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To EC or not to EC

Presented by Caroline Francis, AstraZeneca

Meet the Speaker

Caroline Francis

Title: Associate Director, Standards Developer

Organization: AstraZeneca

A former Statistical Programmer with over 15 years in the Pharma industry, I have recently moved into a full time standards role with AstraZeneca. I started with a small Biotech in Manchester UK, tasked with introducing the SDTM standard, not knowing this would fuel a career in Statistical Programming with a passion for Data Standards.

I have a degree in Mathematics, Statistics, Operational Research and Economics from the University of Warwick, UK.

Apart from data standards I enjoy singing acapella, swimming and water polo, although not all at the same time.

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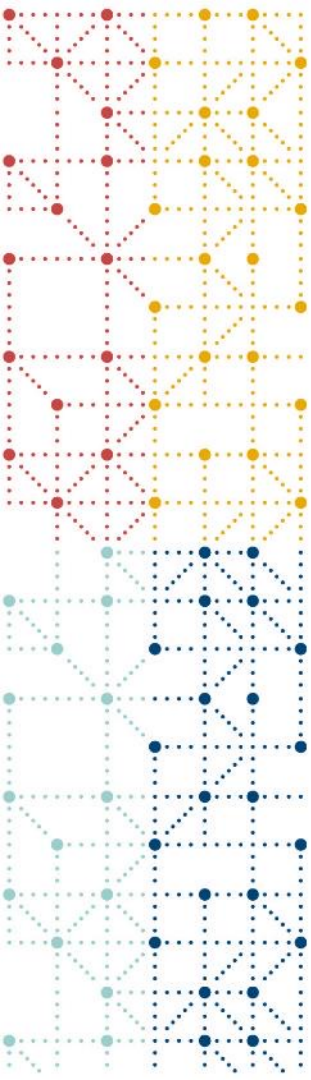
- *The views and opinions expressed in this presentation are those of the author(s) and do not necessarily reflect the official policy or position of CDISC.*

- *The author(s) have no real or apparent conflicts of interest to report.*

Agenda

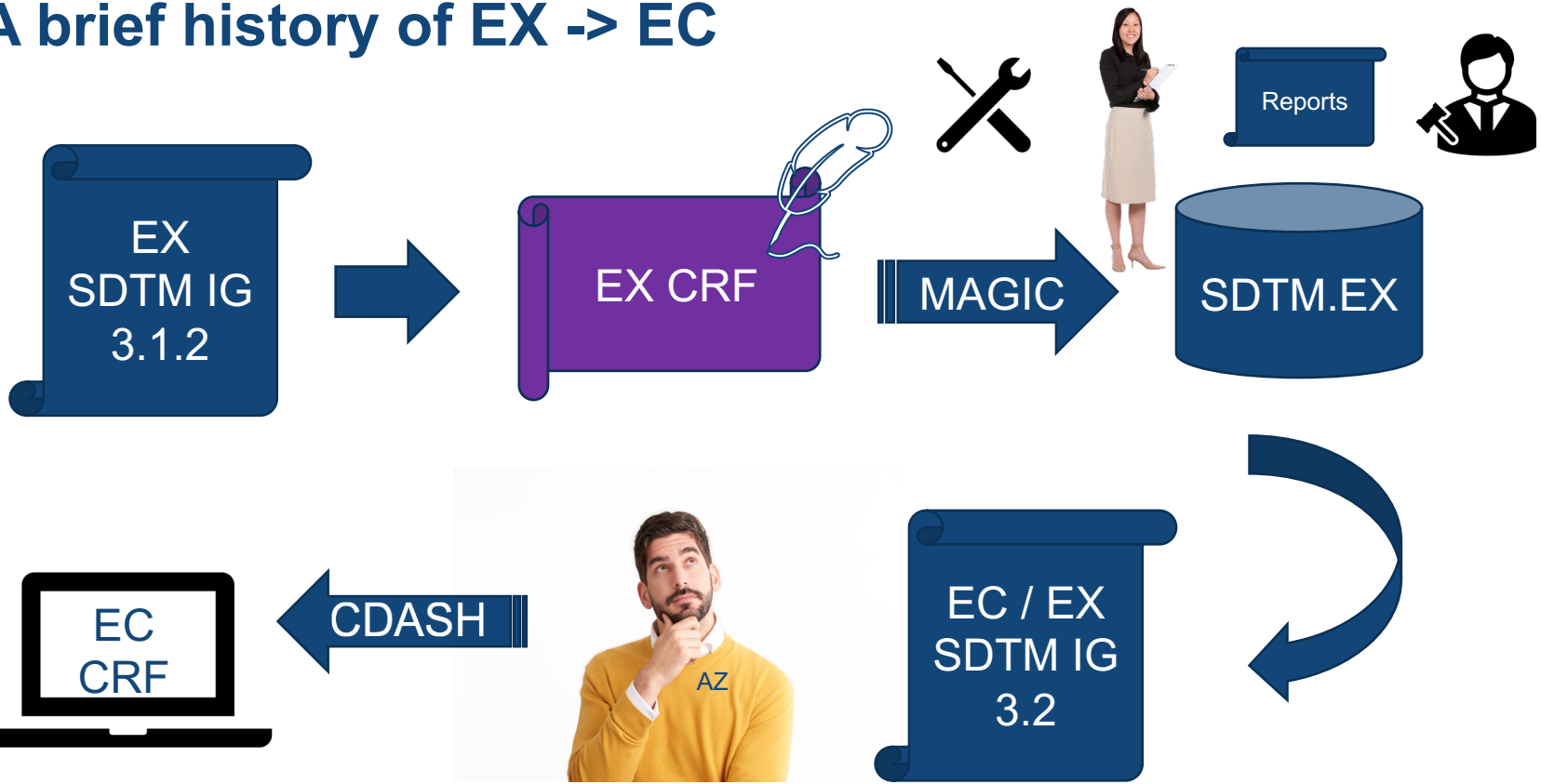
1. Introduction to EC
2. The chosen solution
3. Governance and implementation
4. Summary



Introduction to EC

To EC or not to EC, that is the question?

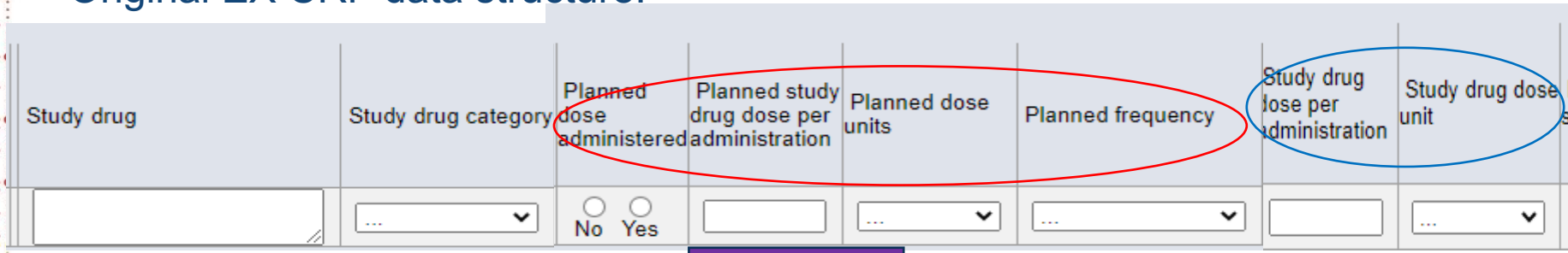
A brief history of EX -> EC



Exposure as Collected (EC) vs Exposure (EX)

Introduction of ECMOOD:

Original EX CRF data structure:



EC structure:

ECTRT	ECMOOD	ECCAT	ECDOSE	ECDOSU
WonderDrug	SCHEDULED	Therapy Category 1	25	mg
WonderDrug	PERFORMED	Therapy Category 1	20	mg
Placebo	SCHEDULED	Therapy Category 1	25	mg

EC in CDASH

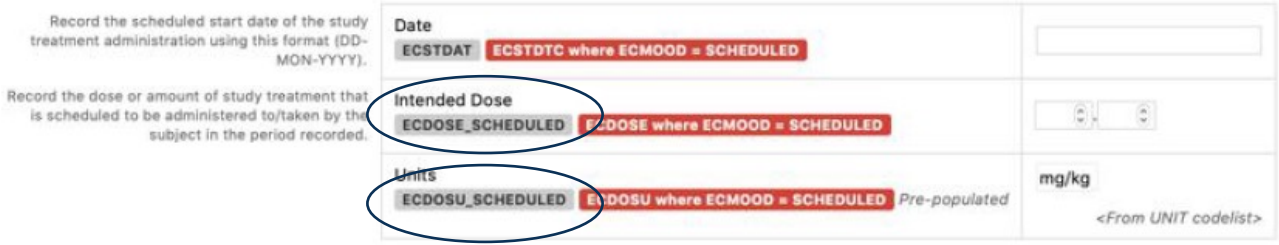
- The ECMOOD variable is available:

CDASHIG Definition	Question Text	CRF Completion Instructions	Mapping Instructions	Implementation Notes
Mode or condition of the record specifying whether the intervention (activity) is intended to happen or has happened.	Does this record describe scheduled [study treatment/dose] or performed [study treatment/dose]?	Indicate if this record has happened or is intended to happen.	Maps directly to ECMOOD. When implemented, ECMOOD must be populated for all records.	"SCHEDULED" is for collected subject-level intended dose records. "PERFORMED" is for collected subject-level actual dose records. "Planned" or "Scheduled" can be pre-printed as the CRF name or section header, as applicable. If collecting both the scheduled and performed dosing in the same horizontal record, the sponsor may choose to append "_SCHEDULED" to the ECDOSE/ECDOSTXT variable name to delineate the scheduled dose from the performed dose. The performed dose would just be collected with ECDOSE/ECDOSTXT and ECDOSU.

Example from the CDASH IG v2.2:

Example 3

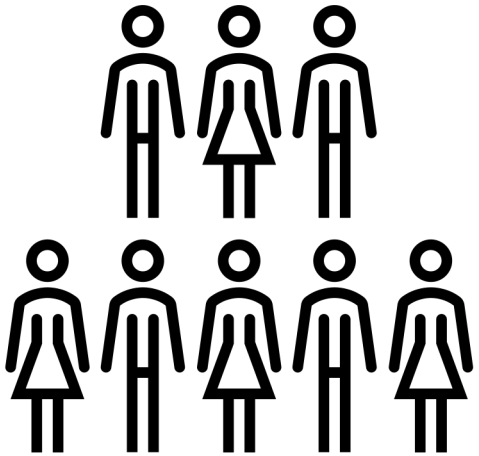
Title: Exposure as Collected - Scheduled vs Performed



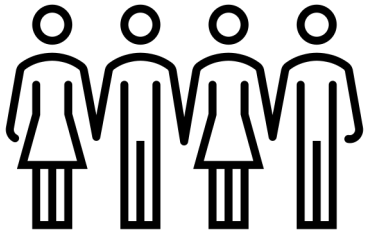
Standards Governance at AZ

Corporate Standards Management is split into 2 at AZ:

- Data Collection Standards (DCS)



- Data Analysis and Reporting Standards (DARS)



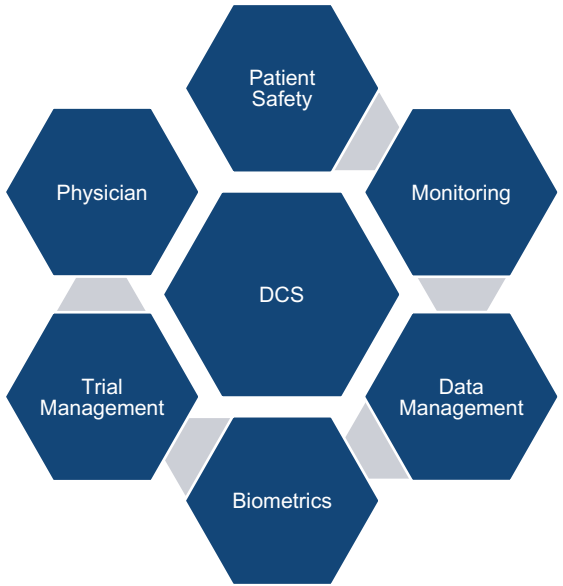
Database Revision

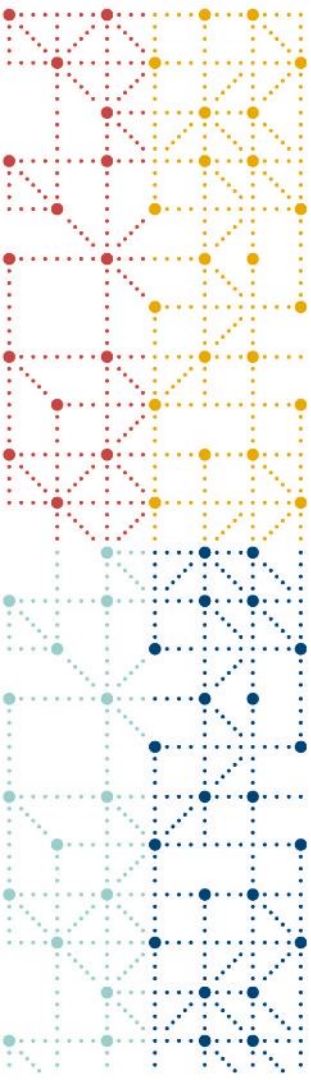
DCS ran the project:

To update the collection instruments to use EC rather than EX:

- A team was created with SMEs from various functions.
- Discussions around:
  - Database design
  - Reducing configurations of the module
  - Evaluating the importance (required/not) of each data point
- Updated data collection components in Q3 2022

Governance Team





SDTM Mapping

The chosen solution

SDTM mapping

Now we have a CDASH compliant EC database we need to update the SDTM mapping:

DARS found we had 3 options:

1. Update the database structure to separate planned and actual dosing
2. Map the current database to SDTM using ECMOOD
3. Map to EC, ignore ECMOOD and put planned dosing in SUPPQUAL

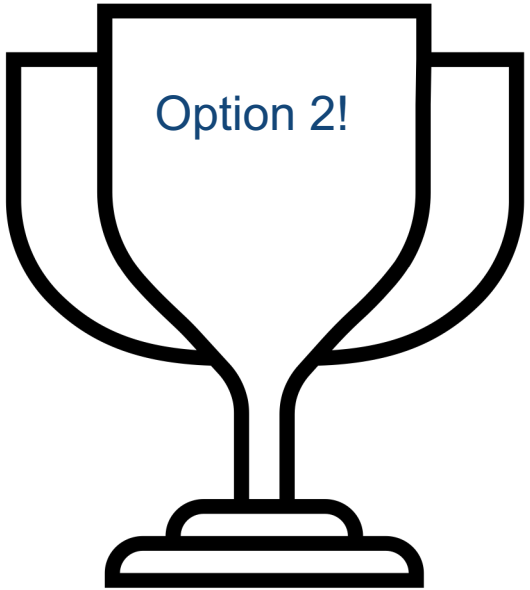
Considerations:

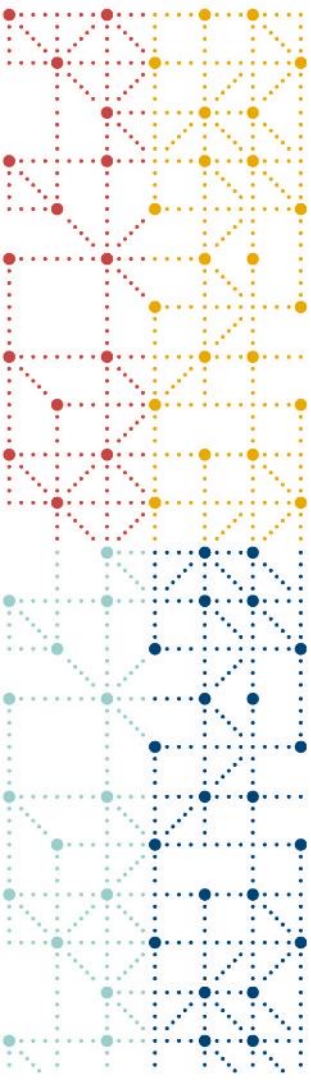
1. Not feasible, given the project had just concluded.
2. Difficult SDTM mapping from a horizontal collection structure to a more vertical structure
3. Easy! But not compliant with CDISC SDTM EC intended structure

And the winner is…

Next steps

- Annotate the CRF with SDTM EC variables
- Create prototype mapping
- Mapping SDTM EC to EX:
  - When can CRF EC be mapped directly to SDTM EX.
  - Prototype mapping of SDTM EC to EX.
  - Update mapping Placebo EXDOSE to zero

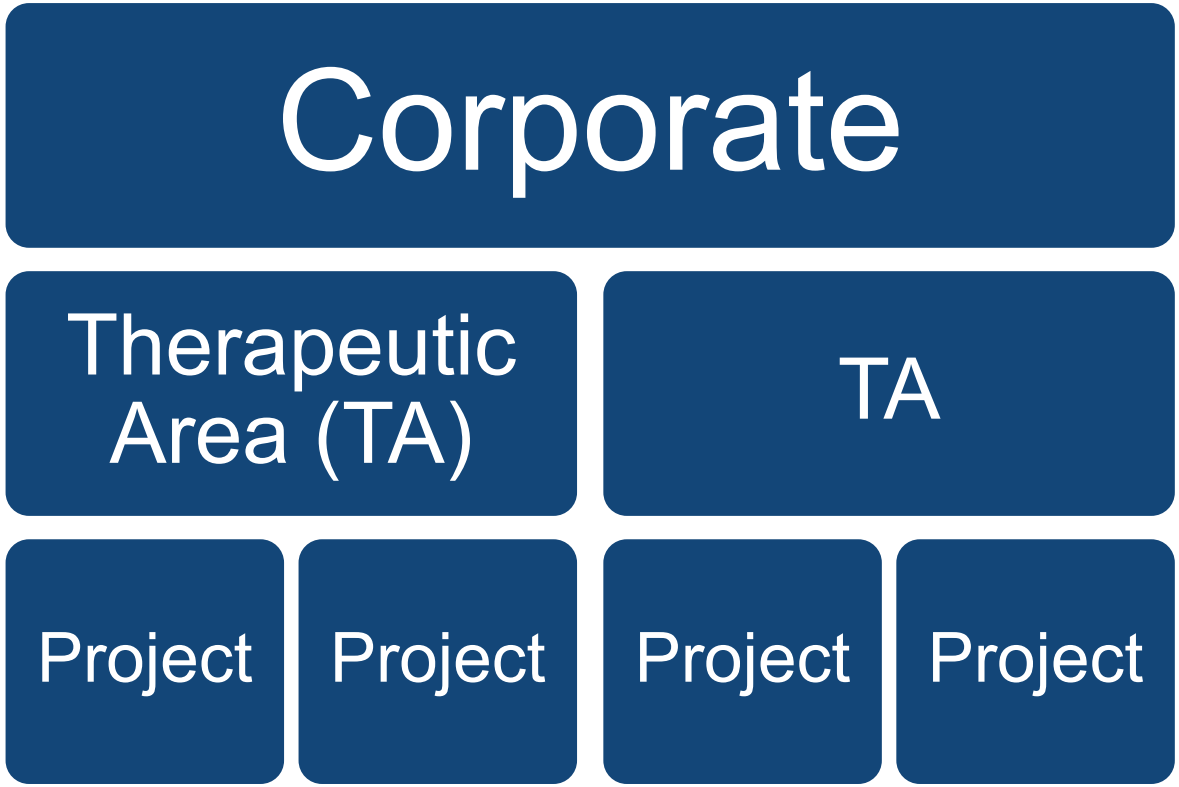




SDTM Mapping

Governance and Implementation

Clinical Data Standards Governance

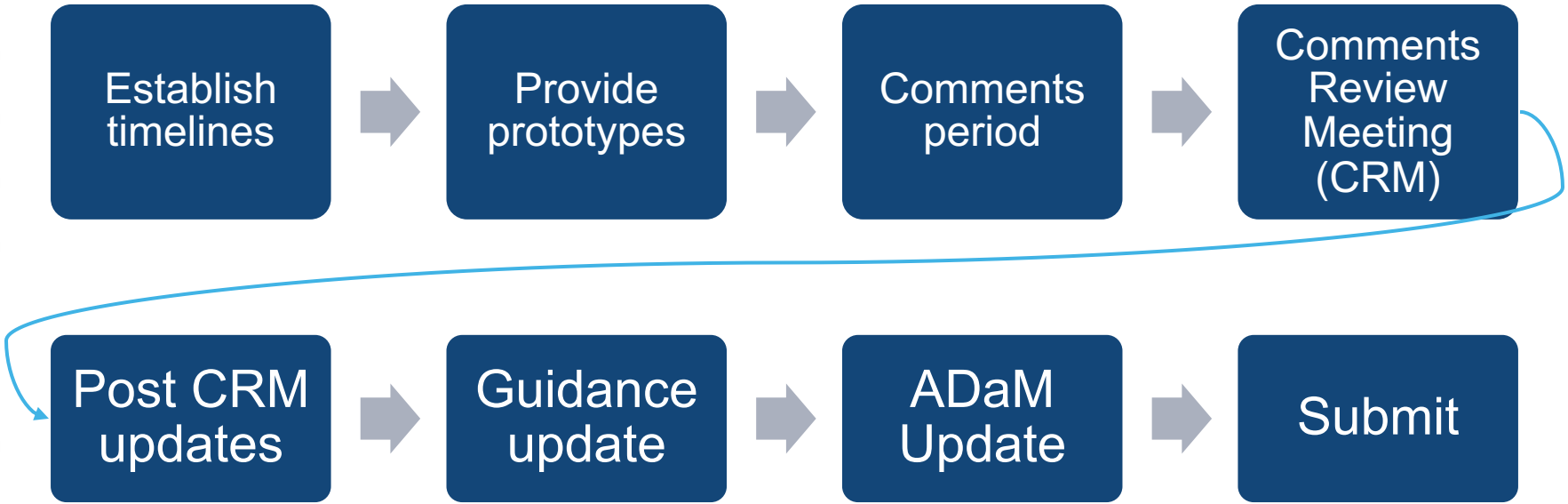


Governed by Corporate + SMEs to make Standards Review Team (SRT)

Governed by TA Standards Development Teams (TASDT)

Project standards receive guidance

Review and governance with TASDT



Submission and Implementation

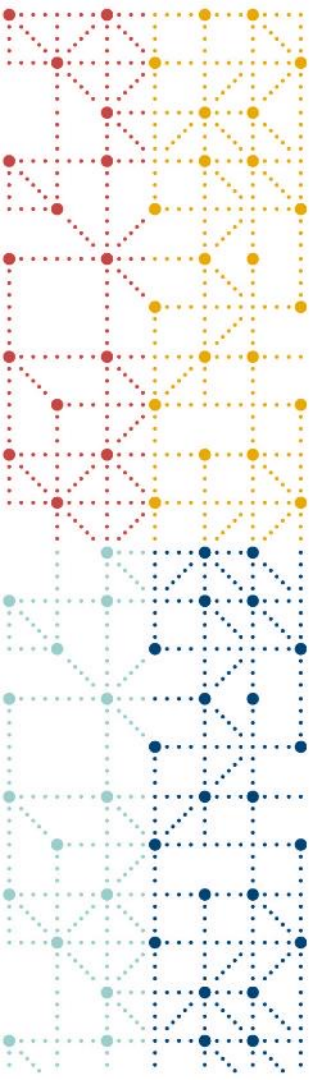
Next steps:

- Approval in the change request system
  - Opportunity for further comments from SRT / TASDT on revised elements.
  - Comments log updated to the system for full traceability.
- Standards update:
  - SDTM
    - Ensure EC metadata is available in the MetatData Repository (MDR).
    - Update EX metadata to reflect the updated mapping (e.g. remove planned variables from SUPPEX)
    - Update the mapping of EC in our MDR mapping tool.
    - Ensure this mapping is useable in our SDTM SAS program builder tool.
    - Update our SDTM Guidance document.
  - ADaM
    - Add any new variables to our ADEX analysis dataset (OCCurrence Data Structure)
    - Update the Value Level Metadata for ADEXSUM Basic Data Structure dataset

Submission and Implementation

Next steps:

- Standards update ctd:
  - Output template
    - Add a programming note warning of EXDOSE=0 for Placebo
- Quarterly release
  - Run the standards extraction macros
  - Validate, QC and update
  - Email notification
  - Education sessions
- Maintenance
  - Address any questions
  - Review requests via the CR system



Summary

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Conclusions:

- More active participation is required from SDTM experts when a data collection instrument is updated.
  - To get the required outcome of a more straightforward SDTM mapping.
- Input of TASDT was invaluable
- SDTM EC mapping was straightforward, the mapping to EX was much more challenging!
  - EC mapping in MDR as complex as anticipated.
- ‘Throwaway’ inclusion of setting Placebo dose caused most post-CRM work
  - End to end impact
  - Updates to ADaM & Output template

Thank You!

Questions?