



CDISC India Day

SEND 4.0 Unleashed:

The Next Evolution in Nonclinical Data Standards

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Speakers



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Anuj Gandhi is a Lead Statistical Programmer at Clantha Research, Ahmedabad, India, with extensive experience in clinical data standards and statistical programming. He specializes in SDTM, ADaM, SEND, TLFs, data quality, and regulatory submissions, supporting clinical and nonclinical research studies through CDISC-compliant solutions. Anuj is passionate about data standardization and leveraging innovative approaches to enhance efficiency, traceability, and research data value across the drug development lifecycle.

Agenda

1. Why did SEND need to evolve?
2. What has changed in SEND 4.0?
3. Why do these changes matter?
4. How should organizations prepare?





Why SEND Exists?

Regulators receive thousands of toxicology studies every year.

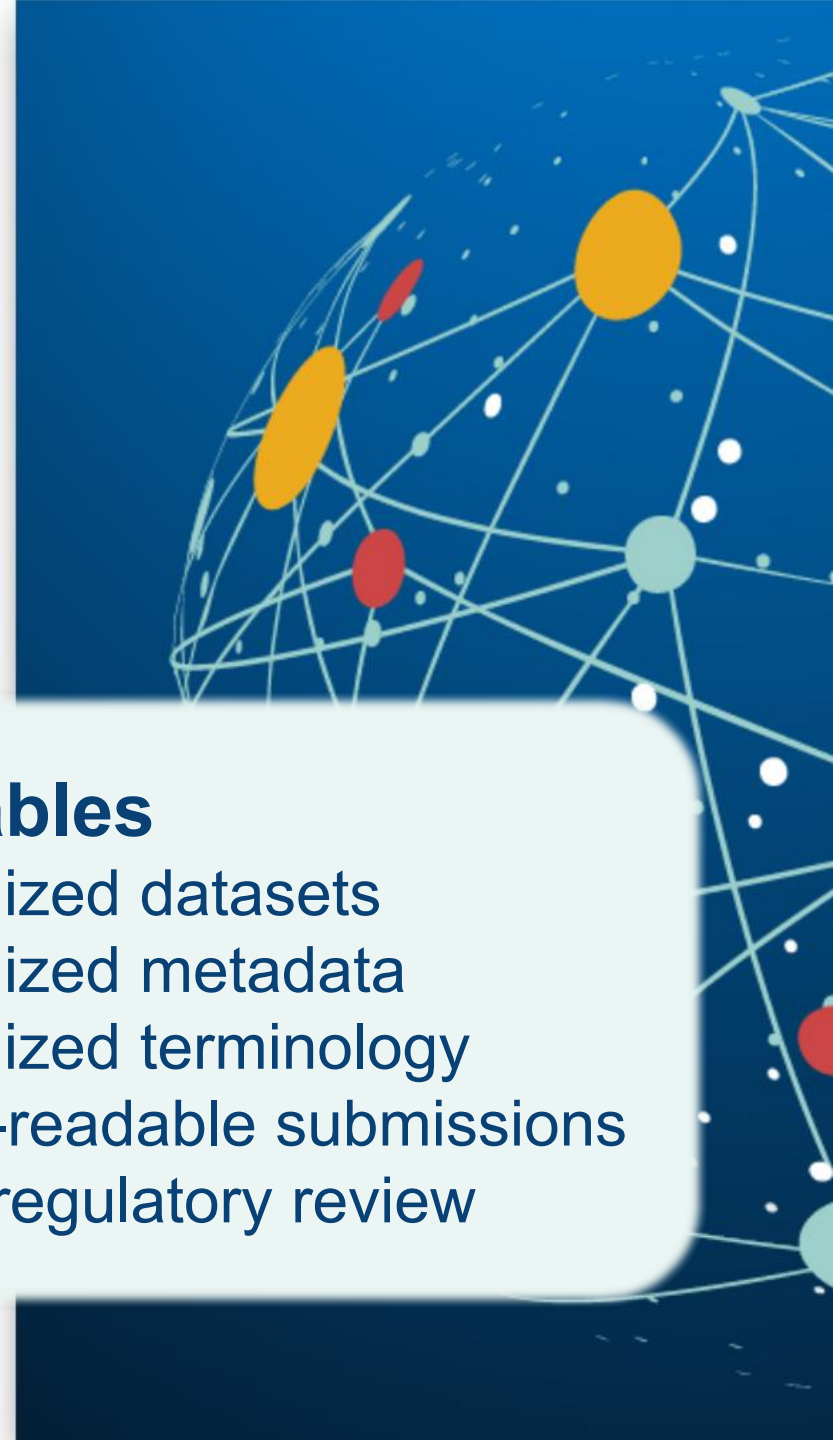
Without standardization:

- Inconsistent variable names
- Inconsistent terminology
- Manual review
- Difficult cross-study comparison
- Limited automation



SEND enables

- Standardized datasets
- Standardized metadata
- Standardized terminology
- Machine-readable submissions
- Efficient regulatory review



Why Are We Talking About SEND 4.0?

- **Evolving Regulatory & Data Landscape**

- Increasing **complexity** of nonclinical studies
- Expanding **study types and endpoints**
- **Higher expectations** from regulatory reviewers
- Demand for **greater traceability and data quality**
- Need for **machine-readable** and **reviewer-friendly** submissions

SEND 4.0 is designed to make data more **interoperable, traceable, and meaningful.**

The largest change to SEND in its history

Why this release is not routine??

8

new domains

The biggest single addition ever made to SEND

2

domains retired

TF and BG deprecated —

~all

existing domains touched

Improvement with more clarity to existing SEND implementation

3.1.1 was one theme — cardiovascular and respiratory safety pharmacology



4.0 hits neurology, dermatology, ophthalmology, immunology, PK methodology and measurement metadata at once.

Four Pillars of SEND 4.0

Domain Modernization

Dedicated domains standardize emerging nonclinical endpoints

Variable Harmonization

A consistent, intuitive metadata model across domains

Structural Modernization (NS Domains)

NS Domains replace SUPPQUAL with a cleaner data structure

Better Study Interpretation & Regulatory Readiness

Clearer study design and modern digital review

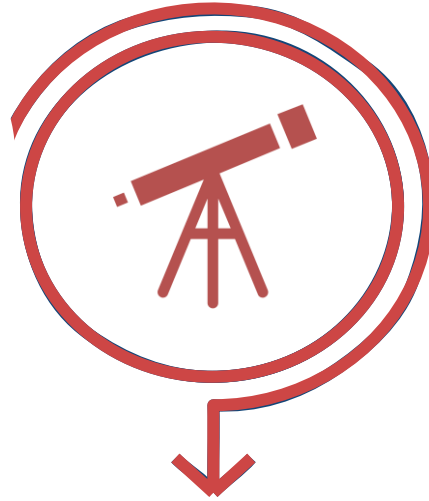
Together, these four pillars transform SEND from a submission-focused standard into a data-centric framework.

1. Domain Modernization



Objective

- ✓ Standardize emerging nonclinical **endpoints** with dedicated domains.



Key Enhancements

- ✓ New domains for Nervous System, Skin, Ophthalmology, GV Immunogenicity, Cell Phenotyping, PK Input, and Scoring Scales
- ✓ Reduces reliance on custom domains



Impact

- ✓ Better standardization
- ✓ Enhanced data interoperability

Domain Specification updates

Old Structure

Laboratory Test Results – LB

lb.xpt, Laboratory Test Results - Findings Domain. Multiple records per subject, Tabulation.

New Structure

Attribute	Value
File Name	lb
Label	Laboratory Test Results
Class	Findings
Definition	A findings domain containing laboratory test results collected during the study.
Structure	One record per laboratory test result per visit/time point.
Purpose	Tabulation

Metadata Structure Mapping: Old vs New

Old Structure

Variable Name	Variable Label	Type	Controlled Terms, Codelist, or Format	Role	CDISC Notes	Core
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New Structure

												
Variable Name	Variable Label	Type	Codelist	Allowed Controlled Terms	Format	Role	Variable Group	Root Variable C-code	Root Variable Definition	Notes	Examples	Core
Name of the variable.	Descriptive label for the variable.	Data type of the variable.	Reference codelist associated with the variable.	Permissible values from the codelist.	Format or pattern of the data.	Role of the variable in the dataset.	Grouping of related variables.	SDTM C-code of the root variable.	Definition of the root variable.	Additional notes about the variable.	Examples of the variable.	Indicates if the variable is core.

New from SDTM

2. Variable Harmonization



Objective

- ✓ Create a **more consistent** and intuitive metadata model



Key Enhancements

- ✓ **Harmonized** variable across domains
- ✓ Improved controlled terminology alignment
- ✓ Reduced ambiguity in variable usage



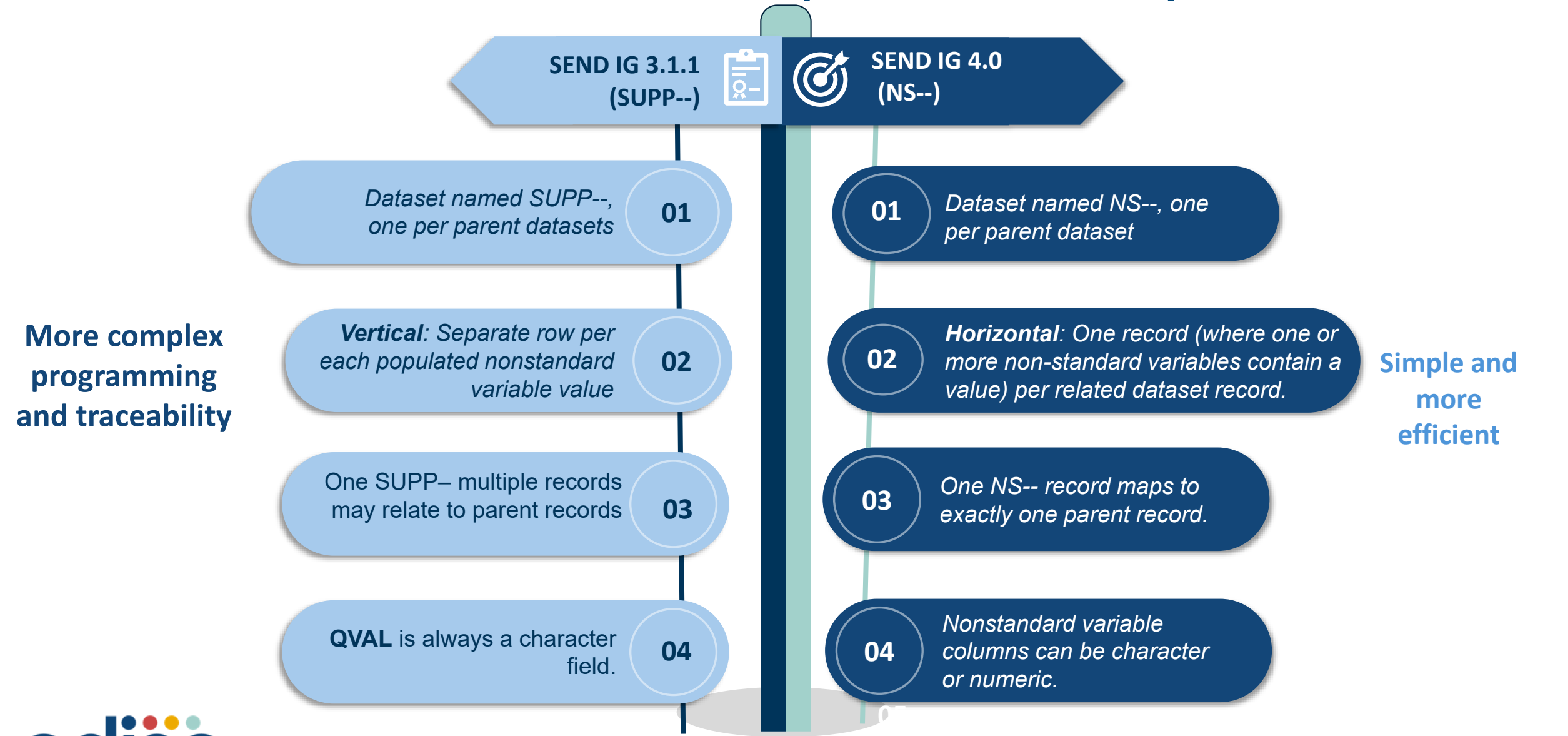
Impact

- ✓ Easier programming
- ✓ Simplified validation
- ✓ Improved Cross domain consistency

New, Removed and Updated Variables

<u>Area</u>	<u>Summary</u>
Baseline Handling	Legacy baseline flags (e.g., BWBLFL, CVBLFL, EGBLFL, LBBFLFL..) removed and replaced by Last Observation Before Exposure concepts (LOBXFL variables).
Element Tracking	New ELEMENT and ETCD variables added across finding domains to support Trial Elements.
Timing Variables	VISITDY-Planned study day of collection removed from several domains; new interval and repetition-related variables (--REPNUM) introduced.
Controlled Terminology	Multiple codelists updated (SPOSIT, PKUNIT extensions, SPMETHOD, SEGTST, SEGTSTCD, etc.).

3. Structural Modernization (NS Domains)



LB Example: Comparing SUPPLB to NSLB

lb.xpt

Convert LBSEQ from numeric to character

Row	STUDYID	DOMAIN	USUBJID	LBSEQ	LBTEST	LBORRES	LB DTC
1	1996001	LB	99-401	1	ALT	35	2023-01-05
2	1996001	LB	99-567	1	AST	42	2023-09-25

supplb.xpt

Transpose

Row	STUDYID	RDOMAIN	USUBJID	IDVAR	IDVARVAL	QNAM	QLABEL	QVAL	QORIG	QEVAL
1	1996001	LB	99-401	LBSEQ	1	LBFAST	Fasting Sample	Y	CRF	
2	1996001	LB	99-401	LBSEQ	1	LBREPT	Repeat Sample	N	Derived	
3	1996001	LB	99-567	LBSEQ	1	LBREPT	Repeat Sample	Y	Derived	

nslb.xpt

Row	STUDYID	DOMAIN	USUBJID	IDVAR	IDVARVALN	LBFAST	LBREPT
1	1996001	LB	99-401	LBSEQ	1	Y	N
2	1996001	LB	99-567	LBSEQ	1		Y

NSLB metadata

Variable	Label	Type	Codelist	Role	Origin Type	Origin Source
LBFAST	Fasting Sample	Char	(NY)	Non-Standard Qualifier	Collected	Investigator
LBREPT	Repeat Sample	Char	(NY)	Non-Standard Qualifier	Derived	Sponsor

4. Better Study Interpretation & Regulatory Readiness



Objective

- ✓ **Improve** study design and **support** modern regulatory review



Impact

- ✓ Faster submission preparation
- ✓ AI- and automation-ready datasets
- ✓ Better subject **traceability**



Key Enhancements

- ✓ Improved metadata consistency
- ✓ Better Define-XML integration
- ✓ Enhanced machine readability
- ✓ Reduced ambiguity in baseline identification

Refined Baseline Handling

Supports multi-period, crossover and repeat dose baseline logic.

Remove --BLFL

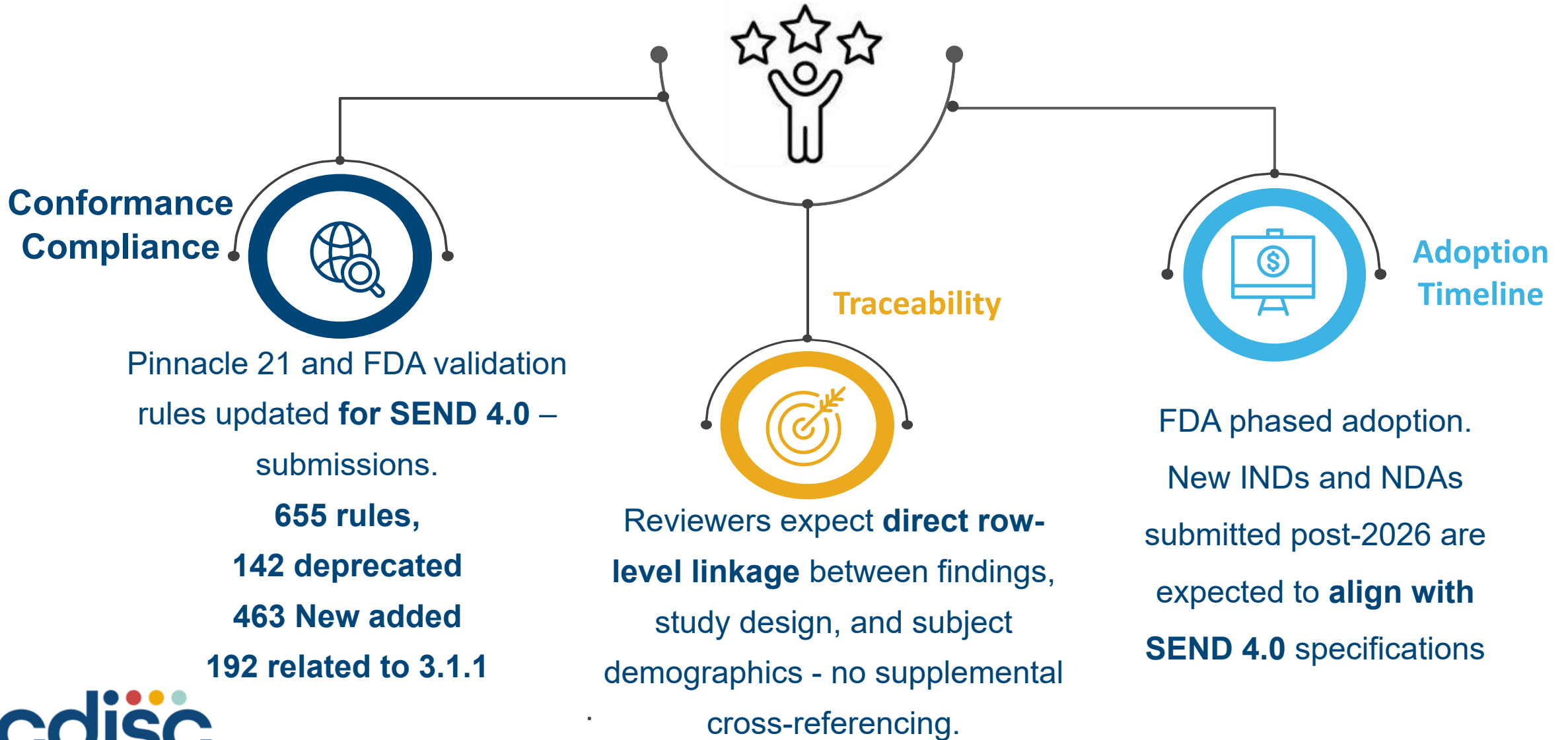
In SEND 3.1.1, baseline identification was not standardized, resulting in inconsistent implementation across studies using VISIT flags, date logic, or comments.

Refined Baseline

Introduction of --LOBXFL

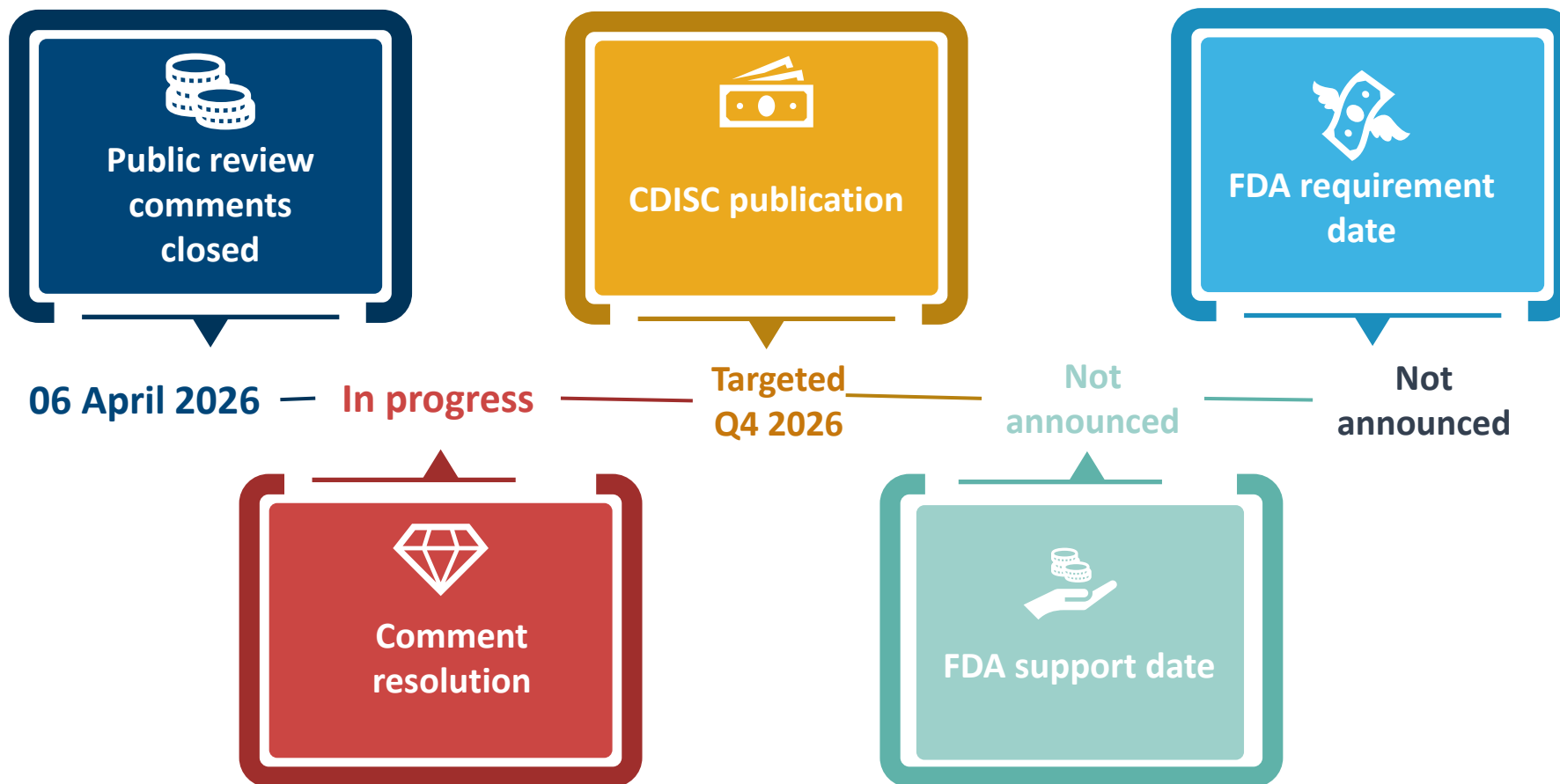
In SEND 4.0, --LOBXFL standardizes baseline identification by flagging the last non-missing assessment before first treatment exposure.

What Regulators Expect in 2026



Progress and Milestones

Where things actually stand



From Compliance to Innovation



Practical Considerations

- **Scan:** Spot SEND 3.1.1 to NS--dataset gaps early.
- **Code:** Update programming, validation, and Define-XML processes
- **Sync:** Connect Data Management, Biostatistics, and Regulatory teams
- **Evolve:** Turn migration tasks into a modernization win.



Strategic Outcome

- **Speed:** Faster, automated regulatory reviews.
- **Clarity:** Seamless traceability across all domains.
- **Precision:** Enhanced mapping and Machine-readable Dataset
- **Value:** Compliance shifts from a cost to an asset.



“A well-structured SEND 4.0 dataset to be easily interpreted, connected, validated and reducing reviewed effort”

Thank You!

