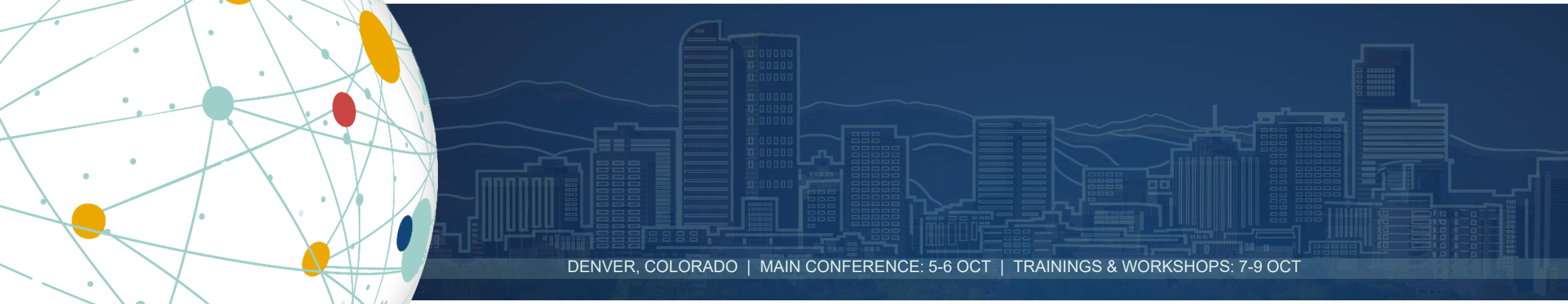


cdisc®

2026 US Interchange

THE FUTURE IS CONNECTED: STANDARDS AND AI POWERING DIGITAL TRANSFORMATION



From Framework to Practice: Practical ADaM Implementation

Jie Yang, Biostatistician, SGS Pharma Clinical Research

Speakers

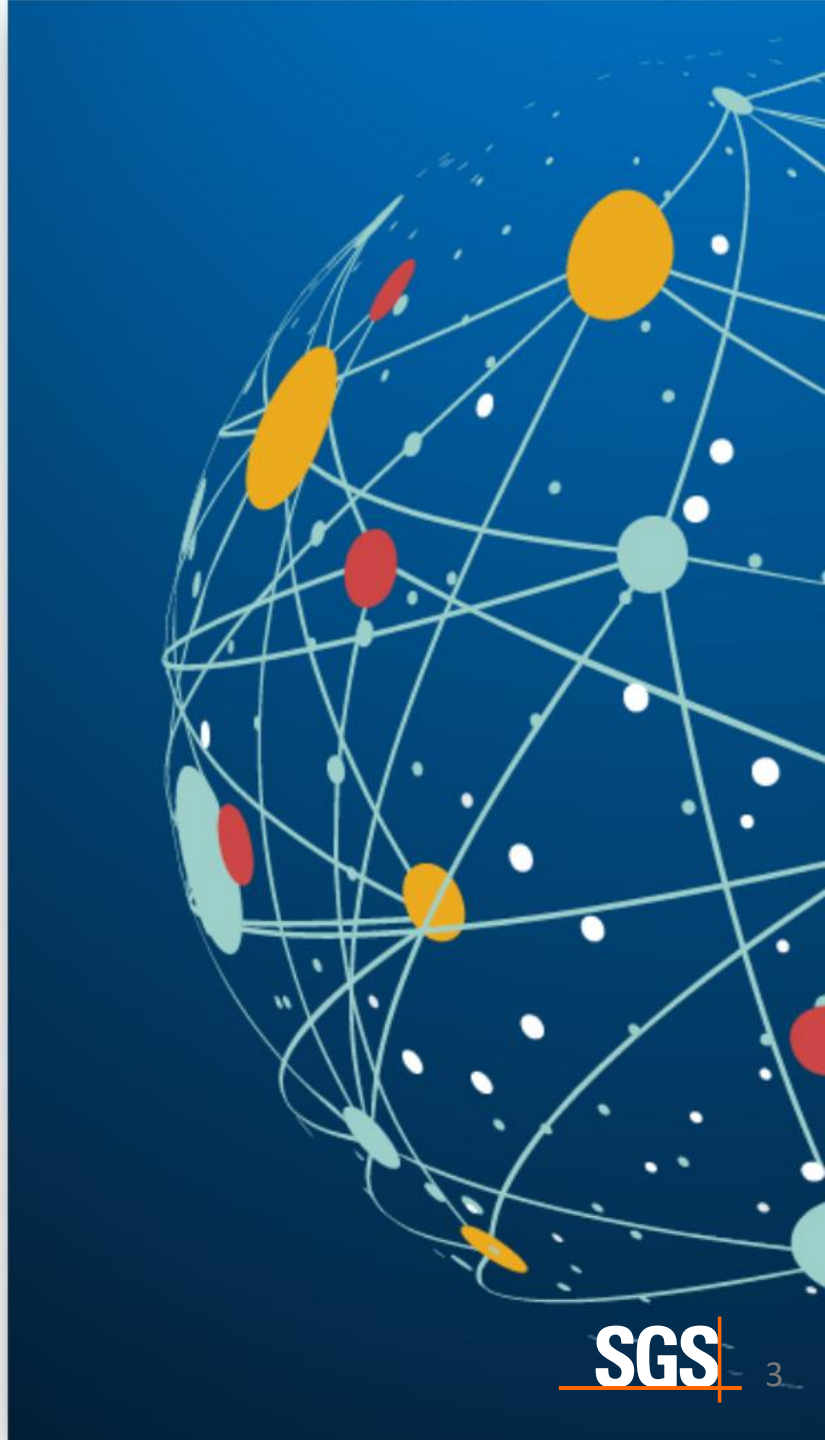


Jie is a biostatistician at SGS, supporting clinical trials across Phase I-IV. Her expertise includes SAP development, CDISC ADaM implementation, TLFs and Define-XML deliverables. She has a particular interest in reproducible workflows and pipelines, open-source technologies, and the evolution of data standards and governance.

Jie Yang
Biostatistician
SGS Pharma – Clinical Research

Disclaimer and Disclosures

- *The views and opinions expressed in this presentation are those of the author and do not necessarily reflect the official policy or position of CDISC or SGS Pharma.*
- *The authors have no real or apparent conflicts of interest to report.*



Agenda

1. The Implementation Gap and PHUSE White Paper (WP-092)
2. ADaM Implementation and Key Decisions
3. Study Example
4. Key Takeaways

The Implementation Gap and PHUSE White Paper (WP-092)

The Implementation Gap

- The ICH E9 (R1) estimand framework is well established across the industry
- However, operationalizing it within clinical trial workflows remains a key challenge
- Diverse and inconsistent implementation across companies/organizations (e.g. ADICE dataset with different variable conventions)

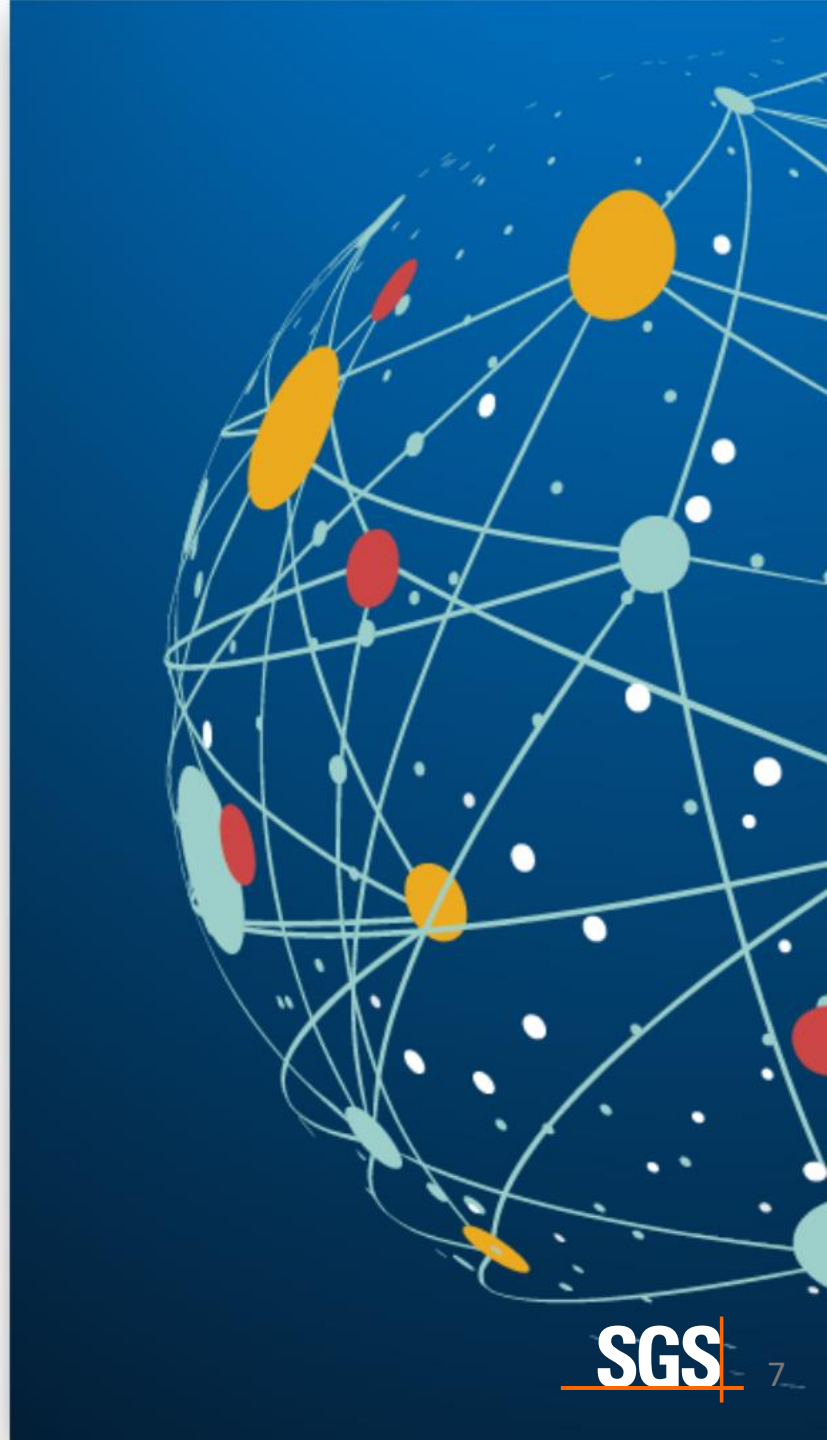
"A framework to align planning, design, conduct, analysis and interpretation"
- ICH E9 (R1) addendum

PHUSE White Paper (WP-092)

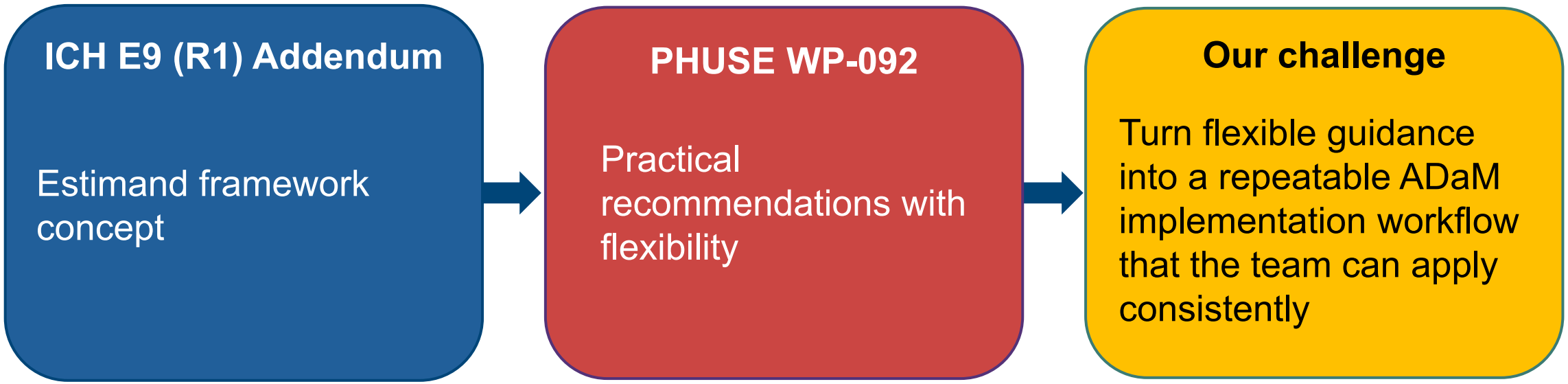
- Implementation of ICH E9 (R1) Estimands Framework using Data Standards
- Published in May 2025 by PHUSE working group "*Optimizing the Use of Data Standards*"
- WP-092 does not redefine the estimand framework
  → Provides practical recommendations across the entire clinical data flow, including data collection, tabulation, analysis, and documentation

  → Supports consistent implementation while preserving flexibility



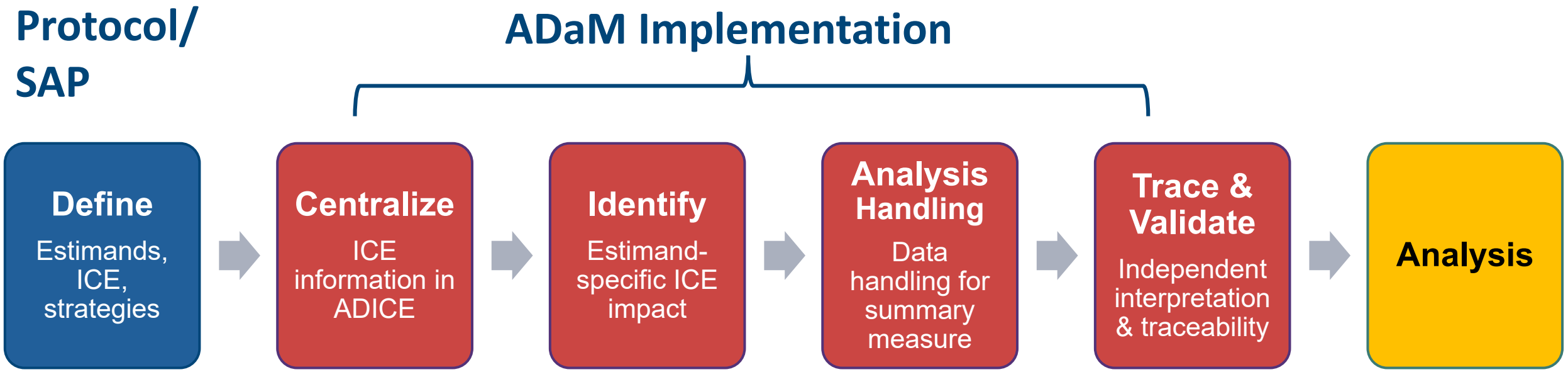


From Estimand Framework to ADaM Implementation



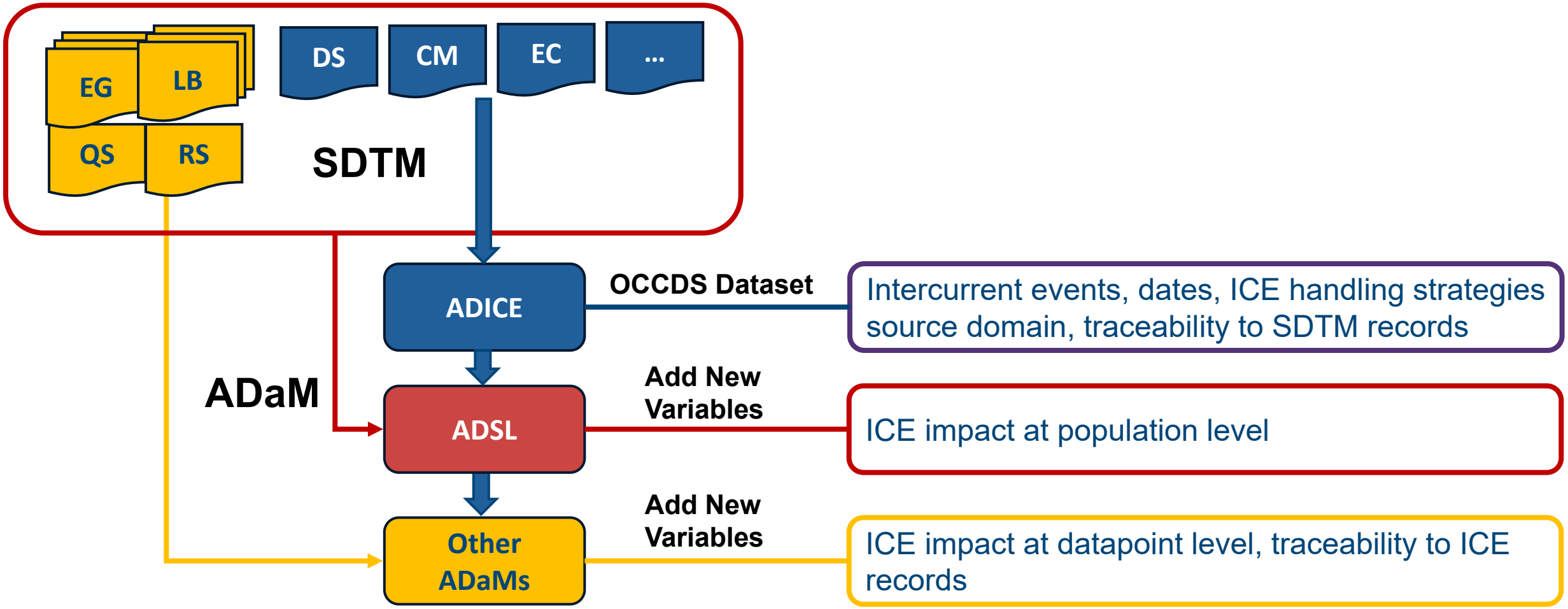
ADaM Implementation and Key Decisions

ADaM Implementation - Workflow



The workflow is standardized while the scientific decision remains study-specific

ADaM Implementation



Where to Capture Intercurrent Events?

SGS preferred approach

1 ADSL

Store ICE information directly in the ADSL for simple trial

2 Existing OCCDS

Store ICE information across relevant occurrence datasets such as ADAE, ADCM, etc

3 Dedicated ADICE

Consolidate ICE information in a single ADaM dataset

Benefits



Traceability

Source→ICE→estimand handling strategies→analysis



Scalability

multiple estimands and complex ICE scenarios



Consistency

reusable implementation across studies and teams



Efficiency

simpler programming logic, less validation and maintenance effort

ADICE (Intercurrent Events Analysis Dataset)

Key features	Core Variables
Identifiers and sequence	STUDYID, USUBJID, SUBJID, ASEQ
Events	ATERM, UDECOD
Standardized classification	ADECOD1, ACAT1
Dates	ASTDT, AENDT
Handling strategy	ESTzzSTP, ESTzzSTA
Source	SRCDOM, SRCSEQ

Variable	Notes
ESTzzSTP	Planned handling strategy for estimand zz
ESTzzSTA	Actual handling strategy for estimand zz Copy of ESTzz*STP or blank

When multiple ICEs occur for the same subject and estimand, the priority rule must be specified in the SAP before programming

Strategies for Addressing Intercurrent Events

Different ICE handling strategies lead to different programming requirements, analysis populations, and analysis data derivations

Strategy	Analysis Principle	Impact Scope	Typical Implementation
Treatment policy	Use all observed data regardless of ICE	None	None
Hypothetical	Estimate outcome as if the ICE had not occurred	Post-ICE datapoints	Exclude or replace impacted datapoints per SAP
Composite	ICE becomes part of endpoint definition	Post-ICE datapoints	Derive unfavorable outcome (e.g., non-responder, impute with worst value)
While on treatment	Use observations collected before the ICE	Post-ICE datapoints	Exclude post-ICE datapoints
Principal stratum	Target population defined by potential ICE occurrence	Population-level	Restrict analysis population

Impact identification ≠ Data handling

Datapoint-Level Impact: Which Approach?

Approach	Question Answered	Strengths	Limitations	Variables Proposed by WP-092
Per estimand	Is the datapoint impacted for this estimand?	Simple for analysis	Less granular for ICE type; priority rule needed	ICEzzS, ICEzzF
Per ICE categorization modalities	Does this ICE modality impact the datapoint?	Attractive for study where same ICE definitions and impact rules apply consistently across the estimands	Less precise traceability to the estimand; Problematic when different estimands handle the same ICE differently	ICCyS, ICCyF
Per estimand and ICE categorization modalities	Does this ICE modality impact this datapoint for this estimand?	Most detailed	Many variables lead to a large dataset	ICCyEzzS, ICCyEzzF

Datapoint-Level Impact: Which Approach?

Approach	Question Answered	Strengths	Limitations	Variables Proposed by WP-092
Per estimand	Is the datapoint impacted for this estimand?	Simple for analysis	Less granular for ICE type; priority rule needed	ICEzzS, ICEzzF

SGS Preferred Approach

- Selection criteria: analysis objective, simplicity and maintainability
- Capturing impact directly at the estimand level keeps the implementation aligned with the clinical question and avoids potential ambiguity

Population-Level Impact: ADSL

In case of estimands with principal stratum strategy, the impact is at population-level

Variable	Label	Description
PSyFL	Principal Stratum y Set Flag	Subject considered for principal stratum y (N/Y)



PSyFL is a participant-level population flag → It's not an ICE occurrence flag

Study Example

Study Example Overview

- **Context**: Chronic Inflammatory Demyelinating Polyneuropathy (CIDP) is an autoimmune disease resulting in impairment of arms and legs
- **Population**: Adult participants diagnosed with CIDP
- **Treatment**: Test drug or placebo, weekly administration
- **Assessment variable**: aINCAT disability scale total score (range 0-10), collected every 4 weeks
- **Endpoint**: Binary aINCAT responder status at Week 12
  - Responder: ≥1 point reduction in aINCAT score from baseline at Week 12
  - Non-responder: <1 point reduction from baseline at Week 12

Study Example - Estimands

Attribute	Primary Estimand	Supplemental Estimand
Population	Adult participants with a confirmed CIDP diagnosis who would remain compliant to investigational medicinal product	Adult participants with a confirmed CIDP diagnosis
Treatment	Test drug or Placebo	
Variable (Endpoint)	aINCAT responder status at Week 12 (Responder/Non-responder)	
Population-level summary	Difference between Test drug and placebo in the proportion of responders	Difference between Test drug and placebo in the proportion of responders

Two estimands, same endpoint, different clinical questions

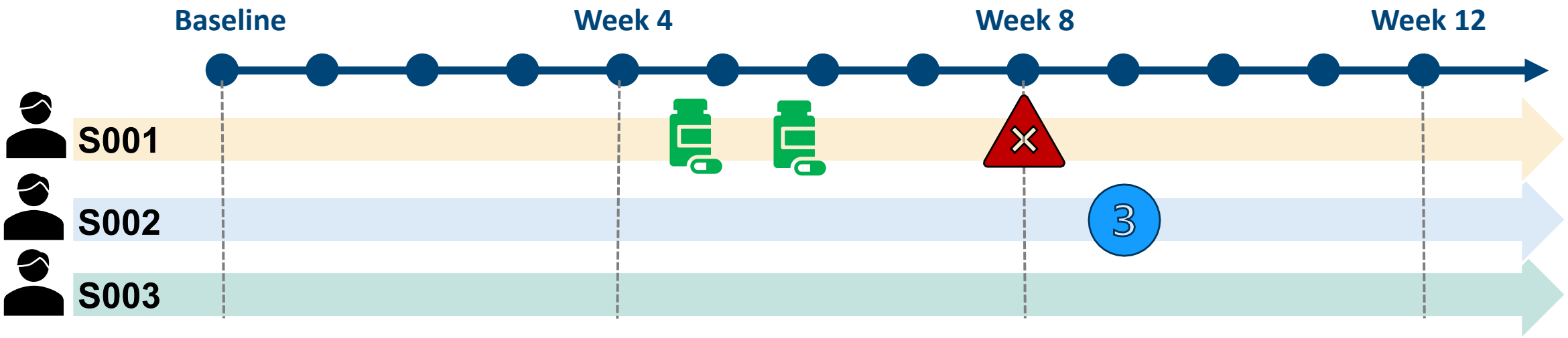
Study Example - Estimands

Attribute	Primary Estimand	Supplemental Estimand
ICE #1: Use of prohibited medication	Composite strategy	Treatment policy strategy
ICE #2: Early treatment discontinuation	Composite strategy	Treatment policy strategy
ICE #3: 3 or more consecutive missed doses	Principal stratum strategy	Treatment policy strategy

- **Composite strategy**: data obtained after the ICE will not be considered, and the subject will be considered as non-responder
- **Principal stratum strategy**: retain all data, and analysis is restricted to the target principal stratum (subjects who would not experience the ICE)
- **Treatment policy strategy**: data obtained after the ICE will be considered, if available

- **Priority rule**: the earliest ICE occurrence per subject and estimand

Study Example - Timeline



ICE #1: Use of prohibited medication

ICE #2: Early treatment discontinuation

ICE #3: Three or more consecutive missed doses

The alNCAT score is collected every 4 weeks regardless of ICE occurrence

ADICE

USUBJID	ASEQ	ATERM	UDECOD	ACAT1	ASTDT	SRCDOM	SRCSEQ
S001	1	IVIG	IVIG	USE OF PROHIBITED MEDICATION	03FEB2026	CM	5
S001	2	CORTAN	PREDNISONE	USE OF PROHIBITED MEDICATION	05FEB2026	CM	12
S001	3	ADVERSE EVENT	ADVERSE EVENT	EARLY TREATMENT DISCONTINUATION	02MAR2026	DS	3
S002	1	3 OR MORE CONSECUTIVE MISSED DOSES		3 OR MORE CONSECUTIVE MISSED DOSES	16FEB2026	EC	2

EST01STP	EST01STA	EST02STP	EST02STA
COMPOSITE VARIABLE	COMPOSITE VARIABLE	TREATMENT POLICY	
COMPOSITE VARIABLE		TREATMENT POLICY	
COMPOSITE VARIABLE		TREATMENT POLICY	
PRINCIPAL STRATUM	PRINCIPAL STRATUM	TREATMENT POLICY	

Same ICE, different handling strategies per estimand

ADICE

Reported treatment from CMTRT

Coded term from CMDECOD

Standardized ICE categorization per SAP

USUBJID	ASEQ	ATERM	UDECOD	ACAT1	ASTDT	SRCDOM	SRCSEQ
S001	1	IVIG	IVIG	USE OF PROHIBITED MEDICATION	03FEB2026	CM	5
S001	2	CORTAN	PREDNISONE	USE OF PROHIBITED MEDICATION	05FEB2026	CM	12
S001	3	ADVERSE EVENT	ADVERSE EVENT	EARLY TREATMENT DISCONTINUATION	02MAR2026	DS	3
S002	1	3 OR MORE CONSECUTIVE MISSED DOSES		3 OR MORE CONSECUTIVE MISSED DOSES	16FEB2026	EC	2

EST01STP	EST01STA	EST02STP	EST02STA
COMPOSITE VARIABLE	COMPOSITE VARIABLE	TREATMENT POLICY	
COMPOSITE VARIABLE		TREATMENT POLICY	
COMPOSITE VARIABLE		TREATMENT POLICY	
PRINCIPAL STRATUM	PRINCIPAL STRATUM	TREATMENT POLICY	

EST01STA is populated for the first ICE, which is the driving ICE per SAP priority rule

EST02STA is blank for ALL records due to treatment policy strategy

Same ICE, different handling strategies per estimand

ADSL

USUBJID	FASFL	SAFFL	PS1FL
S001	Y	Y	Y
S002	Y	Y	N
S003	Y	Y	Y

Target principal stratum: participants who would not experience dose omission (3 consecutive missed doses).

Illustrative implementation: Subject S002* is assigned PS1FL='N'.

**For illustration, PS1FL is used to support principal-stratum analysis. True principal-stratum membership cannot be determined solely from observed ICE occurrence.*

ADQS (Efficacy ADaM)

USUBJID	PARAMCD	AVISIT	AVAL	CHG	CRIT1	CRIT1FL
S001	aINCAT	BASELINE	8		REDUCTION >= 1 POINT FROM BASELINE	
S001	aINCAT	WEEK 4	8	0	REDUCTION >= 1 POINT FROM BASELINE	N
S001	aINCAT	WEEK 8	7	-1	REDUCTION >= 1 POINT FROM BASELINE	Y
S001	aINCAT	WEEK 12	6	-2	REDUCTION >= 1 POINT FROM BASELINE	Y
S002	aINCAT	BASELINE	8		REDUCTION >= 1 POINT FROM BASELINE	
S002	aINCAT	WEEK 4	8	0	REDUCTION >= 1 POINT FROM BASELINE	N
S002	aINCAT	WEEK 8	7	-1	REDUCTION >= 1 POINT FROM BASELINE	Y
S002	aINCAT	WEEK 12	6	-2	REDUCTION >= 1 POINT FROM BASELINE	Y
S003	aINCAT	BASELINE	8		REDUCTION >= 1 POINT FROM BASELINE	
S003	aINCAT	WEEK 4	8	0	REDUCTION >= 1 POINT FROM BASELINE	N
S003	aINCAT	WEEK 8	7	-1	REDUCTION >= 1 POINT FROM BASELINE	Y
S003	aINCAT	WEEK 12	6	-2	REDUCTION >= 1 POINT FROM BASELINE	Y

All subjects have CHG ≤ -1 at Week 12 and are therefore observed responder

Endpoint: responder status at Week 12 (≥1 point reduction from baseline in aINCAT score)

ADQS (Efficacy ADaM)



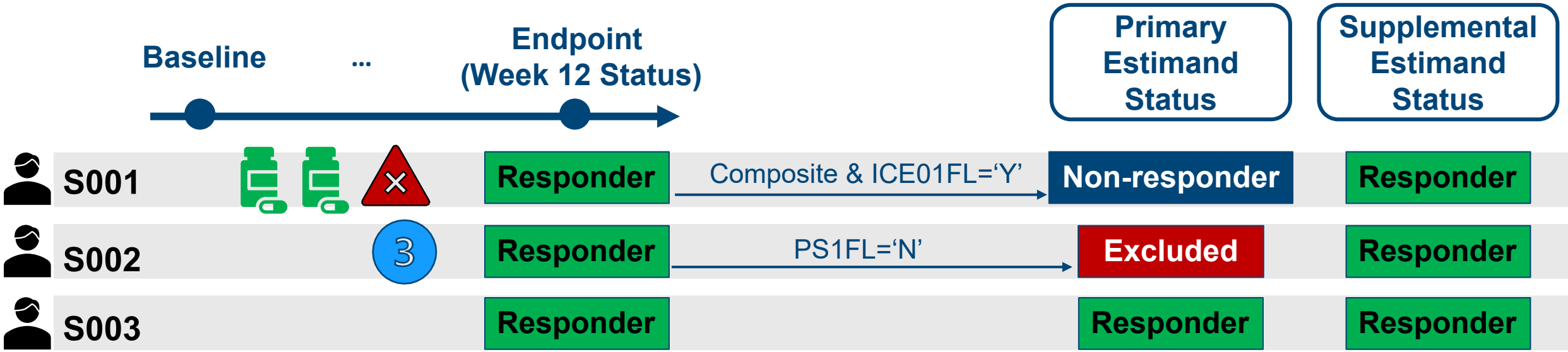
Driving ICE: Use of prohibited medication, IVIG starting between week 4 and 8

Supplimental estimand: impact variables are blank for ALL records due to treatment policy strategy

USUBJID	PARAMCD	AVISIT	AVAL	CHG	CRIT1	CRIT1FL	ICE01F	ICE01S	ICE02F	ICE02S
S001	aINCAT	BASELINE	8		REDUCTION >= 1 POINT FROM BASELINE					
S001	aINCAT	WEEK 4	8	0	REDUCTION >= 1 POINT FROM BASELINE	N				
S001	aINCAT	WEEK 8	7	-1	REDUCTION >= 1 POINT FROM BASELINE	Y	Y	1		
S001	aINCAT	WEEK 12	6	-2	REDUCTION >= 1 POINT FROM BASELINE	Y	Y	1		
S002	aINCAT	BASELINE	8		REDUCTION >= 1 POINT FROM BASELINE		Y	1		
S002	aINCAT	WEEK 4	8	0	REDUCTION >= 1 POINT FROM BASELINE	N	Y	1		
S002	aINCAT	WEEK 8	7	-1	REDUCTION >= 1 POINT FROM BASELINE	Y	Y	1		
S002	aINCAT	WEEK 12	6	-2	REDUCTION >= 1 POINT FROM BASELINE	Y	Y	1		
S003	aINCAT	BASELINE	8		REDUCTION >= 1 POINT FROM BASELINE					
S003	aINCAT	WEEK 4	8	0	REDUCTION >= 1 POINT FROM BASELINE	N				
S003	aINCAT	WEEK 8	7	-1	REDUCTION >= 1 POINT FROM BASELINE	Y				
S003	aINCAT	WEEK 12	6	-2	REDUCTION >= 1 POINT FROM BASELINE	Y				

S002: PS1FL='N', all the datapoints are considered to be impacted

Data Selection and Handling



The endpoint data remain the same, the estimand interpretation changed

Key Takeaways

Key Takeaways

- **Start with well-defined estimands and ICE strategies**

- **Separate ICE occurrence from interpretation**
  - Distinguish what happened from what it means and how it is handled under a specific estimand

- **Let the estimand decisions drive ADaM implementation**
  - The scientific question determines how intercurrent events are interpreted and handled, not the other way around

- **Maintain a clear traceability path**
  - Ensure that ICE representation, impact assessments, and downstream data handling can be traced back to the specified estimand and SAP decisions

References

- ICH E9 (R1) addendum on estimands and sensitivity analysis in clinical trials to the guideline on statistical principles for clinical trials. International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use (ICH). Updated Nov 20, 2019

- PHUSE. (2025, March 3). *Implementation of ICH E9(R1) Estimands Framework using Data Standards* (Doc ID: WP-092). https://phuse.s3.eu-central-1.amazonaws.com/Deliverables/Optimizing+the+Use+of+Data+Standards/WP-092.pdf

- PHUSE. (2025, March 3). *Implementation of ICH E9(R1) Estimands Framework using Data Standards – Example Document* (Doc ID: WP-092). https://phuse.s3.eu-central-1.amazonaws.com/Deliverables/Optimizing+the+Use+of+Data+Standards/WP-092-APP.pdf

Thank You!

Contact SGS

www.sgs.com/pharma

sgs.com/linkedinpharma

clinicalresearch@sgs.com



Questions?

Contact SGS

www.sgs.com/pharma

sgs.com/linkedinpharma

clinicalresearch@sgs.com

