Statistical Review and Data Standards: It's Gettin' Better All The Time

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FDA/OMPT/CDER

2017 PharmaSUG

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Disclaimer

This presentation reflects the views of the speaker and should not be construed to represent FDA's views or policies

It’s Getting’ Better

- Our Shared Mission
- It’s Getting’ Better
  - Submission
  - Review
  - Science/Standards
  - Awareness
  - Collaboration
- Challenges

Our Shared Mission

- … responsible for protecting the public health by assuring the safety, efficacy and security of human and veterinary drugs, biological products, medical devices, ….
- … responsible for advancing the public health by helping to speed innovations that make medicines more effective, safer, and more affordable and by helping the public get the accurate, science-based information they need to use medicines and foods to maintain and improve their health…

https://www.fda.gov/downloads/aboutfda/reportsmanualsforms/reports/budgetreports/ucm298331.pdf

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Patients

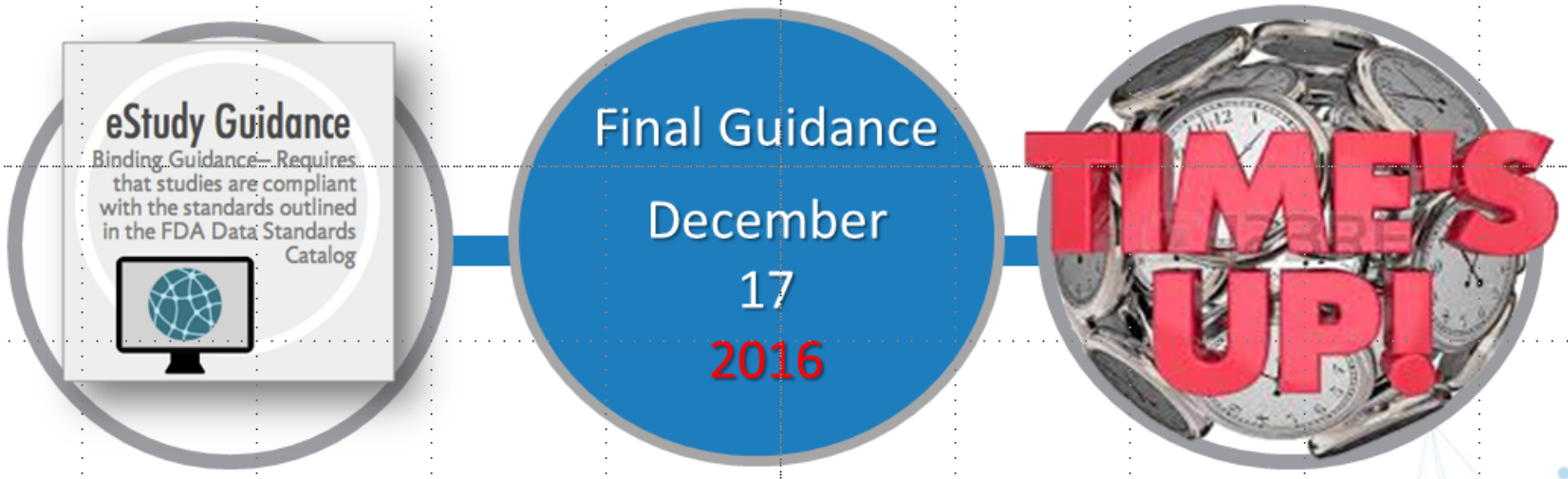
People

Us

https://www.fda.gov/downloads/aboutfda/reportsmanualsforms/reports/budgetreports/ucm298331.pdf

Submission: PDUFA V

FINAL ESTUDY DATA GUIDANCE + 2 YEARS



Adopted from Fitzmartin, 2017

Submission: PDUFA VI

5. Enhancing Capacity to Support Analysis Data Standards for Product Development and Review

- FDA will develop the staff capacity to efficiently review and provide feedback to sponsors on the readiness of submitted analysis data sets and programs for statistical review.
- … support pre- and post-submission discussion of standardized datasets and programs, and maintain the knowledge of and engage in collaborations about standards models used in the design, analysis and review of clinical and non-clinical studies.

https://www.fda.gov/downloads/forindustry/userfees/prescriptiondruguserfee/ucm511438.pdf

Review:
Data Review Committee (DRC)

From the OB/SPC Data Review Committee Charter

- Describe and assess OB practice for the receipt and handling of review data
- Develop necessary OB-wide Standard Operating Procedures (SOPs)
- Collaborate with internal data standards organizations
- Liaise with outside organizations and activities (e.g., CDISC, PhUSE, PharmaSUG, TransCelerate, CPath Institute, CFAST, DIA, HL7, SCDM and ASA) to influence and improve …
- Develop external communication plans for data policies
- Coordinate with the OB Training Committee to provide periodic reassessment of OB training needs.

Review:
Analysis Review Files

SS07 : Overview and Application of the HCV Vertical Resistance Analysis Template

Yan Xie, Abbvie

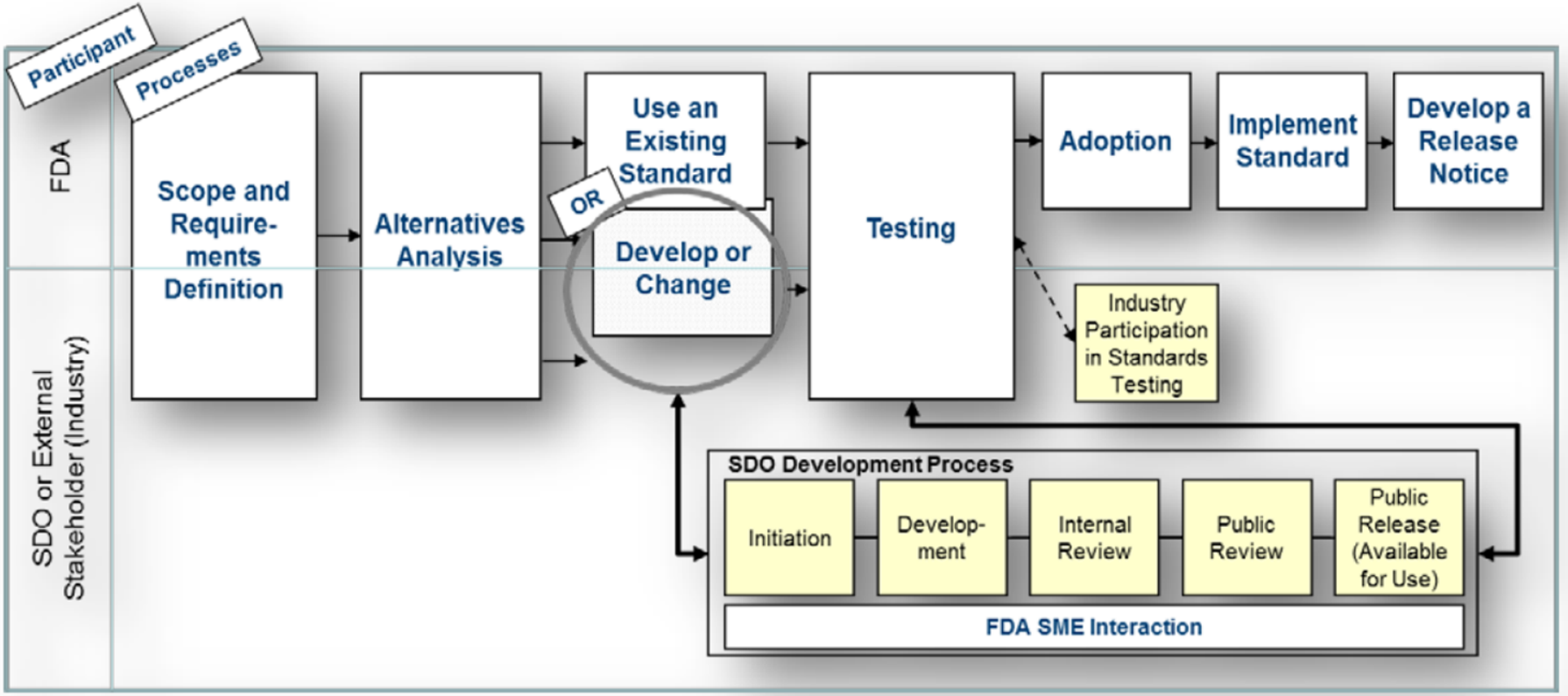
Tuesday, 4:00 PM - 4:20 PM, Location: Key Ballroom 10

FDA proposed a new hepatitis C (HCV) vertical resistance draft template on March 2016, which is quite different from the existing guidance for submitting HCV resistance data. The new vertical template is not published yet and is still under review, but FDA encourages and expects the sponsors to submit the resistance data using the new template. Compared to the previous horizontal template, the new vertical template is more advanced because: 1. it is compatible with current SDTM and ADaM standards, 2. it reduces numerous variables by applying the streamlined and simplified vertical format, 3. it can hold the Next Generation Sequencing (NGS) data, and 4. it can hold multiple targets and HCV subtypes in one dataset. The variables in the new vertical template include three categories of variables, subject level characteristics, pharmacogenomics results, and phenotypic results. ...

http://www.pharmasug.org/us/2017/papers.html#SS07

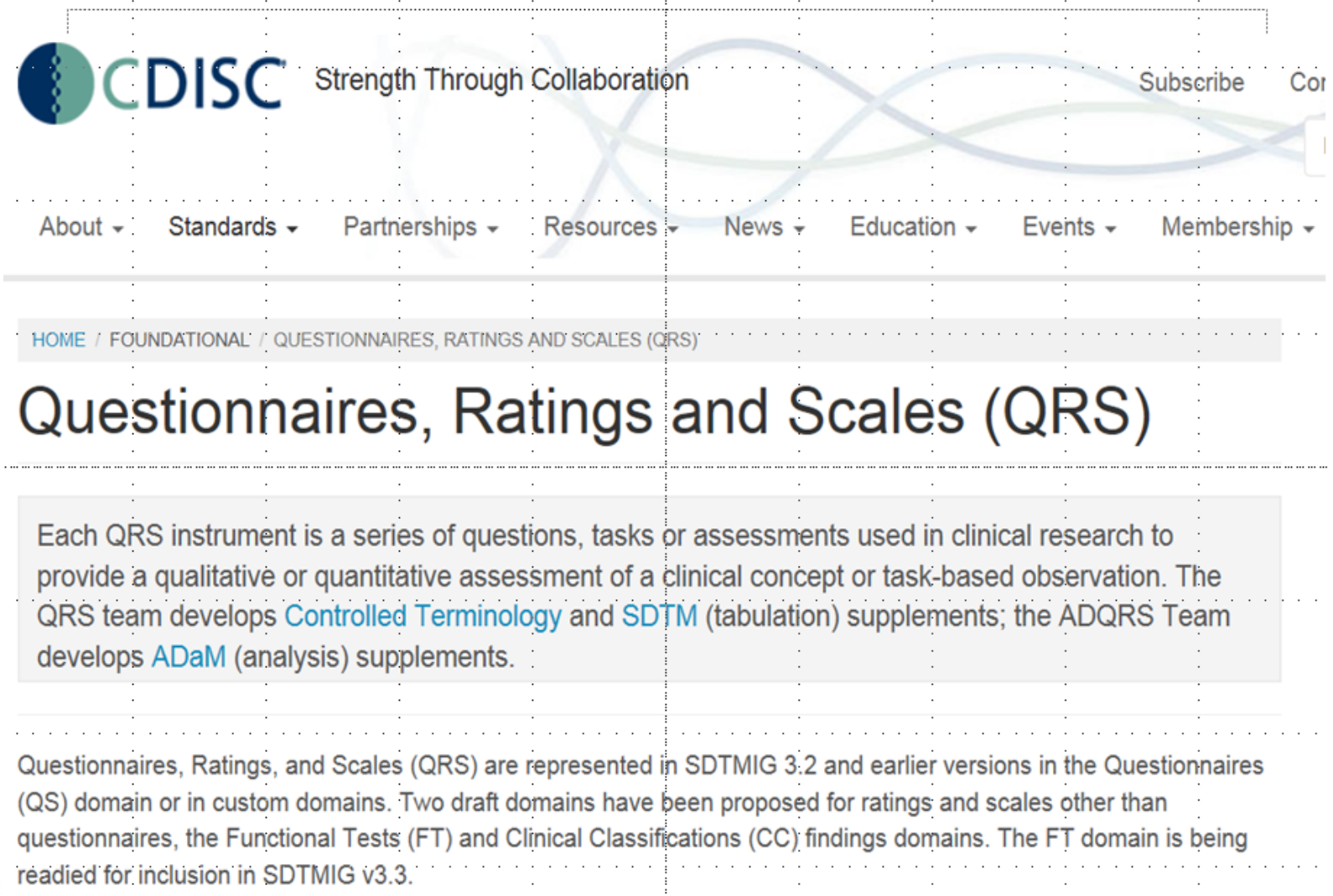
Science/Standards: Therapeutic Areas and Analysis

Figure 1. Collaborative Standard Development Process



https://www.fda.gov/downloads/drugs/developmentapprovalprocess/formssubmissionrequirements/electronicsubmissions/ucm371691.pdf

Science/Standards: COAs & the CDISC QRS Team



https://www.cdisc.org/foundational/qrs

Science/Standards: PRO CTCAEs

https://healthcaredelivery.cancer.gov/pro-ctcae/

Awareness: NIH/FDA Protocol

<Title>

The title should be easy to remember, recognizable by administrative support staff, and sufficiently different from other protocol titles to avoid confusion. Brevity with specificity is the goal.

Protocol Identifying Number: < Number>

Principal Investigator: < Principal investigator>

IND/IDE Sponsor: <Sponsor name, if applicable>

Do not include IND/IDE number

Sponsor means an individual or pharmaceutical or medical device company, governmental agency, academic institution, private organization, or other organization who takes responsibility for and initiates a clinical investigation.

Funded by: < NIH Institute & Center (IC)>

Draft or Version Number: v.<x.x>

<Day Month Year>

All versions should have a version number (v.0.x (for draft) or v.x.0 (for final); i.e., v0.1 for the first draft and v.1.0 for the first final version) and a submission date. Use the international date format (day month year) and write out the month (e.g., 23 June 2015).

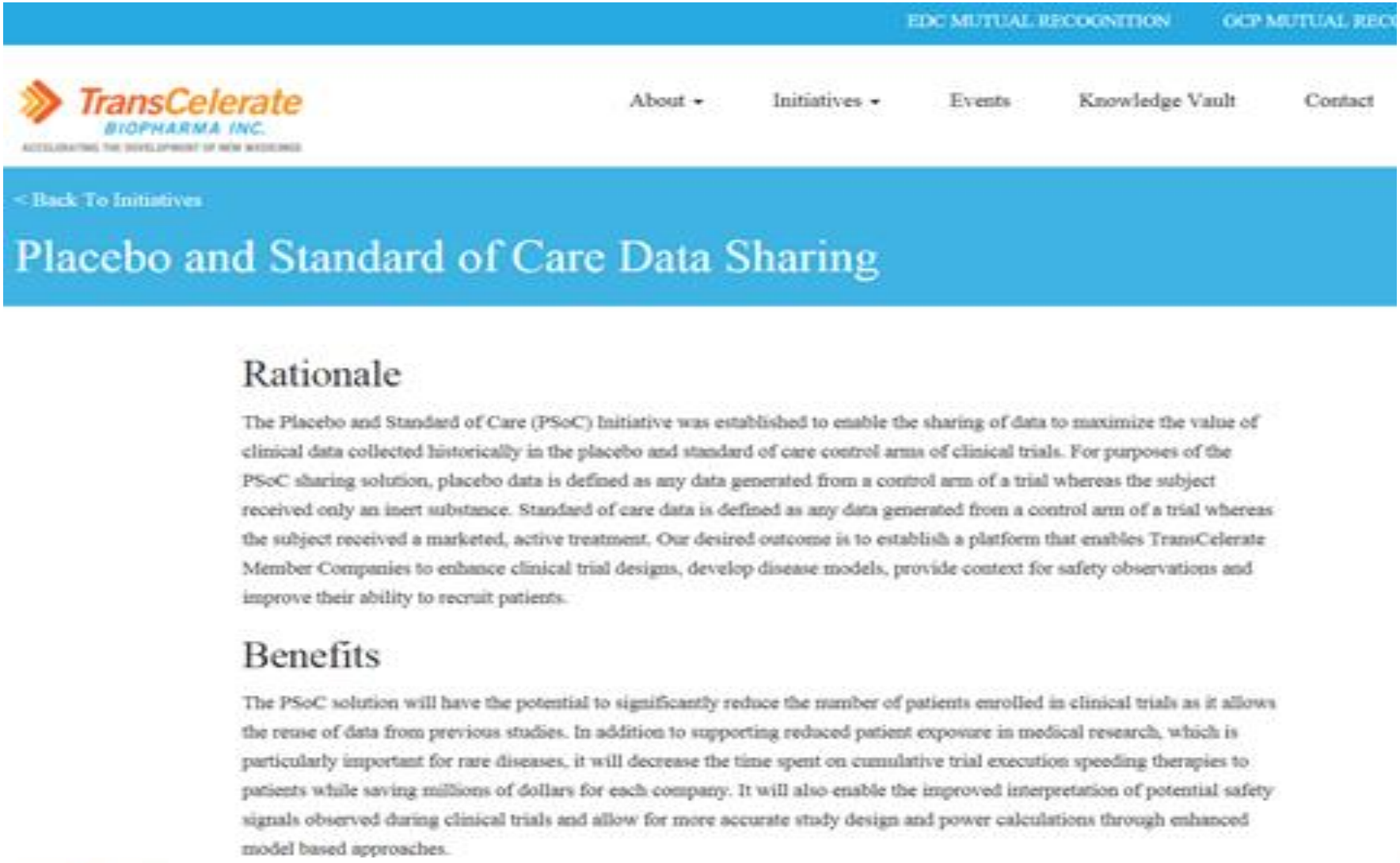
http://osp.od.nih.gov/sites/default/files/Protocol_Template_V1.0_040717.docx

Awareness:
Data Transparency Initiatives

EMA continues to strengthen their position as the patients' advocate in Europe with another important deliverable that helps define the landscape and educate on the critical opportunities from data sharing. CDISC supports and embraces all moves towards greater transparency and structure of patient data through the use of global, freely available consensus-based clinical data standards that will facilitate data sharing to advance research at an optimum rate and more readily unlock cures.

Rebecca D. Kush Founder, President and CEO, Clinical Data Interchange Standards Consortium (CDISC)

Awareness: TransCelerate Biopharma



EDC MUTUAL RECOGNITION OCP MUTUAL REC

TransCelerate BIOPHARMA INC.

About Initiatives Events Knowledge Vault Contact

< Back To Initiatives

Placebo and Standard of Care Data Sharing

Rationale

The Placebo and Standard of Care (PSoC) Initiative was established to enable the sharing of data to maximize the value of clinical data collected historically in the placebo and standard of care control arms of clinical trials. For purposes of the PSoC sharing solution, placebo data is defined as any data generated from a control arm of a trial whereas the subject received only an inert substance. Standard of care data is defined as any data generated from a control arm of a trial whereas the subject received a marketed, active treatment. Our desired outcome is to establish a platform that enables TransCelerate Member Companies to enhance clinical trial designs, develop disease models, provide context for safety observations and improve their ability to recruit patients.

Benefits

The PSoC solution will have the potential to significantly reduce the number of patients enrolled in clinical trials as it allows the reuse of data from previous studies. In addition to supporting reduced patient exposure in medical research, which is particularly important for rare diseases, it will decrease the time spent on cumulative trial execution speeding therapies to patients while saving millions of dollars for each company. It will also enable the improved interpretation of potential safety signals observed during clinical trials and allow for more accurate study design and power calculations through enhanced model based approaches.

http://www.transceleratebiopharmainc.com/initiatives/placebo-standard-of-care/

Awareness: Global – Europe, Japan, China

- EMA – Registries, Compliance, Data Transparency
- PMDA – Required CDISC Submission for regulatory review
- Global Data Standards Become a Hot Topic in China … Linda Wang (C3C)
- CDISC & PhUSE User Groups and Meetings in Europe, Japan and China

Collaboration: Constancy of Purpose

From W. Edwards Deming's 14 Points

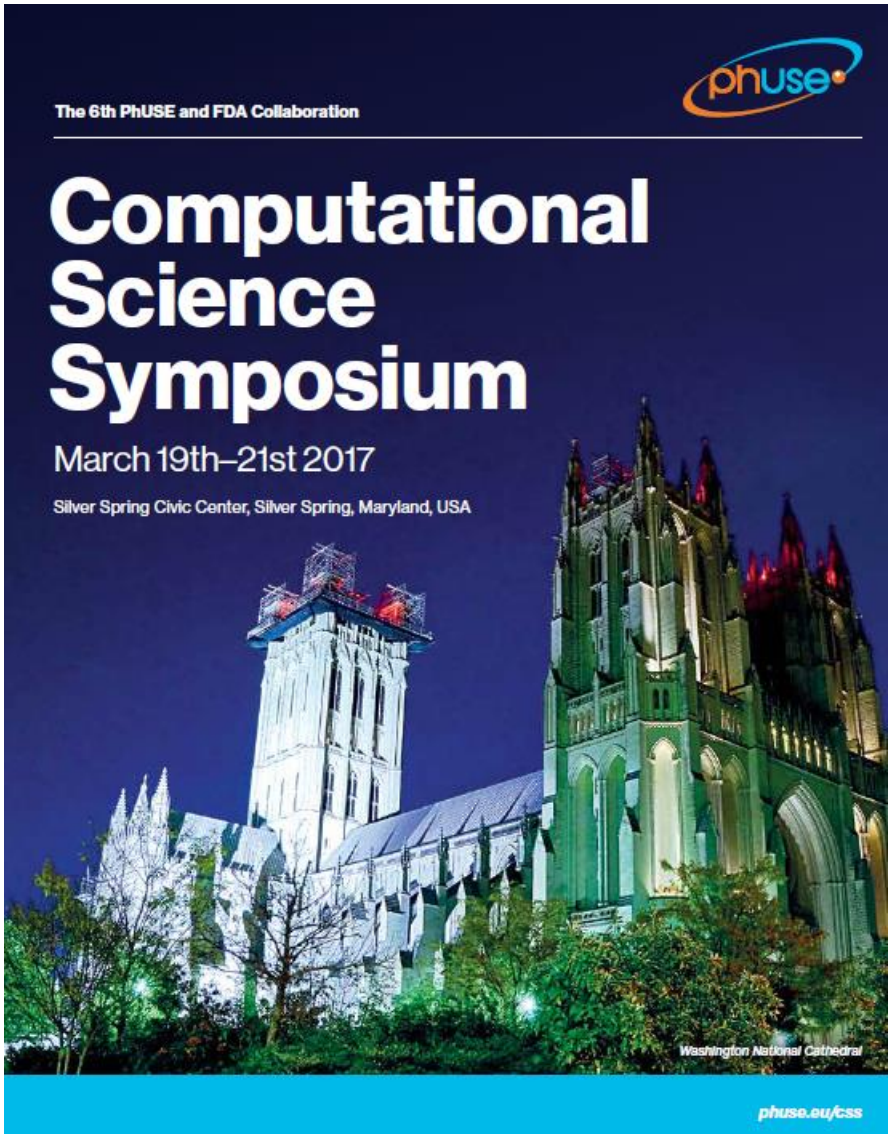
- Create constancy of purpose toward continual improvement of products and services …
- Improve constantly and forever the system of production and service …
- To stay in business requires that leaders spend time on innovation, research and education. They must constantly improve the design of their product and service

Collaboration: Constancy of Purpose*

* The SDS (Submission Data Standards) Team (2004?)

Collaboration:
FDA's "Tom Sawyer Model"

Collaboration: FDA/PhUSE



Collaboration: FDA/PhUSE

Page | Read | View source | View history | Search

Navigation trail: PhUSE Wiki

PhUSE Wiki

- Home
- Categories
- Recent changes
- New Pages
- Popular Pages

Projects

- CSS Working Groups
- Annual Conference
- Therapeutic Areas
- Good Programming Practice
- Data Transparency
- QSPI

PhUSE Wiki Help

Welcome to the PhUSE Wiki

The PhUSE Wiki is an PhUSE/FDA/Industry collaboration to provide a medium to share information specifically relating to clinical trial informatics.

Welcome to the Wiki

CSS Working Groups

Join a Working Group now!

Annual Conference Edinburgh 2017

Good Programming Practice Guidance

Currently 4,523 users are helping to ***Share, Contribute and Advance*** clinical informatics.

All content on this wiki is non-binding. All content expresses opinions of users and not necessarily that of their employer nor PhUSE. See our Disclaimers page.

Collaboration:
Standard Analyses and Code-Sharing

Standard Scripts

Working Group Overview

Name/Vision/Goals	Presentation

Name

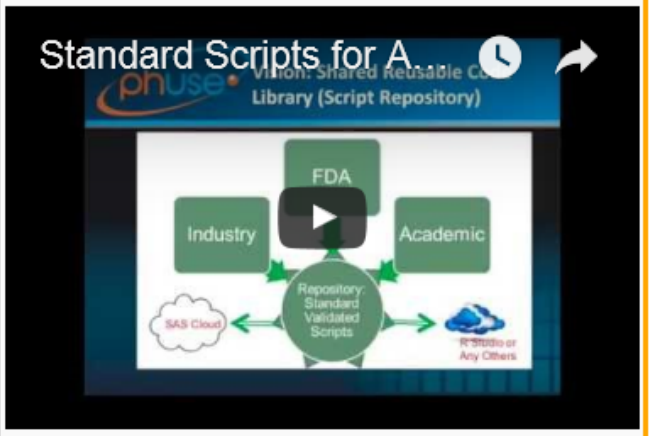
- Standard Analyses and Code Sharing (formerly Development of Standard Scripts for Analysis and Programming)

Vision

- Leverage crowd-sourcing to improve the content and implementation of analyses for medical research, leading to better data interpretations and increased efficiency in the clinical drug development and review processes.

Goals

1. Establish and maintain a publicly available repository for storing program code to be used as analytical tools for medical research.



Contents [hide]

Collaboration:

ASA Section on Statistical Programming and Analysis (SSPA) ?

- ***From the Charter of the SSPA Scientific Working Group (SWG)*** *(Organized 2015)*
- **Scope and Key Responsibilities**
- Participate in the development and maintenance of standard Tables, Listings and Figures (TFLs) to be used in new drug submission or related documents to regulatory agencies with an objective to expedite the review process.
- Establish and maintain liaison with other scientific working groups (e.g., PhUSE, Transcelerate) as appropriate
- Participate in (and initiate, as necessary) broad discussions on [with] … stakeholders
- . Developing tools (e.g., programs, modules) to achieve the objectives ...

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Challenges: 21st Century Cures

Challenging Innovations:

21st Century Cures Act, PDUFA VI Legislation and Beyond

- Tutorials: Graphical Methods & Biosimilarity/Interchangeability
- The Opioid Abuse Epidemic
- Alternative Data Sources
- Novel Trial Designs / Anti-microbial Drugs
- Model-Based Decisions for Drug Development
- Immunotherapy Oncology Studies
- Communication as a tool to spread innovation
- Novel Statistical Methods in Oncology Studies

Challenges:
Constant Improvement / Change

FDA singles out Avicenna Alliance to form part of EU delegation

Next week of 15 May -18 May, the Avicenna Alliance will have a busy week ahead. The FDA has invited the Avicenna Alliance to visit the FDA for high level talks on the future of regulation of in silico medicine will take place on 15 May [2017].

http://avicenna-alliance.com/news/news/fda-singles-out-avicenna-alliance-to-form-part-of-eu-delegation/

Challenges: "Situational Awareness"

- What are the questions?
- What has changed?
- What needs to change?
- How do we make the right changes and in what order?
- Can we plan for and assess improvements?
- What are the benefits and risks?
- Who are the stakeholders?
- Who needs to be involved?
- How do we "socialize the deliverables"?
- How do we get involved? How do we stay relevant?
- How do we help each other continuously be aware of/thinking about where we are?
- How do we efficiently/effectively communicate?
- Where do we find the time?

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ARE YOU WITH US?

It's Gettin' Better All the Time…

THANK YOU FOR THAT!