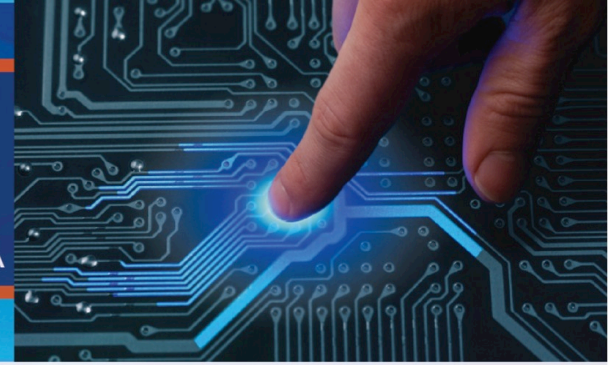




**FDA/PhUSE Annual
Computational Science Symposium**

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Challenges, Gaps and Opportunities from FDA Initiatives CBER Perspective

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Overview

- 2011 Sets Stage for 2012
- Gaps
- Challenges
- Opportunities



2011 Sets Stage for 2012

- eStudy Data Guidance
 - The purpose of this guidance is to promote the use of data standards in the electronic submission of study data to the FDA
 - Comment period closes April 21, 2012
- Janus
 - Data model re-designed to allow for future submission of CDISC and HL7 formatted electronic data
 - First prototype of repository will be available for internal testing summer of 2012



2011 Sets Stage for 2012

- CBER Legacy Data Conversion
 - Converted 12 vaccine studies to SDTM and created 36 analysis datasets
 - Additional 13 studies and 39 analysis datasets will be created in 2012
 - Collecting lessons learned to inform on improvements in Agency business processes, CDISC standards and new analysis paradigms



2011 Sets Stage for 2012

- Spotfire
 - Pilot to evaluate value added to existing toolbox
 - Installation in progress, evaluation will occur in 2012
- Amalga
 - Agency initiative from Office of Chief Scientist
 - Initial pilot two use cases, 1 CDRH, 1 CBER
 - Evaluate:
 - Effectiveness with standardized versus non-standardized data
 - User interface and visualization capability
 - Ability to mix data from multiple sources in multiple formats



GAPS

- Gaps in SDTM Identified to Date
 - Reproductive Findings
 - Macroscopic Findings (gross findings, seen with naked eye)
 - Microscopic Findings (seen with microscope)
 - Procedures
 - Non-subject findings
 - Elimination/Continuation Criteria
 - Sponsors want a define.xml for ADaM
 - Reviewers want to be able to print the define.xml



GAPS

- We Need Business Rules
 - What are the relationships between data elements and how does this impact the standard(s)
 - Where should we put specific data?
 - Is there one answer? This may be dependent on the study design
 - Submit everything that is collected, what does that mean? Should you create a SUPPQUAL to send us the initials of the subjects? Need a business rule that indicates this is not relevant data.
 - How to handle a follow up or add on study where dosing was done in study #1, study #2 has no exposure domain and two separate study numbers were assigned?



- We Need Business Rules
 - MedDRA Coding:
 - How do you code pain from broken leg from a car accident? Do you code as Neurological SOC, Musculoskeletal SOC or Injury?
 - Should it be coded to the root cause if known?
 - Should we follow business rules used on post market side?
 - Use English



– Documentation Rules

- How to identify variables that are on the CRF that were collected and submitted versus variables that were not collected or were collected and not submitted?
- Should you include an annotated CRF and define.xml with the datasets whether it is an original submission, supplement or amendment?
- Is it required to attach or include diary cards and other questionnaires with annotated CRF and annotate these documents as well?



GAPS

– Analysis Traceability

- How to improve clarity between the tabulation data, the analysis datasets and the clinical summary report

– Validation Results

- Are they a result of
 - Legacy data conversion (fitting a square peg in a round hole)
 - Gaps in standard
 - Rule not written properly to obtain desired result



CHALLENGES

- Not enough hours in the day
- We don't always know what we do not know
- All clinical trials were not created equal
- Science changes
- Everyone has a day job
- The standards are evolving and are incomplete xpt as a transport mechanism is ineffective
- Standardized terminology is key to an effective solution



CHALLENGES

- Not all tools created equal, reviewers need a tool box not just one stop shopping to complete their work
- Regulatory requirements are becoming more complex and the Agency has to identify ways to modernize the review process



Opportunities

- Partnership with SDOs and Industry to develop solutions to some of the challenges that face us today
 - Collaboration between CBER, CDER and CDRH to harmonize, where possible
 - Collaborative Agreements with organizations such as Johns Hopkins for the PACES Project (Partnership in Applied Comparative Effectiveness Science)
 - Evaluate new methodologies for analysis
 - Evaluate new adaptive clinical trial design



Opportunities

- Participation in standards development activities with CDISC and HL7
- CDER Grants Program for Data Standards Development
- FDA/PhUse Computational Science Symposium
 - Not a two day event but a living collaboration that is intended to persist after the meeting is over
 - Six Working Groups with co-leads from FDA and Industry
 - PhUse Wiki a collaboration workspace



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