DRAFT PROGRAM (as of 8/28/24) Timing and Speakers Subject to Change.

Wednesday – Thursday, September 4-5, 2024 *(Hybrid Event)*

(See website for logistical details https://www.ipacrs.org/biologics-workshop)

Workshop Organizing Committee Co-Chairs:
Chris Gruenloh, PPD, a part of Thermo Fisher Scientific
Chris Vernall, Intertek
Alan Watts, Catalent

Day 1: The Inhaled Biologics Landscape, their Critical Quality Attributes, and Aggregation Considerations

Day 1 – Wednesday, September 4, 2024 8:30 AM – 4:30 PM US ET	
8:00 - 8:30 am	Workshop Check In Continental Breakfast
8:30 - 9:00 am	***Housekeeping and Rules of Engagement*** Mary Devlin Capizzi, IPAC-RS Secretariat ***Welcome, Workshop Objectives, & Introductions*** Chris Vernall, Intertek, (Co-Chair)
Day 1 Moderator: Chris Gruenloh, PPD, a part of Thermo Fisher Scientific (Co-Chair)	
9:00 - 9:45 am	***Classes of Inhaled and Nasal Biologics: Current Trends in the Industry*** Tomaso Guidi, Chiesi Farmaceutici SpA. Biological drugs, also known as biologics, have revolutionized modern medicine due to their high specificity, potency, and safety profiles. In recent years, the interest in inhaled and nasal biologics has grown significantly, offering a non-invasive route for local and systemic drug delivery. This presentation aims to introduce the topic by starting with some clarifications on the routes of administration generally associated with the concept of inhalation and by providing definitions for the types of products present in this arena. The focus will then shift to the analysis of products that have reached the market or are in clinical development, attempting to highlight their main characteristics and trends. Finally, a look will be given to the preclinical world, where research in the field of inhalable biologics is exploding, including a vast number of innovative technological solutions.
9:45 – 10:30 am	***Overview of Regulatory Landscape*** Ruth Cordoba-Rodriguez, AstraZeneca Inhaled biologics cover a wide range of products that promise to deliver convenience and efficacy to the end-user. Development of these products include novel molecular formats, formulations and manufacturing processes aiming at delivering product via a device into the airway. Despite challenges to manufacture biologics that are stable and possess the physical attributes needed for effective delivery, there is a growing number of products that are being developed for use in the clinic, with the majority of these for indications in the area of respiratory disease. From the perspective of regulatory strategy, development of these products relies on guidance that is not specific to inhaled biologics. This presentation provides an overview of the current available guidance and discuses aspects to consider in the CMC development of inhaled biologics as well as challenges and opportunities.

10:30 - 10:45 am	*Break*
10:45 - 11:30 am	***Testing Requirements for Protein Biologics Therapies*** Wai Lam Ling, Catalent This presentation will cover CMC testing considerations and requirements for Biologics to be administered by injection. Manufacturing workflow for Drug Substance and Drug Product with their corresponding testing will be described.
11:30 am - 12:15 pm	***Preclinical Toxicology: Navigating the Respiratory Tract Barrier*** Emily Resseguie, Labcorp Early Development Laboratories The respiratory tract is designed to keep foreign matter out of the body and provide gas exchange with the blood. Once a therapeutic biologic is effectively delivered, preclinical safety assessment must be scientifically sound to identify potential toxicity and support clinical development. This presentation includes preclinical study design considerations for inhaled and nasal biologics.
12:15 - 1:00 pm	*Lunch*
1:00 - 1:45 pm	***Testing for Inhaled and Nasal Oligonucleotide and mRNA Products*** Ashleigh Wake, Intertek Inhaled /nasal delivery of oligonucleotides and mRNA therapeutics presents many potential advantages from overcoming bioavailability challenges often encountered for this modality of product to improved patient experience and reduced dependency for healthcare lead administration of vital vaccines. Given the complexity of these molecules' strategic characterisation and quality control programs are required to be in place which concentrate on evaluation of the physiochemical, structural and in some instances biological activity of the product to ensure both continued efficacy and safety as well as establishing the performance of the delivery system. The aim of this presentation is to discuss an overall analytical strategy for characterisation and ongoing QC of such an inhaled or nasally delivered material, concentrating on the critical quality attributes, and what infers this criticality, in terms of the modality and how these analytics are combined with inhaled /nasal delivery performance in putting together an overall testing specification.
1:45 - 2:30 pm	***Relevance of Protein Aggregation in the Lung*** Markus Fridén, AstraZeneca The presence of drug protein aggregates in aerosol formulations has been a lingering concern for inhaled biologics due to the perceived risk of causing immunological responses. The process of protein aggregation may be induced by protein unfolding at the large air-water surface created in an aqueous aerosol of a nebulizer product or, for a dry powder formulation, in the process of de-hydration e.g. spray-drying. Assessment of aerosol product quality therefore typically includes detection of higher molecular weight species by chromatographic methods and insoluble particle analysis. This presentation reviews the state of knowledge around the relevance of aggregates for augmenting immunogenic responses. What should be expected with regards to aggregate formation and disposition in the micro-environments of the lung? What data exists on in vivo detection of protein aggregates in the lung? What is the evidence that aggregates cause immunogenic responses? Based on these considerations, avenues for bio-relevant aggregate testing of inhaled biologics are discussed.
2:30 -2:35 pm	*Wrap Up and End of Day 1 For Virtual Attendees*
2:35 – 2:45 pm	***(For in-person attendees only)*** Instructions for Breakouts
2:45 - 3:00 pm	*Break*

3:00 - 4:15 pm	***Breakouts*** *Registrants will breakout into concurrent breakout sessions to facilitate small group discussions.* ***Breakout Topics:*** **(A) Delivery and Manufacturing of Biologic Products** Moderators: Mireia Puig, Vectura and Alan Watts, Catalent **(B) Analytical Testing & Control Strategy** Moderators: Chris Gruenloh, PPD and Chris Vernall, Intertek **(C) Safety & Toxicology Testing** Moderators: John Patton, Kindeva
4:15 – 4:30 pm	*Break* [to allow breakout moderators and notetakers to prepare readouts]
4:30 -5:00 pm	Breakout Readouts
5:00 – 6:30 PM	Networking Reception – for all in-person attendees

Day 2:
Chemistry, Manufacturing and Controls for Inhaled Biologic Drug-Device Combinations

Day 2 – Thursday, September 5, 2024 - 8:30 AM – 3:00 PM US ET	
8:00 - 8:30 AM	Continental Breakfast
8:30 - 9:00 am	***Welcome & Workshop Objective - Day 2*** Alan Watts, Catalent (Co-Chair)
Day 2 Moderator: Alan Watts, Catalent	
9:00 - 9:45 am	***Excipients for Respiratory Delivery of Large Molecules*** Diana Fernandes, invoX and Michael Shultz/Kim Shepard, Lonza The intra- and inter-molecular interactions exhibited within, and between, complex macromolecules can have a critical impact on their function and stability. These interactions can be further influenced by excipient choice in drug formulations, affecting their bioavailability and immunogenic response. When combining a large molecule with one or more excipients, factors such as their own properties, route of administration, dosage form and processing conditions, need to be considered. This presentation will summarize the role of different classes of excipients for the respiratory delivery – pulmonary and nasal – of large molecule liquid and solid formulations with APIs ranging from nucleic acids to peptides, proteins, and more. Formulation considerations for liquid dosage forms delivered by nebulizers and soft mist inhalers will be contrasted with those of injectables. Dry powder formulations, and their specific requirements, will also be discussed. The current regulatory landscape of excipients approved for pulmonary and nasal delivery is also assessed, and gaps identified.
9:45 - 10:30 am	***Spray Drying of Biologics*** Sune Klint Andersen, Janssen
10:30 - 10:45 am	*Break*
10:45 - 11:30 am	***A Platform Approach to Spray Dried, Thermostable, Mucosal Vaccines*** Reinhard Vehring, Access to Advanced Health Institute To achieve thermostability and improved efficacy via mucosal delivery, two adjuvanted subunit vaccines, indicated against tuberculosis and COVID, and an sa-RNA influenza vaccine were converted into respirable dry powders via spray drying. The formulation platform, which used trehalose as stabilizer and an optional shell former excipient, was found to be compatible with all vaccines and provided an outstanding level of thermostability, reducing cold chain reliance. The powders were compatible with inexpensive, single-use delivery devices that allow straightforward, needle-free vaccination.
11:30 – 12:15 pm	**Influence of *Device* on Aqueous Stability** Ronan MacLoughlin, Aerogen
12:15 - 1:00 pm	***Particle Precision: The Importance of Sample Preparation in Insoluble Particle Analysis in Inhaled Biologic Powders*** Scott Sides, AstraZeneca Spray drying process is utilized to produce inhalable protein-containing powders. During the spray drying process, proteins may unfold due to their interaction with the air/liquid interface during drying. Unfolded proteins may aggregate, forming insoluble particles upon the reconstitution of the powder. These protein aggregates raise safety concerns due to their potential to elicit immune responses in patients. The quantification of particles upon reconstitution serves as a common method for quality control. However, this metric is heavily influenced by the reconstitution methodology employed, rendering it unreliable for establishing direct in vivo correlations. This abstract emphasizes the need for caution in the interpretation of in vitro particle data and highlights the complexity of correlating such data with clinical outcomes. Therefore, monitoring product quality and development of control strategies for sub-visible particles present in protein-based spray dried powder formulations for inhaled delivery is challenging and requires a fundamental understanding of the impact

	that the reconstitution process for powders has on protein aggregation. In this case study multiple variables were assessed for impact on protein related insoluble particle formation and sample stability post reconstitution such as: protein concentration, diluent composition and pH, order of addition, scale of preparation, and container type. Analytical methods for enumeration were farther refined to allow for differentiation between sub-visible particles related to proteinaceous species versus other foreign particulate matter to support an overall control strategy for sub-visible particle analyses and characterization as related to product quality.
1:00 – 1:45 pm	*Lunch*
1:45 – 2:30 pm	***Collection and Detection (Compendial) Strategies for Inhaled Biologics*** Philip J. Kuehl, Lovelace Biomedical Christopher J. Gruenloh, PPD, a part of Thermo Fisher Scientific Successful characterization of the performance of device-generated aerosols and sprays requires careful consideration on the part of the analytical chemist and testing laboratory. Prior to introducing a test apparatus (e.g., test chamber, dose filter, NGI, etc.), one needs to develop an understanding of how the biologic sample can be handled both from the perspective of analyst safety as well as not wanting to alter the active that's being studied. Here, questions like stability of the active in various recovery solvents/buffers as a function of concentration should be explored along with investigations into recovery from the different types of collection media that the biologic may encounter during the testing process (e.g., filter materials, glass/plastic/stainless steel materials, liquid impingement collection, etc.). Other questions to be answered involve understanding whether delivery from the medical device results in any degradation, aggregation or loss of biological activity and whether the analytical techniques enable this to be measured without artifacts. Assuming the active drug can be handled in a safe manner that minimally reduces the biological activity including recovery from test apparatus, selection of an appropriate detection scheme to support performance testing provides for a final challenge. The merits of different detection schemes for a few classes of inhaled biologics will be explored and the application of these methods across in vitro and in vivo systems detailed.
2:30 – 3:30 pm	***Panel Discussion - Key CMC/Analytical Issues/Gaps to Address*** **Moderator:** Alan Watts, Catalent (Co-Chair) **Panelists:** • Ruth Cordoba-Rodriguez, AstraZeneca • Philip Kuehl, Lovelace Biomedical • John Patton, Kindeva • Michael Shultz, Lonza • Hailin (Sheena) Wang, OPQAIII/CDER/US Food and Drug Administration
3:30 – 3:45 pm	Closing Remarks – Chris Vernall, Intertek (Co-Chair) End of Workshop

Workshop Organizing Committee

Chris Gruenloh, PPD, a part of Thermo Fisher Scientific; Co-Chair, Workshop Organizing Committee
Chris Vernall, Intertek; Co-Chair, Workshop Organizing Committee
Alan Watts, Catalent, Co-Chair, Workshop Organizing Committee
Ruth Cordoba-Rodriguez, AstraZeneca
Diana Fernandes, invoX Belgium N.V.
Felicia Gioiello, Chiesi
Tomaso Guidi, Chiesi
David Lechuga-Ballesteros, AstraZeneca
John Patton, Kindeva
Mireia Puig, Vectura
Atish Sen, AstraZeneca
Isabel Lopes, invoX Belgium N.V.
Kim Shepard, Lonza
Keith Ung, Kindeva
Ashleigh Wake, Intertek
IPAC-RS Secretariat (Lana Lyapustina, Mary Devlin Capizzi, Dede Godstrey, Lee Nagao)

Workshop Faculty

Sune Klint Andersen Janssen
Ruth Cordoba-Rodriguez, Ph.D., Senior Director, AstraZeneca
Diana Fernandes, Ph.D., Technical Project Lead, invoX Belgium
Markus Fridén, Ph.D., Senior Principal Scientist, AstraZeneca
Christopher (Chris) Gruenloh, Ph.D., Research Fellow, PPD, a part of Thermo Fisher Scientific
Tomaso Guidi, M.Sc., Head of Formulation and Process Development, Chiesi Farmaceutici SpA.
Philip J. Kuehl, Ph.D., Sr. Director Non-Clinical Drug Development, Lovelace Biomedical
Wai Lam W. Ling, Ph.D., Vice President, Scientific Advisory, Catalent
Ronan MacLoughlin Aerogen
John Patton, Head of Kindeva's Scientific Advisory Board
Mireia Puig, PharmD, Ph.D., Team Leader – Technology Science and Innovation, Vectura Limited
Emily Resseguie, Ph.D., Scientific Specialist, Labcorp Early Development Laboratories
Kim Shepard, Ph.D., Director, Lonza (Bend)
Michael Shultz, Ph.D., Manger - Inhalation, Lonza
Scott Sides, B.S. (Biochemistry), Director, AstraZeneca
Reinhard Vehring, Ph.D., Professor, Access to Advanced Health Institute; University of Alberta, Department of Mechanical Engineering
Chris Vernall, MChem, Commercial Director, Intertek
Ashleigh Wake Intertek
Hailin (Sheena) Wang, Ph.D., Lead Interdisciplinary Scientist, Office of Product Quality Assessment III (OPQAIII), Center for Drug Evaluation and Research (CDER), US Food and Drug Administration
Alan B. Watts, Ph.D., Director – Innovation & Partnerships for Orally Inhaled Products, Catalent