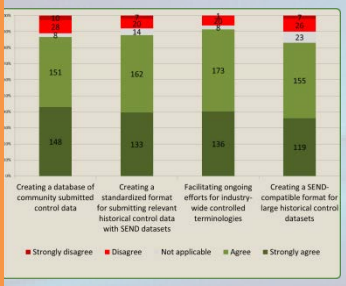
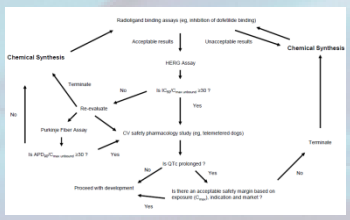
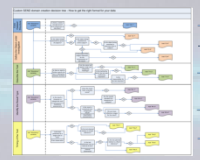
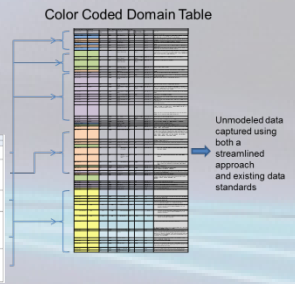
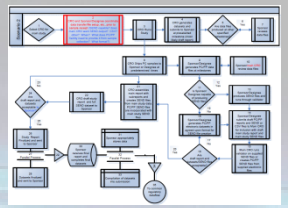
Nonclinical Working Group Update CSS 2014











Nonclinical Working Group

6 projects with significant accomplishments over the past year

- White paper published (3/14):

  "Interconnectivity of Disparate Nonclinical Data Silos for Drug Discovery and Development"

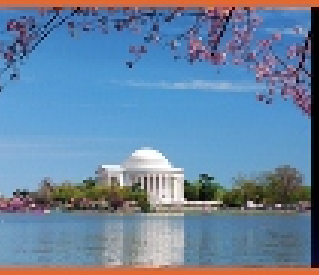
- Manuscript developed on industry use of Nonclinical Historical Control Data

- Expansion of SEND Wiki, with QA perspectives on SEND – poster

- Compared Clinical vs Nonclinical Study Data Reviewer's Guide – poster

- Development and testing of interorganizational flow of e-data – 2 posters

- "How to Design a Custom SDTM Domain for Nonclinical Data"

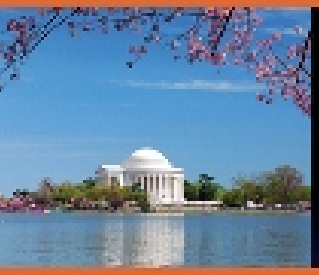


CSS PhUSE 2014 Theme Developing Collaborations

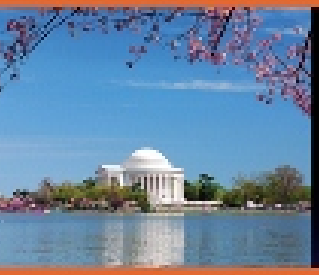
Our Sessions

1. Panel discussion – "How are clinical and nonclinical data coming together in your environment?"
   - 3 presenters shared experiences (vendors, sponsors, consortia)
2. Develop collaborations across PhUSE and others –
   - Interactive discussion on possible projects with Emerging Technologies, IMIeTox, and Transcelerate
   - Goal to increase potential for collaborative new projects
3. Team time
   - Opportunity for NC projects to get feedback from full WG on accomplishments and future directions
   - New project idea triage and action plans
4. Leveraging Deliverables
   - "Table Teams" contributed their experience Socializing the Deliverables

New Outcomes & Actions for 2015

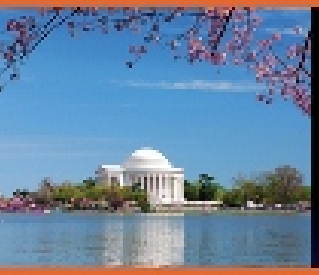


- Presentation of Standards Roadmap project: *"How to Design a Custom SDTM Domain for Nonclinical Data"*
  - Action decided: Pilot this design process on new SEND domains for Safety Pharmacology and Repro - to "vet" the process and domains
- New historical control projects proposed:
  - Recommendation on study level metadata valuable to nonclinical historical control data.
  - SEND representation of domain relevant historical control values or best practices for submitting HC information in SEND data sets
  - Catalog of available HC resources
- New NICE project proposed:
  - Utilizing information on Drug Labels to derive useful conclusions on clinical/nonclinical outcomes, by pharmacologic class



New Outcomes & Actions for 2015

- New Project: Nonclinical Source System Providers Engagement & Education
  - Facilitate greater participation of data system vendors in development and implementation of data standards
  - Onboarding tools
- New collaborative projects to explore with Emerging Tech
  - to validate variable alignment between SDTM and SEND using RDF models
  - to use RDF model as a validation tool to check data set against req, exp, perm variables
- Nonclinical SDRG new activity:
  - Explore opportunities to contribute to management of SEND validation rules (develop examples and process to address errors and warnings)
- Consolidate “Leveraging Deliverables” feedback to publish on WIKI

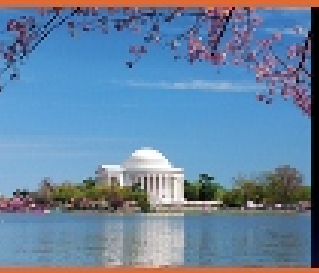


New Outcomes & Actions for 2015

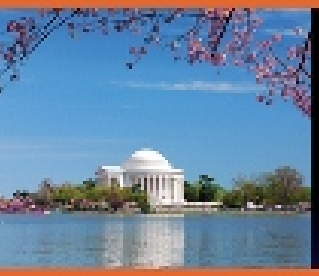
- *AND……..*

  Turbocharge the SEND Implementation User Group!

  - New members, WIKI tools, communication subteams
  - Increase resources to manage FAQ page
  - Develop communication package for EU
  - Develop Onboarding tools




BACKUP
- project status slides



SEND Implementation User Group

- Goals of the project
  - Stand up wiki for knowledge base
  - Stand up forum capability for implementers to ask and discuss issues
- Project status: nearing completion
- Ambitions and/or Accomplishments
  - Wiki receiving continual updates
  - Forum capability decided and tested
  - Official notice in March

- Troy Smyrnios, Lynda Sands
- SEND Implementation User Group page

Nonclinical Data Interconnectivity for Endpoint Predictivity (NICE)

- Goals of the project
  - Explore means by which nonclinical data can be interconnected in ways that will facilitate its use in predicting outcomes in humans.
- Project status:
  - Group is in transition after consolidating two groups: Endpoint Predictivity and Data Interconnectivity
- Accomplishments
  - Accepted for publication, March 2014: ***"Interconnectivity of Disparate Nonclinical Data Silos for Drug Discovery and Development"*** in Therapeutic Innovation & Regulatory Science
- Goals
  - Establish new core objective for group

  Possible projects to explore:
  - Using compound metadata for evaluating nonclinical data and making predictions for clinical safety based on known safety issues for a drug class.
  - Developing data analysis flow charts
  - Identifying and discussing software/in silico predictivity tools
  - Collaborating with other clinical working groups on predictivity

Nonclinical Data Interconnectivity for Endpoint Predictivity (NICE)

Questions for Nonclinical Working Group

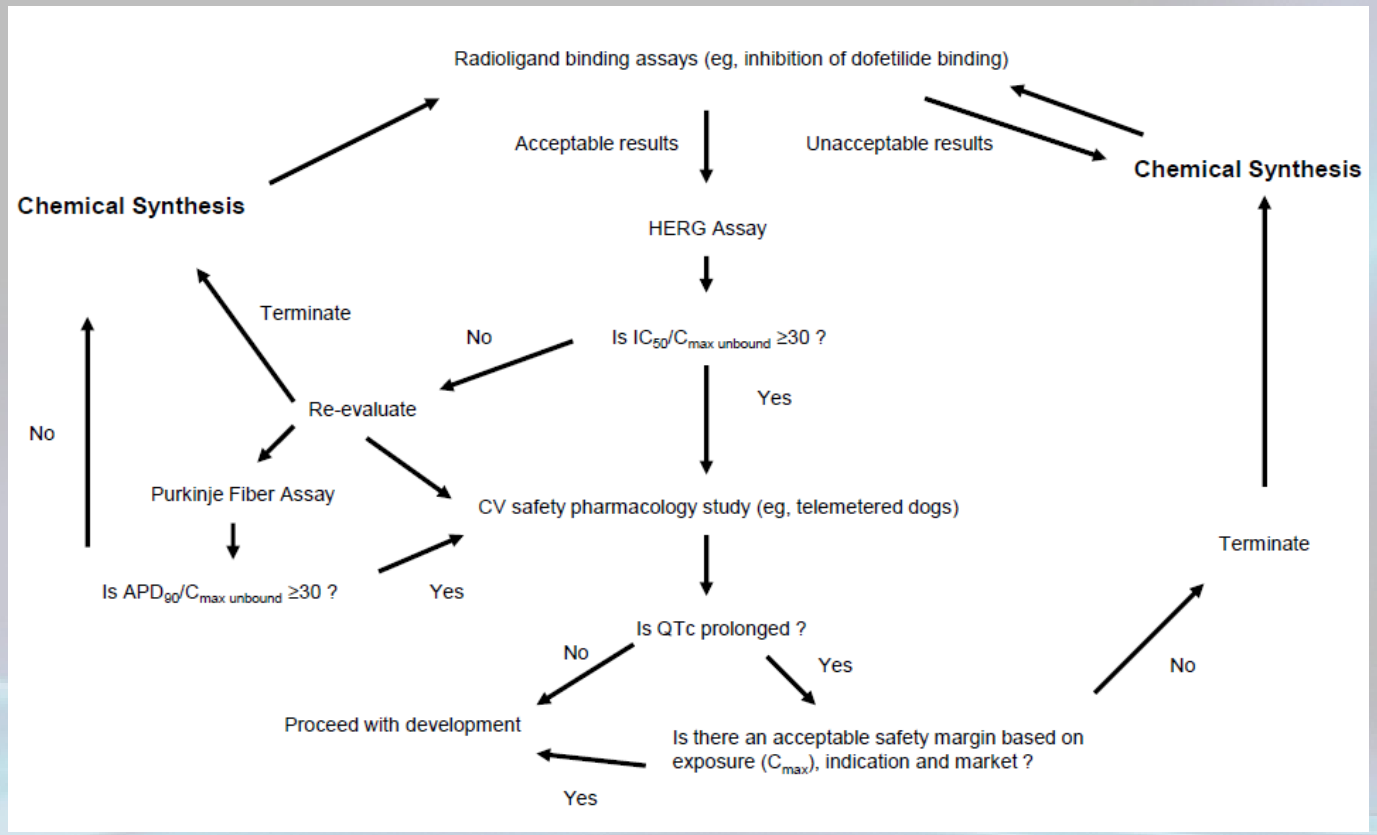
1. Should NICE identify specific safety concerns and attempt to analyze nonclinical and clinical data ?
2. Should the focus of NICE be to explore general or theoretical models for analyzing nonclinical data to predict for human safety ?
3. Is there interest for developing models for correlating toxicity data with pharmacologic class ?
4. Would flow charts for data analysis, modeling and yes/no outputs be of interest for evaluating a specific safety issue (see next slide)
5. How should nonclinical metadata be used for data analysis, hazard identification and risk assessment ? Is this a viable topic for the group to explore ?

Membership: Alan Brown, Paul Brown, Jyotsna Kasturi, Joelle Ibanes, Paul Bradley, Jon Kimball, Jane Reed, Ron Filler, Laura Kauffman, Latha Prabakar

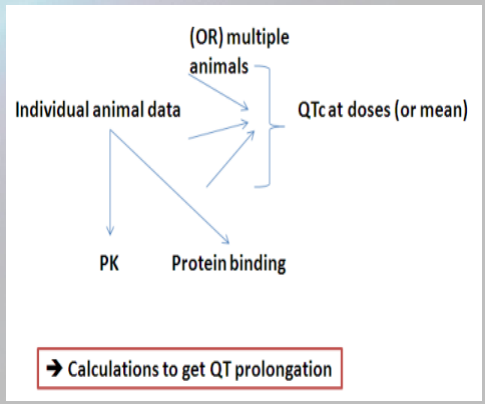
http://www.phusewiki.org/wiki/index.php?title=NICE

Nonclinical Data Interconnectivity for Endpoint Predictivity (NICE)

Data Analysis Flow Chart – Example for QTc Prolongation



Data Integration of QT and PK



Standards Roadmap Team

- Goals of the project
  - Identify priorities and opportunities in nonclinical data based on the current status of data standards.
- Project status
  - Ongoing - We transitioned from our white paper to creating a resource titled, “How to Design a Custom SDTM Domain for Nonclinical Data”
- Ambitions and/or Accomplishments
  - Posted white paper on Wiki entitled, “**The Roadmap for Nonclinical Data Standards and Elements to Improve Data Access.”** Room for additions if topics warrant further discussion.
  - Completed first draft of “**How to Design a Custom SDTM Domain for Nonclinical Data”** resource.
  - Aim: Use the “Custom Domain” resource on three different data types.
- If interested, contact Gitte Frausing and Bob Dorsam
- Link http://www.phusewiki.org/wiki/index.php?title=WG6_Nonclinical_-_Standardization_Roadmap

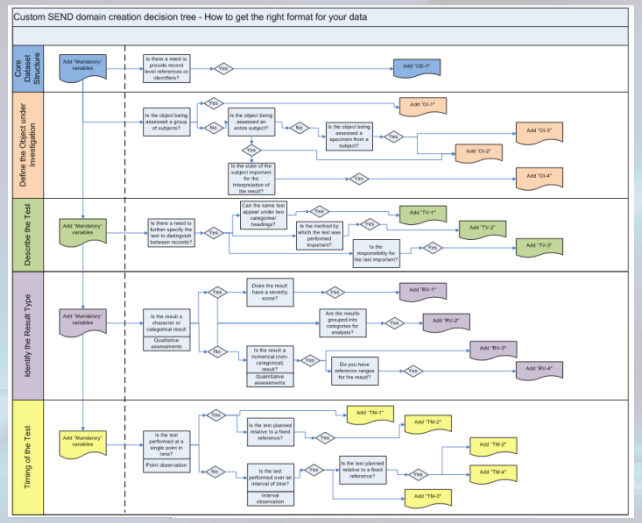
Standards Roadmap Team

"How to Design a Custom SDTM Domain for Nonclinical Data"

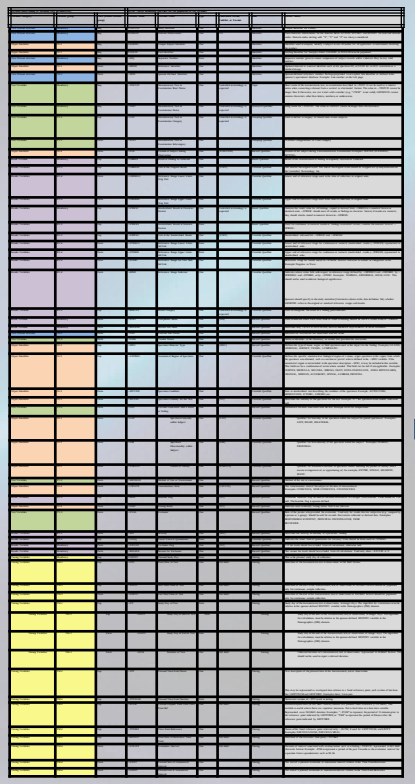
Unmodeled data

Instructions

Decision Tree



Color Coded Domain Table



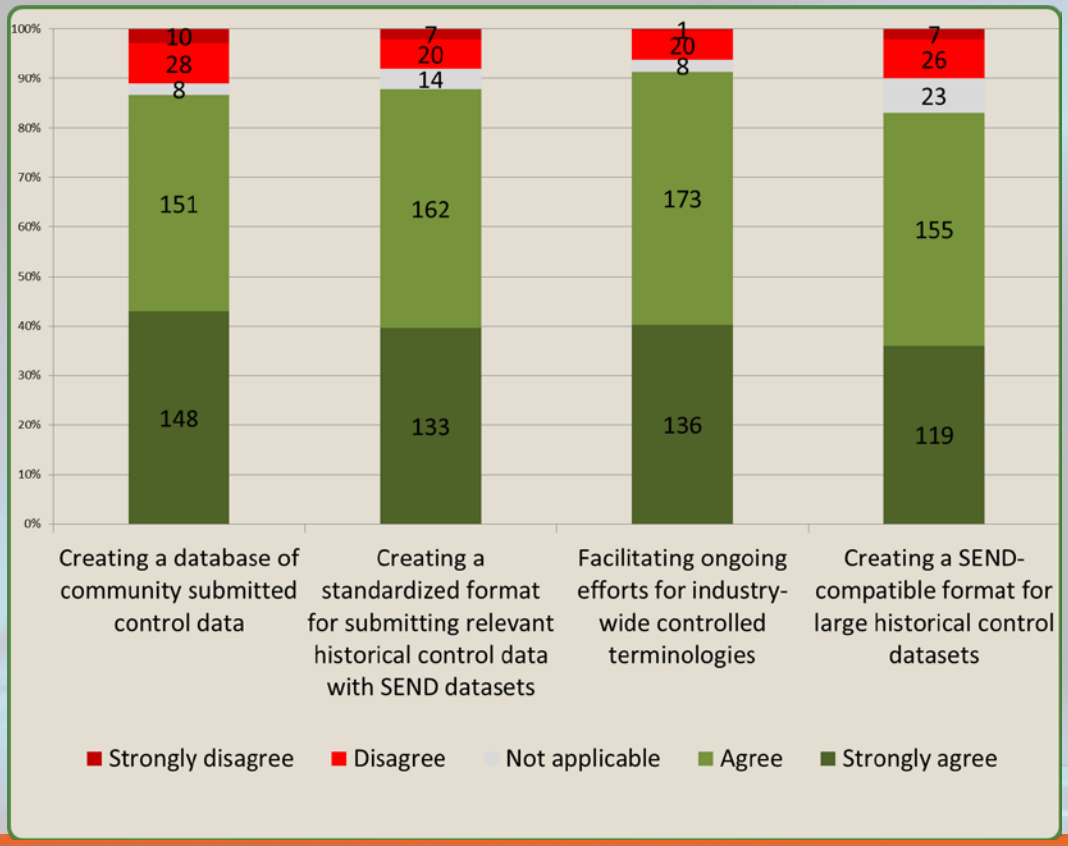
Unmodeled data captured using both a streamlined approach and existing data standards

Historical Controls

- Goals of the project
  - creation of a concise definition of historical control data,
  - identification of published resources that discussed historical control data
  - creation and distribution of survey to assess current and desired use of historical control data
  - and analysis of the survey results
- Project status: Near completion
- Ambitions and/or Accomplishments
  - Survey complete
  - White paper in clearance
- Co leads: Lauren Mihalcik & Jen Feldmann
- http://www.phusewiki.org/wiki/index.php?title=WG6_Nonclinical_-_Historical_Controls

Visual for project

What projects involving historical control data do you think would be a useful undertaking for the nonclinical community?



Interorganizational SEND

- Goals of the project
  - Identify and tackle the highest priority concerns related to inter-organizational SEND dataset creation and use.
- Project status: Ongoing
- Accomplishments (Posters)
  - PP08 Selecting a CRO for Creating and Integrating SEND Datasets from Multiple Organizations
  - PP12 Application of a Quality System to the Generation and Submission of SEND Files
  - PP13 SEND Datasets from Studies Conducted at Multiple Organizations: An Update Based on Current Practices
- Contacts: William Houser, Debra Oetzman
- Link to project WIKI and membership: http://www.phusewiki.org/wiki/index.php?title=Interorganizational_SEND

Study Data Reviewers Guide ~Nonclinical Perspective~

- Goals of the project
  - To evaluate the Clinical SDRG template developed by the Optimizing Standards PhUSE WG to determine: 1) Is the clinical SDRG template appropriate for nonclinical? 2) If not, can it be modified? 3) Is a new nonclinical SDRG template needed?
- Project status:
  - Analysis completed
  - Next step: Develop Nonclinical template modelled on the Clinical template with appropriate adaptations
- Accomplishments
  - The clinical SDRG template & examples were used to develop a nonclinical SDRG for a complex and a simple study.
    - Sections were compared and assessed for usefulness and applicability
    - Comparison to Draft Data Technical Conformance Guide
  - Recommendation for suitability of Clinical template completed
- Goals for coming year
  - Complete Nonclinical SDRG Template with a guide for use
  - Develop useful examples from Repeat Dose Tox Studies
  - Publish on the PhUSE WIKI for public use