

Building (and Rebuilding) the CDISC Toolbox

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Background

- CDISC data and documentation standards have had a significant impact pharma and CRO work flow and processes
- The standards have not always been warmly received
- But they can be used not just for regulatory compliance but to improve workflow efficiency
- This presentation describes tools we've used and developed for CDISC implementation at Rho over the last 10+ years
- We'll talk about missteps as well as successes

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Organization

- Our Lessons Learned approach is most effective if we follow the timeline as we learned the lessons.
- Shortly pre-CDISC to present day is divided into 6 phases.
- For each phase we discuss changes to the regulatory environment for data standards and models, what tools we developed or adopted, and how workflow was affected.

and you may say ... 3

But Wait, Haven't We Been Here Before? Repeatedly?



urban DICTIONARY

1. **beating a dead horse** 📺 📺 📺 📺 📺

It doesn't matter how much you want to continue riding beating a dead horse is not going to get you anywhere.

If something is already done and over with there is no point in still talking about it.

Overview: Development Phases

Frame the discussion around development phases at Rho.

Note:

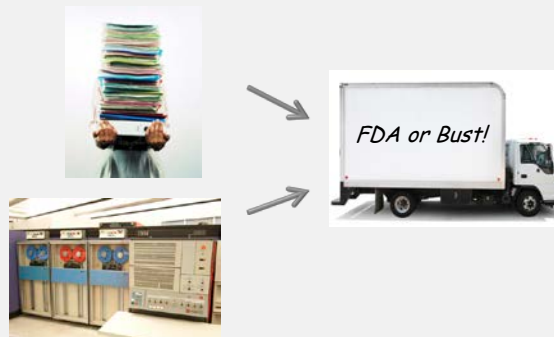
- Pretty arbitrary
- Fairly sequential
- Somewhat overlapping



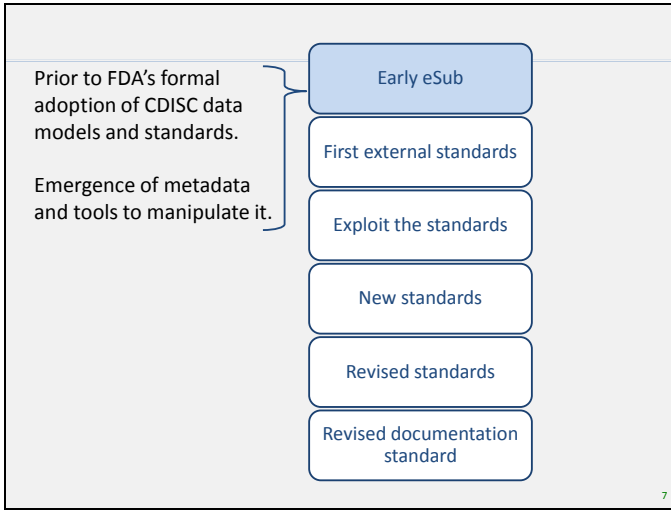
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Not on the List: Pre eSub

Actually more complex than this slide implies, but this is the essence of the process.



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Early eSub: Summary

CDISC

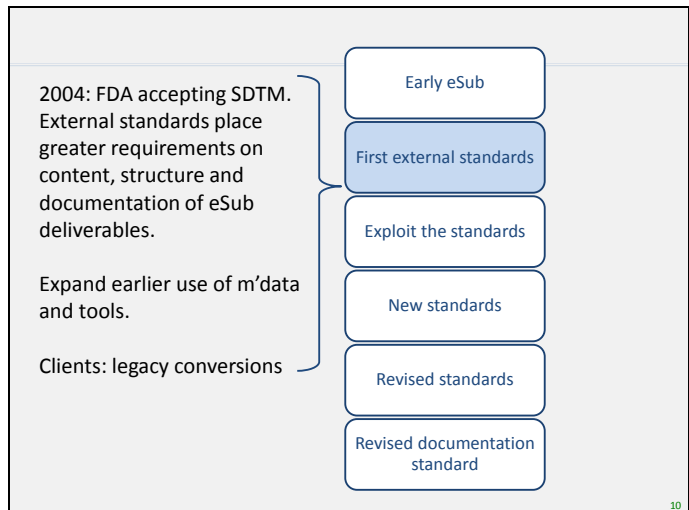
- c. 1997: "a good idea" but no mandate for implementation
- Early ODM, SDTM suggest importance of metadata
- FDA still accepting non-standardized data, define.pdf

Highlights

- Initial (non-CDISC) metadata
- Awareness of need for *tools* to use the metadata
- Move away from Word docs as programming specs

Early eSub : Comments

<p>Standards</p> <ul style="list-style-type: none"> 1999 regulatory submission guidance CRT dataset and documentation format not rigorously defined 	<p>Metadata</p> <ul style="list-style-type: none"> Initially, focus on satisfying creation of XPTs, define.pdf Seeded from SAS Dictionary Tables Store using SAS/Share, Excel Key: structured, machine-readable
<p>Tools</p> <ul style="list-style-type: none"> Print specs from m'data rather than Word Create %attrib stmts from m'data; also var. renaming, formatting, ... Use m'data when building XPTs, define.pdf 	<p>Other</p> <ul style="list-style-type: none"> Train users in the basics: meaning, entry of m'data; use of tools Key: need for m'data <i>and</i> tools to make it easily accessible



First External Standards: Summary

CDISC

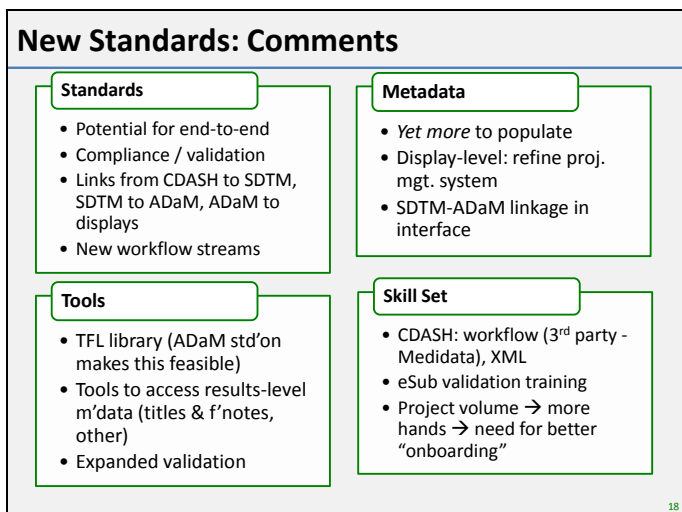
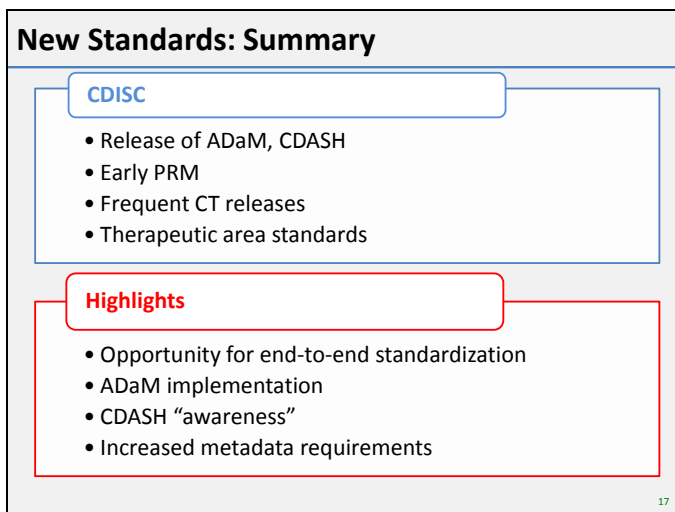
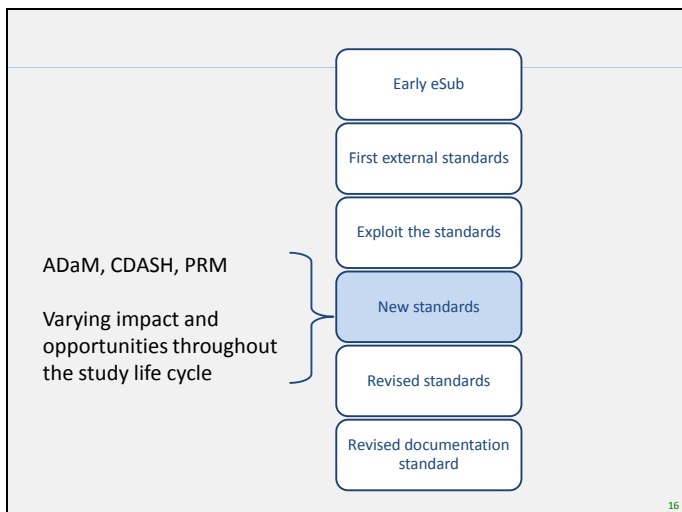
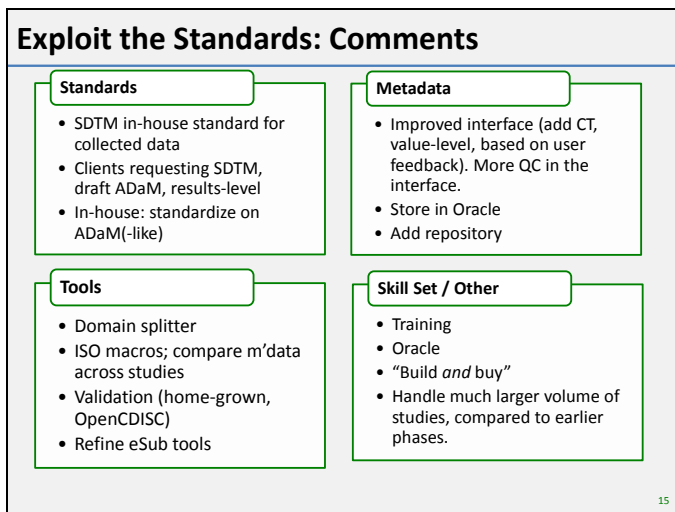
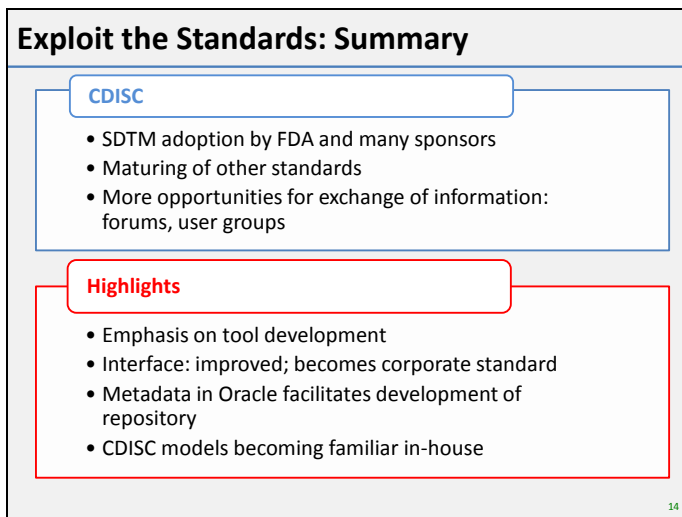
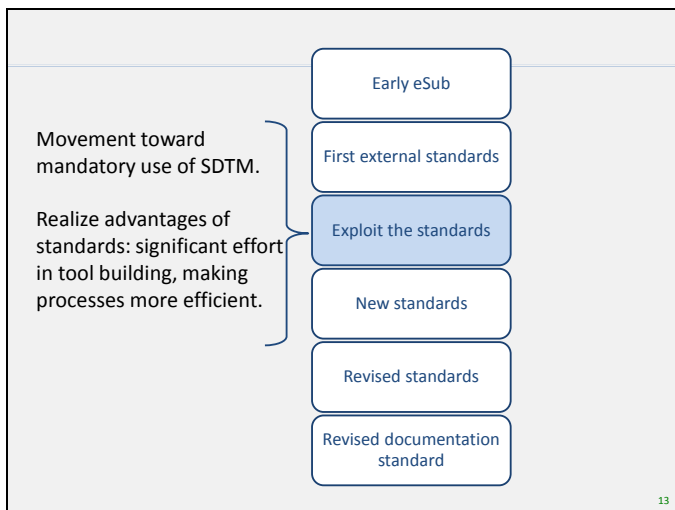
- Initial SDTM: data standard, presented as metadata
- Documentation standard: define.xml
- Relatively little implementation guidance

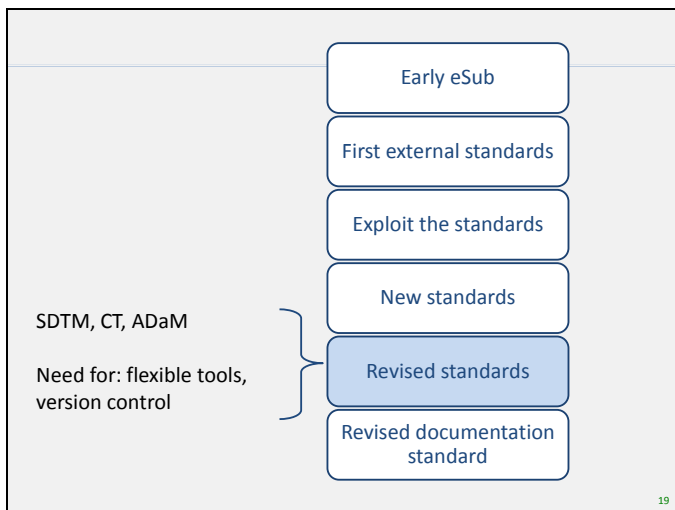
Highlights

- Expanded skill set (XML, XSL)
- Validation to the standard
- Altered work flow
- Learn as we go. Combine R&D with project work. Not pleasant.

First External Standards: Comments

<p>Standards</p> <ul style="list-style-type: none"> Compliance / validation Education / training Dual annotation of CRF New (SDTM) workflow stream 	<p>Metadata</p> <ul style="list-style-type: none"> More to populate Create "Gold Standard" Refine interface (consult end-users) Re-think storage: MDB
<p>Tools</p> <ul style="list-style-type: none"> Updated spec printer (for SDTM) Domain programming tools Validation (Domains, XML) Revise study setup Build XML and render as PDF Legacy conversions 	<p>Skill Set</p> <ul style="list-style-type: none"> Familiarize w/ XML, XSL, SAS XML mapper Define and manage revised workflow (for SDTM) Heavier use of ODS





Revised Standards: Summary

CDISC

- Accelerated pace of updates
- Need for identification of changes across non-harmonized standards
- Clients: standardize on a version throughout a study, or use different ones, then adjust for ISS/ISE?

Highlights

- Automate population of new versions' Gold Standard
- Enhance tools for validation, study setup
- Implications of more people creating eSub deliverables

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Revised Standards: Comments

Standards

- New IGs for SDTM, CTs, others
- Maintain version continuity throughout study
- Our, 3rd party tools need to keep pace

Metadata

- Database management to apply different versions
- Plus coding updates for interface
- CDASH m'data library

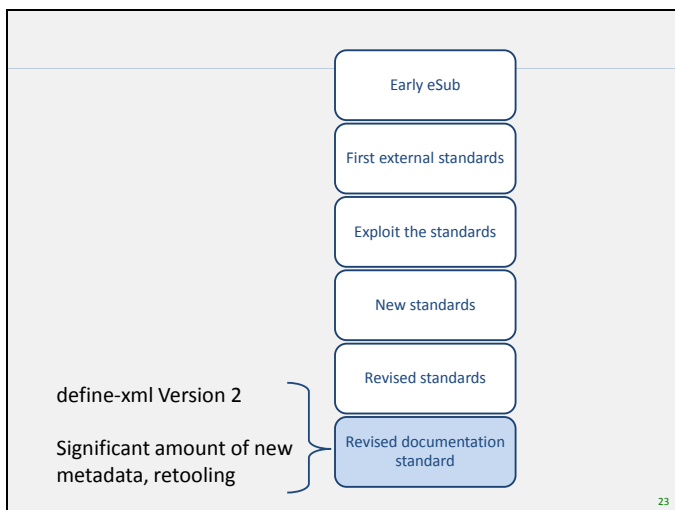
Tools

- Project setup: assign, maintain SDTM, CT versions for all studies
- OpenCDISC (compare checks; create new version config files; how to handle "semi-false" positives)

Other

- Control the beast: soft dev Best Practices (better doc'on, version control)
- Fewer client-specific accommodations needed, requested

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Revised Documentation Standard: Summary

CDISC

- Define-XML Version 2
- Significant amount of new metadata
- Eventual implementation of Results metadata

Highlights

- Opportunity for retooling:
 - Harmonized SDTM-ADaM interface
 - Updated define.xml/pdf and support programs
- Need for new documentation, (re-)training

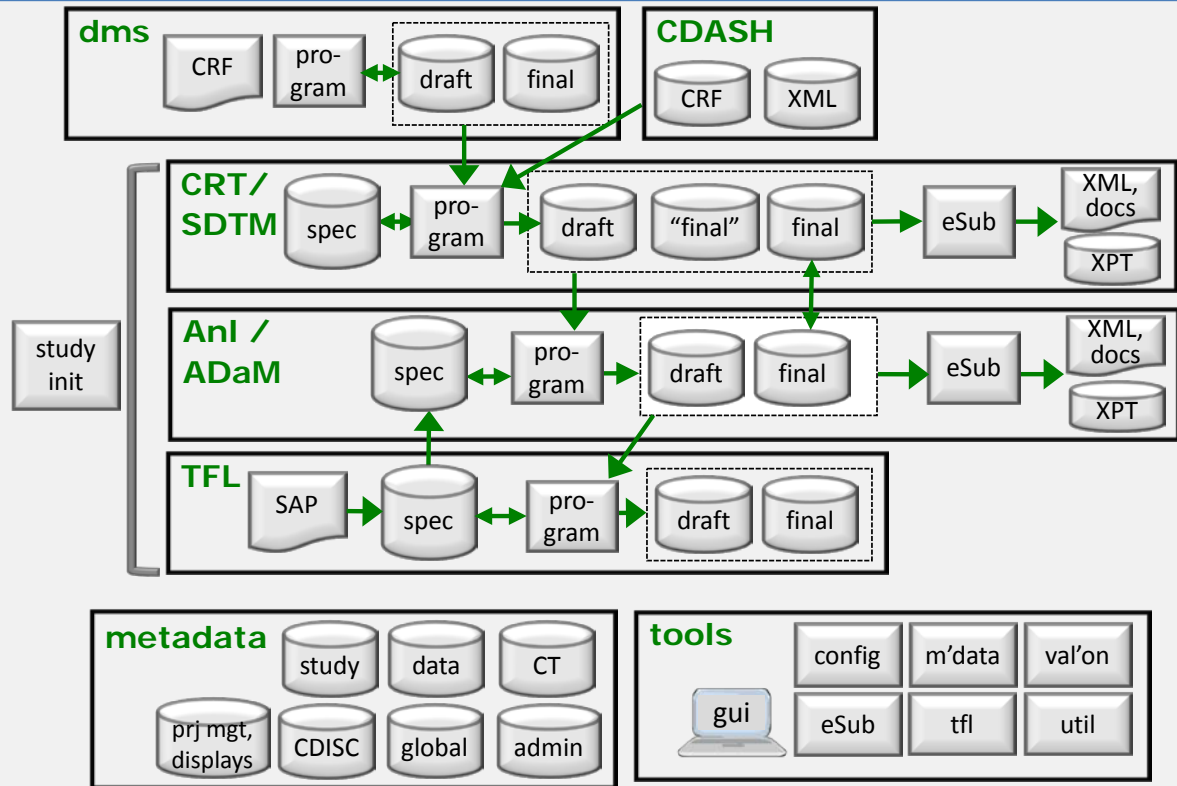
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Revised Documentation Standard: Impact

Standards <ul style="list-style-type: none">• New Define-xml not just incremental change• Will incorporate Results-level• More complex validation	Metadata <ul style="list-style-type: none">• Much more to populate• Single SDTM-ADaM GUI• Create new tables (study-level, global settings)• Look to integrate results-level from other in-house system
Tools <ul style="list-style-type: none">• Complete rewrite of older (10+ year-old) tools• Validation (3rd party + in-house)• Autopopulating some m'data becoming possible• Harmonize Results (proj. tracker) with eSub systems	Other <ul style="list-style-type: none">• Standardize on CDISC style sheet (modify XSL if client requests)• Documentation: updated, new• Training (both "old" and new hires)

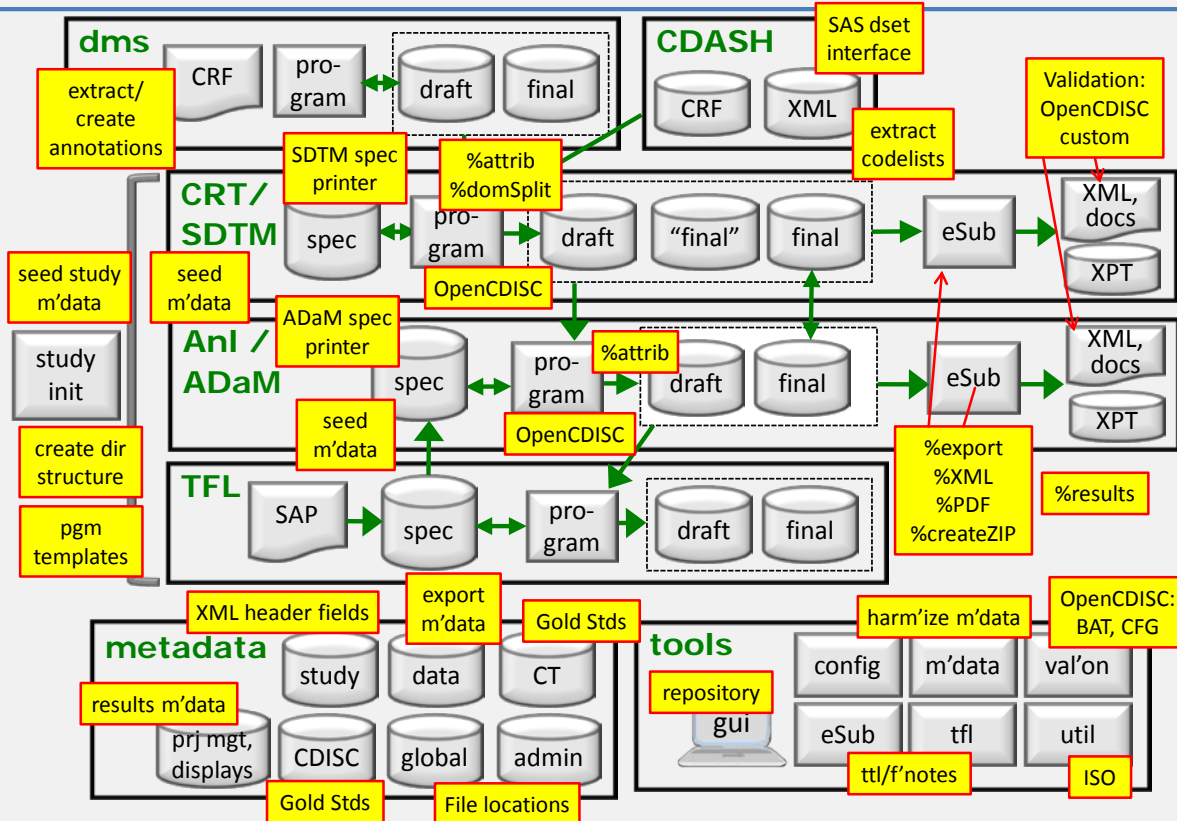
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Summary: Workflow, Tools, Metadata



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Summary: Workflow, Tools, Metadata



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Key Lessons Learned

- Store data specs in **machine-readable** metadata format (for re-use).
- Importance of **seamless access** to metadata: interface, tools
- Treat metadata as a **valued resource** – Oracle (or similar), not Excel(!)
- Validation**: complex, time-consuming
- The CRO dilemma: exploit the Standards but **maintain flexibility** in tools: every sponsor wants their own version
- Tools – built or bought – must be **adaptable**, reacting quickly to changes in standards
- Best soft dev practices** for tools SAS/other tools (doc'on, life cycling, validation)

Looking Ahead: “Phase Next”

- Models**
 - Better end-to-end integration of CDISC models, especially PRM, CDASH
- Strategy, Coding**
 - Better manage OpenCDISC checks; automate inclusion of output into Reviewer’s Guide
 - Extend reach of standard displays (using Results-level metadata)
 - Auto-generated code from metadata
 - Continually review the market, revisiting subsystem “Build or Buy”
- Training**
 - More documentation
 - Clearly identify eSub/other m'data needs
 - Clear, shared understanding of what 's required for eSub completeness
 - Documentation of validation errors and anomalies
- Constant Change!**
 - Building and maintaining systems requires ongoing organizational commitment to R&D

Thanks for coming!

- Questions?
- Comments?

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