Short Course: Science and Risk Based Stability Strategies: Applications of Predictive Tools

Co-Sponsored by: IQ International Consortium for Innovation & Quality in Pharmaceutical Development

Many drug products today are being developed at unprecedented speed, particularly those designed as breakthrough products. It remains imperative that the stability of both drug substances and drug products be understood at the time of product submission and throughout the product life cycle. This understanding is critical for formulation and packaging/device decisions, shelf life determinations for clinical supplies and proposed commercial products, specifications justification, and demonstration of equivalence to support pre- and post-approval changes. These objectives are traditionally approached using long-term and accelerated stability data collected at only two conditions. This experimental design does not support accelerated development because it takes long periods of time and does not necessarily result in an in-depth understanding of the stability of the product.

This short course is designed to clarify the applicability of science and risk-based stability approaches to optimize the stability protocol in order to develop an in-depth knowledge of stability performance of pharmaceutical products (APIs and drug products).

Learning Objectives:

- Discuss when and where to apply science and risk based predictive stability approaches in product development.
- Explore how science and risk based predictive stability approaches are aligned with regulatory guidances.
- Examine case studies of where science and risk based predictive stability approaches have received acceptance globally from regulatory agencies.

Presentations

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

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Workshop Planning Committee

Yan Wu, Ph.D., Merck Sharpe & Dohme
Megan McMahon, MS, Pfizer
Brian Regler, Ph.D., Merck

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Workshop Agenda

Sessions will take place in the Washington Convention Center, room 206

Sunday, November 4, 2018	
9:00 am – 9:20 am	**Introductions and Objectives**
9:20 am – 10:45 am	**Accelerated Stability Modeling Overview** Donald Clancy, GlaxoSmithKline
10:45 am – 11:00 am	Coffee Break
11:00 am – 11:30 am	**Applications of Accelerated Stability Models in Product Development** Brian Regler, Merck
11:30 am – 12:15 pm	**Stability Risk Assessments - What, When and How** Robert Timpano, Pfizer
12:15 pm – 100 pm	**Defining Meaningful Stability Parameters (timepoints, storage conditions, tests)** Anthony Rainosek, B.S., Baxter Cherokee Hoaglund-Hyzer, Ph.D., Eli Lilly
1:00 pm – 2:00 pm	Lunch Break
2:00 pm – 3:00 pm	**Application of Accelerated Stability Modeling Tools in Regulatory Filings** Dennis Stephens, Abbvie Yan Wu, Ph.D., Merck
3:00 pm – 3:15 pm	Coffee Break
3:15 pm – 4:20 pm	**Applying Science and Risk Based Stability Strategies Globally** Megan McMahon, M.S., Pfizer Donnie Pulliam, M.B.A., Biogen
4:20 pm – 5:00 pm	**Panel Discussion**

Speaker Abstracts and Biographies

Accelerated Stability Modeling Overview

This presentation provides an overview of the models and methodology used for accelerated stability. The theory, the underlying assumptions, and the resulting equations will be discussed. Differences between approaches developed between various Pharmaceutical companies will be compared and contrasted. The models needed for liquids and sold oral doses will also be compared. Case studies will be presented of the approaches in action for prediction of impurities, tablet disintegration time, tablet dissolution, hydrate formation, de-solvation, and possible application for assay decline of biologics.

Donald Clancy, GlaxoSmithKline

Don's background is in Chemical Engineering, graduating with a B.S. from Texas Tech University in 1994, then an M.S. in 1996. Don began work as process engineer for Mobil Oil in 1994, doing thermodynamic models to optimize oil and natural gas plants, with particular focus on poorly-understood operations such as high-pressure gas separation using membrane processes. Prior to working for GSK, Don worked seven years in R&D for Cabot Performance Materials developing processes to make powders that go into electronic capacitors. Within GSK for the past 13 years, Don has worked with a variety of teams, and has been responsible for facilitating the process understanding, Quality by Design (QbD), process control, PAT, and development of process models for GSK's late-stage pharmaceuticals.

Applications of Accelerated Stability Models in Product Development

This presentation will focus on the application of accelerated stability models in product development. How various approaches throughout pharmaceutical development have been leveraged to predict stability of products, justify shelf-life and specifications will be discussed; from study design to data interpretation.

Brian Regler, Ph.D., Merck

Brian Regler is currently an Associate Principal Scientist at Merck & Co., Inc. in Rahway, NJ where he serves as a supervisor and analytical project leader for product development in Merck Animal Health. Prior to Merck, he served as an analytical lead in Schering-Plough working on a number of early phase projects. Over the past several years, he has become involved in predictive stability efforts in pharmaceutical drug development. Currently he serves as a subgroup leader on the IQ Risk Based Predictive Stability Working Group. Dr. Regler received his Ph.D. in Chemistry from Rutgers University where he studied surfactant and surface chemistry. He also holds B.A. degrees in chemistry and molecular biology & biochemistry from Rutgers University.

Stability Risk Assessments - What, When and How

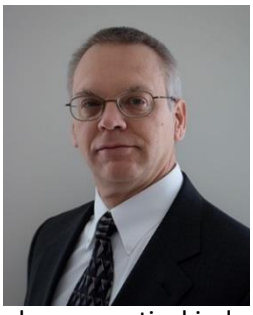
Session description unavailable.

Robert Timpano, Pfizer

Robert Timpano Director/Team Leader in Analytical Research and Development Pfizer Worldwide Research and Development Groton, Connecticut USA. Mr. Timpano received his B.S. in Chemistry from the University of Connecticut. Mr. Timpano has worked at Pfizer Worldwide R&D in Groton Connecticut since 1990 and currently is a Director and Team Leader in Analytical Research and Development. He has led management and scientific teams in Analytical R&D and currently leads a clinical stability group which is responsible for phase 1 to phase IV stability testing and regulatory submission activities. He has been a major contributor to 6 Marketing Applications and 8 external publications. Rob is chair of Pfizer's Stability Council.

Defining Meaningful Stability Parameters (timepoints, storage conditions, tests)

Presenters will lead a discussion on how to choose meaningful stability study parameters while complying with current stability guidance for pharmaceuticals. Time points, storage conditions, and tests will be outlined. Leveraging risk assessments and overall stability knowledge for a compound or product in designing lean stability strategies will be highlighted.



Anthony Rainosek, Baxter

Anthony Rainosek is Senior Manager of Global Stability at Baxter Healthcare, leading teams in Europe, China, and the United States. His global team develops stability strategies and study designs and performs subsequent data assessments supporting the development and maintenance of premixed drug, IV, nutrition, and renal solution products. Anthony received his bachelor's degree in Chemistry from the University of Texas at Austin and has 30 years of experience in the pharmaceutical industry, including leadership roles in analytical method development/validation and stability testing.

Cherokee Hoaglund-Hyzer, Eli Lilly

Cherokee S. Hoaglund Hyzer is a Sr. Research Advisor in the Analytical Small Molecule Design and Development area at Eli Lilly & Co. She has a Ph.D. in Analytical Chemistry from Indiana University, Bloomington, IN and 17+ years of experience in small molecule analytical control strategy development. Her experience spans analytical development for pre-FHD clinical phases through product submissions. She is also an active member of the IQ Consortium analytical RBPS and Lean Stability working groups and of AAPS.

Application of Accelerated Stability Modeling Tools in Regulatory Filings

The presentation will focus on regulatory aspects of Risk Based Predictive Stability (RBPS). A broad overview of how RBPS has been used in the industry will be presented. Specific details regarding regulatory experience will be discussed. Real world case studies of RBPS used in regulatory filings will be reviewed. In addition, the key elements of a regulatory template that leverages collective industry experience will be presented. Attendees will obtain a comprehensive view of how RBPS can be leveraged to accelerate drug development.

Dennis Stephens, Ph.D., Abbvie

Dennis Stephens is a Director in Drug Product Development at Abbvie. He received his BS in chemistry from Saint Xavier University and his PhD in Analytical Chemistry from the University of Illinois. He has worked in drug development for over 25 years on a wide variety of dosage forms (parenteral, controlled release, implantable depot, and solid oral) as an Analytical Chemist. He has been involved with all phases of drug development (pre-clinical, Phase I-III, Market Authorization Application). He currently leads the Engineer Testing and Analysis Group within the Combination Products Organization. He is currently serving as a member of the Small Molecules 2 Expert Committee for the USP. He is the 2018 Chair for the Analytical Leadership Group within the IQ Consortium. In addition, he chairs the IQ Working Group Focused on Regulatory Aspects of Risk Based Predictive Stability. He has over forty publications covering a wide range of topics.

Yan Wu, Ph.D., Merck

Yan Wu, Ph.D., is Principal Scientist of Analytical Chemistry in Development and Supply at Merck, in West Point, PA, where she is responsible for analytical development of drug products in late clinical stages and supports new product filing and launch activities. Prior to that, she had experience leading Stability Project Management, Stability Sample and Data Management groups that were responsible for stability study design, execution, and filing for late stage development and commercialization of drug products. Before joining the Stability group at West Point, PA in 2005, she held positions in Analytical Research within Merck Research Laboratories, where she was responsible for analytical method development of API throughout different clinical stages of product development and supporting market launch activities.

Applying Science and Risk Based Stability Strategies Globally

Attendees will learn about the current pharmaceutical regulatory landscape with respect to approaches for pharmaceutical product stability strategies to justify commercial licensure and post-marketing CMC changes. The presenters will share results from a recent industry survey related to usage of approaches used to justify reduced stability testing approaches relative the ICH guidances (e.g. Q1A and Q5C) and will overview recent case studies illustrating examples of applications of these approaches.

Megan McMahon, M.S., Pfizer

Megan McMahon is a Director in Global Regulatory CMC at Pfizer in Connecticut. Megan received her B.S. in Chemistry from Purdue University and M.S. in Regulatory Affairs/Quality Assurance from Temple University. Megan started her career at Pfizer in Chemical R&D as an analytical chemist and has worked in Regulatory CMC for the past 11 years. She is a member of Pfizer's Impurity Council and Stability Council. Megan was a founding member of the AAPS Chemical and Biological API Focus Group in 2009 and served as chair in 2012 and 2013. Megan is currently an active member of the AAPS CMC Community steering committee and has taken a leading role on the AAPS Virtual Round Table series. In addition to her support of AAPS, Megan is an active member of the IQ Analytical Leadership Group, Risk Based Predictive Stability Working Group, and leads the Lean Stability Working Group.

Donnie Pulliam, Biogen

Donnie Pulliam is a global regulatory commercial product lead in the Regulatory Affairs-CMC department at Biogen in Research Triangle Park, NC. Donnie has 10 years of experience designing stability studies for pharmaceutical products to support clinical development and new product registration, and to justify cold chain distribution and handling. He also collaborates with other companies through the International Consortium of Innovation and Quality in Pharmaceutical Development, or IQ Consortium, as a subteam leader in the Lean Stability working group. Donnie obtained his MBA from North Carolina State University, where he also obtained bachelor's degrees in chemical engineering and chemistry.

Organizing Committee Biographies

Yan Wu, Ph.D., Merck Sharp & Dohme

Yan Wu, Ph.D., is Principal Scientist of Analytical Chemistry in Development and Supply at Merck, in West Point, PA, where she is responsible for analytical development of drug products in late clinical stages and supports new product filing and launch activities. Prior to that, she had experience leading Stability Project Management, Stability Sample and Data Management groups that were responsible for stability study design, execution, and filing for late stage development and commercialization of drug products. Before joining the Stability group at West Point, PA in 2005, she held positions in Analytical Research within Merck Research Laboratories, where she was responsible for analytical method development of API throughout different clinical stages of product development and supporting market launch activities.

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