USP-APEC Center of Excellence for Advanced Therapies

Pilot Virtual Training Workshop on "Starting and Raw Materials for Advanced Therapies"

1, 3, 8, 9 March 2021 (Americas) / 2, 4, 9, 10 March 2021 (Asia)

Draft Program – *Updated 19 February 2021*

Background

For many years and still today, USP staff and external expert volunteers have collaborated to develop standards applicable to medicines, excipients and other common raw materials found in small molecule and biologic therapeutics. Almost two decades ago, USP began building its work on cell, gene and tissue engineered products, with an initial focus on best practices applicable to raw materials used in manufacturing of these therapies. As a result, USP published a series of general chapters, documentary and physical Reference Standards, with support from Expert Committees and Panels. To support the standards setting activities and engage with stakeholders in this space, USP organized and delivered courses, and workshops on cells, tissues and gene therapies to bring together experts to debate and determine solutions to common problems. Recognizing that some of these concerns and the best approaches to mitigate their risks were not fully understood, USP staff have also provided dozens of talks around the world in leading advanced therapy conferences, as well as developing and delivering training webinars to build capability among developers and regulators. The proposed training program for regulators is designed by USP in collaboration with the Regulatory Harmonization Steering Committee and other experts to build on the Advanced Therapy Products Core Curriculum with a special emphasis on:

- Understanding shared versus unique considerations of raw materials for advanced therapies versus other purposes
- How to select and characterize raw materials to demonstrate that they are high quality and fit for purpose
- Help the audience, identify and implement, when applicable, national and international standards that can be used to support quality
- How to mitigate supply chain and quality risks throughout the product life cycle
- Learning from real world case studies in cell therapy, gene therapy, and tissue-based products

The training will include pre-reads and pre-assessments for attendees, opportunities to ask questions of the instructors, and a post-assessment to ensure that the training was effective.

Day 1: – 3 hours

- **Introduction: Welcome and Objectives for the Program**
    - **Dr. Fouad Atouf, Vice President, Global Biologics, USP**

- **Session 1: Terminology: Definitions and examples of starting, raw, and ancillary materials**
    - **Mr. Rajesh Patel**, Quality Assurance Manager, Raw Materials and Deviation Investigations, Bristol-Myers Squibb, will focus on an introduction to raw materials and excipients, guidances and standards (compendial and non-compendial) that exist to support their quality and demonstration of suitability, and introduce specific considerations when used for advanced therapies. The following objectives will be covered:
        - Explain definitions of starting, raw and ancillary materials as defined by ICH, and describe the regional differences between these definitions.
        - Using examples, explain commonalities and differences between raw materials used for small molecule drugs versus those used in advanced therapies.
        - Define excipients and their relationships to starting, raw and ancillary materials.
        - Explain compendial grade raw materials.
        - Understand ISO and pharmacopeial standards for raw, ancillary and starting materials and what to do when no standard exists.
        - Describe the following starting materials for advanced therapies: cell banks, types of starting materials, and quality considerations for viral vectors
    - **Nicole Larmore**, Janssen will continue with more specific concerns for materials used to manufacture advanced therapies and differences between different grades of materials, including the following objectives:
        - Explain that raw materials include cell culture supplements, enzymes, cytokines, and cell stimulating beads.
        - Explain common misunderstandings about “GMP grade” raw materials.

- **Session 2: Advanced Therapies- Raw material expectations from different regulatory bodies**
    - **Objectives:**
        - Each regulator from Japan, Canada, and the United States will explain the expectations on raw materials for advanced therapies from different regulatory bodies, including the APEC region.
    - **Speakers:**
        - **Dr. Masaki Kasai**, Principal Reviewer, Pharmaceuticals and Medical Devices Agency, Japan
        - **Dr. Martin Nemec**, Senior Biologist/Evaluator, Health Products and Food Branch, Health Canada
        - **Dr. Irina Tiper,** Biologist, US FDA, Center for Biologics Evaluation and Research, Office of Tissues and Advanced Therapies

- **Discussion/Q&A Session moderated by Dr. Fouad Atouf**

Day 2: – 3 hours

- **Session 3: Selection and sourcing of materials**

- **Moderator: Dr. Mohammad Heidaran**, Vice President, Technical, Parexel

    - **Speakers will cover risk-based approaches to demonstrating suitability of use for materials used to manufacture advanced therapies and how to ensure the supply and quality of those materials:**

        - **Dr. Claudia Zylberberg**, Chief Executive Officer, Akron Biotech will share her perspectives as a supplier, including the following objectives:
            - Understand how to reference vendor master files and how to access confidential supplier information.
            - Understand selection and suitability for intended use information as it relates to starting, raw and ancillary materials.

        - **Mr. Heath Coats**, Principal Consultant, Parexel International will share his perspective as a previous regulator and now consultant

on best practices to decrease risks to quality and supply between manufacturers and suppliers, including the following objectives:

- Understand how raw materials can lead to process failure
- Explain supplier qualifications, what a quality agreement is, and how to use a risk-based approach to evaluate a supplier's quality systems.

- **Mr. Aaron Mack**, Senior Engineer, Biogen will focus on qualification of raw materials in relation to process requirements and ways to mitigate risk, including the following objectives:

  - Explain and give examples of human source materials and common donor requirements.
  - Explain and give examples of animal source materials and additional testing that may be required.
  - Understand feeder cells and describe their use(s) as starting, raw and ancillary materials.
  - Understand typical qualifying tests for recombinant proteins used as starting materials.
  - Understand typical qualifying tests for other biologically-derived materials, such as amino acids, peptones, etc. used as starting materials.
  - Explain risk management tools as outlined in USP <1043> and FMEA.
  - Describe how raw materials can be assessed based on risk and provide examples of this strategy.

- **Dr. James Brown**, CEO of Agathos Biologics and Consultant to Aldevron. He will share his perspective from a contract manufacturer and raw material supplier including the following objectives:

  - Explain quality considerations for nucleic acids
  - Explain the role of plasmid DNA in gene therapy, cell therapy, and mRNA-based therapies

- **Discussion/Q&A Session moderated by Dr. Mohammad Heidaran**

Day 3: – 3 hours

- **Brief Recap of Days 1 & 2: USP**

- **Moderator: Judith Arcidiacono,** US FDA, Center for Biologics Evaluation and Research, Office of Tissues and Advanced Therapies

- **Session 4: Case studies to cover raw/starting materials and finished products**
  - **Objectives:**
    - Demonstrate an understanding of requirements and considerations of starting, raw and ancillary materials as related to Cell Therapies including donor requirements and assurance of quality.
    - Demonstrate an understanding of requirements and considerations of starting, raw and ancillary materials as related to Gene Therapies including plasmid DNA, transfection reagents, and cell lines for virus production.
    - Demonstrate an understanding of requirements and considerations of starting, raw and ancillary materials as related to Tissue Engineered products including donor tissue selection, screening, processing enzymes, and sterility assurance.
  - **Each speaker will share case studies regarding the following types of products illustrating principles presented in Days 1 and 2:**

    - **Case Study I: Gene therapy products**
      Dr. Richard Snyder, Vice President for Science and Technology, Pharma Services, Viral Vector Services, Thermo Fisher Scientific

    - **Case Study II: Cell-based or genetically modified cell therapy products**
      Dr. Michael Havert, Senior Director, Regulatory & CMC, bluebird bio

    - **Case Study III: Tissue engineered product**
      Dr. Nikhil Gheewala, Director of Product Development, Cytex Therapeutics

- **Discussion/Q&A Session – moderated by Judith Arcidiacono**

Day 4: – 3 hours

- **Session 5: Lifecycle Management of raw materials in advanced therapy products**

- **Moderated by Dr. Maura Kibbey,** Senior Scientific Fellow, Global Biologics, USP

    - **Speakers:**
        - **Dr. Christopher Bravery**, Director, Advanced Biologicals Ltd will share case studies illustrating common issues during a product's lifecycle when raw materials must be substituted or later in formulation, including the following objectives:
            - Describe common mistakes that manufacturers may make when managing raw materials across a product's life and how to mitigate these issues.
            - Describe how to demonstrate that a replacement material is suitable and leads to a comparable product
            - Explain additional expectations for excipients in formulated products

        - **Dr. Mohammad Heidaran**, Vice President, Technical, Parexel will share common regulatory expectations due to changes and how they are best addressed, including the following objectives:
            - Explain how to manage changes to raw materials post-approval
            - Understand types of changes and resulting US FDA notification

- **Closing session moderated by Maura Kibbey**
    - Questions for the speakers
    - Summarize the learnings
    - Identify future training opportunities and discuss next steps