CDISC standards when programming is outsourced (*Managing difference of opinion/interpretation*)

CDISC

- Why and how CDISC is important?
  - Easy review by FDA. Saves time for the reviewer and can spend more time in analyzing the data rather than understanding the data.
  - Common language across the departments and industry. Clear & unambiguous communication, Treasability, Machine readable metadata and Analysis ready (ADaM).
- Without CDISC the outsourcing would be even more complicated.
  - CDISC defines the specifications for how the data should be presented, traceability and analysis ready.
  - But not every minute detail is defined in CDISC. And also there is some flexibility and grey area of how the CDISC can be interpreted. This gives rise to confusion.
  - As more companies are implementing it, the grey area is getting narrowed down, leading to less confusion.
  - Remember that CDISC does not solve all problems.

Reasons for outsourcing

- Lack of CDISC expertise
- Not enough Programming Resources
- Not enough Time
- More economical in some situations
- Convenience

- Whatever is the reason, the CRO is expected to have the CDISC expertise.

Kinds of outsourcing

- FSP – Functional Service Provider
  - Sponsor: Have full access and control over many aspects.
  - CRO: Becomes strategic partner
- 100% outsourcing – Spec preparation, Primary programming and Validation
- Partial Outsourcing – Both the sponsor and CRO share responsibilities in the Spec preparation, Primary programming and Validation.

Right partnership

- Choose the right partner
  - Scope of the project/s
  - Time zone differences
  - Team size
  - CDISC expertise
- Pilot studies
- Acceptance checks should be done by the sponsor on the work done by the CRO

Scope of the agreement

- Version of the CDISC standards (SDTM, ADaM, Control Terminology, MedDra, WHODRUG) used
- Sponsor standards
- Resources from both sides
- Timelines and meeting schedules
- Budget
- Data storage and transfer
- Expectations from both sides
- How to handle changes/amendments. Deviation to the original plan

Collaborative effort

- Things that need to be reviewed between Sponsor and CRO
- Timely communications and progress meetings
- Be on the same page

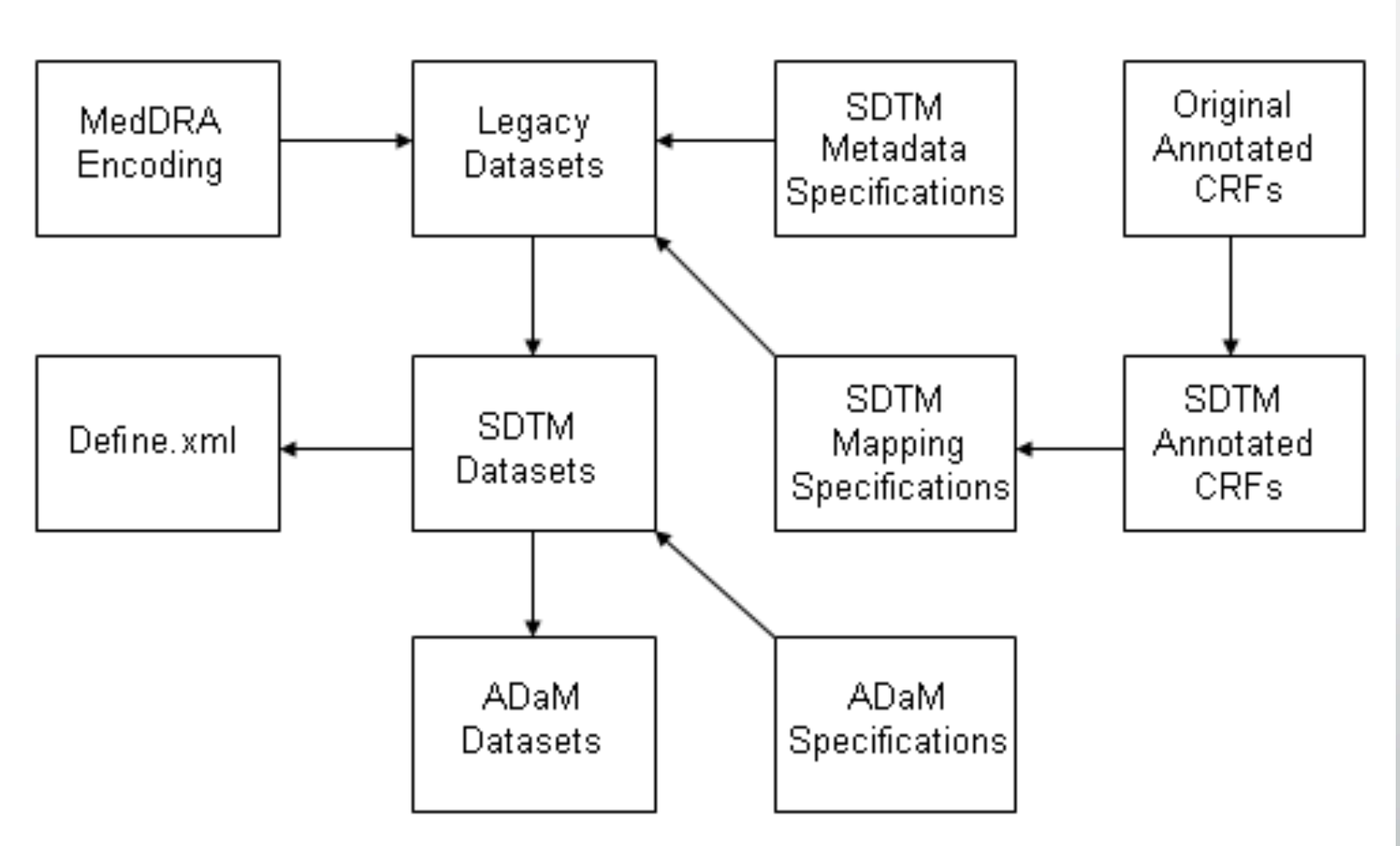
Communication

- Regular and frequent communication is key
- Project Status/Progress updates
- Quality review
- Method of communication

Timelines/Milestones

- Define the whole process from start to end
- Agree upon the timeline
- Milestone work breakdown –> Sub-milestones

Workflow



- Reference: **Outsourced Data Integration Project with CDISC SDTM & ADaM Deliverables**

Christine Teng, Merck Research Labs, Merck Sharp & Dohme Corp.

Margaret Coughlin, Merck Research Labs, Merck Sharp & Dohme Corp.

Recommendations

- TLF Mock shell annotation is highly recommended at the time of ADaM specification preparation.
- This will avoid lot of double work, and eliminate unnecessary work.

Methodologies

- SDTM → ADaM (Preferred and most widely used)
- Non-Standard/ Legacy → ADaM/AdaM Like (Bridging document)

Who is working

- Define the roles and responsibilities of personnel involved
- Programmer/s, Data Managers, Statisticians

CDISC Training / Education

- Should not be overlooked
- Initial investment
- Increases the Quality
- Reduces the rework
- Down the line saves money
- Saves time and resources

Managing difference of opinion/interpretation

- It is highly recommended that the sponsor/CRO maintain a library of PARAM, PARAMCD to maintain consistency across the studies and avoid confusion, because multiple people will be working on different projects.
- ANLzzFL (Analysis Flag) could be present in any of the BDS dataset and it could have a different definition in each dataset. This could get really complicated if it is not properly handled.
- Similar issues with CRITzz and CRITzzFL variables.

Managing difference of opinion/interpretation (Continued)

- With in the study, the analysis and/or criteria flags can have different definitions in different datasets. In ISS and ISE when multiple studies are pooled this could get more complicated if they are not handled properly.

- Different Interpretation of the same specification. → Make sure the specs are "Clear and unambiguous". Review and discuss them thoroughly.

- Anticipate the areas/topics where potential difference can come based on the previous experiences.

Managing difference of opinion/interpretation (Continued)

- Handling the grey areas in CDISC. E.g
  - 1) Having all the flag variables in each domain or not.
  - 2) Having all the ADSL variables in all ADaM datasets.
  - 3) Having a new variable vs new observation.
  - 4) Keeping detailed observations along with the Summary observation.
  - 5) SUPPQUAL vs FA (Findings About).
  - 6) Flexibility in the CDISC standards: Good and bad.

New Ideas

- ADBL
- Introducing new SDTM domains to accommodate wide range of requirements in various therapeutic areas
- Always there is a scope for improvement. CDISC standards are subjected to continuous evolution. New and better ideas are implemented overcoming the existing problems.
- Upgrade the systems and templates accorrdingly.

Review/Validation/ Acceptance checks

- Who is doing the validation? (Sponsor or CRO)
- Whether Acceptance checks are being performed or not?

Reviewing

- Statistical Analysis Plan
- Annotated Case Report Form
- TLF mock shell annotation
- SDTM Mapping Specifications and/or ADaM Specifications
- The reviewing process should be done as early as possible to eliminate double work and save resources.

Acceptance checks

- To assure the QUALITY.
  - Factors influencing the quality: Resources, Time and Subject Expertise
- CDISC Compliance checking (e.g Open CDISC and/or sponsor's own proprietary tools)
  - SDTM checks
  - ADaM checks
  - Define.XML checks
- Sponsor Compliance checking

Questions

Thank You

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