

Standardization of Auxiliary Medicinal Products (AxMPs) in Clinical Trials

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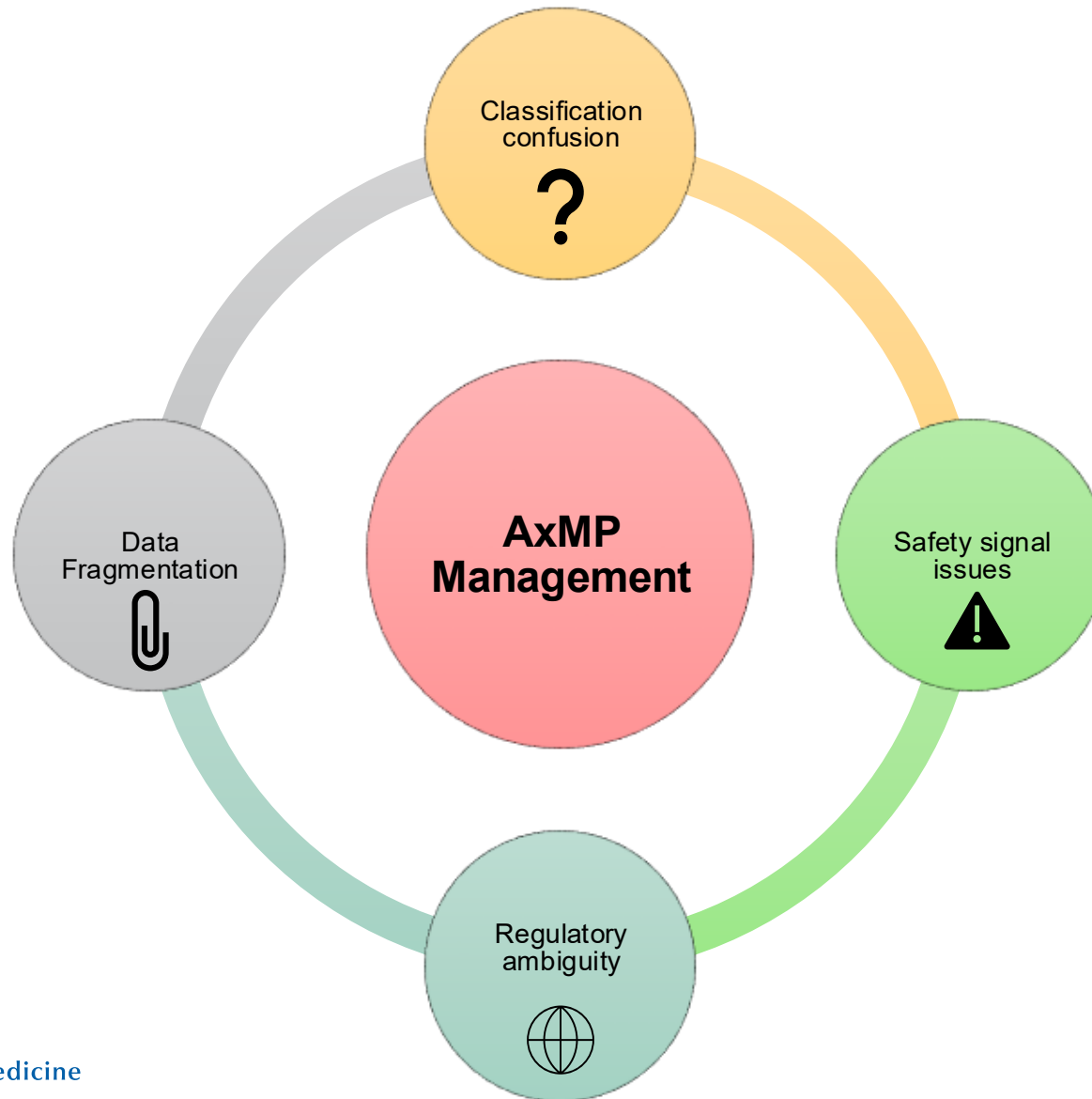
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Event: PhUSE (APAC)

Agenda

1. Title & Context
2. Problem Statement & Motivation
3. AxMP: Definitions & Types
4. AxMPs vs IMPs vs Concomitant Medications
5. EUCTR Perspective & Regulatory Expectations
6. Conventional vs Standardized AxMP Data Collection
7. Strategic Response: Novartis E2E AxMP Framework
8. Methodology: Building the Framework
9. CDISC-Compliant AxMP CRFs & Metadata
10. Analysis & Reporting
11. Benefits & Measured Outcomes
12. Conclusion, Future Direction

Problem Statement & Motivation



AxMP: Definition & Types

Auxiliary medicinal product means a medicinal product used for the needs of a clinical trial as described in the protocol, but **not** as an investigational medicinal product (EU CTR, Art. 2, No. 8) but to

- Support the application of IMP(s)
- Maintain trial integrity



AxMPs vs IMPs vs Concomitant Medications

IMP (Investigational product)	AxMP (Auxiliary Medicinal Product)	Concomitant Medications
• Primary object of Investigation • Defined in protocol • Primary focus is safety evaluation • Included in EUCTR dossier • Well established CDISC standards	• Supports trial conduct, safety. • Defined in protocol • Crucial to AE causality & analysis • Included in EUCTR dossier • Historically inconsistent, now being standardized	• Subject's routine or incidental medications • Not controlled by protocol • Contextual • Generally, not (unless safety critical in protocol) • Well established CDISC standards

EUCTR Perspective & Regulatory Expectations

Why AxMPs Matter for Safety Evaluation?

EUCTR positions AxMPs as regulatorily visible:

- Must be defined and justified in the protocol
- Require appropriate quality and safety oversight

Safety evaluation perspective:

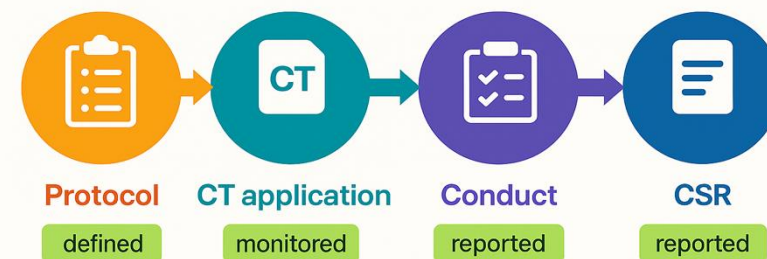
AxMPs can:

- Modify efficacy outcomes (e.g., background standard of care)
- Create or mask safety signals (drug-drug interactions)
- Affect causality assessments for AEs/SAEs if not clearly captured

Regulators expect:

- **Traceability of AxMP exposure** to subject-level events
- Clear distinction from IMP and ConMeds in safety reports and CSRs

EUCTR emphasizes consistency, transparency, and traceable documentation of all medicinal products impacting trial conduct.



Conventional Way

- ❖ **AxMPs buried in ConMed CRFs**
- ❖ **Protocol not explicit on AxMP definitions**
- ❖ **No dedicated AxMP indicators or metadata**
- ❖ **Limited ability to trace AxMPs to AEs and endpoints**
- ❖ **Limited, non-standard TFLs, often post-hoc.**

Strategic Response: End-to-End AxMP Framework

- ❖ Development of an end-to-end (E2E) framework
- ❖ Cross-functional, phased approach

Objective: A structured, end-to-end framework for AxMPs, covering:

- Early identification & classification (protocol stage)
- Standardized CRFs & metadata (CDISC aligned)
- Controlled data collection in EDC
- Clear SDTM/ADaM mapping
- Statistical analysis planning
- Integrated reporting in TFLs & CSRs

Contd...

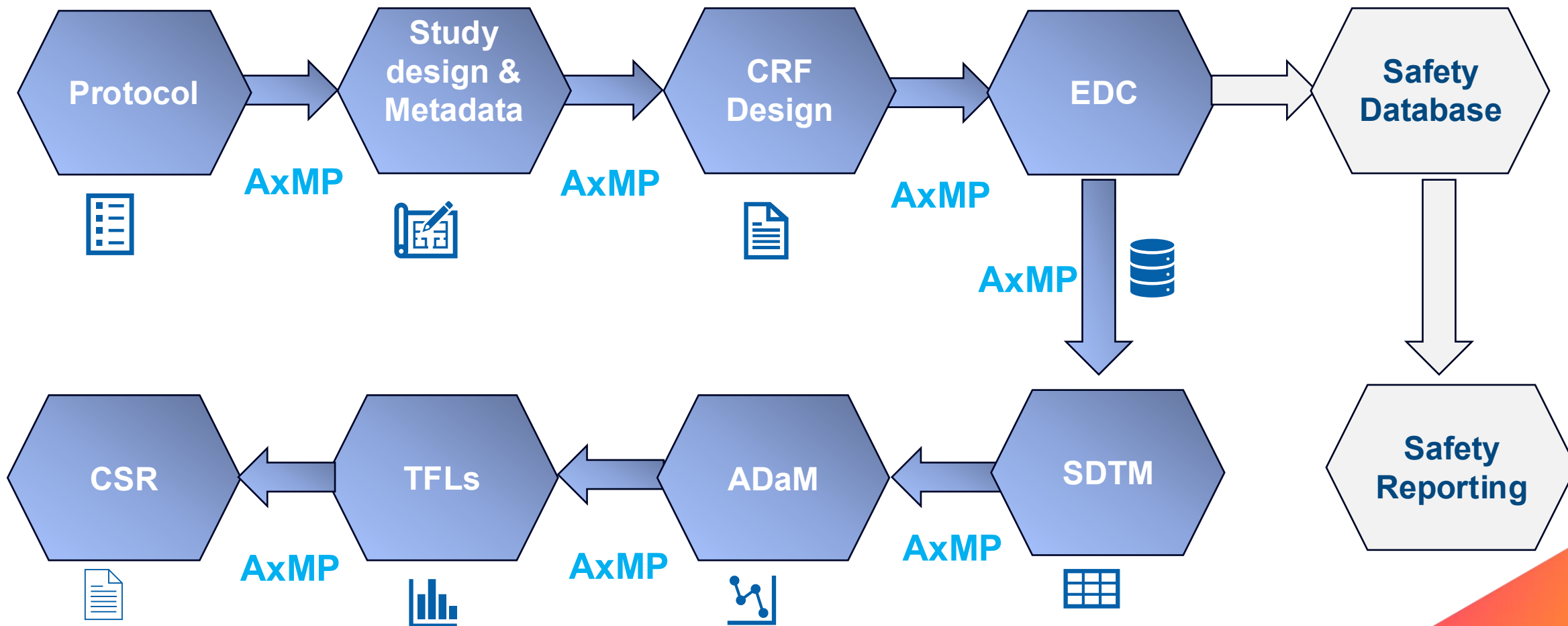
❖ Cross-functional participation

- ✓ Clinical Data Standards
- ✓ Clinical Development
- ✓ Pharmacovigilance / Safety
- ✓ Biostatistics & Programming
- ✓ Regulatory Affairs
- ✓ Clinical Operations

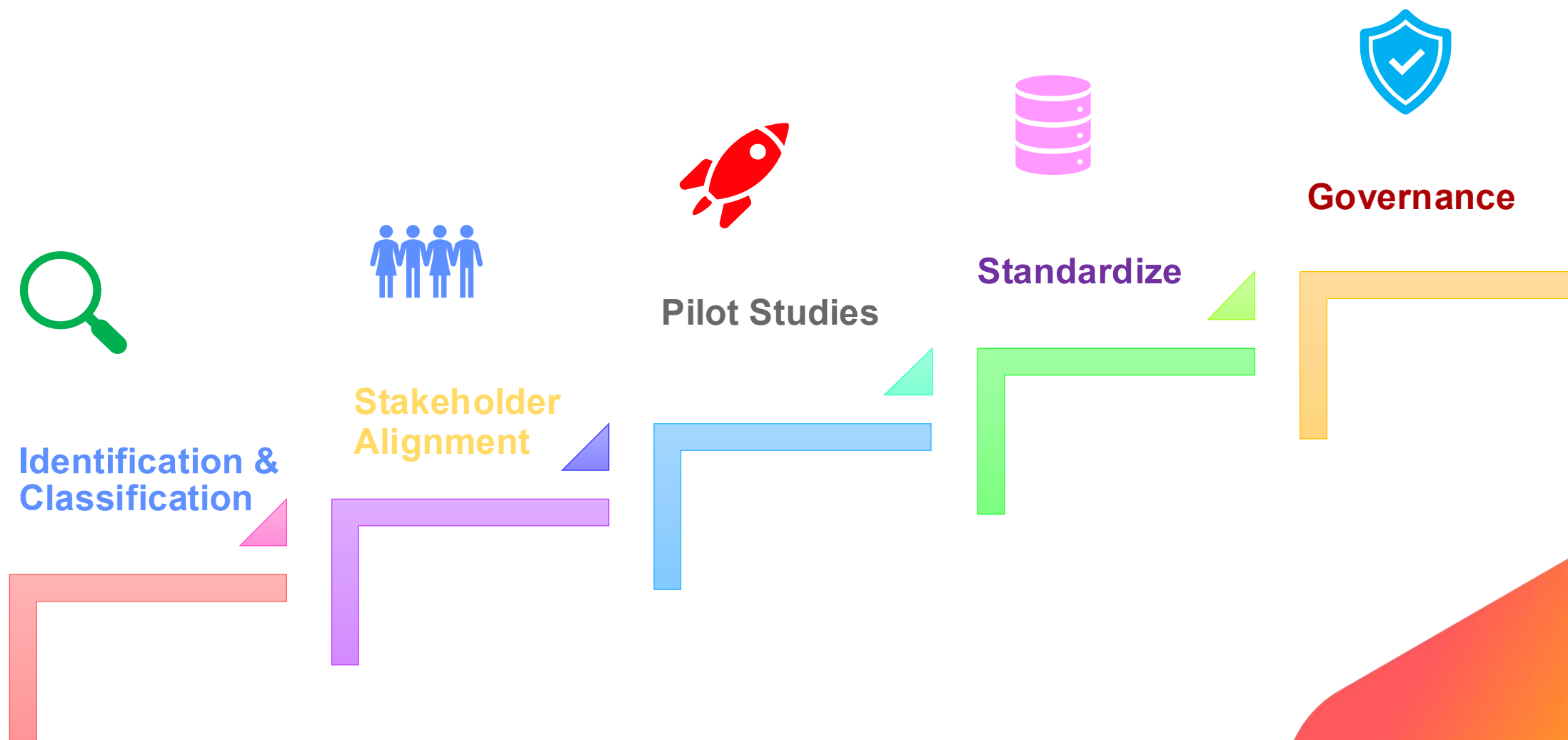
Cross-functional participation



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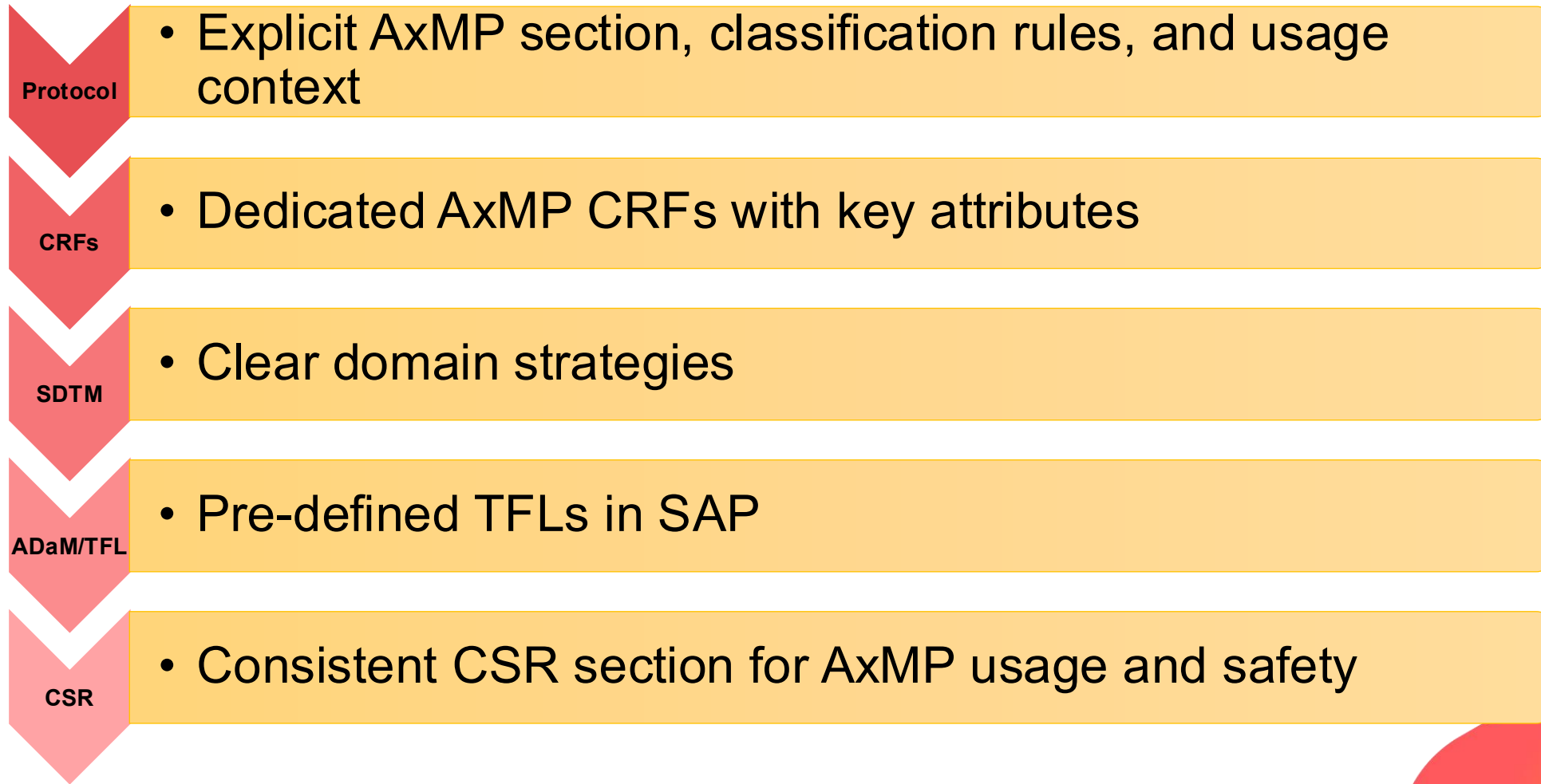


Methodology: Building the Framework

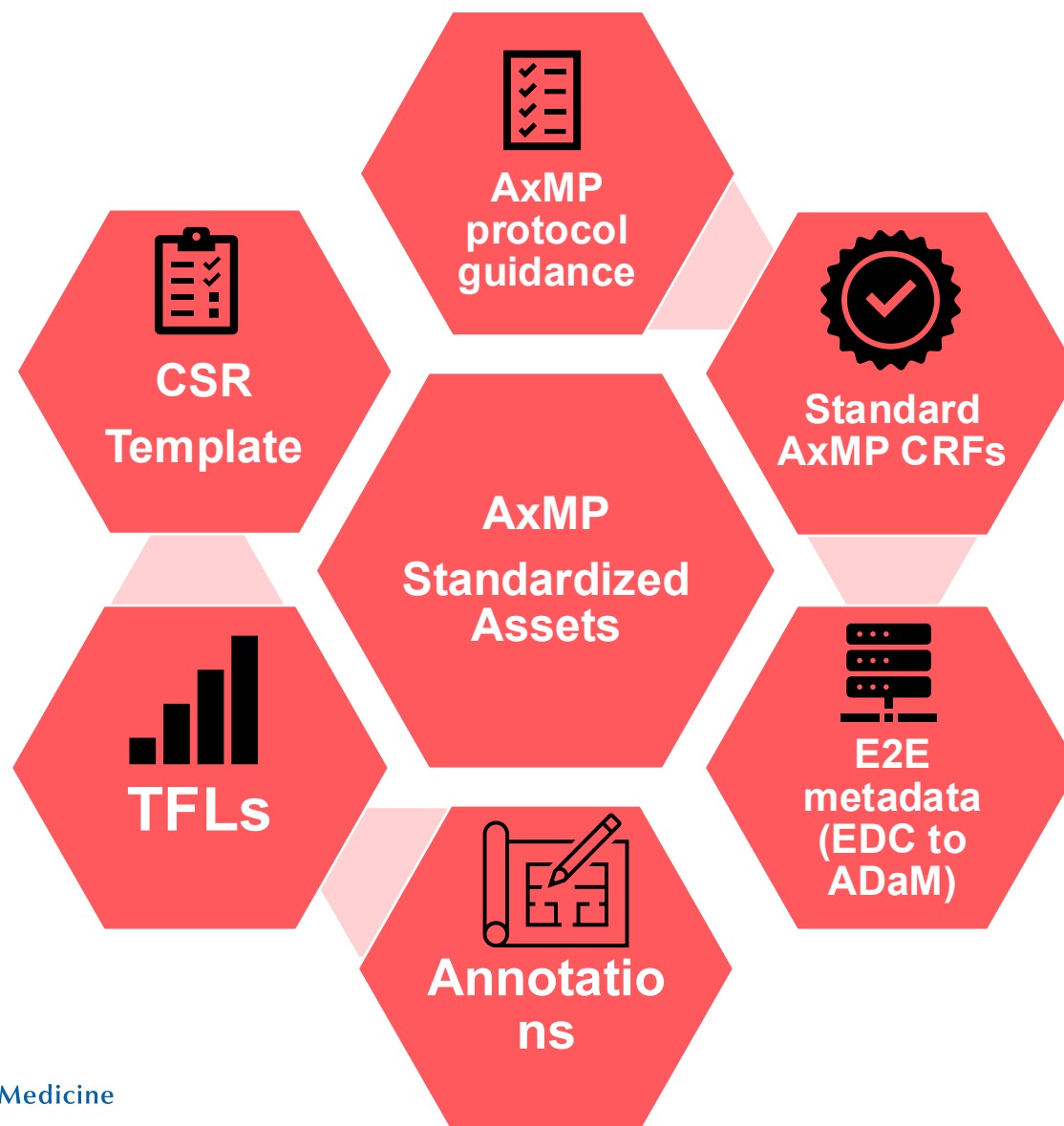


Standardized AxMP Data Collection

Novartis Approach: Protocol to TFL alignment:



Assets Released



CDISC-Compliant AxMP CRFs & Metadata

Design principles

- Reuse core CDISC concepts where possible. OR Align with CDISC concepts (e.g., EX, CM) while maintaining AxMP specificity.
- Maintain clear separation from IMP and ConMed CRFs. OR Minimize duplication; reuse core ConMed fields where appropriate.
- Enable straightforward mapping to SDTM (e.g., EX, CM, SUPP domains with AxMP indicators).

Key data elements

- Product name, formulation, route, regimen.
- AxMP role (background / challenge / rescue / supportive).
- Start/stop dates and relationship to dosing of IMP.
- Reason for use (linked to protocol-defined procedures)

Metadata-driven implementation

- AxMP CRFs defined as reusable metadata objects in the EDC library.
- Controlled terminology and code lists for AxMP roles and types.
- Central governance for changes and version control.

Analysis & Reporting Framework

PV



- Regulatory reporting (SUSAR/PSUR/ASR etc.)
- Risk Monitoring
- Signal/Pattern detection

CSR



- Table/Listing : AEs/SAEs related to AxMPs
- Summary of AxMPs
- Sponsor defined TFLs

Exploratory Analysis



- Drug-Drug interaction
- Other

Benefits of the Standardized Approach



**Improved
protocol design**



**Enhanced safety
surveillance**



**Operational
efficiency**



**High-quality
Data capture**



**Regulatory
readiness**

Roadmap for AxMP Standardization

Today



**Internal
framework**

Novartis-developed
E2E AxMP Framework for
trial integrity and subject safety

Near-term



**Broader
adoption**

Expand implementation
across studies
And functions

Future



**Industry-wide
standards**

Collaborate with
industry and regulatory bodies
For future alignment

THANK YOU



Questions?