Industry Experiences Submitting Standardized Study Data to Regulatory Authorities

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Contents

1. Introduction

1.1. Background

The Optimizing the Use of Data Standards – Industry Experiences Submitting Standardized Study Data to Regulatory Authorities Project is a collaborative, non-competitive PHUSE forum for industry to share submission experiences and develop best practices including submission strategy and planning, regulatory requirements, and interactions with the regulators. The project team was formed to:

1) investigate and recommend a strategy and planning practices for preparing data for a regulatory submission
2) recommend communication practices within sponsors and between sponsors and regulators that can facilitate an effective exchange of the standardised study data and the submission-related information.

1.2. Problem Statement

The FDA and PMDA have provided the industry with guidance documents and technical guides for submitting standardised study data. Over the course of implementation, the industry has recognised that the requirements differ among FDA review divisions and between regulatory agencies across the globe. The evolution of standards during the regulatory submission life cycle further compounds the challenges. Industry approaches to meeting these requirements and challenges vary across companies. The submission activities involve different groups and organisations, both within and outside the sponsor company, which makes the process more complicated.

1.3. Scope

This white paper, which focusses on two regulatory authorities, the FDA and PMDA:

- presents an overview of submission activities that outlines the scope of the submission work
- compares regulatory requirements and differences between FDA and PMDA submissions
- discusses legacy data conversion
- explores the ways to incorporate and optimise the use of the Study Data Standardization Plan (SDSP)
- describes communication strategies and methods within sponsors and between sponsors and regulatory authorities that can facilitate an effective exchange of the standardised study data and the submission-related information.

1.4. Abbreviations, Acronyms and Definitions

Term	Description
ADaM	Analysis Data Model
ADRG	Analysis Data Reviewer's Guide
ARM	Analysis Results Metadata
ANDA	Abbreviated New Drug Application
BLA	Biologic License Agreement
CBER	Center for Biologics Evaluation and Research
CDER	Center for Drug Evaluation and Research
CDISC	Clinical Data Interchange Standards Consortium
CP	Clinical Pharmacology
cSDRG	Clinical Study Data Reviewer's Guide
CSR	Clinical Study Report
eCTD	Electronic Common Technical Document
FDA	Food and Drug Administration
IND	Investigational New Drug
Legacy Data	Study data that does not conform to the standards by the date of requirement specified in the published Data Standards Catalog. Unless specified, Legacy Data can refer to either tabulation or analysis data.
NDA	New Drug Application
PHUSE	Pharmaceutical Users Software Exchange
PK	Pharmacokinetics
PMDA	Pharmaceutical and Medical Devices Agency
SDSP	Study Data Standardization Plan
SDTM	Study Data Tabulation Model

2. Overview of Submission Activities

2.1. Time Course and Description of Activities

The key to a successful acceptance of standardised study data for a BLA or NDA is to have a clear path to follow through the submission process. The submission team needs to identify the requirements, scope of work, when and what resources are required throughout the submission workflow. This section aims to provide a high-level overview of the type of activities, along with potential functional areas involved in the activity.

Figure 1 depicts a standard submission time course. The figure starts at Phase I, first in human studies, through the NDA/BLA filing. There are activities prior to the first in human studies such as pre-clinical studies and submission of the IND, but for the purposes of this paper, the time course will begin with the first in human studies. Communication with regulatory authorities, development of the SDSP and legacy data conversion planning will be discussed in detail later within this paper. The figure below can vary across the industry.

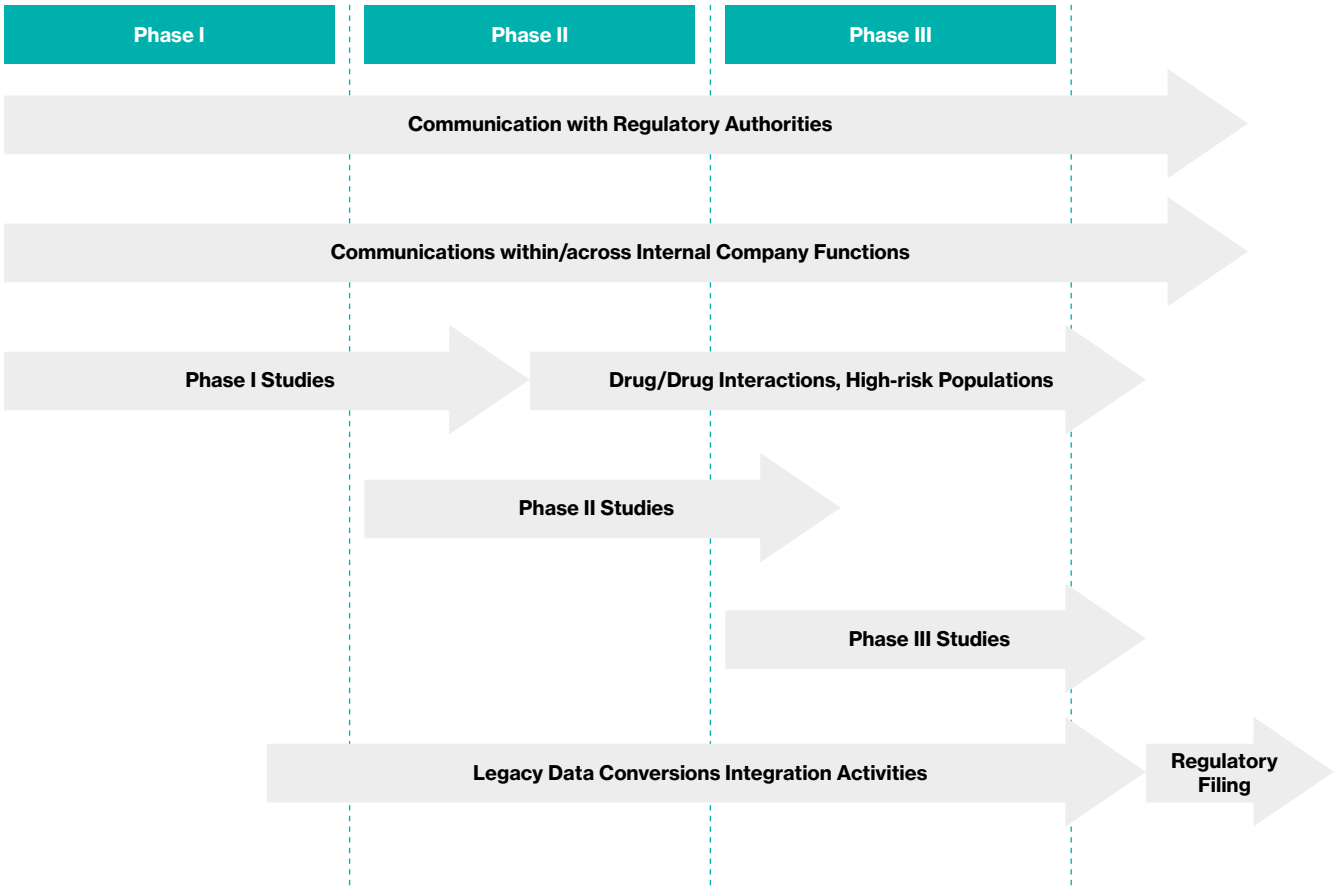

Table 1 lists the activities required throughout the submission life cycle, encompassing all the clinical development phases. Often these activities could be done in parallel in order to expedite the timeline for the filing of the submission. Suggested functional areas involved are also included in the table below.

Submission Activity	Suggested Functional Area Involvement
Develop/Update the SDSP (includes all studies completed, active or planned)	Biostatistics/Statistical Programming, Data Management, Clinical, Regulatory Affairs
Prepare topline results from completed studies for briefing materials in preparation of a regulatory meeting	Biostatistics/Statistical Programming, Clinical, Medical Writing
Draft protocol and statistical analysis plan for studies planned in next phase of the clinical development	Biostatistics, Clinical
Draft proposal/questions for regulatory meeting	Regulatory, Biostatistics/Statistical Programming, Clinical
Prepare standardised data packages (i.e. CDISC or Legacy) for all studies being submitted to regulatory authorities	Biostatistics/Statistical Programming, Data Management
For studies that have been converted into a different format, perform reconciliation on key analysis results using the new data format	Biostatistics/Statistical Programming, Data Management
Submit Bioresearch Monitoring (BIMO) deliverables to CDER	Biostatistics/Statistical Programming, Regulatory Affairs, Clinical
Submit packages to regulatory authorities	Regulatory Affairs

2.2. Exceptions to the Standard Submission

Besides the standard submission, whose time course and activities are depicted in Figure 1 and Table 1, there are other types of submissions that have different regulatory requirements and timelines:

1) orphan submission for rare disease
2) breakthrough and fast track therapies
3) abbreviated new drug application for generics

These designations are given to shorten the overall timeline of the product reaching the market. Further information on submission types and designations can be found on the FDA website (*Designating an Orphan Product: Drugs and Biological Products*; *Fast Track, Breakthrough Therapy, Accelerated Approval, Priority Review*; *Abbreviated New Drug Application*).

At the PMDA, similarly, priority review is conducted for orphan drugs and specific drugs selected by the Ministry of Health, Labour and Welfare (MHLW) based on the seriousness of the

target disease and the medical usefulness. Priority review status is also granted to products designated under the SAKIGAKE Designation System [1,2].

Just as there are different regulatory requirements for the type of submission, differences also exist depending on which regulatory authority is reviewing the application, which will be discussed in *Section 3 Study Data Submission Requirements*.

In addition to the different types of submissions, there is also an opportunity for a joint submission in which two pharmaceutical companies develop a compound and submit to the regulatory authorities. Generally, it follows the same submission strategy flow and folder structure as the standard submission.

2.3. Timing of Submitting Data Submission Packages

There are no requirements to submit data to the FDA prior to the planned filing date. However, the FDA offers a process to validate a sample eCTD and/or standardised study data for sponsors. If sponsors choose to do so, they may refer to the FDA *Sample Submission Validation Process*. In order to test the Electronic Submissions Gateway (ESG) prior to the official filing, follow the FDA *Instruction for Guidance Compliant Test Submission*. From a data delivery perspective, you can submit your data submission packages to the FDA at the time of the planned submission together with the rest of the filing dossier.

According to the PMDA Technical Conformance Guide [3], the data submission package to the PMDA can be filed up to five weeks before the scheduled application date. In practice, some sponsors choose to deliver the electronic data package early to ensure a successful submission without jeopardising the scheduled application date. Prior to the delivery of the package, there is a requirement to have consultation meetings regarding study data submission.

The next section discusses the requirements and differences between the FDA and PMDA.

3. Study Data Submission Requirements

It is essential to understand the regulatory requirements to plan, develop and submit a study data package.

Sponsors should consult the FDA Data Standards Catalog [4] to understand the study data requirements. If a study used an earlier version of a CDISC standard after the support date ended in the Data Standards Catalog4, the study may require up-versioning or a waiver (refer to *Section 6.1.2 Waiver*).

According to the PMDA Guidance, they mandate submissions that occur on or after 01 April 2020 should adhere to CDISC standard format regardless of study start. The PMDA also has a Data Standards Catalog [5] that lists their supported standards. Waivers/exemptions are allowed under certain conditions based on the PMDA guidance (refer to the FAQ1-5 of FAQs on Electronic Study Data Submission [6]).

Although industry may comply with the standards, experiences have shown that the FDA may have strong preferences to follow a later standard that is ahead of the mandatory schedule if the standard is currently supported in the FDA Data Standards Catalog [4].

While both agencies require standardised data per their respective data standards catalog, there are differences in the validation rules, other requirements, and documentation that sponsors are expected to address. A complementing PHUSE white paper "FDA and PMDA Study Data Submission Distinctions" will be published on the PHUSE website under *Final White Paper Deliverables & References from Working Groups Projects*. It contains comprehensive FDA and PMDA requirements to address similarities and differences between these two agencies. The details of the differences between these two agencies are not part of this paper due to the comprehensive content.

The next section shares a case study and frequently asked questions to help industry plan and prepare study data submission.

3.1. Case Study: FDA and PMDA Submission Experience from a Sponsor

Project Description: The sponsor prepared a submission that contained two studies. The sponsor submitted the same data submission package to the FDA and PMDA.

Sponsor Experience:
- The sponsor followed the conformance validation rules applied to all SDTM and ADaM. Conformance issues found were explained in the cSDRG. The packages for both studies were accepted by the FDA.
- The same submission package was delivered to the PMDA. One study that only contained "ERROR" issues was accepted, with the "ERROR" issues being properly explained in the cSDRG; however, the second study was rejected because it contained "REJECT" issues.

Lessons Learned:
Although both agencies have adopted CDISC standards, the regulatory validation rules, including severity categories, are different. What is acceptable to the FDA may not be acceptable to the PMDA. Therefore, it is essential to execute validation checks using both FDA and PMDA validation rules; resolve "REJECT" issues; and share the "ERROR" issues with the PMDA at the meeting named Consultation on Data Format (refer to *Section 6.2 PMDA Communication Strategy*) ahead of the submission.

3.2. Frequently Asked Questions (FAQ): Planning for FDA and PMDA Submissions

Can we create a single study data package and submit it to both the FDA and PMDA?
This limits the sponsor's ability to create a single study data package that satisfies both the FDA and PMDA. The differences include:

- requirement to implement a version of standards from the respective Data Standards Catalog [4,5]
- severity of the validation rules
- file naming conventions
- software programs format

- Analysis Results Metadata (ARM) (strongly recommended by the PMDA)
- potential update to the cSDRG and ADRG due to the PMDA officer's recommendations.

What do you recommend if a study is submitted to both the FDA and PMDA?

- Adopt the latest CDISC model and implementation guide of SDTM, ADaM, and controlled terminologies supported by both agencies, per their respective Data Standards Catalog [4, 5].
- Ensure checks are performed against the CDISC conformance rules and regulatory authorities' business and validation rules.
- Resolve rejection issues and address (resolve or justify) remaining issues.
- Open a dialog with the authorities as early as possible.
- Use the ARM to facilitate the review of key analyses.

What if I do not know if we are submitting to the PMDA?
The implications could be severe and could require significant re-work. Hence, plan and be prepared. Regardless of which regulatory authority, sponsors should run compliance checks against CDISC conformance rules and the agency's validation rules to ensure there are no 'REJECT' issues.

4. Legacy Data Conversion

As the industry is transitioning into the requirement of standardised study data, it is common that a sponsor may have some studies that used a legacy data format, or an early version of a standardised data format no longer supported per the Data Standards Catalog [4, 5]. The sponsor must assess the situation and be prepared for legacy data conversion (including up-versioning) in order to meet regulatory requirements discussed in the previous section. Performing legacy data conversion (including up-versioning) is complex and resource-consuming. It is crucial for a successful submission to have a comprehensive strategy and implementation plan at the early stage of the product life cycle. Information regarding the legacy data conversion should be documented in the cSDRG and/or ADRG when submitting to the FDA and PMDA, depending on where the conversion took place.

4.1. Assess the Scope of Conversion and Up-versioning

4.1.1. Conversion/Up-versioning Methodologies

There are two types of studies that may need conversion or up-versioning:

- Study data that does not conform to the supported standards per the agency's respective Data Standards Catalog [4, 5]
- Studies that followed an earlier model and implementation guide of a standard that is no longer supported by regulatory authorities per the agency's respective Data Standard Catalog [4, 5]

There are multiple approaches for conversion/up-versioning. Each approach has limitation, as discussed in the FDA Study Data Technical Conformance Guide [7], which needs to be evaluated. The FDA does not recommend an approach but emphasises that the issues associated with a certain approach must be properly addressed in the Legacy Data Conversion Plan and Report within the cSDRG and/or ADRG.

- Legacy tabulation-> SDTM, legacy analysis -> ADaM, independently
  When CSR outputs were produced using legacy data, teams need verify that key outputs could be reproduced using the converted SDTM and ADaM. (For PMDA submission, traceability between converted SDTM datasets and converted ADaM datasets needs to be clearly explained; if converted ADaM datasets are to be submitted, they should be created from converted SDTM datasets. Therefore, this may not be the best approach for PMDA submission.)

- Legacy tabulation -> SDTM -> ADaM, sequentially
  - **CSR using legacy as source.** Since CSR outputs were produced using legacy data, teams should take steps to verify that key outputs could be reproduced using converted SDTM and ADaM. This approach has a higher cost due to ADaM rederivation and has higher possibility of discrepancies between original CSR outputs and new ADaM datasets.
  - **CSR using ADaM as source.** This approach could best maintain the traceability. An early anticipation on potential legacy data conversion allows action to be taken earlier to take advantage of this route.

Regardless of which approach is taken, traceability must be maintained, and data flow must be represented clearly. For traceability reasons, the FDA may still request legacy data.

4.1.2. Additional Cost for Conversion

Significant cost occurs during the conversion process that requires resources to:

- convert the datasets
- run a compliance check and address the issues
- create the cSDRG/ADRG with the Legacy Data Conversion Plan & Report
- produce more detailed metadata files to create the Define-XML, which may include ARM strongly recommended by the PMDA
- verify that the converted data reproduces the key results created using legacy data.

4.2. Decide on the Legacy Data Conversion Strategy and Planning

There are factors that need to be considered:

- Ensure the regulatory requirements are met (mandatory timelines for electronic study data submission by the FDA and PMDA, as specified in their respective Data Standards Catalog [4, 5]).
- Refer to previous discussions with regulatory authorities.
- Evaluate cost and benefits, including the impact on resources and timelines.
- Consider the key objectives of the study and the role the study will play in the submission, such as PK, safety, efficacy.
  - Pivotal studies may carry more weight on converting; and in most cases, pivotal studies will be converted.
  - Supporting studies including earlier phase studies, such as healthy volunteer studies, PK studies and CP studies, may have some flexibility within the boundary of mandatory requirements by conducting partial conversion on selected important domains.

- Consider the stage of analysis and reporting activities.
- Review pooling needs.
- Ensure the plan can facilitate regulatory review.

During the process, it is recommended to engage internal cross-functional teams, such as regulatory affairs.

For FDA submissions, sponsors have the option to request a waiver for studies that do not conform to the FDA Data Standards Catalog [4]. Refer to FDA Guidance for Industry – Providing Regulatory Submissions in Electronic Format – Standardized Study Data [8].

For supporting legacy studies that do not require a waiver, find examples of legacy data conversion strategy and planning that could be considered below:

- Submission of only legacy CRT package
- Submission of legacy CRT package plus selected converted SDTM domains based on the key objectives of the study
- Submission of legacy CRT package plus a full set of converted SDTM domains
- Submission of legacy CRT package plus a full set of converted SDTM domains plus ADSL
- Submission of legacy CRT package plus a full set of converted SDTM domains plus ADSL plus ADaM datasets that are related to key analyses

For all these examples, the legacy source data and analysis data that were used in the CSR are provided. Also, the submission of SDTM datasets would allow the FDA to run their automated tools, such as data fitness check, and to load the source data into their data repository.

Once the strategy, including what studies will be converted and how to convert them, is identified, an action plan needs to be created. It is recommended that harmonising various versions of standardised study data, including SDTM, ADaM and dictionaries, be implemented at the pooled level rather than at the study level. The plan should include resource allocation (both quantity and experience) and timelines for the overall conversion objective and for each deliverable.

In addition, the strategy needs to be communicated properly with regulatory authorities. Refer to *Section 6 Communications with Regulatory Authorities* for more details.

5. Incorporate and Optimise Use of the Study Data Standardization Plan (SDSP) in Submission Strategy and Planning

The FDA recommended the industry to include a study data standardisation plan to summarise the adoption of data standards for completed, ongoing and planned studies. The SDSP helps to identify legacy data formats, which enables sponsors to make decisions on the plans for submitting study data. Planning and communication with regulatory authorities would set expectations and align on the use of data prior to an application. While the SDSP is not applicable to PMDA submission, it can still be regarded as a useful tool to support study data standardisation planning.

5.1. Development of the SDSP

Gathering study-level information is the first step to authoring the SDSP. It requires cross-functional support from both nonclinical and clinical teams. Obtaining the inventory of trials and supportive data standards requires orchestration between functional areas which may not typically have regular interactions. The collection of historical information is an investment in time and resources. Refer to the PHUSE SDSP Sponsor Implementation Guide [9].

5.1.1. Initiating the SDSP and Content Assembly

Individuals with oversight to the filing strategy and touchpoints with functional areas during the product development cycle could have a main role in authoring the SDSP. There is no single approach to implementing the SDSP in an organisation, and various experiences have yielded successful process outcomes in developing and sharing the SDSP. Below are additional approaches to organisations coordinating the SDSP assembly:

Practice #1: Statisticians and programmers initiate and facilitate the content ownership and collection on the use of data standards. Once the document is ready, the SDSP would be handed over to the regulatory affairs team for FDA sharing.

Benefits:

- The programming team has study knowledge of SDTM and ADaM implementation while statisticians have study-level and integrated analysis knowledge.
- Cross-functional areas (e.g. data management, clinical, nonclinical) would be supportive content providers.

Practice #2: The regulatory affairs team owns and initiates the SDSP while data management in clinical and nonclinical facilitates the collection of content.

Benefits:

- Assign content ownership to the team with the study standard implementation knowledge. Data management/statisticians identify the exchange standards and terminology standards for each study and pool (integration).
- Leverage the project management skills from data management/statisticians to maintain the document through the product life cycle.
- Cross-functional areas (e.g. statistics, programmers, clinical, nonclinical) would be supportive content providers.

Practice #3: The data standards team initiates the document and distributes the SDSP to the study-level, cross-functional teams to review, confirm and complete an accurate SDSP. Once the document is ready, the SDSP would be handed over to the regulatory affairs team for FDA sharing.

Benefits:

- A single point of contact oversees defining study data standards as early as possible, including:
  - organising data standards up-versioning
  - ensuring a successful and timely assembly of the content

  - implementing consistency
  - reducing duplicated efforts
  - promoting the study data standards awareness.
- While each function has study-level knowledge, it is still efficient to have a single point of contact who would coordinate the activities.
- Centralising the creation of the document enables consistency across all submissions within the company.

Risk: The standards team representative heavily relies on other functional areas to provide their respective information.

5.1.2. Retrospective SDSP Implementation Considerations

For a new development programme, it is recommended to start the SDSP process as early as the IND. However, industry is still applying a retrospective application of the SDSP and is challenged with recovering versions of exchange and terminology standards that supported earlier studies.

Scenario #1: Implementing SDSP in-life for the first time in a programme that has a long product development.

Recommendations:

- Leverage the knowledge of a cross-functional team to coordinate and communicate the history of standards implemented for the study.
- Be flexible working within the team. Although a company procedure may assign a specific role to complete the SDSP, it is important to find the historians who have access to archived supportive documents and can correctly reflect the exchange and terminology standards applied in earlier product development.

Scenario #2: Products that are ready for submission and the SDSP has not been previously shared.

Recommendation: When possible, submit the SDSP in the application based on the exchange and terminology standards implemented in the submission. In practice, if timelines are sensitive, there were cases where the alternative approach was to apply the SDSP towards supplemental applications.

5.1.3. Frequently Asked Questions (FAQ): Development of the SDSP

How do you establish support and structure in your organisation to commit to completing the SDSP?
- Identify the leaders in your organisation who have the current information and background to support the reporting of accurate information.
- Refer to the PHUSE SDSP Sponsor Implementation Guide [9].

During the development of the SDSP, who knows when a product transitions from nonclinical to the first clinical study?
The owner of the SDSP, as described in *Section 5.1.1. Initiating the SDSP and Content Assembly*, has the oversight to the product development life cycle and can assist in bridging the information from nonclinical to clinical development.

How frequently should sponsors update and review the SDSP internally?
Refer to the PHUSE SDSP Sponsor Implementation Guide [9].

What are the expectations for identifying the pooled analysis when there is not a clear plan to integrate data so early on in the product life cycle?
- Authoring the SDSP early in the product development life cycle can bring challenges for sponsors when the plans for pooled analysis or the use of data to support analysis have not been developed. Early in the product development life cycle, the plans for integrated data may not exist in early releases of the SDSP. As the product reaches the End of Phase II meeting or 12–15 months prior to a submission, sponsors are encouraged to discuss the plans for pooling safety and efficacy data and to document it in the SDSP.
- As studies approach submission, authors will be expected to adjust the studies in the pooled analysis at stage gate milestones and finalise the document at the time of submission.

When is the optimal time to share the SDSP?
The PHUSE SDSP Sponsor Implementation Guide9 contains recommendations for sharing the SDSP at stage gate meetings. If sharing the SDSP too late, sponsors may not have the opportunity to vet the request and gain alignment on the approach to submitting data, thereby jeopardising the submission, for example:
- missed opportunity for legacy conversion at an earlier stage or waiver request
- implementing a standard that is no longer supported by the Data Standards Catalog
- miscommunicating expectations (e.g. pooling analysis strategy).

If you have plans to convert legacy data to standardised data, how do you document it in the SDSP?
Refer to the PHUSE SDSP Template [10] and the SDSP Completion Guidelines [11].

What to do when indications are designated as rare disease, orphan, breakthrough or unmet medical need?
The scope/volume of protocols may be smaller. The structure and practice to implement the SDSP remain the same.

Do we include all studies that we run or just the ones that we submit?
Sponsors should include all studies that were opened under the IND regardless of whether it is planned for the original or supplemental application. Refer to the PHUSE SDSP Sponsor Implementation Guide9 and the PHUSE SDSP Template [10].

5.2. Use of the SDSP as a Strategy and Planning Tool

Once the SDSP is drafted, the next step is to identify the gap from trials that were not developed in accordance to the Data Standards Catalog. Studies that do not conform to standards will require an assessment on the submission strategy.

Option 1: Plan activities to conform to the expected data standards.

- Refer to *Section 4.2 Decide on the Legacy Data Conversion Strategy and Planning* as a guide for possible considerations to the decision-making process.
- Action: Ensure you revisit the SDSP to reflect the exchange and terminology standards implemented at the time of submission.

Option 2: Apply for a waiver to seek alignment on expectations for submitting data. Refer to *Section 6.1.2 Waiver* for further details.

NOTE: Sponsors may implement multiple options within the submission.

If regulatory input is required to determine the data submission strategy, the sponsor should interact with the regulatory authorities on their position and rationale by utilising the SDSP. The next section will discuss the practices of regulatory interactions.

6. Communications with Regulatory Authorities

Decisions and strategies must be organised and communicated internally before presenting the situation for regulatory agreement. Once sponsors decide to engage regulatory authorities, pre-work is needed to prepare the briefing materials in advance of the meeting. Functional areas, who have responsibility for submitting standardised study data, should proactively lead and/or engage in the related discussions. This may include developing certain sections of briefing materials and responses, preparing the team to speak on behalf of study data standards.

Tools for communicating the plan with regulatory authorities include:

- Share the SDSP at each stage gate interaction with the FDA, to align on the strategy and planning through the submission life cycle and process. (The SDSP can be attached to the briefing document for each interaction, and discussions and agreements reached can be added back to the SDSP for further actions and future communications.)
- Consult with the PMDA on electronic study data submissions utilising Form A and Form B.

6.1. FDA Communication Strategy

Refer to the 2017 FDA draft Guidance for Industry12 that describes the Formal meetings between the FDA and Sponsors or Applicants of PDUFA products.

When addressing submission of study data to regulatory authorities, sponsors should communicate the following:

- Deviation from the deliverables outlined in the FDA Guidance for Industry: Providing Regulatory Submissions in Electronic Format – Standardized Study Data8 and the FDA Data Standards Catalog [4]
- Up-versioning that may include a Legacy Conversion Plan and Report in cSDRG and/or ADRG
- Studies or approaches that require regulatory agreement prior to submission
- Review of the pooled analysis plan

6.1.1. The SDSP

The SDSP is a living document that should be shared with CDER or CBER at stage gate meetings and at the time of submission. To make best use of the regulatory interaction, it is recommended to identify trials that require reviewers' agreement on the use of data standards to support the submission. It is recommended to submit the SDSP no later than the End of Phase II meeting.

While CDER wants to be informed on the development and adoption of data standards shared at stage gate meetings, CBER seeks additional information in a CBER Appendix. The content contains metadata details that facilitate CBER review and could affect sponsors' mappings. For CBER submissions, sponsors should allow enough time to gain concurrence on the information presented in the CBER Appendix.

6.1.2. Waiver

Waiver request applies to study data that no longer have a version of the data standards supported in the FDA Data Standards Catalog [4]. Refer to FDA Guidance for Industry – Providing Regulatory Submissions in Electronic Format – Standardized Study Data [8].

The waiver process should be the first line of communication to share the rationale for non-conformance of legacy data or retired standards. Once agreed upon, sponsors should document the outcome in SDSP Section 6: FDA Data Standards Discussions.

6.1.3. General Correspondence

Sponsors have additional options to communicate with the FDA:

- Contact the project manager via email or phone with applicant-specific questions.
- Raise non-applicant-specific enquiries directly to the CDER or CBER edata mailbox.

6.2. PMDA Communication Strategy

Consultation on study data submission can be requested multiple times during the product life cycle. Form A or Form B should be prepared prior to the consultation. More details can be found in the complementing PHUSE white paper "FDA and PMDA Study Data Submission Distinctions", to be published on the PHUSE website under *Final White Paper Deliverables & References from Working Groups Projects*.

Sponsors can request the following meetings with the PMDA (refer to the FAQ1-5 of FAQs on Electronic Study Data Submission [6]):

- **Clinical Trial Consultation** (normally, End of Phase II) – Identify the study data and/or analysis data planned for electronic submission necessary for a new drug application.
- **Consultation Meetings for Submission of Electronic Study Data** include:
  - **Consultation on Exemption** – Discuss and reach agreement on the exemption to submit electronic study data submission or acceptance of study data and analyses in non-CDISC format
  - **Consultation on Preparation** – Discuss and review the following:
    - methods for storing data (e.g. custom domains) and handling variables

    - approaches to legacy data conversion
    - submission method to send study data
  - **Consultation on Data Format** – Discuss validation results
- **Pre-NDA Meeting** – Occurs approximately 1–3 months prior to the planned filing date for final confirmation on the submission package

If the meeting is granted, the PMDA will identify the meeting in the following format:

- face-to-face
- teleconference (at the PMDA's discretion)
- video conference system at the PMDA in Osaka to connect to the PMDA office in Tokyo

7. Recommendation

Submitting standardised study data to regulatory authorities is a critical and complex process and it requires strategy, planning, and communication. Sponsors need to proactively identify and prepare for challenges throughout the submission life cycle.

It is essential to start the process early and revisit it by taking steps, as discussed in this white paper, to deliver a high-quality and compliant submission package in a lean, resourceful, and cost-effective way.

8. Disclaimer

The opinions expressed in this document are those of the authors and should not be construed to represent the opinions of PHUSE members' respective companies/organisations or regulators' views or policies. The content in this document should not be interpreted as a data standard and/or information required by regulatory authorities.

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