

Using a Waiver Process as a Change-Control Tool for ADaM Standards Governance

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Karin LaPann's Biography

- Karin LaPann is Associate Director Clinical Standards at Shire, and is the Shire team lead for CDISC ADaM Standards and TFL's. Karin has worked in the Pharmaceutical industry since 2001. She is an active member of PhUSE in the white papers group, has been on the CDISC ADaM team since 2010, and is co-lead of the ADaM Questionnaires Ratings and Scales (ADQRS) sub-team. She holds an MS in Information Systems from Drexel University.



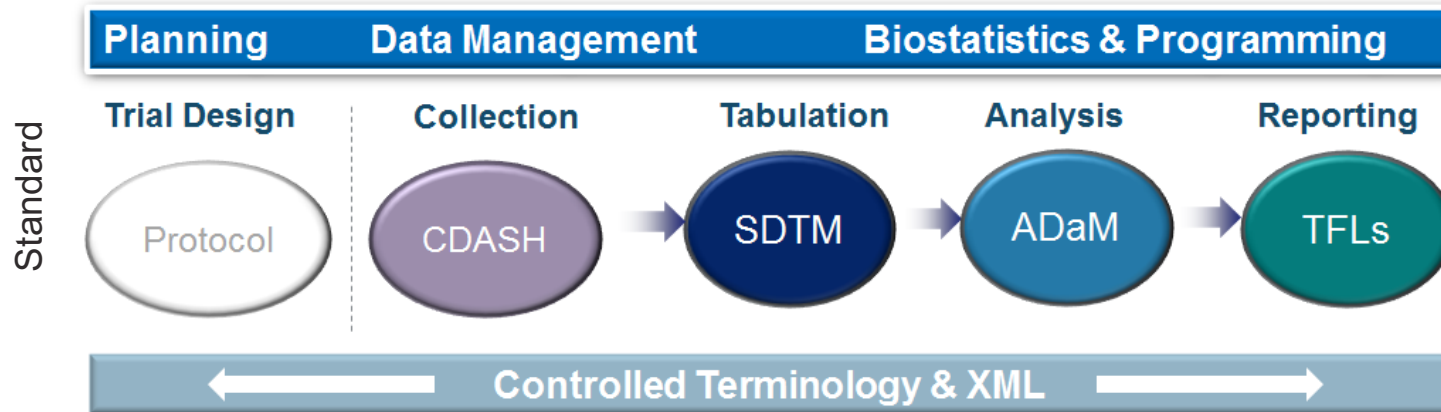
CDISC Standards are in Place –

- The CDISC standards are at a mature state
- The PhUSE organization and CDISC are in close collaboration with FDA on implementation
- Adoption of beginning-to-end standards is now a reality for Sponsor Companies
- The question remains:

How do we implement them and ensure compliance?

Current Situation

- Shire is early adopter of the standards
- Standards are more powerful when implemented beginning-to-end



- Keeping variations to a minimum there is more re-use of:
 - Protocol templates (and SAPs)
 - Mapping from CDASH to SDTM
 - Programs and macros for data conversion
 - Programs and macros for SDTM to ADaM
 - Programing for standard reporting outputs (not currently CDISC standard)

Interpretation of Published Standards

- Detailed Standards documentation provided by these documents
 - ADAM Model 2.1 (2009-12-17)
 - ADaM IG 1.0 (2016-02-12)
 - ADaM IG 1.1 (2016-02-12)
 - ADaM OCCDS, ADaM ADTTE (2012)
- Still some grey areas that require interpretation and guidance for study teams
 - Permissible variables that are required by Sponsor
 - Therapeutic Area specific implementations Studies using legacy standards inherited through acquisitions

What is a Waiver

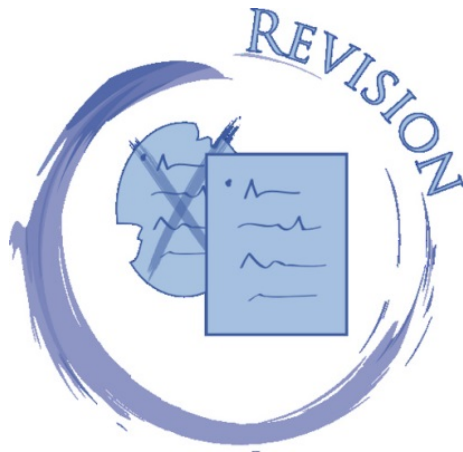
Waivers are a way to track deviations from Sponsor-Specific Standards and Controlled Terminology (CT)

- “Waiver” is a borrowed term from the FDA
- Process starts as a question to the Standards team
- Requests allow for a departure from a Sponsor- approved standard
- Provide an avenue for feedback on Standards and CT
- Documentation acts as Lessons Learnt



Importance of Waivers

- Waivers provide an avenue for feedback to the Standards team
 - Provide potential need for an update
 - Helps to drive future development of standards
 - The documentation created in the waiver process provides traceability for consistent decision-making

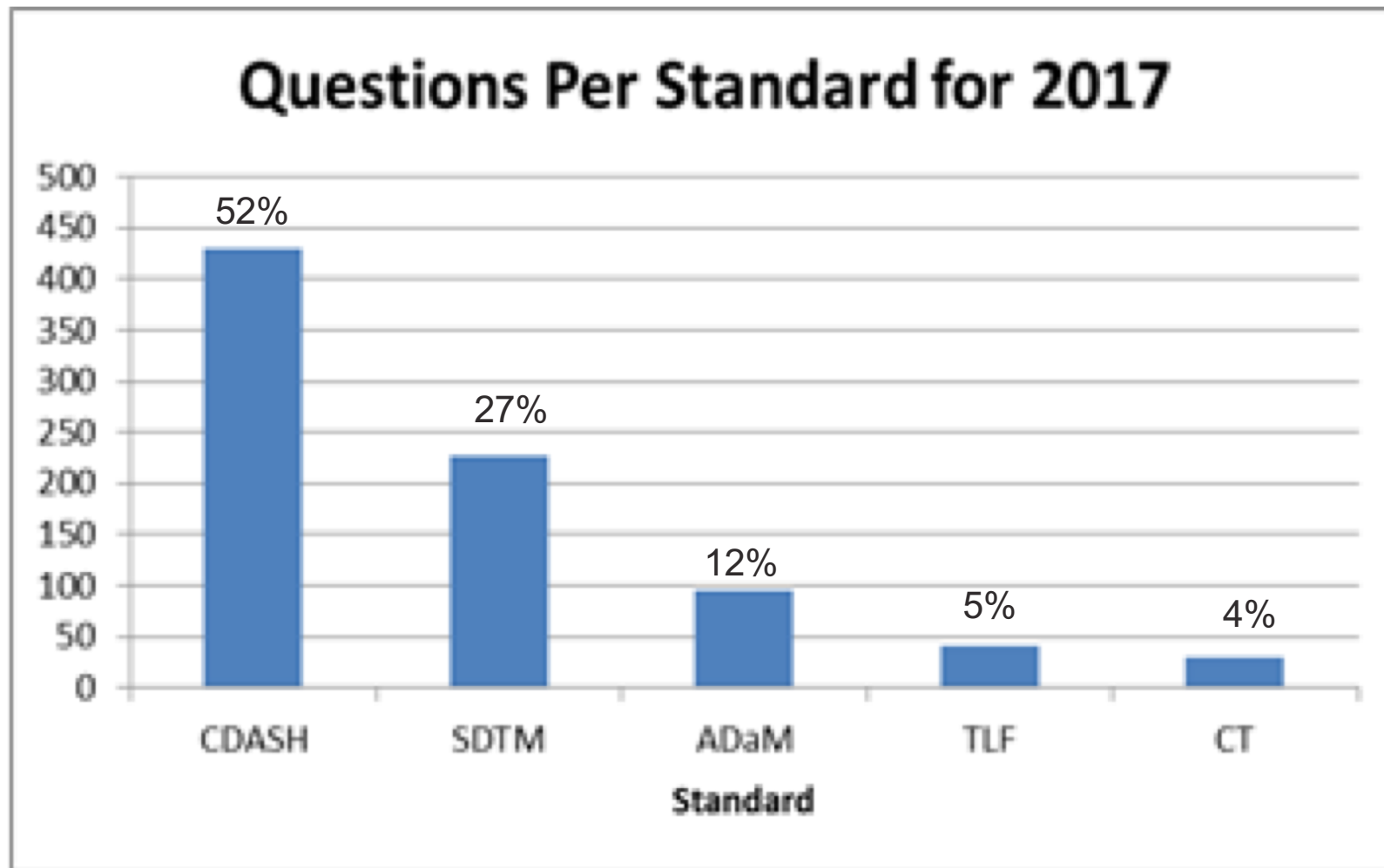


Sample Waiver Form

Standards LT Assessment	
	Recommendations/Rationale from Standards LT.
CDASH	☐
SDTM	☐
ADaM	☐
TFL	☐
CT	☐
Standards Decision Date	Date at which Standards has made a decision to either reject or submit to the board.

- Impact of one waiver assessed for beginning-to-end standards
- If it affects ADaM, does it affect SDTM, TFLs?
- Standards team evaluates each waiver together
- Determine overlap to other standards

Metrics for Standards Questions



Use Cases for AdAM Standards Compliance.

- Following are three examples of use cases for the waiver process and compliance checklist
- Compliance reports may contain the following:
 1. Datasets not specified in Toolkit
 2. Variables in a specified dataset not in Toolkit
 3. Changes to standardized derivations marked in black
 4. Variables marked 'Shire Required' not in final specification
 5. Output from additional ADaM Metadata Compliance Checklist

ADaM Waiver Use Cases (1)

Dataset Type	ADaM Business Rule	Use case	ADaM Question Tracker	Waiver Needed	Discussion / Rationale
All ADaM	The Sponsor will indicate the minimum requirements for the ADaM-Compliant Datasets (ADaMIG v1.1)	The team wants to exclude Sponsor-Required Variable	Y	Y	All the ADaMIG v1.1 required variables are also required by the Sponsor. In addition, some CDISC standards variables marked 'Cond' for Conditional are clarified and also required by Sponsor documentation. Sponsor-required variables will be mandatory unless the study design clearly does not or cannot support them. This aligns to the TFL standards which are annotated with the expectation that the variables will be available in ADaM.

ADaM Waiver Use Cases (2)

Dataset Type	ADaM Business Rule	Use case	ADaM Question Tracker	Waiver Needed	Discussion / Rationale
OCCDS	New datasets in the Occurrences Data Structure (OCCDS) may be created as long as they conform to the ADaM metadata rules.	Can the team create new datasets that are compliant to OCCDS data structure?	Y	N	New datasets similar to ADAE or ADCM (OCCDS) such as ADSURG for surgical procedures, do not need a waiver as long as they follow the same naming conventions for the variables in the CDISC OCCDS documentation.

ADaM Waiver Use Cases (3)

Dataset Type	ADaM Business Rule	Use case	ADaM Question Tracker	Waiver Needed	Discussion / Rationale
OTHER	New datasets not conforming to the ADaMIG v1.1 should be the exception.	Can the team create new datasets that are not compliant to BDS or OCCDS?	Y	Y	New datasets of the type OTHER that are not defined in the ADAMIG 1.1. or Toolkit or OCCDS 1.0 document will need a waiver.

Waiver Governance Process

- Begins with questions raised to the Standards team by Study teams
 - SDTM – questions from Data Management and programmers
 - ADaM – questions from Statistical programmers and statisticians
- Standards team leads (CDASH, SDTM, ADaM, TFL and CT) get together and triage the waiver requests.
- If decided that requires a waiver, then send to the Standards Governance Board.
 - Otherwise, approve as an acceptable non-waiver deviation
- The standards process is supported with Executive Sponsorship.



Conclusion

- Waiver process is an important tool to encourage compliance to CDISC standards
- Begins the conversation with the Study teams
- Questions are tracked and answered providing lessons learnt
- Is measurable and traceable
- Actual waiver is last resort after all options have been explored
- Provides feedback to improve the standards

Questions



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