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2026 Europe Interchange

THE FUTURE IS CONNECTED: STANDARDS AND AI POWERING DIGITAL TRANSFORMATION

Crosswalk to Compliance: Bridging FDA and PMDA eData Expectations

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Agenda

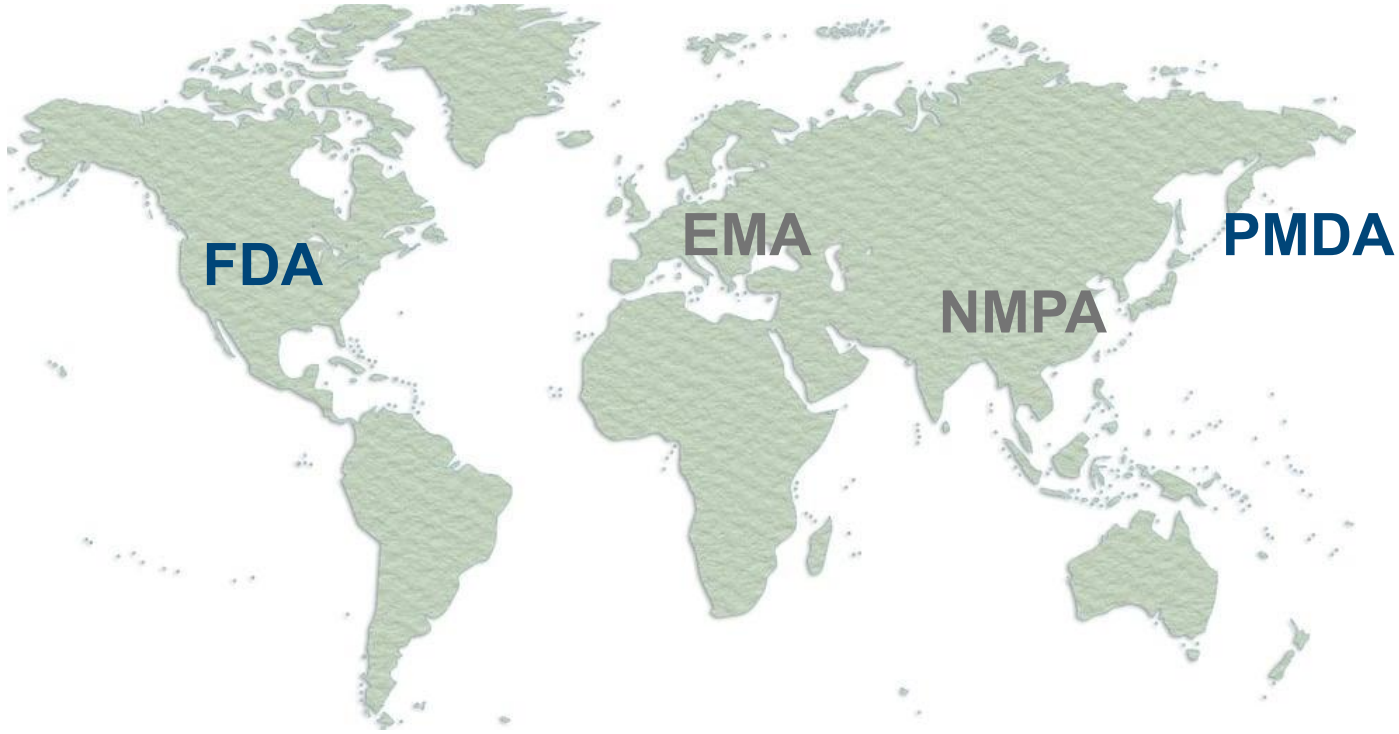
1. Setting the scene
2. The Project Case
3. From FDA-ready to PMDA-ready: The eData Package
4. Walls / Wins / Wisdoms

Setting the Scene

Global Submissions: Why It Matters

- More and more clinical programs follow global submission pathways (FDA, EMA, PMDA, NMPA).
- Submission packages are no longer “single-authority only”.
- Efficient reuse of validated deliverables is now a key strategic advantage.

- **But… reusability is not automatic: each authority interprets CDISC differently.**



FDA and PMDA:
Shared CDISC, Different Expectations

FDA

- FDA Validator
- Standard metadata structure
- ARM optional for many submissions
- Issue Management often sponsor-driven

PMDA

- PMDA Validator with Japan-specific rules
- Metadata must explicitly document derivations
- ARM required and expected to be more narrative
- Formal expectations for issue justification

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Regulatory Intelligence: The Missing Link

What Makes the Difference

- Understanding not just the guidelines, but how each Authority **interprets** them.
- Anticipating PMDA **expectations** before building the package.
- Using FDA **experience as a baseline**, not a template.
- **Supporting decisions** with evidence, rationale, and documentation

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The Project Case

Real Multi-Agency Submission Challenge

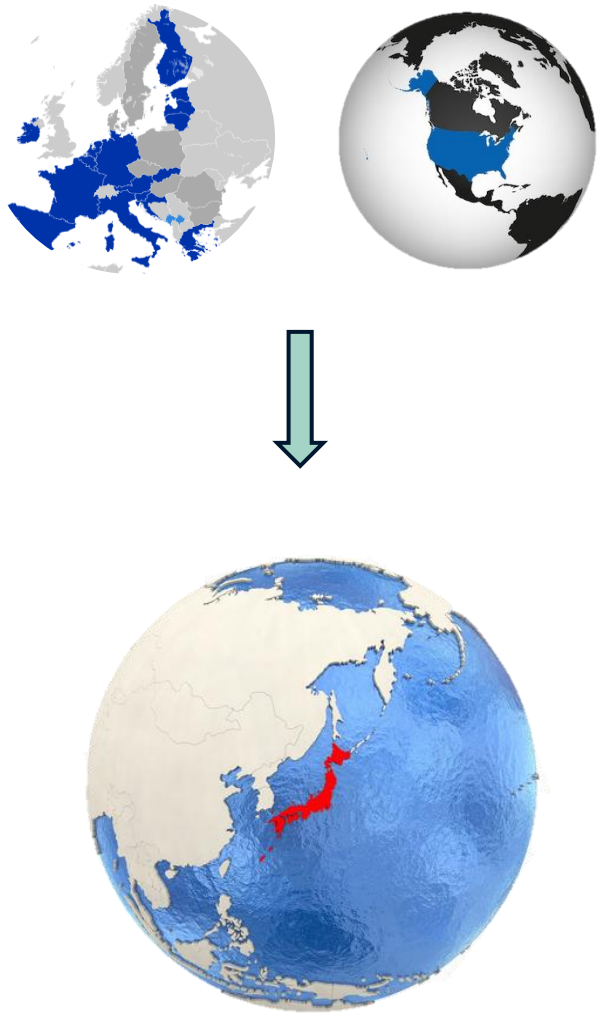
The **program** was **originally designed** for **FDA** and **EMA** submissions.

eData package prepared and finalized according to **FDA expectations**.

Later, the program entered a **Japanese** regulatory **pathway**.

This required adapting the existing FDA-ready package to PMDA requirements — **without rebuilding from scratch.**

*This triggered a **structured process** of **crosswalk, remediation**, and **governance**.*



Overview on Drug Development process

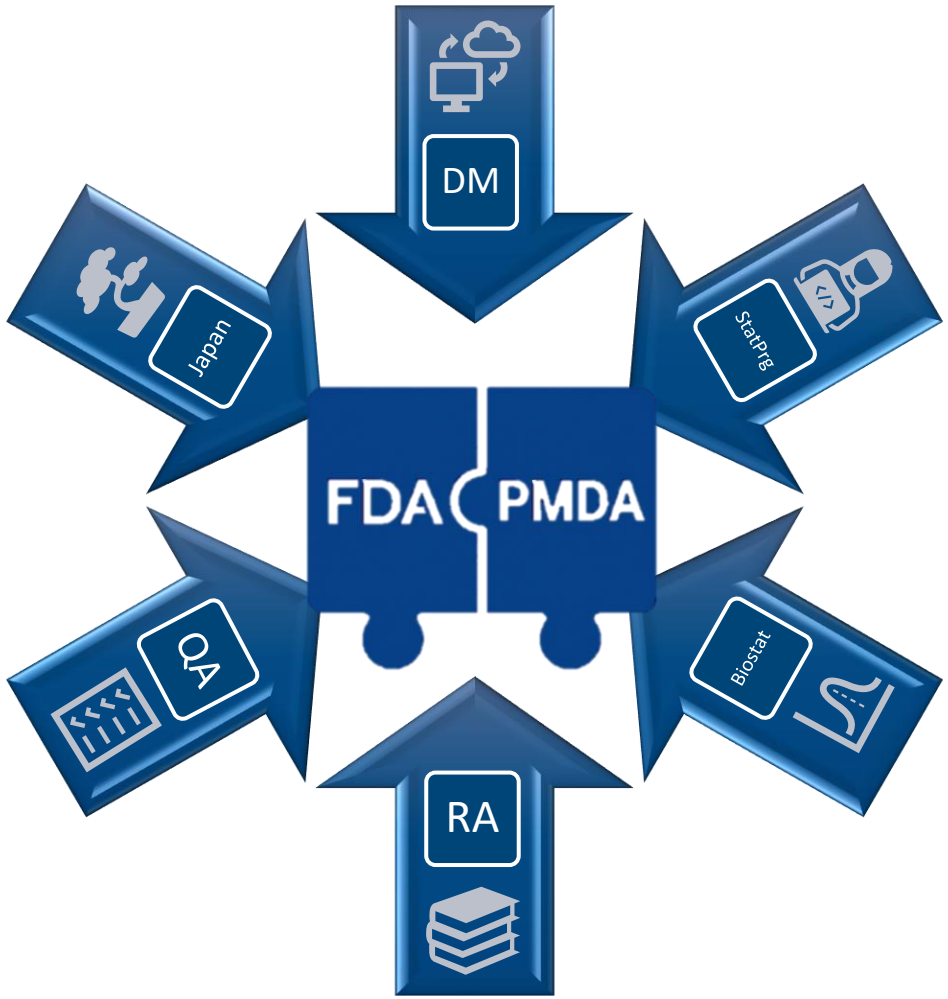
Integrated working model: Data Management, Statistical Programming, Biostatistics, Regulatory Affairs , QA, and Japan affiliates.

Clear ownership of each remediation stream (SDTM, ADaM, Define, ARM, Validator issues).

Decision log to track interpretation, rationale, and alignment across functions.

Focus on **maximizing reuse of FDA deliverables** while adapting only where PMDA required deeper documentation or different validation behavior.

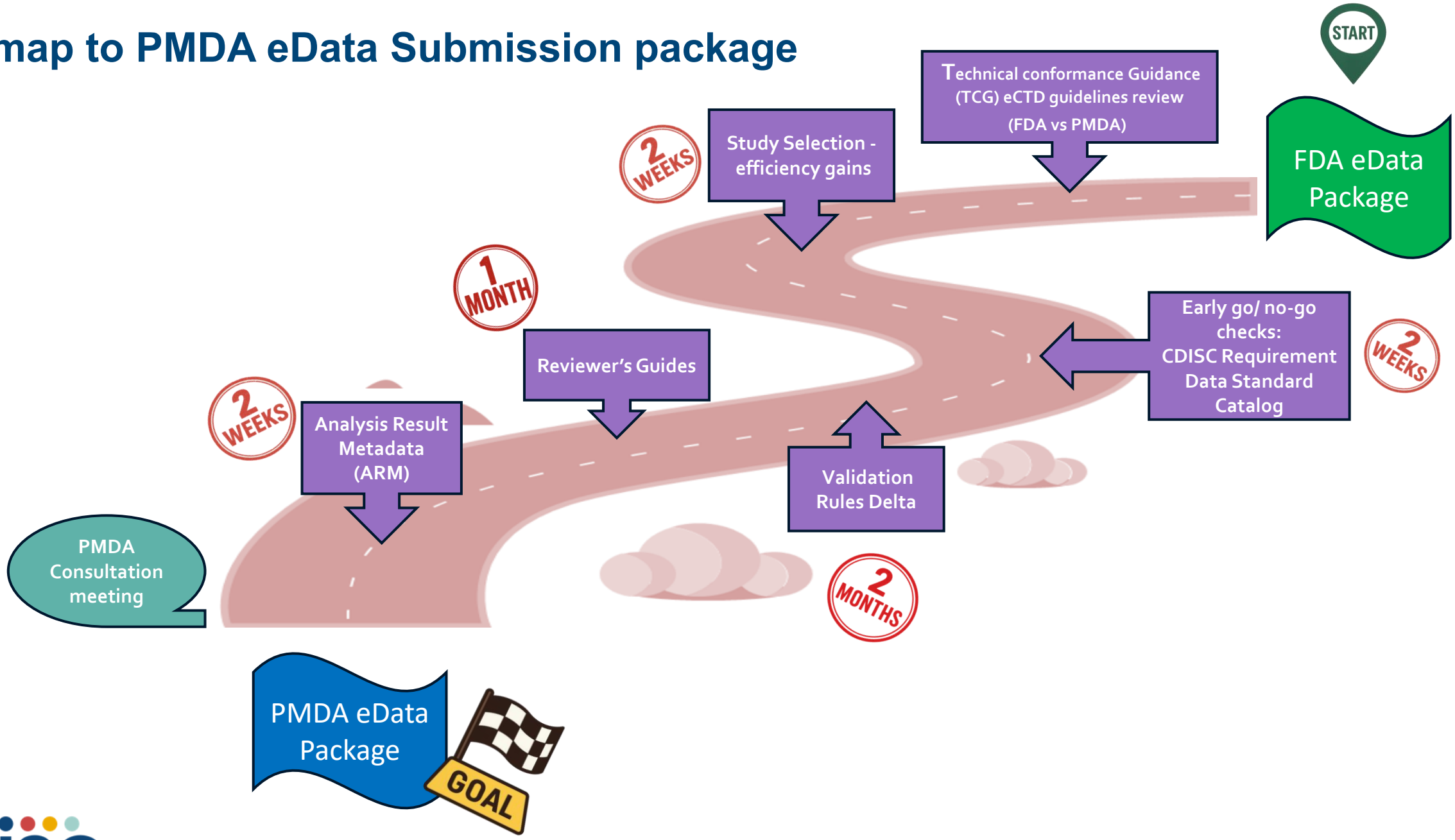
Continuous coordination ensured consistency, traceability, and reduced rework.



From FDA-ready to PMDA-ready: The eData Package

A streamlined approach to aligning eData package for FDA and PMDA requirements

Roadmap to PMDA eData Submission package



Estimation : time might change based on the number of studies included in the data package.

Key Elements of the eData Submission Package

DATABASES: SDTM and ADaM

XPT V5 or above

ANNOTATED CRF

aCRF.pdf

PROGRAMMING CODE

Readable and understandable
No external program calls;
Avoid nested macros, macro
document spec . can be included;
No update file extension as .txt

DATA DEFINITION FILES

including ARMs *

.xml or .pdf
**included in .xml or as separate PDF*

DATA REVIEWER'S GUIDE

.pdf as default format – no specific requirment

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Study Selection: efficiency gains

PMDA REQUIRES*

Data for efficacy/safety analyses relevant to JP review

Handle legacy/non-CDISC studies via narrative if conversion is not feasible

EXAMPLE

Ph2 and Ph3 studies / Pivotal efficacy and safety studies

Ph1 with Japanese and non-Japanese population

QT/QTc

Integrated analyses (ISS) in ADaM

Chiesi Strategy

FDA package = PMDA-required studies included
Grouping as:

- Evaluation Studies:
  - Substantial efficacy/safety evidence
  - Supported dose selection
  - Key PD info (e.g., cardiac effect)
- Reference Studies:
  - Supportive/non-critical studies

GOAL

Provide sufficient evidence

Keeping eData scope lean

Note: PMDA 's agreement at Clinical consultation

*Provisional Translation (as of April 2024) - https://www.pmda.go.jp/files/000267942.pdf

Early Go/No-Go Checks

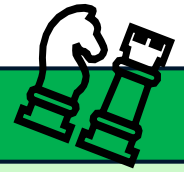
PMDA REQUIRES*

Submission date* = primary driver for validation rules and standards to be applied

Study start dates = determine if CDISC format is mandatory (after Oct, 2016).

*FDA primary driver for validation rules and standards to be applied = study start date

Chiesi Strategy



FDA study's standard vs **latest PMDA Data Standard Catalog**

Run Pinnacle 21 current **PMDA (Japan-specific) engine**

Identify **Reject** = **lead to a halt** if not explained/verified during consultation meeting

Review other findings type: figure out adjustments

EXAMPLE

Rule ID SD0002 NULL value in CMTRT variable marked as Required --> Reject

Data Issue = SF subject: explained and verified on consultation meeting (risk/applicability balance evaluation)

GOAL

Avoid high rework risk: not compromise reuse strategy

Prevent unacceptable packages and consultation surprises

*Provisional Translation (as of April 2024) - https://www.pmda.go.jp/files/000267942.pdf

Validation Rules Focus

Summary of Focus		
Feature	**FDA Validation Focus**	**PMDA Validation Focus**
Stringency	High; Focus on Data Interpretation	Very High; "Fail-fast" (Reject)
Key Priority	Data Analysis & Comprehensiveness	Strict Compliance & Consistency
Process	Interpretive/Flexible	Formalized/Structured

Chiesi Strategy

Run **both** agency-specific engines in P21 but **focusing first on PMDA JPN-specific**.

PMDA's validation engine can trigger "**Rejections**" or "**Errors**" despite data package passed FDA validation.

GOAL

Ensure compliance with both Healthy Authorities;

"Reject" level focus: avoid rework/compromise data package acceptability.

Validation Rules Delta

PMDA REQUIRES*

PMDA checks cross-layer consistency (SDTM↔ADaM↔define)

Strong checks on TS, demographics, and metadata completeness

Unresolved ERROR findings documented in RG

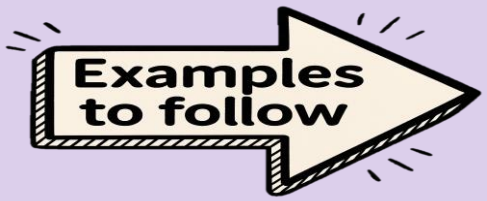
Chiesi Strategy

Pinnacle P21 PMDA JPN-specific engine:

- Reject/Error/Warning gaps with FDA's P21 engine
- Justification's Evaluation vs potential rework
- FDA justifications evaluation: consistent vs refine

2 MONTHS

EXAMPLE



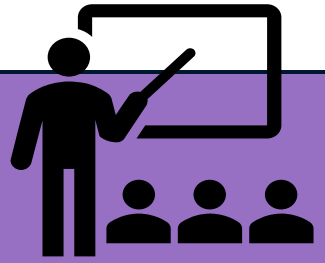
GOAL

Non-breaking adjustments (metadata, docs)
Avoid dataset rebuilds
Zero REJECT
Explain residual ERRORs with impact

Run P21 (PMDA Engine) Identify JPN-specific Reject / Error / Warning → Gap Assessment (Is it justifiable?) → Identify Potential Rework If not justifiable → Compare FDA vs PMDA Shared Rules → Reuse FDA Justifications or Refine for PMDA (emphasis differences) → Finalize Strategy Support Reusability

*Provisional Translation (as of April 2024) - https://www.pmda.go.jp/files/000267942.pdf

EXAMPLE



Rule ID	Findings Text	Severity	Explanation
		SDTM	
SD2244	Invalid TSVCDREF value for FCNTRY	Error	Data have been kept as originally prepared for the FDA, it is an old study and “ISO 3166” is stored in TSVCDREF instead of ‘ISO 3166-1 alpha-3’ as recently introduced.
SD0025	--DTC is after --ENDTC	Error	Error in source data discovered after database lock. Decision was taken not to amend as it did not affect PK analysis. Subject ID AA579 , --DTC 2023-04-25, --ENDTC 2023-04-23.
		ADaM	
AD0141	Inconsistent value for PARAM within a unique PARAMCD	Error	UROBIL has quantitative (PARCAT2= QUANT) and qualitative (PARCAT2= QUAL) results coming from 2 different sources (SRC1 and SRC2), one with unit and one without unit. PARAM values are different because is created concatenating Parameter name and Unit.

AEs Causality/ Relationship Definitions

PMDA REQUIRES*

Causality categorization: related/not related - probable/possible/unlikely/unrelated.

Unrelated is considered **Not related**;

Other categories = **Related,** including **unlikely related**

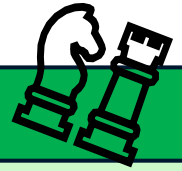
EXAMPLE

Unlikely related = Unrelated

Reason: consistency with internal medical governance and conservative safety interpretation.

Impact: # records affected; AE counts impact summarized in a table + full mapping logic documented in ADRG.

Chiesi Strategy



Causality/relationship PMDA definitions vs collecting data in CRF.

Impact for interpretation and analysis of AEs

Potential differences: explanation in ADRG/ evaluate to add new TLFs based on PMDA-specific causality/relationship.

GOAL

Enhancing Clarity/Compliance

Avoid risk of more PMDA questions

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*https://pharmasug.org/proceedings/2025/SS/PharmaSUG-2025-SS-254.pdf

Reviewer's Guides

PMDA REQUIRES*

Mandatory

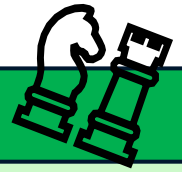
No specific template requirements

Persistent Error/Bug: explanations needed (data acceptability)

Rule IDs

SI unit conversion table

Chiesi Strategy



Reused the FDA template = PHUSE template

Updates:

- ✓ P21JPN outputs (Error/bug)
- ✓ RuleID
- ✓ SI unit conversion table
- ✓ Japan-relevant mapping decisions, terminology use, and traceability expectations

EXAMPLE

List of Japanese vs non-Japanese sites

Causality/relationship AE granularity detailed

GOAL

Turn technical findings into fast, unambiguous review narratives

Adding Japan-relevant information

*Provisional Translation (as of April 2024) - https://www.pmda.go.jp/files/000267942.pdf

ARMs

PMDA REQUIRES*

Required

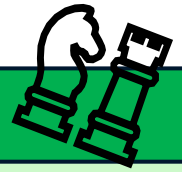
Embedded in ADaM define xml (v2.0)

Alternative approach: standalone PDFs.

EXAMPLE

	Table XX.X.X.X
Display	Clinical Study Report xx.xx.xx Primary Analysis of the Primary Endpoint: Change from Baseline in XXXX for Visits Through Week 24 (ITT SET)
Analysis Result	Change from Baseline in XXXX for Visits Through Week 24
Analysis Parameter(s)	PARAMCD = "xxxxxx" PARAM = "xxxxxxxx"
Analysis Variable(s)	ADRE.CHG (Change from Baseline)
Analysis Reason	SPECIFIED IN SAP Section X.X.X Primary Efficacy Analysis
Analysis Purpose	PRIMARY OUTCOME MEASURE
Data References (incl. Selection Criteria)	ADRE [PARAMCD = "XXXX" and ITTFL= "Y" and AVISIT in ("Week 12" "Week 16" "Week 24")]
Documentation	Add link to documentation i.e. SAP
Programming Statements	add relevant programming steps

Chiesi Strategy



Standalone PDFs

Focused on subset on key endpoints: populations, endpoints, censoring, algorithms, code traceability

Keep define.xml lean

GOAL

Transparency

Reducing XML complexity

Simplifying compliance processes without losing data traceability.

*Provisional Translation (as of April 2024) - https://www.pmda.go.jp/files/000267942.pdf

PMDA Consultation Meeting*

Consultation meeting (held more than once) :

Formats

Conformance data error

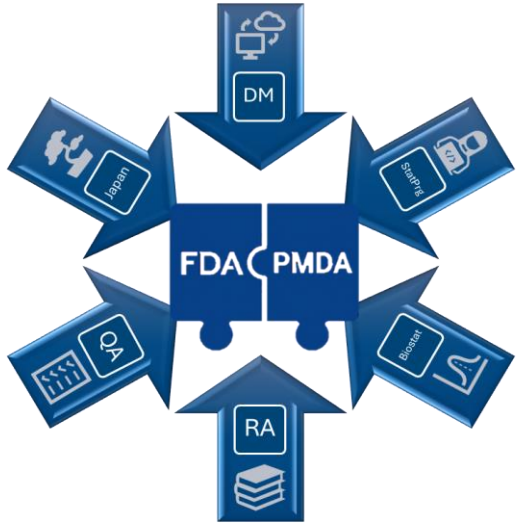
2 meeting types:
- fee-charged with minutes
- charge-free without minutes.

In preparation of consultation meeting

Specific Form 8, which is similar to the FDA requirements, it is crucial to specify the following:

- Validation results reports
- Submission data strategy
- Submitted before the Pre-consultation meeting

It is useful to have the data package prepared at least 2 months in advance of the consultation meeting.



https://www.pmda.go.jp/files/000274654.pdf

Walls, Wins, Wisdoms

Conclusion

WALLS

1. **Regulatory intelligence needed**
   CDISC is shared, but agency-specific expectations are not always documented.

2. **ARM expectations higher**
   PMDA expects deeper narrative, stronger traceability, and clearer rationale compared to FDA.

3. **Validator behavior shifts the focus**
   i. PMDA P21 rules are stricter and reveal issues not highlighted in the FDA workflow.
   ii. Some FDA deliverables (like the Reviewer's Guide) require redesign.

WINS

1. **Strong FDA package quality**
   High reusability of FDA datasets and metadata enabled minimal re-work.

2. **Effective cross-functional alignment across all teams**
   DM, StatProg, Stat, RA, QA, and Japan teams aligned quickly on decisions.

3. **Reusable FDA→PMDA crosswalk for future submission**
   It turns FDA experience into a ready-to-apply blueprint for PMDA submissions.

Himeji Castle, 1333 CE

WISDOMS

1. **Build multi-authority standards**
   Plan ahead: think global from day one.

2. **Anticipate divergence — use regulatory intelligence**
   PMDA aligns with CDISC globally, but maintains unique expectations.

3. **…and a dream — true global interoperability**
   One day, a single submission package may satisfy FDA, PMDA, NMPA, EMA without re-engineering.

The Great Buddha of Kamakura, 1252 CE

A big big thank to..

The eData Package Team (Beyond the Speakers)

Glauco Cappellini — Chiesi Disease Area Stat Lead
Marco Musca — Chiesi Senior Statistical Programmer
Luís Magalhães — Chiesi Clinical Program Leader
Natalia De Grandis — Chiesi Clinical Operations Lead
Laura Loche — Chiesi Senior Global RA Manager
Ananth Bheemavarapu — Gossamer Head of Stat Progr

Thank You!

Questions?