Short Course: Immunogenicity Data Evaluations and Clinical Interpretation

The detection, characterization, and interpretation of Anti-Drug-Antibodies (ADA) formed in response to biotherapeutics are greatly influenced by the data evaluations methods used during pre-study validation and in-study sample analysis. Despite several white-paper publications and guidance documents over the past decade, there are significant gaps in the understanding and implementation of appropriate data analytic methods across the entire spectrum of Immunogenicity method development, validation, implementation, and clinical impact assessments.

This short course will provide an overview of regulatory expectations and experience with data reviews, in-depth statistical guidance for a broad range of topics, case-study illustrations of some common challenges, along with a demo of some simple data analysis templates/tools.

Learning Objectives:

- Understand the regulatory expectations on immunogenicity data evaluations for method validation and in-study implementation.
- Apply a robust approach for the evaluation of various types of cut-points and some key method validation parameters.
- Practice with provided Excel-based tools for preliminary cut point evaluations and some validation parameters.
- Address some of the challenges encountered during sample analysis, pre-existing antibodies, in-study re-validation, qualifying assay reagent changes, assess clinical relevance, etc.

Presentations

All presentations will be available on the workshop website, no later than 24 hours following the short course. Presentations will remain online for registered attendees until August 7, 2019.

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Workshop Planning Committee

Viswanath Devanarayan, Ph.D., FAAPS, Charles River Laboratories

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aaps PharmSci 360 / NOV 4–7 2018 / Walter E. Washington Convention Center

Workshop Agenda

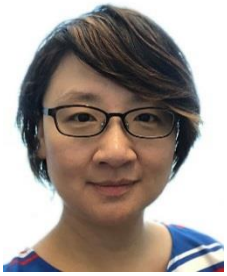
Sessions will take place in the Washington Convention Center, room 146 A

Sunday, November 4, 2018	
9:00 am – 9:15 am	**Immunogenicity Testing Strategy & Regulatory Expectations on Method Validation** Haoheng Yan, Ph.D., U.S. Food and Drug Administration
9:15 am – 10:05 am	**Recommendations for Different Cut Point Evaluations and In-Study Extensions** Ronald Bowsher, Ph.D., B2S Life Sciences
10:05 am – 10:45 am	**Case Study Illustrations of Some Practical Challenges & Resolutions** Robert Nelson, Ph.D., NovImmune
10:45 am – 11:00 am	Coffee Break
11:00 am – 12:00 pm	**Regulatory Experience with Immunogenicity Data Reviews, and Case Studies** Brian Janelsins, Ph.D., U.S. Food and Drug Administration Haoheng Yan, Ph.D., U.S. Food and Drug Administration
12:00 pm – 1:00 pm	**Some Solutions to Frequently Encountered Challenges with Immunogenicity Data Evaluations** Viswanath Devanarayan, Ph.D., Charles River Laboratories
1:00 pm – 2:00 pm	Lunch Break

Speaker Biographies and Abstracts

Immunogenicity Testing Strategy & Regulatory Expectations on Method Validation

This session will provide an overview of immunogenicity testing strategy and essential assay validation parameters.



Haoheng Yan, Ph.D., U.S. Food and Drug Administration

Haoheng Yan, M.D., Ph.D., Chemist, FDA-CDER Dr. Haoheng Yan is a biologics product quality and immunogenicity reviewer in the Office of Biotechnology Products (OBP) in CDER/FDA. Haoheng joined FDA in 2014 as a full-time reviewer. She is the primary reviewer for numerous INDs and several BLAs. Dr. Yan has also gained extensive experience in immunogenicity assay review for monoclonal antibodies, pegylated proteins, fusion proteins, antibody drug conjugates, polypeptides and polynucleotides. She is a member of OBP immunogenicity working group and CDER Center of Excellence in Infectious Disease and Inflammation. Dr. Yan received her M.D. from Peking Union Medical College, Beijing China and her Ph.D. in Molecular and Cellular Biology from the University of Massachusetts, Amherst.

Recommendations for Different Cut Point Evaluations and In-Study Extensions

This presentation will review recommended options for computation of validation and In-study cut points, including Screening, Confirmatory, and Titer cut points. In addition, recommendations will be provided for statistical study designs for efficient determination for cut points for different disease populations and In-study cut points. Lastly this presentation will share our collective experience and broad learning gained by computation of immunogenicity cut points across a wide range of biotherapeutics for many sponsors over a number of years.

Ronald Bowsher, Ph.D., B2S Life Sciences

Ronald Bowsher's career in the pharmaceutical/biotechnology and CRO industries has spanned 4½ decades. He is a recognized thought-leader in the areas of bioanalytical methods development for regulatory-compliant bioanalysis, ADME and immunogenicity assessments of biotherapeutics. He received his M.S. and Ph.D. degrees in Biochemistry & Molecular Biology at the Indiana University School of Medicine (Indianapolis, IN). Currently, he is Partner and CSO at B2S Life Sciences™ (www.B2SLifeSciences.com), a biotechnology laboratory in Franklin, IN specializing in the generation and life-cycle management of custom biological reagents, assay development and ADME to support biotherapeutic drug development. In 2003, Dr. Bowsher retired after more than 30 years at the Lilly Research Laboratories where he led research groups responsible for supporting regulated bioanalysis of biotherapeutics and conventional small molecule drugs. Since 1980, he has published >250 research papers, monographs, and abstracts, has four patents, 75 invited lectures, been a consultant to >100 global companies and has served on several scientific advisory boards. In 2004, Dr. Bowsher was elected as an AAPS Fellow. In 2008, he was given an AAPS Presidential citation for his efforts to establish educational training programs. In 2011, Dr. Bowsher received the AAPS BIOTEC Section distinguished service award.

Case Study Illustrations of Some Practical Challenges and Resolutions

This presentation will use real-life case studies to illustrate how technical aspects, such as use of the bridging format, acid dissociation protocols and extraction procedures, may positively and negatively impact immunogenicity assays and the data generated. Topics will include sensitivity and drug tolerance, dealing with low assay signal response and low biological variation, and determination of appropriate screening and confirmatory cut-points.

Robert Nelson, Ph.D., NovImmune

Biography unavailable.

Regulatory Experience with Immunogenicity Data Reviews, and Case Studies

Session description unavailable.

Brian Janelsins, Ph.D., U.S. Food and Drug Administration

Biography unavailable.

Haoheng Yan, Ph.D., U.S. Food and Drug Administration

Biography available above.

Some Solutions to Frequently Encountered Challenges with Immunogenicity Data Evaluations

This presentation will address some frequent questions such as the use of alternative cut point formula, outlier criteria and outlier-resistant methods, when and how to evaluate in-study cut points, pre-existing antibodies, criteria for treatment-boosted ADAs, in-study performance and system suitability criteria, assessing clinical relevance of ADA, etc. Data from several case-study examples will be used to convey the concepts and recommendations. In addition, demo of Excel-based tools for some informal calculations will be provided.

Viswanath Devanarayan, Ph.D., Charles River Laboratories

Devan has 22 years of pharmaceutical research experience from Eli Lilly, Merck, and AbbVie. In addition to leading global teams for over 15 years, his scientific contributions cover a wide variety of statistical methods and applications across drug discovery and clinical research. He has filed 10 patent applications, given over 100 invited talks, and coauthored over 60 manuscripts. This includes several white-papers with regulatory, academic and industry scientists on compound screening, genomics, predictive modeling, machine learning, bioanalytical methods, Immunogenicity and clinical biomarker qualification. He was inducted as a Fellow of the American Association of Pharmaceutical Scientists (AAPS) in 2014. He is currently employed at Charles River Laboratories and is also serving as an Adjunct Professor at the University of Illinois in Chicago.

Organizing Committee Biographies

Viswanath Devanarayan, Ph.D., Charles River Laboratories

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