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Tuesday, April 10, 2018

7:00 am–9:00 am	Pre-Registration Badge Pick-Up

Wednesday, April 11, 2018

7:00 am–9:00 am	Registration Hours
7:00 am–8:00 am	Continental Breakfast
8:00 am–8:15 am	**Opening Remarks** Nanda Subbarao, Ph.D., Biologics Consulting Group, Inc. (Chair) Nina S. Cauchon, Ph.D., Amgen Inc.(Co-Chair)
8:15 am–8:45 am	**FDA Perspective** Kavita Vyas, Ph.D., U.S. Food & Drug Administration (CDER) Peptides and oligonucleotides can be distinguished from both small molecules and larger biological molecules based on size, structural heterogeneity, and manufacturing process. They are more complex than small chemical entities, but are relatively more amenable to characterization than biological molecules. Their intermediate size and complexity often raises scientific and practical issues that may require adoption of specific approaches and strategies for product development and commercialization. This presentation will give an overview of regulatory and scientific considerations that inform the development of a comprehensive control strategy for these molecules to assure that product quality is maintained throughout lifecycle.
8:45 am–9:30 am	**EMA Perspective** Brian Dooley, B.Sc. (Pharm), M.Sc., European Medicines Agency This session will provide an overview of EMAs experience of oligonucleotide & peptide containing medicinal products, the relevant legislation and guidelines applicable to such products in the EU and commonly seen issues in marketing authorization and scientific advice applications.
9:30 am–10:00 am	Coffee Break
10:00 am–11:00 am	**Major Considerations for Development of Control Strategies for Oligonucleotides & Peptides** Mohan Sapru, Ph.D., U.S. Food & Drug Administration As a class of novel active pharmaceutical ingredients (APIs), the synthetic oligonucleotides and peptides, which are most commonly manufactured by solid-phase synthesis, are extremely diverse in terms of their structural characteristics and pharmacological properties. Based on adequate product and process understanding, the guiding principle is that a comprehensive control strategy needs to assure

process performance and product quality throughout the product lifecycle. This presentation will aim to discuss salient considerations for developing control strategies for: a) synthetic oligonucleotides and peptides, including oligonucleotide conjugates and modified peptides, and b) emerging technology-based continuous manufacturing of synthetic oligonucleotides and peptides.

11:00 am–11:30 am **Special Considerations for Control of Oligonucleotide Drugs: Product Quality Attribute Assessment to Ascertain Criticality**

Robert J. Duff, Ph.D., Amgen Inc.

Small interfering RNA (siRNA) molecules are an emerging class of therapeutics with tremendous potential in the clinic. Generally siRNA molecules have been described as "big small molecules" since they possess attributes of synthetic as well as biologic molecules. Nevertheless, the principles of Quality-by-Design (QbD) apply so the attributes must be assessed and scored for criticality. The purpose of a product quality attribute (PQA) assessment is to provide severity scores ranking the criticality for the molecule's quality attributes. A severity score reflects the expected or perceived impact on the drug's safety or efficacy if the attribute levels were to be out of control (elevated or reduced in comparison to expected levels). Product understanding and the relationship of process parameters to critical product quality attributes is an expectation in regulatory filings for product characterization, analytical method capability, process evaluation (formerly comparability), and justification of control strategy.

11:30 am–12:00 pm **Special Considerations and Regulatory Challenges for Control of Peptide Drugs**

Susanne Kinderman, Ph.D., Roche

To date, over 60 peptide-based drugs have been approved in the United States, Europe, and Japan and over 150 are in active clinical development.

Despite this progress, some challenges remain. Peptides are not easily classified into purely small molecule or biologics categories, because of their varying properties (such as size, potential secondary or tertiary structure and modifications) and manufacturing processes. Therefore, identifying relevant CQAs (critical quality attributes) and defining appropriate control strategies is essential for pharmaceutical development and gaining health authority approval. This presentation will address the control of synthetic peptides, including consideration of starting materials, manufacturing process, product characterization, and release testing. Regulatory aspects/requirements will be discussed.

12:00 pm–12:30 pm **Panel Discussion: Key Challenges for Peptides and Oligonucleotides in the Regulatory Area**

Moderator: Nina S. Cauchon, Ph.D., Amgen Inc.

12:30 pm –1:45 pm Networking Lunch

1:45 pm–2:15 pm **Analytical Methods for Oligonucleotides – Use in Characterization or as Part of Formal Specification**

Claus Rentel, Ph.D., Ionis Pharmaceuticals, Inc.

An overview of analytical methods for characterization, release and stability testing of single-stranded oligonucleotide therapeutics, e.g. as submitted in NDA filings for mipomersen (KYNAMRO®), nusinersen (SPINRAZA™), volanesorsen, (WAYLIVRA) and inotersen, will be presented. Tests for API and the medicinal products will be covered.

2:15 pm–2:45 pm	**Analytical Methods and Specifications for Peptides – A USP Perspective** Dale Schmidt, M.S., U.S. Pharmacopeia (USP) This presentation will provide a historical perspective of methods used in early USP peptide documentary standards, transition to current monograph methods and development of future monographs, with a focus on later monographs based upon their complexity and impurity profiles.
2:45pm–3:15 pm	**Q&A and Panel Discussion: Analytical Methods** Moderator: Nanda Subbarao, Ph.D., Biologics Consulting Group, Inc.
3:15 pm–3:45 pm	Coffee Break
3:45 pm–5:00 pm	**Breakout Group Discussions**
5:00 pm–6:30 pm	Networking Reception

Thursday, April 12, 2018

7:00 am–8:00 am	Registration Hours
7:15 am–8:15 am	Continental Breakfast
8:15 am–8:30 am	**Welcome Remarks** Fouad Atouf, Ph.D., U.S. Pharmacopeia (USP)
8:30 am–9:00 am	**In-Process Controls and Impurities in the Manufacture of Oligonucleotides** Marc Lemaître, Ph.D., ML_Consult We will describe from early stages to late stage manufacturing how to develop a compliant strategy for successful filing
9:00 am–9:30 am	**Development of Control Strategies for Peptides: Regulatory & Industry Perspectives** Ved Srivastava, Ph.D., Intarcia Therapeutics, Inc. The presentation will focus on quality attributes for raw materials and synthetics peptide API, manufacturing process considerations for quality control, process related and product related impurities in synthetic peptides, and analytical control strategies: comprehensive characterization of a peptide.
9:30 am–10:00 am	**Decoding Peptide Degradation-The Whole Nine Yards** Yogita Krishnamachari, Ph.D., Merck Peptides are an intermediate, yet a burgeoning modality in the continuum from small molecules to large molecules. Given the shallow energy curve, they present confounding and complex physical and chemical degradation pathways. In the absence of harmonized regulatory guidance, assessment of stability becomes a time and resource intensive activity. The goal of this presentation is to address some of these challenges by providing a more mechanistic approach, enabled by a montage of new and unique tools, to allow better prediction of such instabilities and define

control strategies for increasing the development speed and robustness of such therapeutics.

10:00 am–10:15 am Coffee Break

10:15 am–10:45 am **Characterization of Critical Quality Attributes of mRNA, A Novel Therapeutic Modality**
Huijuan Li, Ph.D., Moderna Therapeutics
Using mRNA to create new therapeutics is complex and requires overcoming novel scientific and technical challenges. mRNA production process heavily relies on in vitro enzymatic synthesis instead of chemical synthesis due to its length. Recent advances towards mRNA production and delivery prompt a need for robust analytical methods capable of characterizing this new class of drugs.
mRNA product-related impurities include short mRNAs resulting from either premature termination of transcription or in-process degradation, uncapped mRNAs, and point mutations, insertions/deletions. Multiple case studies utilizing a combination of biochemical and biophysical methods will be discussed on characterization of mRNA product- related impurities and variants for successful development of mRNA therapeutics.

10:45 am–11:15 am **MS for Routine Analysis and Impurity Quantitation (Both Oligonucleotides and Peptides)**
Athula Attygalle, Ph.D., Stevens Institute of Technology
Mass spectrometry is an indispensable tool in the analysis and impurity quantifications of pharmaceutical compounds. This presentation will highlight basic fundamentals of mass spectrometry and describe how the technique is applied to analyze pharmaceutical samples. A comparative account of modern gas-phase ion generation, separation, isolation, and fragmentation techniques will be discussed. In addition, the session aims to provide an overview of interpretation of mass spectral data, and quantification protocols based on hyphenation of liquid chromatography with mass spectrometry.

11:15 am–12:00 pm **Panel Discussion: Impurities and Related Substances**
Moderators: Elena Gubina, Ph.D., U.S. Food & Drug Administration and Fouad Atouf, Ph.D., U.S. Pharmacopeia (USP)

12:00 pm –1:00 pm Networking Lunch

1:00 pm–1:45 pm **Breakout Group Discussions**

2:00 pm–2:30 pm **USP Perspective on Reference Standard Development and Uses**
Fouad Atouf, Ph.D., U.S. Pharmacopeia (USP)
In addition to identity and purity tests, reference standards may also support quantitative assays. In the latter case, the reference standard needs to have an assigned content. This presentation will highlight strategies for characterization and development of reference standards as well as data to support their suitability for use. Cases studies from small peptides to large and complex molecules will be discussed.

2:30 pm–3:00 pm **Case Studies - Challenges Faced in Development (Industry Perspective): Oligonucleotides**
Sara Richardson, Ph.D., AstraZeneca

Oligonucleotides are a novel class of therapeutics that have the potential to be developed into drugs for numerous patients with unmet medical needs. Currently there are no regulatory guidelines available for oligonucleotides; they are considered small molecules although relatively large. This session aims to describe challenges faced in the development of synthetic oligonucleotide therapeutics. Focus will be put on analytical challenges – from how to approach analytical controls of oligonucleotides to the complexity of the current quality control methods to the large number of structurally similar impurities that needs to be qualified and quantified. Regulatory aspects around oligonucleotide therapeutics will also be discussed.

3:00 pm–3:30 pm **Case Studies - Challenges Faced in Development (Industry Perspective): Peptides**
Umang Shah, Ph.D., MBA, RAC, Shire
This presentation will provide examples of regulatory challenges faced in the development of (a) synthetic (b) recombinant peptides ranging from characterization to in-process testing and specification setting for lot release and (c)It will also discuss the controls necessary for starting material and impurities for synthetic peptides and for cell substrates, expression constructs as well as the adventitious agents controls for recombinant peptides.

3:30 pm–3:45 pm Coffee Break

3:45 pm–4:15 pm **Challenges of Peptide-Based Personalized Therapeutic Vaccines**
Elena Gubina, Ph.D., U.S. Food & Drug Administration
From the FDA perspective, this presentation will discuss the current challenges associated with the development of peptide-based therapeutic vaccines with a focus on personalized medicine.

4:15 pm–4:45 pm **Q&A and Panel Discussion**
Moderator: James S. Bernstein, Ph.D., Live Oak Pharmaceutical Consulting

4:45 pm–5:00 pm **Closing Remarks**
Nanda Subbarao, Ph.D., Biologics Consulting Group, Inc. (Chair)

Workshop Planning Committee

Nanda Subbarao, Ph.D. *(Chair)*
Biologics Consulting Group, Inc

Kavita Vyas, Ph.D. *(Co-Chair)*
U.S. Food & Drug Administration

Nina S. Cauchon, Ph.D. *(Co-Chair)*
Amgen Inc.

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