How to Prepare a
Study Data Standardization Plan

Tom Guinter
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Next will be the status of validation rules, and how they are expected to evolve.

Future potential topics

- The SDTM Trial Design Model (TDM), how to define EPOCH and ELEMENT to facilitate review
- SDTM key domains (DM, DS, EC/EX), how they work together, and how they impact review
- Baseline Flags or Last-Observation-Before-First-Dose, does it matter for review?

Tom Guinter

- P21 VP Clinical Data Services
- CDISC SDS Team Veteran - 15 years
- FDA Leveraging & Collaboration Award
- 18 Years in Clinical Data eSubmissions

Disclaimer

The opinions expressed here are those of Pinnacle 21 and the speaker, offered as recommendations based on our experiences. We are not representing regulatory agencies, CDISC or PhUSE.

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Topics

- FDA Binding Guidance
- FDA Technical Conformance Guide
- PhUSE SDSP Subteam
- The Big Bang – Theory and Practice
- Validation Rules
- Standards Up-Versioning Considerations
- Conclusion

FDA Binding Guidance (1)

Providing Regulatory Submissions In Electronic Format – Standardized Study Data (December 2014)

- Data Standards Catalog
- Study Data Technical Conformance Guide
  - Non-binding recommendations
- Effective date – December 17, 2016, All Studies
- SDTM, SDTMIG, SEND, ADaM, CT, Define.xml

25536fnl.pdf

FDA Binding Guidance (2)

Providing Regulatory Submissions In Electronic Format – Standardized Study Data (December 2014)

- Waivers
  - Versions of standards, not if using standards
  - No later than time of protocol submission
- Study Data Standardization Plan (SDSP)
  - Use established FDA-sponsor meetings
  - No later than the end of phase 2 meeting
  - Premarketing application meeting too late
  - May request a separate Type C meeting

FDA SDTCG (1)

Study Data Technical Conformance Guide (Version 3.0, March 2016)

- Study Data Standardization Plan (SDSP)
  - "Sponsors should include a plan (e.g., in the IND)"
  - Updated in subsequent communications
- Reviewer's Guides (SDRG, ADRG)
- SDTM general considerations
- ADaM general considerations

ucm384744.pdf

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FDA SDTCG (2)

Study Data Technical Conformance Guide (Version 3.0, March 2016)

- Therapeutic Area Standards (TAUGs)
  - Chronic Hepatitis C
  - Dyslipidemia
- Controlled Terminology (CT)
- Study Data Validation Rules (Conformance & Quality)
  - "…validate … before submission using the most recently published validation rules"
  - "…explain in the Reviewer's Guide"

FDA SDTCG (3)

Study Data Technical Conformance Guide (Version 3.0, March 2016)

> "In summary, the goal of standardizing study data is to make the data more useful and to support semantically interoperable data exchange between sponsors, applicants, and the FDA such that it is commonly understood by all parties."

PhUSE SDSP (1)

Pharmaceutical Users Software Exchange
Study Data Standardization Plan (SDSP)

- Project Overview
  - Template
  - Sponsor Implementation Guide
  - Completion Guidelines
  - Asthma and Oncology Example Documents
- FDA has documents for review
- Next step is an FDA Federal Registry (FR) notice

www.phusewiki.org/wiki/index.php?title=Study_Data_Standardization_Plan_(SDSP)

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PhUSE SDSP (2)

Pharmaceutical Users Software Exchange
Study Data Standardization Plan (SDSP)

- Sponsor Benefit
  - "Brings internal focus and agreement … throughout the project lifecycle"
  - "Important reference for all sponsor groups"
  - "Means of tracking discussions and agreements"
  - "Drive decisions about legacy data conversion and up-versioning … to allow for pooling"

www.phusewiki.org/wiki/index.php?title=Study_Data_Standardization_Plan_(SDSP)

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PhUSE SDSP (3)

Pharmaceutical Users Software Exchange
Study Data Standardization Plan (SDSP)

- Standards to reference
  - Exchange standards (SDTM, ADaM, etc.)
    - More than one exchange format may be listed
    - Document primary source
    - Additions beyond primary source documented in separate section

www.phusewiki.org/wiki/index.php?title=Study_Data_Standardization_Plan_(SDSP)

The Big Bang – in Theory

"In theory there is no difference between theory and practice. In practice there is."

Yogi Berra

The Big Bang – in Practice (1)

- Standards are exploding in different directions
  - Some are directly related
  - Some overlap, some are convergent
- SDTM v1.4 is directly related to SDTMIG v3.2
- SDTM v1.5 is primarily SEND related, but not entirely
- SDTM v1.6 is expected to be PGx related
- SDTM v1.7 is expected to relate to SDTMIG v3.3
- CT is developed independently

The Big Bang – in Practice (2)

- Associated Documents (TAUGs, AP, PGx) exploding
  - Contain multiple standards recommendations
    - SDTM/SDTMIG, ADaM
    - Validation rules?
  - Provisional
    - Available, but different state
    - Not incorporated in SDTM and SDTMIG necessarily at the same time

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The Big Bang – in Practice (3)

- Therapeutic Area User Guides (TAUGS)
  - FDA SDTCG includes
    - Dyslipidemia
    - Chronic Hepatitis C
  - CDISC published (draft or final)
    - Alzheimer's, Asthma, Breast Cancer, COPD, Cardiovascular, Diabetes, Influenza, Multiple Sclerosis, PKD, Pain, Parkinson's, QT Studies, Schizophrenia, TBI, Tuberculosis, Virology

The Big Bang – in Practice (4)

- FDA SDTCG
  - Some things in SDTCG are more prescriptive
    - EPOCH
  - Some things in SDTCG only FDA can define
    - Content
  - Expected to be in sync with standards, but…
    … history suggests otherwise
    - EX/EC in SDTMIG v3.2, EC previously excluded
    - DD in SDTMIG v3.2 previously excluded
  - TAUG acceptance

Validation Rules (1)

- CDISC SDTM, SDTMIG being defined
- CDISC ADaM being updated
- FDA, PMDA business rules
- Define.xml

- Currently by primary source
  - SDTM-IG 3.2, SDTM CT 2015-12-18

- **But will be changing to a-la-carte!**

Validation Rules (2)

a-la-carte Future

- SDTM may define a variable that can be retrospective
- CT may be updated independently
- SDTCG may be updated independently, retrospective
- TAUGs may introduce:
  - Variables that should be checked as NSVs (SUPP)
  - Domains that are not standard, but not custom
- FDA and/or PMDA business rules may be updated
- There may be reason to run multiple validations
  - At time of study lock
  - **Again at time of submission**

Up-Versioning Considerations

Decision Recommended at EOP2 Milestone

- Considering:
  - Standards evolution as it applies to critical data
  - Validation updates – new issues?
  - Ability to maintain linear data flow
  - Pooling expectations
    - May be cost effective to up-version safety data
  - Facilitating review
- Not just because of new validation rules!
  - Can (and should) explain issues in SDRG/ADRG

Conclusion (1)

- FDA Binding Guidance requires:
  - Standards adoption and communication via SDSP
- FDA SDTCG evolves
- Standards evolve
- Validation becoming a-la-carte
- PhUSE SDSP a **great** starting point
- Standards evolution, validation rules evolution, and submission plans will challenge the SDSP to evolve significantly more granular

Conclusion (2)

Hopefully the SDSP is a positive trigger for earlier decisions, better communication, and better review packages. ☺

Questions

Tom Guinter
tguinter@pinnacle21.net