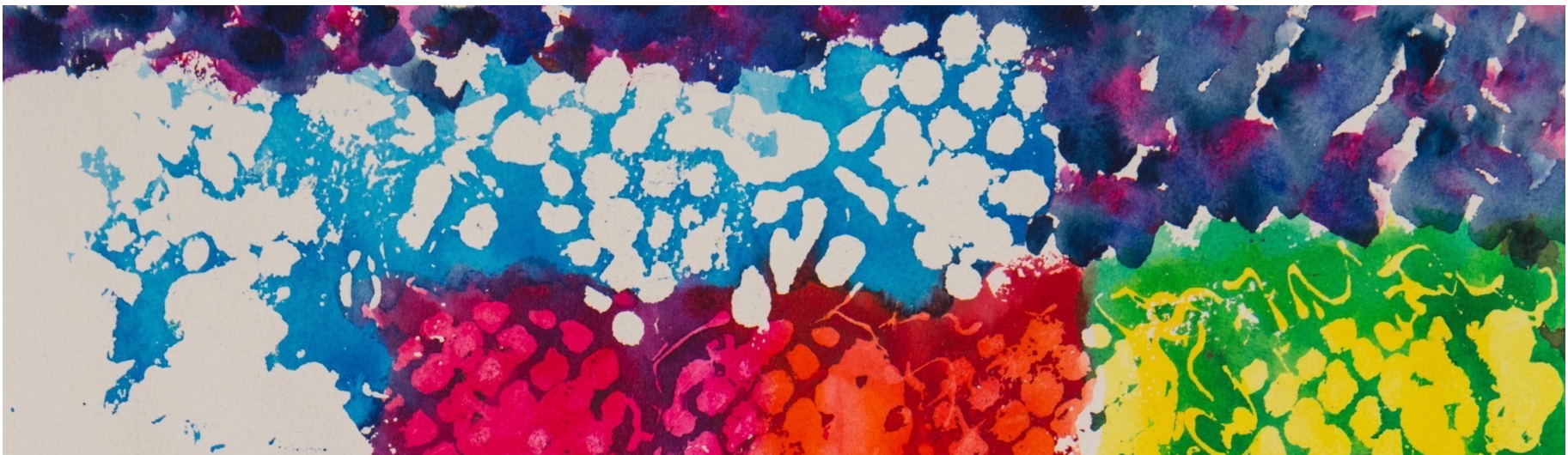




DS10 - A Collaborative Approach to Analysis Standards

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Artwork from The Creative
Center at University
Settlement.

Agenda

Analysis Standards at Janssen

- Who are the players?
- What is included in Analysis Standards?
- Examples of collaboration
- Conclusion

Who are the players?

Who are the players?

Analysis Standards team



- ❖ Programmers and statisticians
- ❖ Experienced in clinical trial analysis
- ❖ **Dedicated** to analysis standards
- Owners of analysis standards development
- Create and maintain all standard related files

Participate in industry groups: CDISC, PHUSE, PharmaSUG, ...
Stay current on industry standards.

Who are the players?

Subject Matter Experts (SMEs)



- ❖ Programmers and statisticians
- ❖ Working on clinical trials
- ❖ Representation of all disease areas
- Provide **input/expertise** on standards development/updates and questions
- Owners of analysis standards content

SMEs are assigned to a topic based on their expertise, e.g. Adverse Events, Lab data.

Who are the players?

Statistical programmers and Statisticians



- ❖ Programmers and statisticians
- ❖ Working on clinical trials

➤ **Users** of standards

Reach out with questions/requests on standards through the SMEs, or enter into Q&A or Change Request tool.

**What is included in
Analysis Standards?**

What is included?

1. Prepopulated templates for Statistical **requirements** documents, e.g. SAP.
2. ADaM **metadata**
3. ADaM dataset and TLG **code**

All elements are **aligned from requirements through metadata and code***.

Options are aligned by use of variants numbers which identify that option throughout requirements, metadata and code.

* Elements are also aligned with data collection/delivery/CRF standards (not in scope of this presentation).

Statistical Requirements templates

- Statistical Analysis Plan (SAP)
- Data Presentation Specifications (DPS)
 - Part 1: List of outputs with mock-ups
 - Part 2: Key/complex analysis/derivation rules for ADaM dataset (to be carried over into ADaM metadata)

Templates are pre-populated with standard requirements

Template conventions:

- Study specific, user-supplied text [light blue shading]
- Optional text **turquoise blue**
- Variants of text denote alternative definitions

Example of optional/user supplied text

The verbatim terms used in the CRF by investigators to identify adverse events will be coded using the Medical Dictionary for Regulatory Activities (MedDRA). All treatment emergent adverse events will be included in the analysis. For each adverse event, the number and percentage of subjects who experience at least 1 occurrence of the given event will be summarized by treatment group.

Summary tables will be provided for:

- AEs
- Serious AEs (SAEs)
- AEs leading to [discontinuation of study agent, termination of study participation]
- AEs by [severity, toxicity grade]
- AEs by relationship to study agent
- AEs leading to [dose interruption, dose modification]

Study specific, user supplied

Optional, can be removed

In addition to the summary tables, listings will be provided for subjects who:

ADaM variable from SAP through code - example

The full analysis set (FAS) includes all [randomized] participants.

The full analysis set (FAS) includes all [randomized] participants who received at least 1 dose of any study intervention.

SAP – 2 variants for full analysis set

DPS Part 2 – translate SAP text into programming details

More technical text for programming

Analysis Set Name	Text	Variable Name	Variant #
Full Analysis Set (FAS)	Subjects who had a non-missing randomized date (DSDECOD=RANDOMIZED and DSSTDTC is not missing).	FASFL	1
Full Analysis Set (FAS)	Subjects who had a non-missing randomized date (DSDECOD=RANDOMIZED and DSSTDTC is not missing) and were treated with at least 1 dose of any study agent.	FASFL	2

VARNAME	VARVER	VERDESC	ORIGCOM	SASMCR
FASFL	1	Randomization.	Subjects who were randomized. Y if there is a record in DS with DS.DSDECOD equal to RANDOMIZED and DS.DSSTDTC is not null. Otherwise N.	%ADFASFL
FASFL	2	Randomization with dosing.	Subjects who were randomized and have at least 1 dose of study agent with a non-missing start date. Y if there is a record in DS with DS.DSDECOD equal to RANDOMIZED and DS.DSSTDTC is not null and at least one EX.EXSTDTC is not null, otherwise N.	%ADFASFL

ADaM metadata – more programming details, including standard macro name

SAS macro call

```
%adfasfl(hdsn = adsl,
          adrule = VERSION1,
          outdsn = adsl101,
          debug = OFF);
```

Mock display to code

TSFAE-ST02: Number of Subjects With [Treatment-emergent Adverse Events] With Frequency of at Least [xx]% in [Any Treatment Group/the Combined Treatment Group] Through [Time Point] by System Organ Class and Preferred Term and [Subgroup]; Safety Analysis Set (Study [Study ID])

	[Active Study Agent]		
	[Placebo]	[Treatment Group A]	[Treatment Group B]
Analysis set: Safety	###	###	###
[Subgroup]: [Category]	###	###	###
Avg duration of follow-up ([units])	###	###	###
Avg exposure ([units])	###	###	###
Subjects with 1 or more [AEs]	### (xx.x%)	### (xx.x%)	### (xx.x%)
System organ class			
Preferred term			
System organ class	### (xx.x%)	### (xx.x%)	### (xx.x%)
Preferred term	### (xx.x%)	### (xx.x%)	### (xx.x%)

Key: AE = adverse event, Avg = average
 Note: Subjects are counted only once for any given event, regardless of the number of times they actually experienced the event.
 Adverse events are coded using MedDRA Version XX.X.

[Output Identifier] [Program Location] [Date/Time of output]

Display Specifications	
Optional parameter(s)	☐ Avg duration of follow-up (specify units) (with corresponding footnote): Click here to enter text.
	☐ Avg exposure (specify units) (with corresponding footnote): Click here to enter text.

Programming Notes:

- Where applicable, apply the frequency cut-off ($\geq x\%$) before rounding.
- Based on Standard Reference Layout TREF-ST001

TSFAEST02 template program

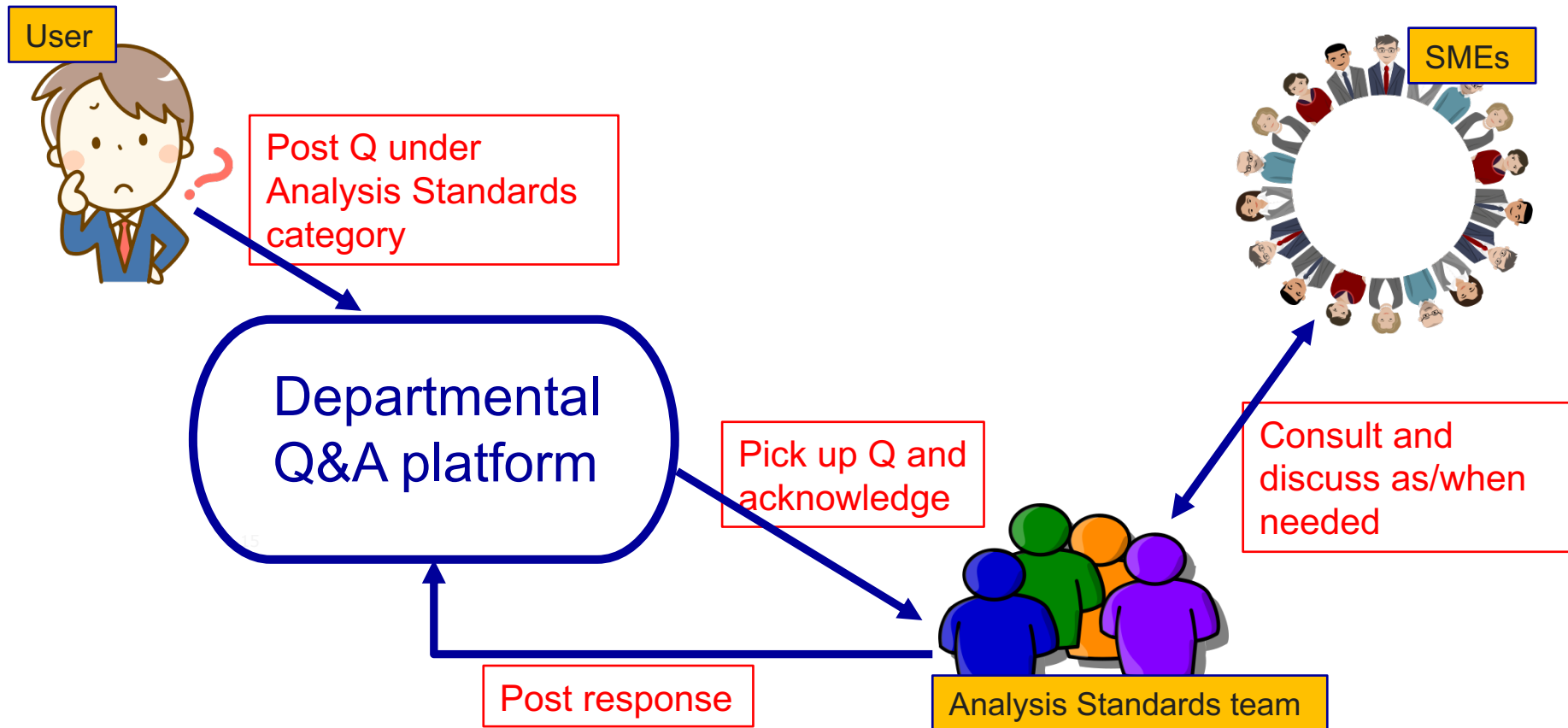
Calls macro %astrefst001

Macro input parameters linked to mock display options:

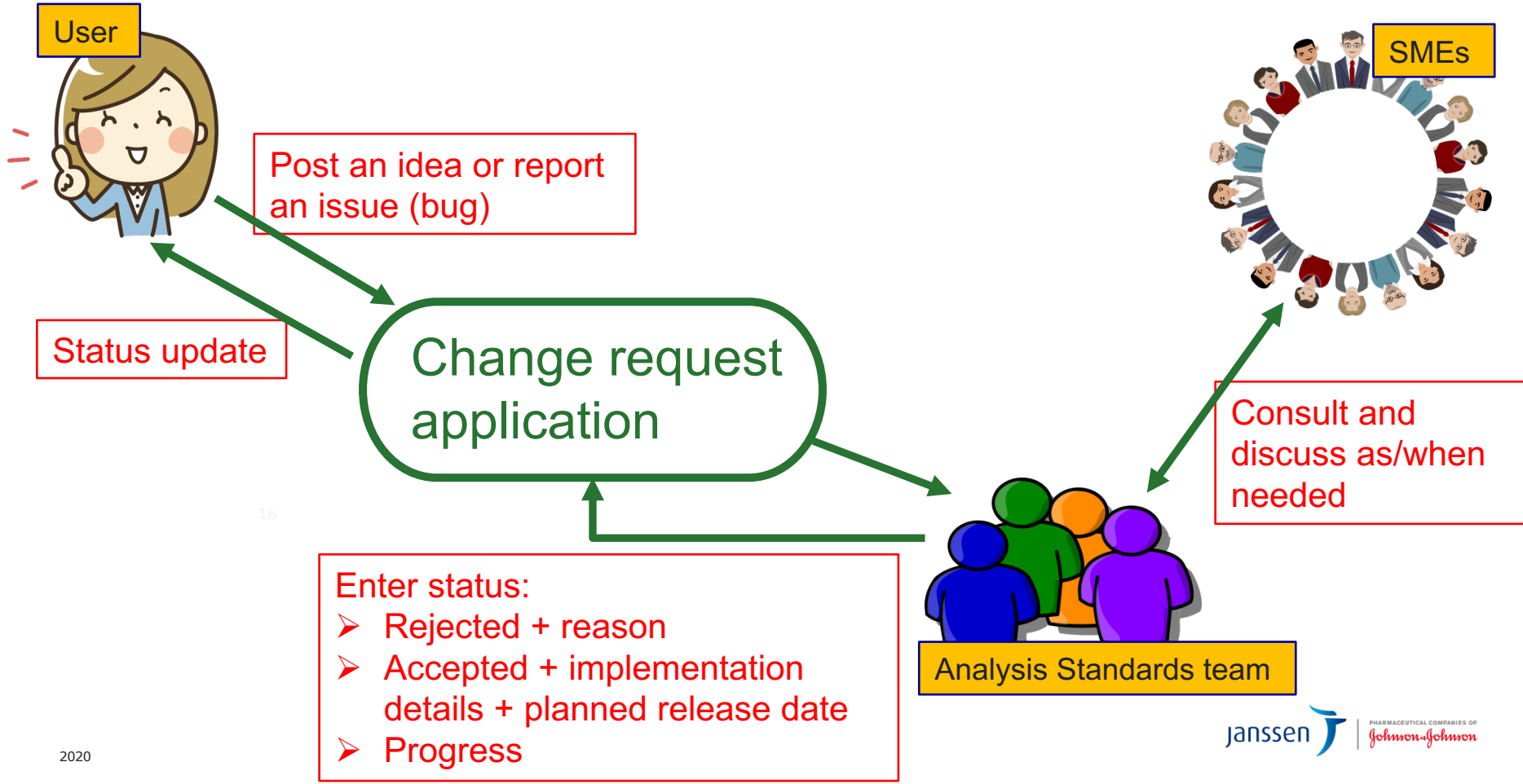
- ☒ where = %str(TRTEMFL='Y')
- ☒ fupvar = studydur
- ☒ expvar = trtdurd

Examples of collaboration

Users can post Questions



Users can enter a Change Request



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Development of Disease Area standards (1)



Analysis Standards team

- ✓ Facilitate meetings
- ✓ Provide guidance on standards
- ✓ Develop DA documents

Standard requirement templates:
SAP, DPS with mock lay-outs and
derivation rules

Global
standards*

*Global standards support routine analysis and
reporting needs across therapeutic areas



Disease Area (DA) team:
Representatives of all
involved functions, i.e.
statisticians,
programmers, medical
writing, clinical, ...

- ✓ Provide functional
DA input/expertise
- ✓ Define DA specific
requirements

Requirements customized for the DA:

- ✓ Options/variants selected based on
DA needs
- ✓ DA specific
requirements added

DA
standards

Development of Disease Area standards (2)

- ✓ Facilitate meetings
- ✓ Provide guidance on standards
- ✓ Plan/manage development of DA metadata and code
- ✓ Add DA specific options/variants to standard metadata and code



Analysis Standards team



Assist in development of DA standards

- ✓ Provide metadata and code that can be leveraged
- ✓ Develop DA specific elements, e.g. efficacy.



Disease Area programming team

Metadata and Code

Metadata

DA Metadata

- Integrated into standards
- DA level is an extract from standards

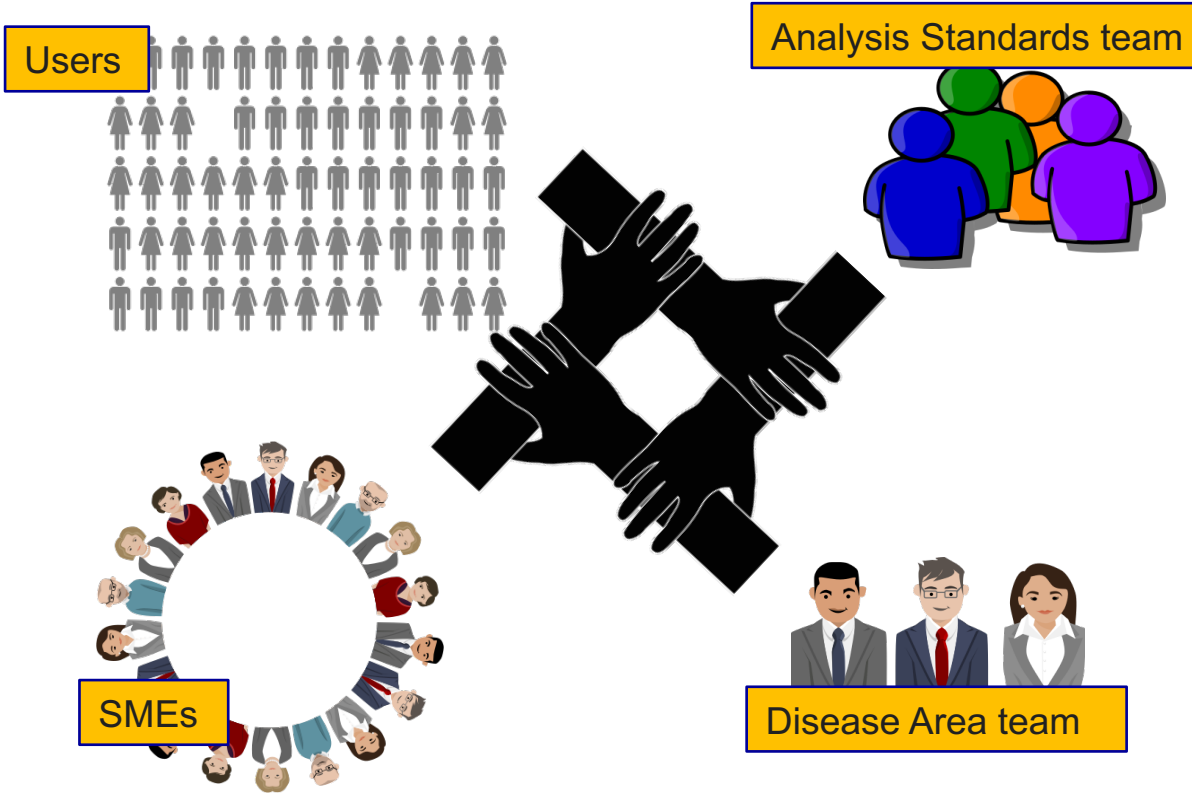
Code

DA Programs and macros

- DA options added to standard code
- DA code added to standard library

Conclusion

Future of standards at Janssen



Continue to enhance standards and develop more DA standards.

Adopt new technology to facilitate maintenance and implementation of standards.

User, SME and DA team involvement and participation trigger enthusiasm for adoption of standards.

Customization of standards for DAs increases the use of standards.



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