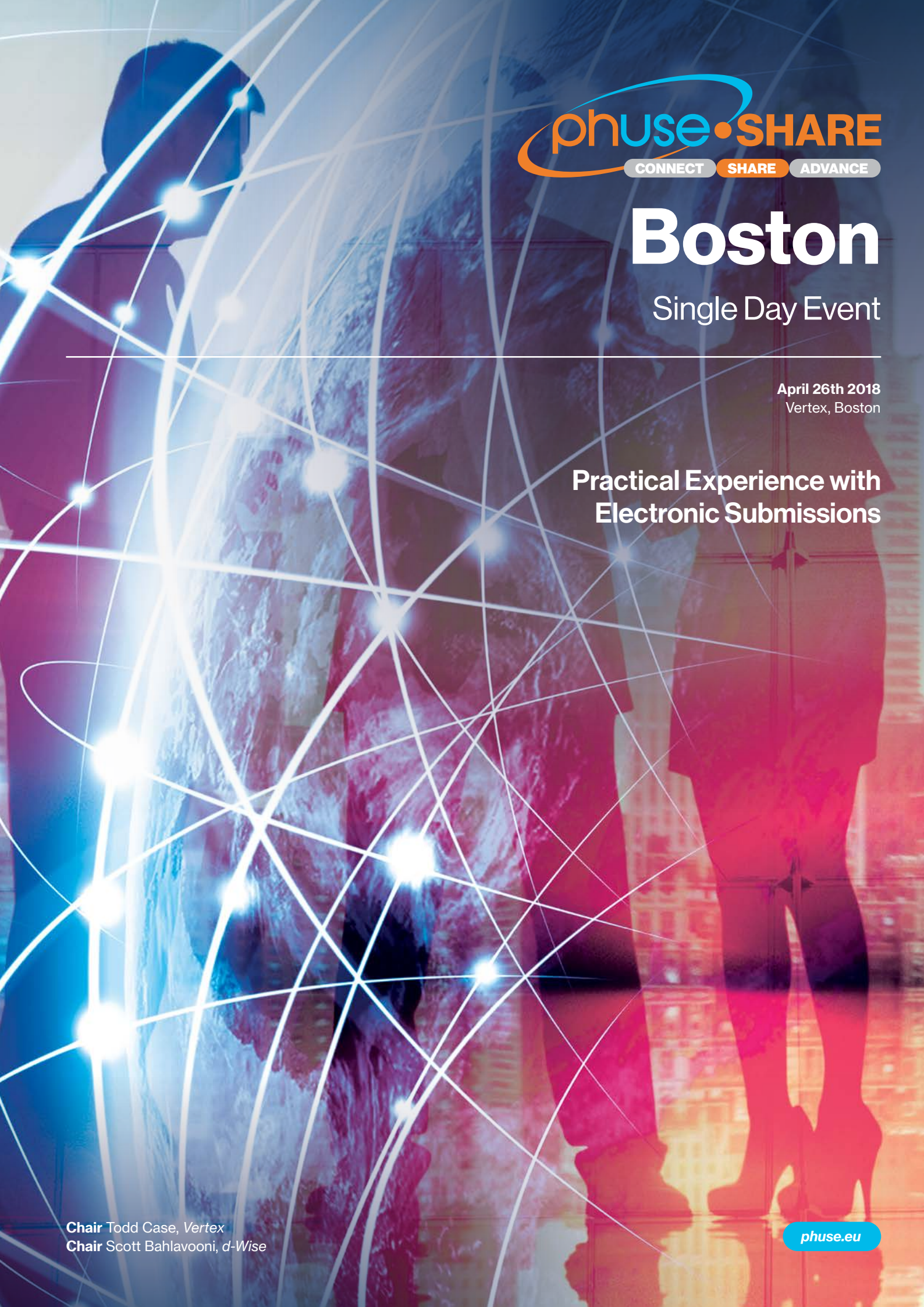

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Boston

Single Day Event

April 26th 2018
Vertex, Boston

Practical Experience with Electronic Submissions

Chair Todd Case, *Vertex*
Chair Scott Bahlavooni, *d-Wise*

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Agenda

Time	Title and Speaker
08:30–09:15	**Registration**
09:15–09:30	**Welcome and Introduction** Mei-Hsiu Ling and Bo Yang, *Vertex*
09:30–10:00	**A Framework for Implementing Evolving FDA Guidance** Todd Case, *Vertex*
10:00–10:30	**CDISC Submissions: A CRO Perspective** Bhavin Busa, *Vita Data Sciences*
10:30–11:00	**Morning break**
11:00–11:30	**Hands-on with the Analysis Data Reviewer's Guide** Shailendra Phadke, *Shire*
11:30–12:00	**PhUSE Working Groups Update** Scott Bahlavooni, *PhUSE Working Groups Director*
12:00–13:00	**Lunch**
13:00–13:30	**Trials and Tribulations: Experiences Using Data Standards and Assisting Staff in Reviewing Submissions** Dr. Jeffry Florian, *FDA*
13:30–14:00	**Standardized Data Sample Submissions: The Key to Improving the Regulatory Submission Strategy** Joanna Koft and Prafulla Girase, *Biogen*
14:00–14:30	**Afternoon break**
14:30–15:00	**Perfecting the Game Plan: The Hand-off from Programming and Stats to Regulatory Operations** Mary Anne Potok, *MMS*
15:00–16:00	**Panel Discussion and Closing Remarks**

"Be heard, be loud, be collaborative."

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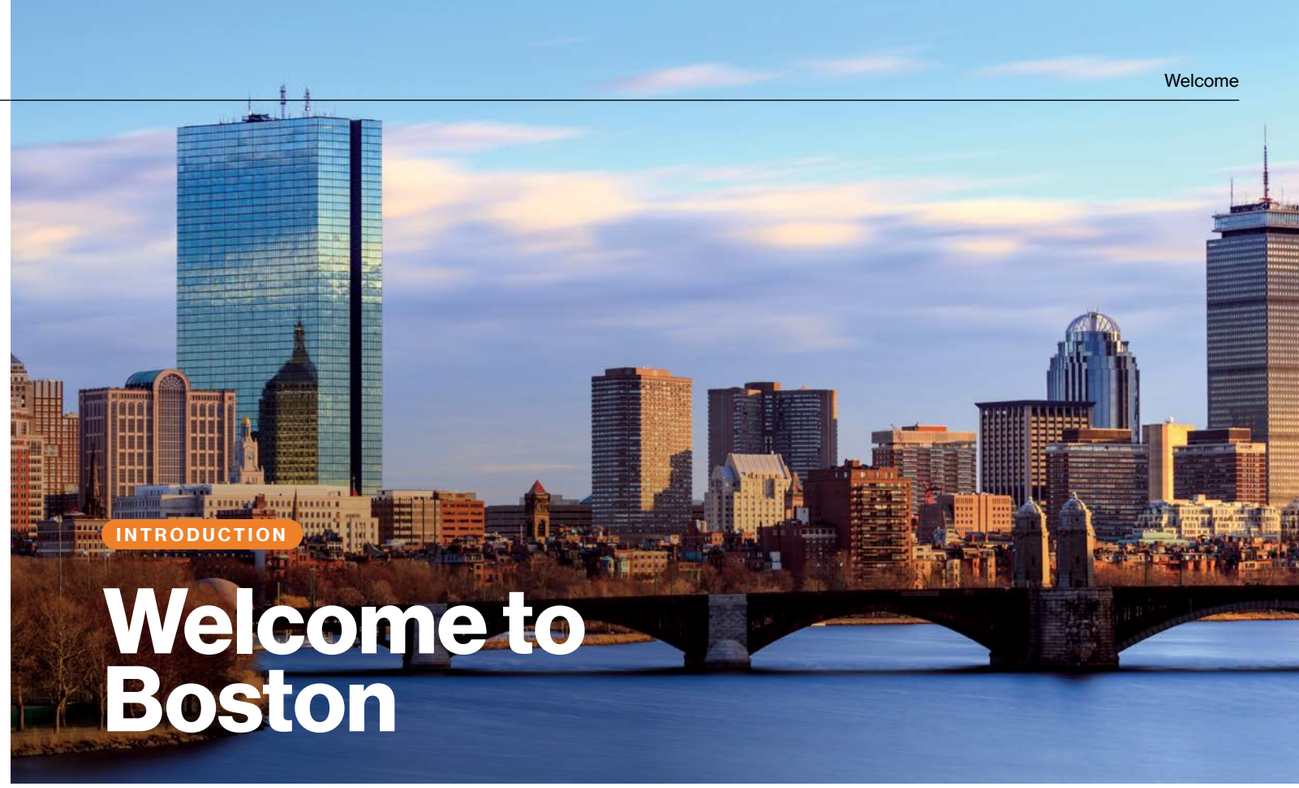


INTRODUCTION

Welcome to Boston

Todd Case
Vertex

Scott Bahlavooni
d-Wise

Chris Hurley
PhUSE Americas Director

Dear Attendees,

Welcome to our PhUSE Single Day Event (SDE) in Boston, MA. Boston is home to distinguished academic and research institutions, world-class medical centers, championship sport teams, and "Dunkies". You probably passed each of these and at least 15 Dunkies on your way to the SDE today. Despite our many stereotypes, Bostonians truly are a collaborative, pragmatic lot. Admittedly, yes, the loud stereotype is accurate...so, we Bostonians are loud, collaborative, and pragmatic.

Our theme today, "Practical Experience with Electronic Submissions", reflects that Bostonian pragmatism. The FDA and PMDA have been requiring standardized study data for certain regulatory submissions since 2016. The regulators have been loud, collaborative, and transparent in sharing their experiences receiving, processing, and reviewing CDISC submissions. The FDA continues that by sharing more trials and tribulations in reviewing standardized study data with us today.

Unfortunately, industry has not been as loud or collaborative in sharing our experiences with standardized study data submissions. We started making some noise during a session at the 2018 Computational Science Symposium and will continue raising our voices at this SDE. We will hear both sponsor and CRO perspectives on CDISC submissions. Several presentations will feature pragmatic approaches to developing and delivering submission artifacts.

Boston played a pivotal role in American history. The first incursions of the American Revolution happened in and around Boston. In 1773, the Boston Tea Party occurred steps from the site of this SDE. We want to channel the spirit of those revolutionaries and today's Bostonians...be heard, be loud, be collaborative. In doing so, we can bring the pragmatism we hear today back to our own companies to make a difference and possibly start a revolution.

Regards,

Todd & Scott

09:15–09:30

Welcome and Introduction

Mei-Hsiu Ling and Bo Yang, *Vertex*

Biographies

Mei-Hsiu Ling is the Executive Director of Biometrics, leading the Statistical Programming group at Vertex Pharmaceuticals. Prior to this, Mei-Hsiu held positions as Director and Senior Director of Statistics at Vertex (leading the Cystic Fibrosis Statistical team), and worked in Respiratory at Novartis for more than 10 years, ending her tenure there as Global Program Head for Respiratory. Before that, she worked as a biostatistician at Schering-Plough. Mei-Hsiu has more than 25 years' industry experience. She received her PhD in Statistics from the University of California at Berkeley.

Bo Yang is the Vice President of the Biometrics group at Vertex Pharmaceuticals, heading the Biostats, Statistical Programming and Modeling and Simulation groups. Previously, Bo held jobs as Global Head of Statistics at AbbVie and Abbott, Sr. Director of BARDS at Merck, and Associate Director of Statistics at Schering-Plough. Bo has over 17 years' industry experience. His research interests include multi-region clinical trials, adaptive design and enrichment design.

09:30–10:00

A Framework for Implementing Evolving FDA Guidance

Todd Case, *Vertex*

Abstract

On July 21, 2004, the US Food and Drug Administration (FDA) announced a format called the Study Data Tabulation Model (SDTM) that sponsors can use to submit data to the agency. 12 years later (on December 17, 2016), the FDA began enforcing the requirement of standardized electronic data submissions in SDTM format and, now, in addition to SDTM, there are multiple sources (and versions) of data standards which impact data supporting applications to the FDA:

- The FDA Data Standards Catalog (primary list and source of standards AND the Study Data Standardization Plan
- The SDTM model (Version 1.4), the SDTM Implementation Guide (SDTMIG Version 3.2), the Analysis Data Model (ADaM) – Version 2.1, the ADaM Implementation Guide (Version 1.1)
- The FDA Guidance for Industry (April, 2017[1])
- The Study Data Technical Conformance Guide (October, 2017)
- Prescription Drug User Fee Act (PADUFA) Version V for fiscal years 2013-2017 (and VI for fiscal years 2018-2022).

At times, these documents, guidances and laws can be contradictory and it's up to the sponsor (when appropriate) to engage with the FDA to determine which 'standard' (of the standards) to adapt, which version(s) to use and when to update versions. The purpose of this presentation is to clearly articulate the definitive source of clinical data standards, what versions of the standards are acceptable and active, and which standards (and guidance/documents) supersede when there are contradictions.

Biography

Todd Case has worked in roles of increased responsibility in the biotech/pharmaceutical industries for over 16 years. During that time he has led multiple groups within biometrics, from project lead to compound lead, to QC lead to TA lead, and is now leading a group responsible for standards, QA/QC and outsourcing operations at Vertex. Along the way, Todd has won numerous awards for leading and managing statistical programming teams to multiple successful FDA (NDA/BLA), EMA (EU), PMDA (Japan) and Rest of World (ROW) filings. He has been a requested presenter and panelist as well as author of numerous papers and presentations at conferences in the US and internationally, including PhUSE, PhUSE SDEs, PharmaSUG, PharmaSUG China, NESUG, SAS Global Forum, JSMs (Joint Statistical Meetings) and the Women's Innovation Network. In addition, Todd has initiated, created and led team and departmental meetings and cross-company meetings, and actively participates in PhUSE and other industry Working Groups.

10:00–10:30

CDISC Submissions: A CRO Perspective

Bhavin Busa, *Vita Data Sciences*

Abstract

Of the several outsourcing models, a Functional Service Provider (FSP) model has become most successful and significant especially in data management, statistical programming and biostatistics service areas of clinical drug development. Most sponsors prefer to have a single, full-service contract research organization (CRO) offering end-to-end services for an entire study including data submission components. However, with the stringent requirements for the CDISC-compliant datasets by the regulatory agencies, the sponsors are at a higher risk of getting a refuse to file (RTF) due to compliance issues with the submitted data. The full-service CRO may not have an all-round expertise in each of the service areas, which will lead to poor quality of the submission deliverables and delays. An FSP model is a perfect fit to these services as it gives the sponsor an ability to access the optimal functional expertise, in addition to the quality and operational needs, to meet their expedited submission timelines. In this presentation, we will discuss a case study where we, as a niche provider, worked with a sponsor towards their final NDA submission packet, even though the sponsor had outsourced these services to a global full-service CRO. We will outline significant gaps identified in the deliverables provided by the full-service CRO, services we offered, and how we rescued this sponsor to be able to meet the quality expectations and submission timeline. In addition, we will summarize lessons learnt during our engagement with this particular sponsor.

Biography

Bhavin Busa, Director of Statistical Programming and Data Analytics at Vita Data Sciences (VDS), a division of Softworld, Inc., is responsible for managing the Statistical Programming and Clinical Data Analytics group at VDS. He has over 12 years' of experience working with both CRO and sponsor companies and is a thought leader in the area of data standards, analytics and regulatory submissions. Before joining VDS, he worked at Cubist, where he led multiple successful submissions, worked on global data standards implementation, and developed SAS-based automated reporting systems.

Bhavin is actively involved with the PhUSE Optimizing the Use of Data Standards Working Group and is currently leading a "SDTM/ADaM Implementation FAQ" project which involves gathering frequently asked questions by the industry and providing a response, which will soon be available to the general public on the PhUSE Wiki.

11:00–11:30

Hands-on with the Analysis Data Reviewer's Guide

Shailendra Phadke, *Shire*

Abstract

The Analysis Data Reviewer's Guide is a very important document. A successful submission with a faster regulatory agency review depends on the quality of the submission package as well as the ease with which the reviewer can interpret the submitted data and understand the analysis and derivations. One of the key elements of the submission package that will help reviewers with data interpretation and understanding study analysis is the Analysis Data Reviewer's Guide (ADRG). This presentation will give an overview of the ADRG, and will talk about a new approach in creating as well as reviewing the ADRG. It shall also discuss some regulatory reviewers' expectations and some dos and don'ts while writing the ADRG.

Biography

Shailendra Phadke has worked in roles of increased responsibility in the biotech/pharmaceutical industries and CROs. He is currently working at Shire as an Associate Director, Statistical Programming. He has led statistical programming teams in successful submissions to different regulatory authorities such as the FDA, EMA and PMDA. He has also presented twice at PharmaSUG on topics such as "Application development to map datasets and

output dependencies using SAS" and "How to maintain quality of a submission package in a partnership model using different techniques".

13:00–13:30

Trials and Tribulations: Experiences Using Data Standards and Assisting Staff in Reviewing Submissions

Dr. Jeffry Florian, *FDA*

Abstract
Clinical review is a crucial component in assessing the clinical efficacy and safety of drug products. With the development and adoption of standards for submitting clinical trial data and documents, staff have some expectation of receiving information in a consistent format. At the same time, clinical reviewers are being asked to understand elements beyond their training. One solution for addressing this need has been the creation of Associate Directors for Biomedical Informatics (ADBMI) positions within a subset of the Office of New Drug Divisions. This presentation will provide information regarding the role of ADBMIs and how they interact within their Division and the review process. The presentation will also cover experiences from ADBMIs and other clinical review staff over the past few years reviewing standardized and non-standardized data.

Biography
Dr. Jeffry Florian received his PhD in Chemical Engineering from the University of Pittsburgh in 2007, where his work focused on dose optimization of cycle-specific chemotherapeutics and empirical modeling for glucose control in critical care and diabetes. Following his PhD, he completed a post-doctoral fellowship with the FDA evaluating how thorough QT trial design may impact results and performing viral dynamic modeling of emerging hepatitis C therapies. Jeffry joined the Division of Pharmacometrics in 2010, working first as a reviewer then as a team leader. His responsibilities included covering various therapeutic areas including cardiovascular/renal, transplant, antiviral, anti-infective, dermatology, reproductive, urology, and bone products. Jeffry has recently transitioned to the Biomedical Informatics and Regulatory Review Science team in the Office of New Drugs, Immediate Office, where he oversees various informatics-related projects within the OND.

13:30–14:00

Standardized Data Sample Submissions: The Key to Improving the Regulatory Submission Strategy

Joanna Koft and Prafulla Girase, *Biogen*

Abstract
Over the course of the past six years, Biogen has submitted (and received approval for) several standardized data submissions to regulatory agencies. Submission strategies have always existed, but have needed a makeover due to the new way of thinking brought on by the increasing demand for standardized clinical data coupled with the evolving regulatory landscape needed to accommodate them. This presentation, composed of two parts, will take you on the journey of how Biogen's submission strategies have evolved and how the "standardized data sample submission" came to be an integral and highly useful component. We will walk through the key parts of a sample submission as well as how to plan and implement one. From here, we will introduce four case study overviews of how we have successfully utilized the sample submission, focusing on the following core areas:

- stakeholders involved
- FDA feedback
- continuous improvement.

As regulatory submission requirements are continuously advancing both in scope and location (PMDA), it is critical to re-evaluate the submission strategy and enhance it with new ideas. These are the keys to successful submissions and, ultimately, getting treatments to patients quicker.

Biographies
Joanna Koft has been in the biotech industry for 18 years, holding various positions within biometrics, statistical programming, vendor relationship management, and clinical data standards and governance. She is currently the Director of Data Standards and Governance within the Global Biometrics department at Biogen, where she leads a team responsible for the development, maintenance, implementation and governance of clinical data standards. In addition, Joanna is responsible for strategy definition and management of operational capabilities for clinical data sharing on behalf of Biogen.

Prafulla Girase has 18 years' experience in the biotech industry including experience of working on six NDA/BLA clinical data submission packages that are currently approved therapies in the market. He currently works as a Principal Analyst in Data Standards and Governance at Biogen, where he is responsible for data standards and governance work related to ADaM, analysis results, and submission standards. Prafulla is an active member of PhUSE and currently co-leads the PhUSE Define-XML 2.0 Completion Guideline Working Group.

14:30–15:00

Perfecting the Game Plan: The Hand-off from Programming and Stats to Regulatory Operations

Mary Anne Potok, *MMS*

Abstract
Programming and statistics outputs are the crucial deliverables upon which an NDA is built. However grueling, their completion signals the start – rather than the finish – of the thrilling and exhausting final quarter of the submission process. Winning submission teams focus on three key elements of teamwork: conditioning, planning, and making adjustments. These steps are especially critical when delivering data packages to regulatory teammates for publishing. "Final" datasets, program files, and TFLs are rarely in a format that is acceptable in eCTD submissions. Data packages must undergo a significant transformation to be included in an application. A proactive effort is needed to maintain the integrity of the data and ensure compliance with current regulatory guidelines. For a recent NDA, our Programming, Statistics, and Regulatory Operations groups worked together to submit over 30 separate data packages from 17 legacy studies, 3 CDISC-compliant global Phase III studies, integrated safety and efficacy, BIMO, and legacy nonclinical studies. This case study will diagram how cross-functional team training, well-drawn and precisely executed transfer plans, and flexibility in the face of adversity can lead to victory for the entire submission team.

Biography
Mary Anne Potok is a Regulatory Operations Technical Manager, having joined MMS in Canton, MI, in 2013. She serves as Global Resource Manager for the Regulatory department and shares resourcing responsibilities within the MMS-Asia headquarters in Bangalore, India. Mary Anne brings 15 years of experimental and operational experience in the academic, clinical, and pharmaceutical arenas. Her campaigns for organizational efficiency, inter-departmental cooperation, and global integration have helped pharma partners of all sizes achieve success. Mary Anne has a strong professional interest in clinical trial transparency and working with small to mid-sized pharma clients, as they navigate the electronic submission process.

In your own words

Notes

EVENTS

Dates for your diary

Dates may be subject to change – for more information, visit phuse.eu/conferences

February

Netherlands SDE
Utrecht
Wednesday 7th

US SDE
Foster City, CA
Thursday 22nd

March

CSS US
Silver Spring, Maryland
Sun 4th – Tue 6th

India SDE
Delhi
Saturday 17th

April

US SDE
Boston, MA
Thursday 26th

May

Japan SDE
Tokyo
Friday 11th

Germany SDE
Frankfurt
Tuesday 15th

US SDE
Collegeville, PA
Thursday 17th

China SDE
Beijing
Friday 18th

India SDE
Bengaluru
Saturday 19th

June

US Connect
Raleigh, NC
Sun 3rd – Wed 6th

Denmark SDE
Copenhagen
Thursday 14th

Switzerland SDE
Basel
Thursday 28th

July

India SDE
Hyderabad
Saturday 14th

Singapore SDE
Singapore
Wednesday 25th

US SDE
Ridgefield, CT
Thursday 26th

August

No events currently planned – keep an eye on the PhUSE website for announcements

September

Canada SDE
Mississauga
Thursday 13th

Belgium SDE
Brussels
Friday 21st

October

Poland SDE
Warsaw
Friday 12th

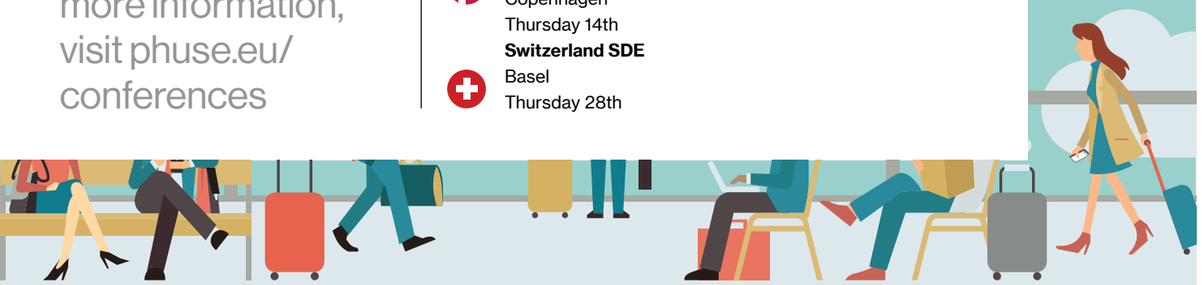
India SDE
Chennai
Saturday 13th

November

China SDE
Shanghai
Friday 2nd

EU Connect
Frankfurt, Germany
Sun 4th – Wed 7th

South Africa SDE
Bloemfontein
TBC



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US 2018

The Clinical Data Science Conference

June 3rd–6th
Raleigh Convention Center
Raleigh, North Carolina, USA

Chair Jim Johnson, *Summit Analytical*
Co-Chairs Jennifer True, *GSK* & Terek Peterson, *Covance*

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