery Solutions
   Thomas Tice, Ph.D., Evonik Corporation

IV. Moderated Q&A Session with the speakers
This webinar is being recorded.

The recording will be posted on the PQRI website at www.pqri.org after the webinar.
Questions

- Submit written questions using the Questions Panel.
- Raise your hand to be unmuted for verbal questions.

*Note: Today’s presentation is being recorded.*
Mission:
PQRI is a non-profit consortium of organizations working together to generate and share timely, relevant, and impactful information that advances drug product quality, manufacturing, and regulation.
What Does PQRI Do?

• Unites thought leaders from regulatory agencies, standard setting bodies, industry and academia to conduct research and share knowledge on emerging scientific and regulatory quality challenges.

• Provides a unique, neutral forum to develop broad consensus among a diverse collection of industry organizations and regulatory bodies.

• Creates opportunities to accomplish mutual goals that cannot be achieved by individual organizations.

• Impacts global regulatory guidance and standards, bringing maximum value to members and patients.
PQRI Structure

- PQRI consists of two governing bodies – a Board of Directors and Steering Committee and three **Technical Committees**, 
- Technical Committees each have a broad disciplinary focus that collectively spans the drug product regulatory lifecycle. They establish and provide scientific guidance, direction and oversight to PQRI working groups and research projects.
- Current PQRI Technical Committees:
  - Biopharmaceutics Technical Committee (BTC)
  - Development Technical Committee (DTC)
  - Product Quality Technical Committee (PQTC)
- This webinar is co-sponsored by the **BTC and PQTC**.
- You can find out more information about the TCs on the PQRI website: [https://pqri.org/about-pqri/](https://pqri.org/about-pqri/)
PQRI Webinars

Posted at https://www.gotostage.com/channel/pqriwebinars

2020 Webinars

• **SEPTEMBER 16, 2020: Regulatory Requirements and Technical Considerations for Biosimilar Products:** Presenters: Stacey Ricci, M.Eng., Sc.D, FDA; Leah Christl, Amgen; Sundar Ramanan, Ph.D., MBA, BioCon – Registration Opening Soon

• **The Challenge and the Promise: Developing Complex Drug Products (April 28, 2020)** Presenters: Wenlei Jiang, Ph.D., FDA and Adrian Goodey, Ph.D., Merck

2019 Webinars

• **Holistic QbD to Enable Product Quality Webinar (October 10, 2019)** Presenters: Ajit Narang, Ph.D., Genentech; Rakhi Shah, Ph.D., FDA; Xavier Pepin, Pharm.D, Ph.D; Divyakant Desai, Ph.D., BMS; Xavier Pepin, Pharm.D, Ph.D., AstraZeneca

• **The Expanding IVIVC Toolbox to Enable Drug Product Quality and Clinical Pharmacology – Complementary Traditional and PBPK Based Approaches (June 7, 2019)** Presenters: Xianyuan (Susie) Zhang, Ph.D., FDA and Filippos Kesisoglou, Ph.D., Merck

2018 Webinars

• **A Science Based Approach to Simplifying the Regulatory Pathway for Topical Drugs (April 9, 2018)** Presenters: Vinod P. Shah, Ph.D., FAAPS, FFIP and Flavian Radulescu, Ph.D.

• **Questions about the Proposed Topical Classification System (TCS) and What To Do With It (June 19, 2018)** Presenter: Sam Raney, Ph.D., FDA

• **Performance Testing in Quality Control and Product Development, Where are We? (October 23, 2018)** Presenter: Raimar Löbenberg, Ph.D., University of Alberta

• **Biowaiver Approaches for Solid Oral Dosage Forms in New Drug Applications (December 6, 2018)** Presenter: Poonam Delvadia, Ph.D., FDA
Pre-Workshop Events

• Pre-Workshop Survey
  • Obtain feedback from possible workshop attendees to understand the types of challenges they have experienced with their own organizations during the implementation of ICH Q3D. The results of the survey will be blinded, aggregated and shared during the November Workshop.
  • Survey to launch on Aug. 3

• FREE Pre-Workshop Preview Webinar
  • To be held on Monday, September 21st.
  • Registration Opening Soon

4th PQRI Workshop on ICH Q3D Elemental Impurities Requirements
November 9-10, 2020
LIVE VIRTUAL EVENT

Registration:  Registration to open August 3rd

See https://pqri.org/4th-pqri-ei-workshop/ for more information
Ms. Skutnik is the Associate Director for Quality Intelligence at Biogen and the current Chair of IPEC-Americas. Her former positions include: Vice President at NSF DBA; and Director /Team Leader of Quality & Regulatory Policy at Pfizer, responsible for working with various trade associations and also developing Pfizer Positions on Quality and CMC issues. She has over 25 years experience and expertise in compendial activities, quality and regulatory policy, and has held a variety of positions with responsibilities in documentation, change control, analytical method validation and product launch. Ms. Skutnik earned a Bachelors of Science from the University of Connecticut in 1994. She is a member of the ICH IWG for ICH Q3D Elemental Impurities, and was also on the EWG for Q3D. She was the Chair of PhRMA's Compendial Liaison Team (2000-2012); and the PhRMA Topic Leader for the ICH Topic - Q4B Regulatory Acceptance of Pharmacopoeial Interchangeability. She is the IPEC Delegate to the ICH Assembly and ICH Informal Quality Discussion Group.
EXCIPIENTS FOR USE IN PARENTERALS

JANEEN SKUTNIK-WILKINSON

BIOGEN
• This disclaimer informs readers that the views, thoughts, and opinions expressed in the text belong solely to the author, and not necessarily to the author’s employer, organization, committee or other group or individual.
EXCIPIENT ROLES IN PARENTERALS

- Solubilizing Agent: increase drug solubility
- pH: minimize oxidation and degradation
- Buffering agent: temperature stability
- Polymers & proteins: stabilize and increase half-life
- Bulking agent: forms the bulk of the lyophilized product
- Preservatives: prevent microbial growth
- Lyoprotectants: protect against freezing/unfolding
COMMON PARENTERAL EXCIPIENTS

• Mannitol
  • Most commonly used in lyo products

• Lactose / Sucrose
  • Bulking agent

• Polyethylene Glycol
  • Lyophilizing agent, co-solvent, viscosity modifier

• Polyvinyl Pyrrolidone (PVP)
  • Solubilizing agent, dispersant, crystallization inhibitor
EXCIPIENT SELECTION

- Influence on Quality, Stability, and effectiveness of the drug product
- Compatibility with drug and packaging system
- Compatibility with manufacturing process
- Amount / percentage that can be added
- Administration route
  - IV, IM, SQ, intracisternal, epidural, intrathecal, intradural
- Dose Volume
  - SVP vs LVP
- Single use or multiple use
- Amount of time the product will be used over (multidose)
EXCIPIENT SELECTION

- based on a comprehensive understanding of their impact on the product across the many events that can occur in product manufacture
  - freeze-thaw
  - time-in-solution
  - filtration, mixing
  - material compatibility
  - formulation/fill process
  - lyophilisation process
  - long-term stability
  - Photosensitivity
  - time-out of refrigeration (TOR),
  - in-use stability (post-reconstitution stability)
  - shipping.
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<th>What is Important</th>
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<td>Risk Analysis necessary for grade determination</td>
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<td>Consistency and traceability</td>
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<td>Supply assurance and compliance</td>
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<td>Packaging suitable for cGMP processing areas</td>
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<td>Segregation of non-animal-derived and animal-derived raw materials</td>
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<td>Specifications</td>
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SPECIFICATIONS

Sterility: free from Yeasts, Molds, Bacteria, Viruses

Particle Free: Must be free of particles over a certain size (unless a suspension)

Endotoxin Free

Pyrogen Free
SPECIFICATIONS

• Additional depending on product
  • Appearance
  • pH
  • Potency
  • Purity
  • Tonicity
  • Specialized (proteins, monoclonal antibodies, vaccines)
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<td>Controls the manufacturer of the pharmaceutical product can introduce, for example:</td>
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<td>Additional Excipient Supplier Supply Chain Controls:</td>
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<td>Change of testing (e.g., every pack or every lot to ensure identity and homogeneity)</td>
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<td>Microbiological testing</td>
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<td>Regular verification of supplier’s Certificates of Analysis</td>
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<th>Additional Excipient Controls</th>
<th>Controls the excipient supplier can introduce, for example:</th>
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<td>Increased auditing by excipient user or third party</td>
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<td>Changes to the excipient manufacturing process or controls</td>
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<td>Higher demand for notification of changes</td>
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<td>Increased oversight and control of shipments, tamper-proofing</td>
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<td>Additional controls the excipient supplier can introduce, for example:</td>
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<td>Increased effectiveness of cleaning (microbiological risk reduction)</td>
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<td>Sanitization (microbiological risk reduction)</td>
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<td>Enhanced filtration of excipient, e.g., Technically Unavoidable Particle Profile (TUPPS) risk reduction</td>
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<td>Altered processing conditions (by-product reduction)</td>
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<td>Exclusion of rework (reduced unknown impurity risks)</td>
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<td>Use of dedicated equipment</td>
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<td>Introduction or change of in-process controls</td>
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6.6 IMPLEMENTATION OF CONTROLS
**CHALLENGES**

- **Some antimicrobial preservatives can induce** Requires screening needed for each excipient at desired drug concentration
- **Protein oxidation by buffer components, antioxidants and trace metals**
- **Lack of trace metals** can also negatively impact media/buffer
- **Certain process-related impurities** could interact with surfactants, resulting in product-related
- **Some excipients** may interfere with analytical methods used for the control of the API
QUESTIONS?

Janeen.skutnikwilkinson@biogen.com
Thomas R. Tice, Ph.D., Senior Director, Technical Global Marketing
Evonik Corporation
tom.tice@evonik.com

Thomas R. Tice, PhD, Senior Director, Technical Global Marketing, Evonik Corporation, provides scientific support to Evonik’s product development, sales, M&A, and intellectual property teams. Dr. Tice is internationally recognized for research in drug delivery and has lectured on the topic throughout the world. His specialties include complex parenteral dosage forms and bioabsorbable polymers. He has over 40 years’ experience developing injectable, extended-release microparticles and implants made with bioabsorbable lactide/glycolide polymers. He led the team and is one of the inventors that developed the first commercial, injectable, extended-release microparticle product. This product is Decapeptyl® SR, a one-month LHRH formulation indicated for the treatment of prostate cancer. Dr. Tice earned his PhD in Biophysics from Syracuse University, New York. He holds 48 US patents with many foreign equivalents and has more than 180 publications, presentations and invited lectures to his credit. He currently serves on the Board of McWhorter School of Pharmacy at Samford University and serves on two United States Pharmacopeia expert committees - the General Chapters-Dosage Forms Expert Committee (Vice Chairman) and the Nomenclature and Labeling Expert Committee.
Thank you for attending the webinar!

For more information on PQRI, visit our website at:
www.pqri.org

Questions? Contact the PQRI Secretariat at:
PQRI_Secretariat@pqri.org

Call for Volunteers
If you or your company is a member of a PQRI member organization (CHPA, FDA, Health Canada, IPEC-Americas, PDA or USP) and you would to participate in any of the PQRI Technical Committees, please contact the PQRI Secretariat (PQRI_Secretariat@pqri.org) for further information.