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Single Day Event

Evolving electronic Data Submission: FDA/PMDA Requirements and the Future of Regulatory Compliance with AI

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Disclaimer

The contents of this presentation represent the opinions of the PHUSE Japan electronic Data submission working group / individual presenters and do not represent the opinions or positions of the organization to which they belong.

Agenda

1. Current status of Japan electronic Data submission working group

2. Future of Regulatory Compliance with AI

3. Evolving electronic Data Submission:
   FDA/PMDA Requirements

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Highlight of our WG in 2025

- Our WG is composed of 17 members (Pharmaceutical company, CRO)
- One sub team was completed, and two sub teams are ongoing

eData for RWD (Completed)	Future of Regulatory Compliance with AI (Ongoing)	Evolving eData Submission: FDA/PMDA Requirements (Ongoing)
• Survey results were presented at PHUSE SDE in 2024 • Final Document was finalized in 2025 • The document was disclosed only to the PHUSE/CJUG ADaM team members who participated in the survey.	• Team started in Sep 2025 • Goal: AI-powered prompt library for regulatory compliance checks • Focusing on eData submissions to the PMDA	• Team started in Mar 2025 • Summarize how it aims to make cross-agency differences easier to understand and apply

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Project Overview & Scope

Primary Project Goal

- Develop an AI-powered Prompt Library to verify compliance with PMDA regulations using Generative AI.

Target Regulatory Authority

- The target authority is PMDA, responsible for approving pharmaceuticals in Japan.

Benefits of Alignment

- Aligning the prompt library with PMDA's eData requirements improves submission accuracy and accelerates approval processes.

Target Artifacts
SDTM
ADaM
Define-XML
SDRG
ADRG

Our Approach & Methodology

STEP 1: Establish the Master Checklist	STEP 2: Develop Cross-Validation Prompts	STEP 3: Ensure Cross-Platform Accessibility
Activity:	**Focus:**	**Target AI Platforms:**
Collect and consolidate validation checks currently performed by various companies.	Creating prompts **to verify cross-document consistency** and data integrity.	Develop the library for use with **Copilot** and **Gemini** to support different user environments.
Output:	**Key Cross-Checks:**	**Validation:**
A comprehensive list of checks that can be executed via Gen AI prompts.	SDTM x define-XML x SDRG ADaM x define-XML x ADRG SDTM x ADaM	Verify that prompts return **consistent results** across both models to ensure high **reliability**.

Future of Regulatory Compliance with AI Team Members

[Alphabetical order]

Eri Sakai	**Novartis Pharma K.K**
Iori Sakakibara	**Johnson & Johnson**
Keita Takahashi	**Chugai Pharmaceutical Co., Ltd.**
Rie Kageyama *Leader *Speaker	**Mebix**
Ryo Watanabe	**A2 Healthcare**
Takashi Kitahara	**Novartis Pharma K.K**
Yasuhiko Ozawa	**AstraZeneca**

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[Agenda]

- Opening
- Our Approach
- How We Created It
- Overview of the New Paper
  - Chapter Structure
  - Chapter Example

Opening

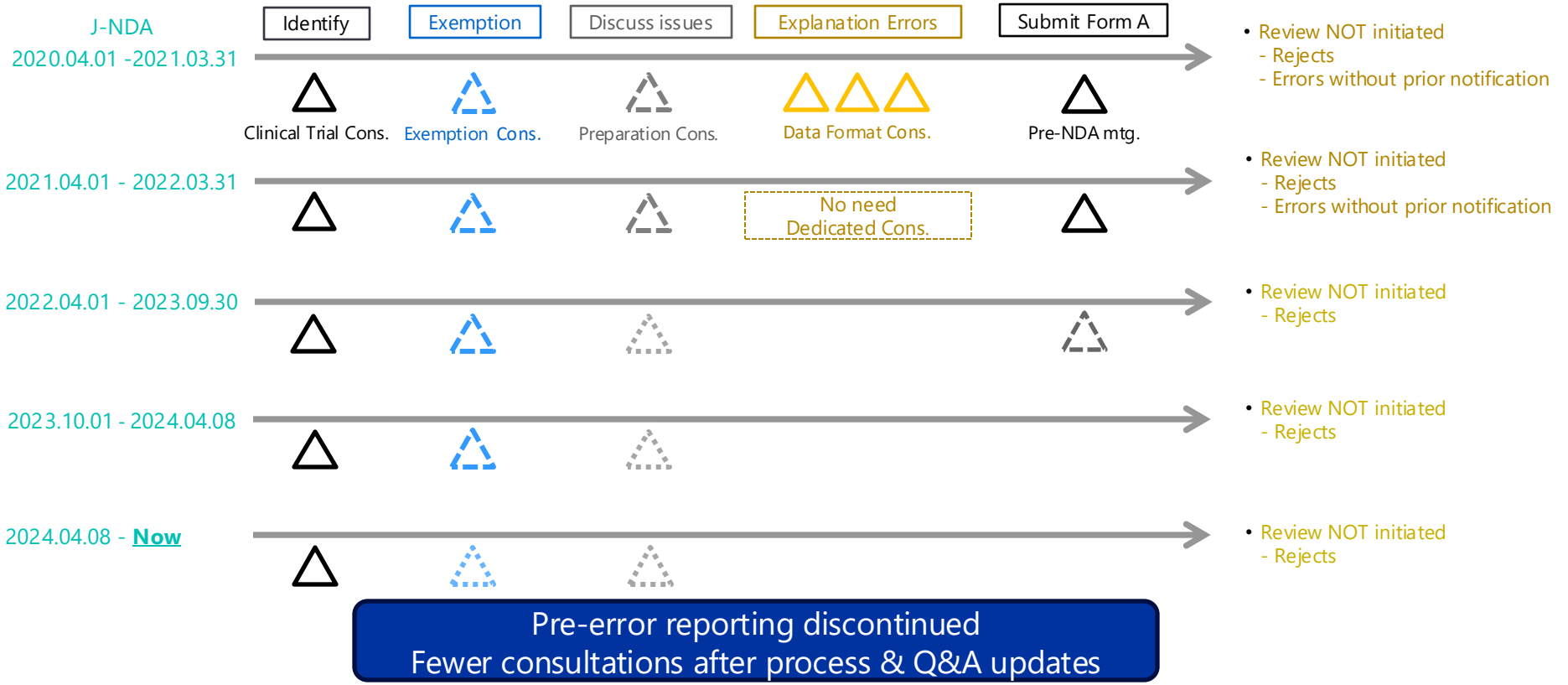
- **~ 9 years since FDA CDISC mandate (2016)**
- **~ 5 years since PMDA requirement (2020)**
  - Both agencies have **refined guidance**

- **WP-047 (2020)** summarized initial comparison
  - Many detailed Comparisons
  - Some **Outdated** rules
  - **PMDA framework stabilized**

Opening

- New paper in progress
  - **Revisiting FDA – PMDA differences**
  - Focus on **practical implications for cross-agency submissions**
- **Overview of new paper:**
  - **Motivation**
  - **Development process**
  - **Planned structure**
  - **Goal:** simplify and clarify **cross-agency differences**
- **Future's Plan:** expand comparison to include **NMPA (China)**

History of PMDA Guidance / Process Update



Our Approach : How We Have Summarized

- **WP-047:** comprehensive summary of FDA–PMDA differences
  - Great as full reference
  - Hard to use for quick comparisons

- **New paper:** focus on **practical use cases**
  - data submitted **FDA -> PMDA** or **PMDA -> FDA**

- Highlight **what to update** and **what to pay attention to**
  - Based on latest guidance from both agencies

Our Approach : How We Have Summarized

- **Impact level** of each difference
  - Evaluated by **associated risks** and **human resource** required
  - Categorized as **High / Middle / Low**

- **Visual indicators:**
  - ⚠ : possible **inquiries / re-submissions**
  - ⏰ : **time-consuming** differences
  - 💡 : **Cautions / Reminder**

- **Assessing deviation and inquiry risk:**
  - Verified with **global colleagues** (across companies)
  - Ensured **realistic, practical risk assessment**

Our Approach : How We Have Created

- **Step 1: Reviewed WP-047**
  - **Re-identified** FDA–PMDA differences
  - Based on **latest notifications** (chapter by chapter)

- **Step 2: Reorganized content**
  - Followed **actual review order**
  - **Merged similar topics** into single sections

- **Step 3: Discussed summarization approach**
  - How to **section related topics**
  - **Refined** the structure based on discussions

- **20+ meetings (1.0 - 1.5 hours)**
- **Outdated notices**
- **Complex multi-agency checks**

Overview of the New Paper: Chapter Structure

1. **Studies/Reports required for electronic data submission**

2. **CDISC Standards and Validation**
   - Standards Version
   - Validation Rules
   - Dictionary Controlled Terminology / MedDRA / WHO-DD
   - Other Dictionaries (Event Problem Codes / LOINC / MedDRA , WHO-DD for ISE/ISS / MED-RT / SNOMED CT / UNII)

3. **Metadata**
   - File size
   - Variable name, length
   - Dataset name
   - Label of dataset and variable

4. **Data Structure**
   - SDTM
   - ADaM
   - TFLs

5. **Reviewer's Guide / Define.xml**

6. **File type / Folder**

New Paper Chapter Example:
1. Studies/Reports in scope for electronic data submission

Key Differences:

- **Electronic Data Submission Scope :**
  Varies across agencies — even for the same drug/indication
- **Completed / Additional Studies after the first NDA:**
  submission may be required for another agency

Risks:

- **Cross-agency submission caution:**
  Same study submission scope can NOT be reused for another agency
- **Resource impact:**
  Preparing additional data for other agencies requires significant effort and time
  -> **Risk level: High** 

New Paper Chapter Example:
1. Studies/Reports in scope for electronic data submission

ID	FDA	PMDA	FDA to PMDA	PMDA to FDA
1.1	To be confirmed through the SDSP (the specific documents subject to submission are not explicitly described).	The data that are subject to electronic submission for new drug applications include evaluation data that are considered to provide the major evidence for the efficacy, safety, and dosage and administration as well as data on studies or analyses that are considered to contribute to the establishment of the dosage and administration and are focused on the evaluation of efficacy, safety, or pharmacokinetics.	H	H

- **Different processes for determining submission scope**

PMDA:
Notification on Handling of Submission of eStudy Data for NDA (2024.Ari.8), 2 (1) b.

New Paper Chapter Example:
3. Metadata - File size

Key Differences:

- **FDA:** Datasets >5GB must be split.
- **PMDA:** Dataset splitting is not required, regardless of file size.

Risks:

- **FDA→PMDA :** Submit only the original unsplit dataset. Remove any split dataset descriptions from the RG to avoid PMDA inquiries. **(L)**
- **PMDA→FDA :** If any dataset >5GB, splitting and explanation in the RG are required. **(H)**

ID	FDA	PMDA	FDA to PMDA	PMDA to FDA
3.1.1	Datasets greater than 5 gigabytes (GB) in size should be split into smaller datasets no larger than 5 GB. Sponsors should submit these smaller datasets, in addition to the larger non-split datasets, to better support regulatory reviewers. The split datasets should be placed in a separate sub-directory labeled 'split' (See section 7.2). A clear explanation regarding how these datasets were split needs to be presented within the relevant data RG. For submissions that are greater than 10 GB, refer to the FDA technical specification Transmitting Electronic Submissions Using eCTD Specifications. (if > 10 GB, use USB drive)	If the total capacity of the files to be submitted in a single operation exceeds 100GB or the size of a single file exceeds 10GB, please contact the Helpdesk in advance. Also, a zero-byte file (empty file) cannot be submitted.	L	H

New Paper Chapter Example:
4. Data Structure – SDTM.LB/QS domains

Key Differences:

- **FDA:** If LB domain > 5 GB, split it by LBCAT. If still too large, further split by LBSCAT. Name the split files sequentially (e.g., lb1, lb2, lb3).

ID	FDA	PMDA	FDA to PMDA	PMDA to FDA
4.1.6	LB domain: by splitting a large LB dataset into smaller datasets according to LBCAT and LBSCAT, using LBCAT for initial splitting. If the size is still too large, then use LBSCAT for further splitting. For example, use the dataset name lb1 (file name 'lb1.xpt') for chemistry, dataset name lb2 (file name 'lb2.xpt') for hematology, and dataset name lb3 (file name 'lb3.xpt') for urinalysis.	–	L	H

Experience Sharing:

When multiple questionnaires were collected, the QS domain was split by each questionnaire (e.g., QSCG, QSHS, QSMT etc.) during mapping to support analysis needs. This approach ultimately resulted in smaller file sizes.

New Paper Chapter Example:
4. Data Structure – ADaM/TFLs program

Key Differences:

- **FDA/PMDA:** The scope of ADaM/TFL submissions is clearly defined
- **FDA:** Submission of safety-related programs is not mandatory

Risks:

- Existing package may lack required submission programs.
- Verify promptly after receipt
- Request missing items immediately (may cause delays)

  -> **Risk level: High** ⚠

New Paper Chapter Example:
4. Data Structure – ADaM/TFLs program

ID	FDA	PMDA	FDAto PMDA	PMDA toFDA
4.2.1	• All programs used for the creation of ADaM datasets and for analysis (primary, secondary efficacy analyses, but not safety) • Programs used to generate additional information included in Section 14 (Clinical Studies) of the Prescribing Information (equivalent to programs used for analysis in the Japanese package insert) • The ADRG must include details of the analysis execution environment, the software utilized, and its version. • macro is not generally required. • explanations for each program (e.g. read me) are not required.	•Submit ADaM and analysis programs (incl. population/simulation) for key efficacy, safety, and dosing rationale. If unavailable, provide specs outlining the algorithms. •Submission does not need to be in a format or content that is directly executable within the PMDA environment. •Provision of macro programs is preferred; however, if this is difficult, submission of documentation such as specifications that clearly describe the analysis •Provide the analysis execution used, and its version in the ADR •Description of ADaM dataset cr analysis programs •Programs can use any software/version, but file names must include the software-assigned extension. If missing, explain the format in the data guide.	H ⚠	L

- **Accepted without extension if Reviewer's Guide specifies the file format**

FDA/PMDA Requirements Team Members

[Alphabetical order]

Hisae Yagishita	**A2 Healthcare**
Kayo Inushima	**Biogen Japan**
Naoki Yoshida *Speaker	**Takeda Pharmaceutical Co., Ltd.**
Sayaka Niiya	**Bristol Myers Squibb K.K.**
Takafumi Kamon	**A2 Healthcare**
Tomohiko Funai *Leader	**Eli Lilly Japan**

Join Us?

Member List

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Eli Lilly	Tomohiko Funai （船井友彦）
Novartis Pharma K.K	Yasuhiro Iijima （飯島康浩）
Novartis Pharma K.K	Eri Sakai （坂井絵理）
Novartis Pharma K.K	Takashi Kitahara （北原孝志）
Johnson & Johnson	Iori Sakakibara （榊原伊織）
Mebix	Rie Kageyama （影山理絵）
Kyowa Kirin	Shinichi Hotta （堀田真一）

Company	Name (mention)
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A2 Healthcare	Hisae Yagishita （柳下壽栄）
A2 Healthcare	Ryo Watanabe （渡部亮）
A2 Healthcare	Takafumi Kamon （嘉門貴文）
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