



CDISC India Day

Global Regulatory Landscape for Clinical Data Submissions: FDA, PMDA, EMA, and NMPA Perspectives on AI-Enabled Submission Readiness

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Speaker



Shirisha is currently working as Manager II, Biostatistics and Programming at Efficacy Lifesciences, with over 12 years of end-to-end clinical research experience. Her expertise includes SDTM programming, regulatory study submissions, ADaM and TFL programming, and macro automation. She also brings strong domain knowledge across multiple therapeutic areas, including Oncology, Ophthalmology, Gynaecology, and Pediatric studies.

She holds a postgraduate degree in Bioinformatics from Sri Venkateswara University. Before joining Efficacy Lifesciences, she worked with leading global Contract Research Organizations (CROs), including ICON, Syneos Health, and Covance. These roles provided extensive experience in clinical data standards, regulatory submissions, and statistical programming across diverse therapeutic areas and global clinical studies.



Agenda

- Introduction & Why Submission Readiness
- Regulatory Comparison: FDA, PMDA, EMA & NMPA
- Challenges & AI Applications
- Future LLMs & Key Takeaways



Why Global Submission Readiness Matters

- Supports Global Regulatory Approvals
- Accelerates Review Timelines
- Enhances Compliance
- Strengthens Traceability
- Improves Submission Quality
- Reduces Operational Costs

“One Clinical Trial. Multiple Regulators. One Goal — Submission Readiness.”

Why Global Submission Readiness Matters

The Challenge – Global Clinical trials often support submissions to multiple regulatory agencies

Agency Expectation

- CDISC compliant SDTM
- ADaM Datasets
- Define.xml
- Reviewers Guide
- High Quality Metadata & Traceable Analysis

One Global Submission Package
CDISC Compliant – Standardized – Traceable – Well Documented



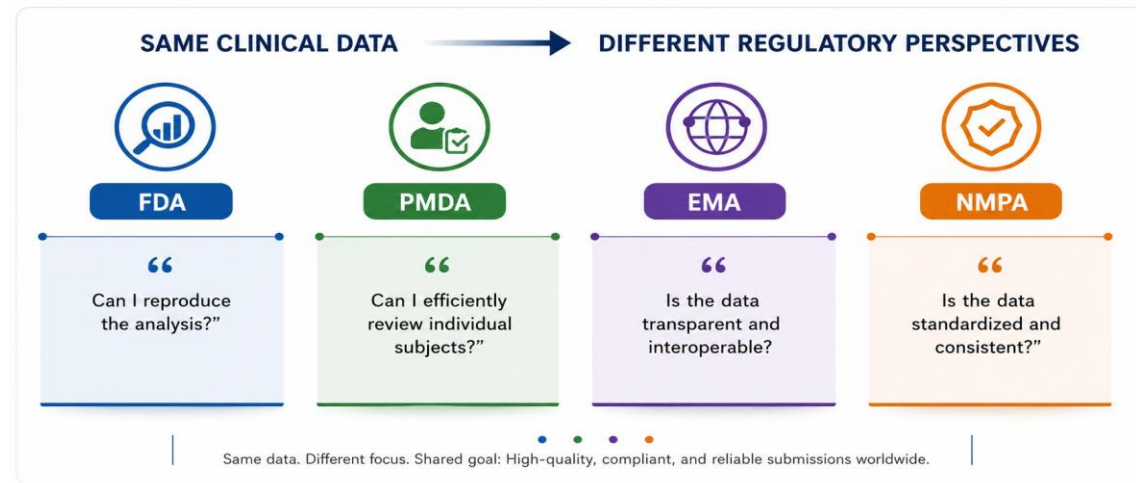
Key Question: How can organizations prepare ONE submission package that satisfies MULTIPLE Global regulators ????



Answer: Strong Standards, governance, high quality metadata, consistent implementation and AI enabled submission

Global regulatory Landscape

Agency	Primary Focus	Review Priority
FDA – US Food and Drug Administration	Reproducibility	Traceability and Analysis
PMDA – Pharmaceuticals and Medical Devices Agency	Subject Review	Metadata & Reviewer Navigation
EMA – European Medicines Agency	Transparency	Interoperability and Data Sharing
NMPA – National Medical Products Administration	Data Quality	Consistency & Standardization



Reference:

1. FDA. *Providing Regulatory Submissions in Electronic Format — Standardized Study Data, Final Guidance*, June 2021.
2. PMDA. *Notification on Practical Operations of Electronic Study Data Submissions*, January 2019.
3. EMA. *External guidance on the implementation of EMA policy on the publication of clinical data for medicinal products for human use, Version 1.5, 2025*.
4. NMPA. *Requirements for the Management of Drug Records and Data (Interim)*, 2020.

FDA Perspective – Submission Expectations

FDA Submission Expectations

- **Analysis reproducibility**
Results can be understood and reproduced.
- **End-to-end traceability**
Results can be traced back to source data.
- **Dataset consistency**
SDTM, ADaM and metadata remain aligned.
- **Define-XML accuracy**
Metadata accurately describes the submission.
- **Reviewer efficiency**
Information is easy to navigate and review.

What the FDA Reviewer Needs to Follow



Key principle: A reported result should be traceable back to the underlying patient-level data.

Common FDA Submission Issues

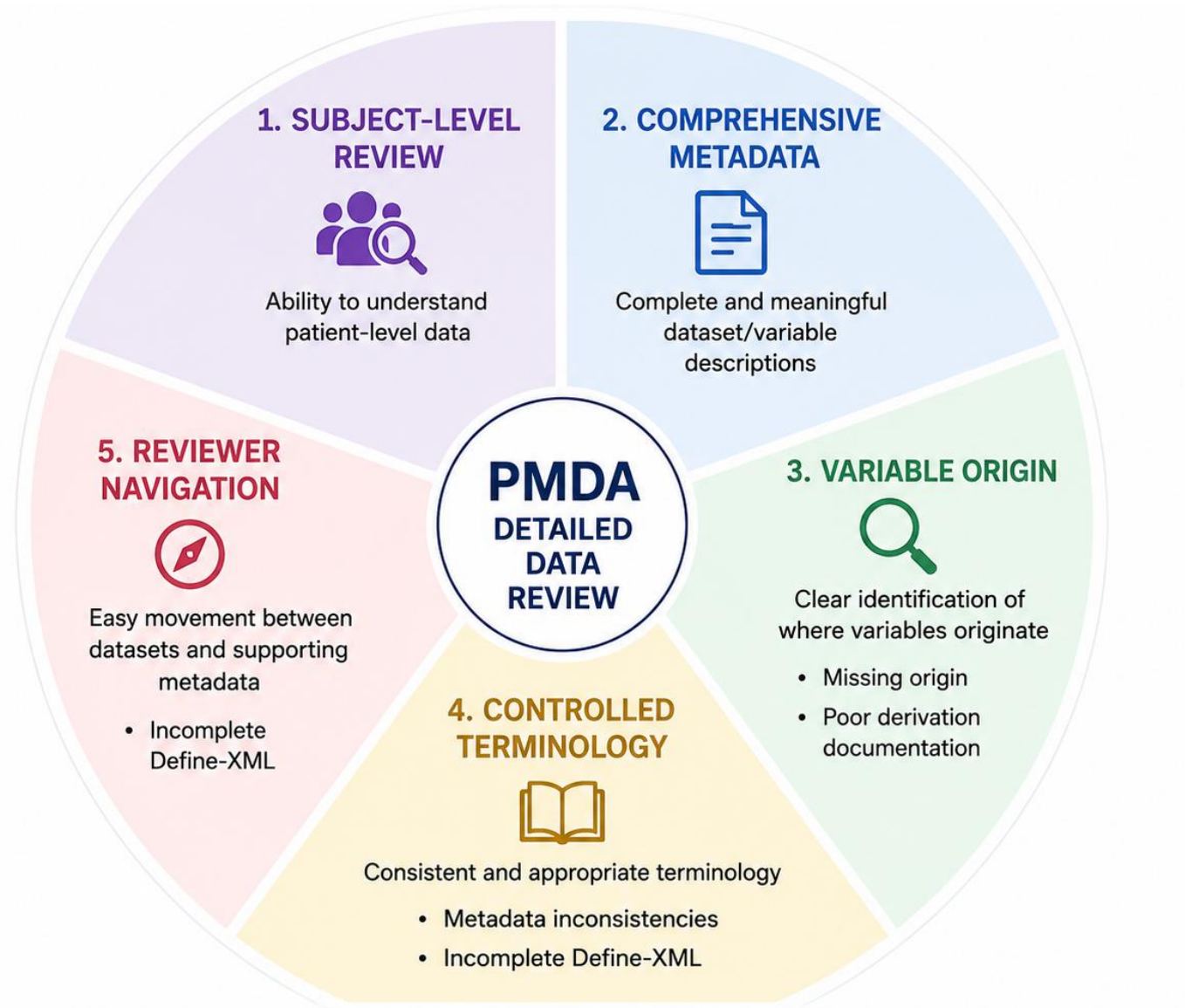
Missing traceability

PARAM / PARAMCD mismatch

Define-XML metadata issues

Reviewer Efficiency

PMDA Perspective



EMA and NMPA Perspective

EMA Focus	NMPA Focus
Transparency	Data Integrity
Fair data principles	Standardization
Interoperability	Data Set Consistency
Future data reuse	Validation Compliance
EMA Expectation	NMPA Observation
Machine readable meta data	Inconsistent controlled terminology
Consistent standards	Missing Metadata
High Quality documentation	Validation failures
	Dataset Discrepancies

Reference:

1. *European Medicines Agency (EMA). European Medicines Agencies Network Data Strategy – Increasing the value of data for the benefit of public and animal health. 2025.*
2. *European Medicines Agency (EMA). Policy 0070: European Medicines Agency policy on publication of clinical data for medicinal products for human use.*
3. *National Medical Products Administration (NMPA). Requirements for Registration Classification and Application Dossiers of Chemical Drugs. 2020.*
4. *NMPA. Drug Administration Law of the People's Republic of China.*

Common submission Challenges

Category	Challenge	Typical Issues	Impact
Metadata Quality	Metadata Inconsistencies	Dataset metadata differs from Define.xml	Reviewer confusion and clarification requests
Metadata Quality	Define.xml Issues	Missing value-level metadata, incorrect origins, incomplete links	Reduced reviewer efficiency
Traceability	Variable Origin Problems	Undocumented or incorrect derivation sources	Traceability concerns
Traceability	Traceability Gaps	Broken links between SDTM, ADaM, and TFLs	Difficulty reproducing analyses
Standards Compliance	Controlled Terminology Mismatch	Non-standard codelist, inconsistent terminology	Validation findings
Standards Compliance	P21 Validation Findings	Errors, warnings, compliance issues	Submission readiness risks
Data Consistency	Cross-Dataset Inconsistencies	Differing subject counts or treatment assignments	Review delays and data quality questions
Operational Efficiency	Manual QC Dependence	Spreadsheet-based reviews and repetitive checks	Higher effort and human error risk

AI Enabled Submission Readiness

Traditional Approach	AI-Assisted Approach
Manual metadata reviews	Automated metadata validation
Spreadsheet-based reconciliations	Continuous consistency checks
Time-consuming traceability review	Automated lineage verification
Reactive issue identification	Early risk detection
Resource-intensive QC cycles	Targeted review of high-risk areas
Submission readiness assessed late	Continuous readiness monitoring

AI Application across Submission lifecycle

Metadata Intelligence

- ✓ Validate metadata completeness
- ✓ Identify discrepancies between datasets and Define.xml
- ✓ Detect missing variable attributes and documentation
- ✓ Verify value-level metadata consistency

Documentation Quality Review

- ✓ Review Define.xml completeness
- ✓ Assess Reviewer Guide quality
- ✓ Detect missing explanations and justifications
- ✓ Identify incomplete submission documentation

Traceability Assessment

- ✓ Verify SDTM → ADaM lineage
- ✓ Detect missing derivation documentation
- ✓ Identify broken traceability links
- ✓ Confirm consistency between analysis outputs and source datasets

Standards and compliance review

- ✓ Validate Controlled Terminology usage
- ✓ Detect non-standard variable implementations
- ✓ Identify CDISC compliance risks
- ✓ Prioritize P21 validation findings by impact

Future: Domain-Specific Regulatory LLMs

General AI understands language — not always SDTM, ADaM, Define.xml, controlled terminology, or agency-specific expectations.

Where general models fall short

- SDTM and ADaM standards
- Define.xml structure
- Controlled terminology
- FDA / PMDA / EMA / NMPA expectations
- Submission-specific QC rules
- Internal SOPs and processes

Built by training / configuring the LLM with

1

Regulatory Knowledge

FDA, PMDA, EMA, NMPA expectations and submission requirements

2

Clinical Data Standards

SDTM, ADaM, Define.xml structure, controlled terminology

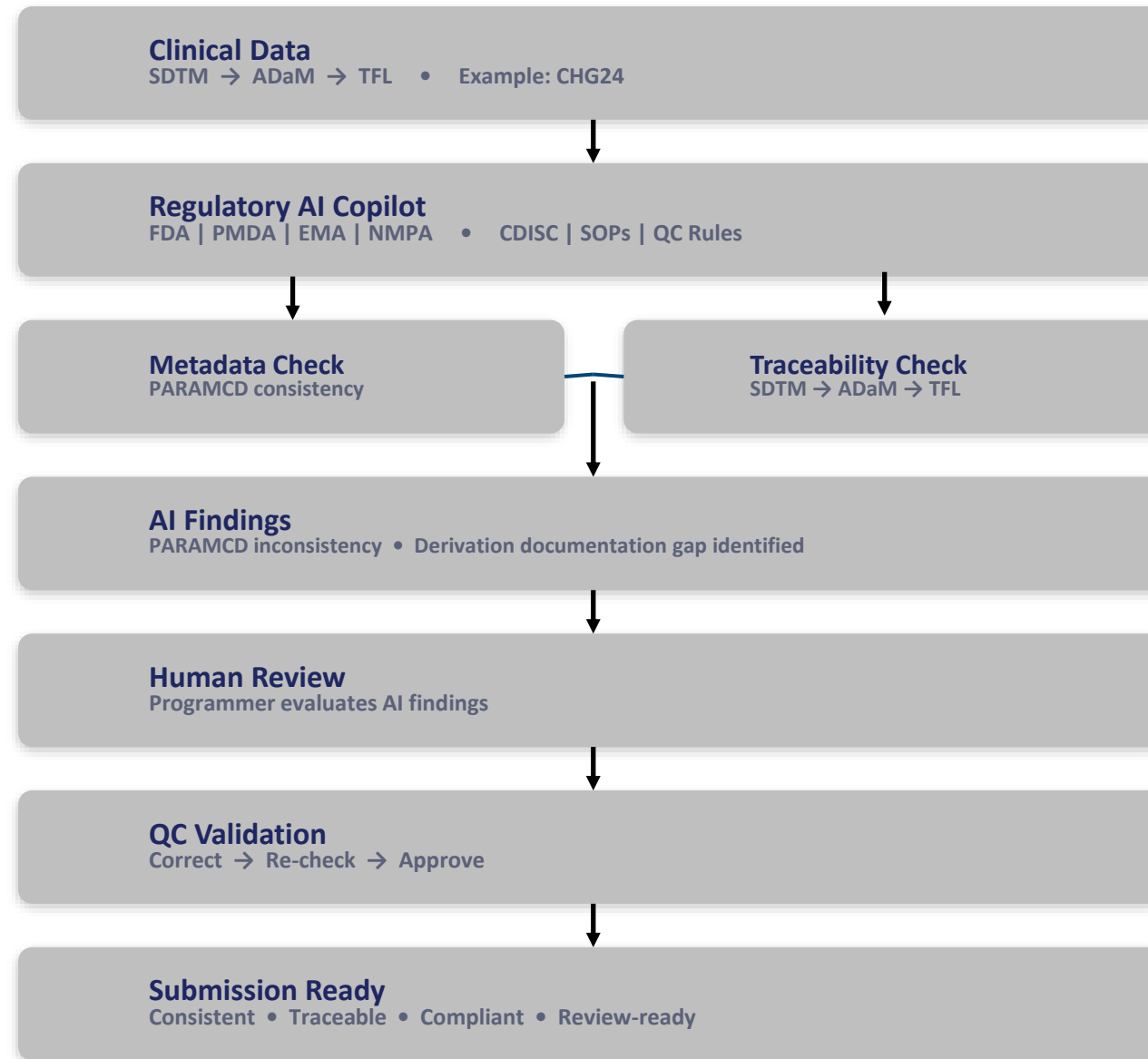
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Organization-Specific Knowledge

Internal SOPs, QC rules, and submission-specific processes

Domain-Specific Regulatory LLM: Example Flow

Example: AI Review of an ADaM Efficacy Endpoint



Key Takeaways

Submission Readiness is More Than CDISC Compliance

Success requires

- High-quality metadata
- Complete traceability
- Consistent standards implementation
- Regulatory-specific preparation
- Strong governance
- AI-assisted quality review

Standardization + Metadata + Traceability + AI = Smarter, Faster, Higher-Quality Global Regulatory Submissions



AI does not replace Statistical Programmers. AI augments submission quality by proactively identifying risks, inconsistencies, and compliance gaps before regulatory submission.





Questions?





Thank you

