

SDTM and SEND: An Integrated View and Approach

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ABSTRACT

Regulatory agencies are requiring the use of standardized data for submission and analysis. While many companies have already been using CDISC standards such as SDTM and ADaM for the submission of clinical data, the use of the SEND CDISC Standard for nonclinical studies has not been as widely implemented at the time the requirement went into effect. SEND is now required by the FDA Data Standards Catalog, although it is currently not a requirement for PMDA. Recently drug development trends show an increase in a globally integrated drug development processes, where similar clinical data packages are used for submission to both PMDA and FDA, and sponsors need to know the differences and similarities across all standards.

The SDTMIG and SENDIG are relatively unique in the world of CDISC standards in that the SDTM model underlies both implementations. Despite sharing the same model, and many of the same standard domains, the processes, terminology, and concepts that support these two implementations are often quite different. This paper focuses on the comparison of SEND vs. SDTM, in the context of Shire's implementation and processes, noting where they are exact reflections of each other and where they are decidedly not.

INTRODUCTION

The data reported by nonclinical and clinical research are submitted to regulatory agencies to bring new therapies to patients. United States (US) Food and Drug Administration (FDA) and Pharmaceuticals and Medical Devices Agency (PMDA) are the leading regulatory authorities that have developed tools to enable the acceptance of electronic study data using CDISC standards.

Clinical trials are research studies that explore whether a medical strategy, treatment, or device is safe and effective for humans. A nonclinical study is one of the many components of research that is required before human clinical trials may begin, and during which important feasibility, iterative testing, and drug safety data are collected.

FDA has Federal Food, Drug, and Cosmetic Act (FD&C Act), Section 745(a) and has signed the Food and Drug Administration Reauthorization Act (FDARA). This new law includes the reauthorization of the Prescription Drug User Fee Act (PDUFA) (2018-2022) which governs the requirement for data standards. PDUFA provides FDA with the necessary resources to maintain a predictable and efficient review process for human drug and biologic products. To support this effort, FDA Center for Biologics Evaluation and Research (CBER) and Center for Drug Evaluation and Research (CDER) have published FDA Data Standards Strategy (2018-2022) to reinforce the ongoing commitment to the development, implementation, and maintenance of a comprehensive data standards program that will facilitate the pre- and post-market regulatory review process. FDA has communicated these study data requirements to the industry on "FDA Study Data Resources" page that includes Data Standards Catalog (DSC), Study Data Technical Conformance Guide (TCG). The DSC lists the FDA acceptable standards, formats, and terminologies that are used to represent electronically submitted study data. The current version of the FDA DSC v5.0 lists the Study Data Tabulation Model (SDTM) and Standard for Exchange of Nonclinical Data (SEND) for clinical and nonclinical study data.

The Japanese cabinet passed the special corporation rationalization plan in December 2001 and enacted the PMDA Law in December 2002. At this time the PMDA started handling all consultation and review work from the preclinical stage to approvals and post-marketing surveillance. The PMDA has published their own requirements, similar to the FDA's DSC and TCG that provides the expectations of the study data. The current version of the PMDA DSC vMarch03, 2017 lists the expectation of SDTM for clinical data and has not yet listed SEND as a requirement for nonclinical data.

Shire has a Standards Governance framework that includes a Clinical Standards Board and Standards Governance Team for each of the CDISC Foundation standards, starting from data collection through to submission and Table, Figure and Listings (TFLs).

SDTM AND SEND:

The SDTM is the CDISC model that standardizes the organizing and formatting of collected data for submission. With SDTM as the underlying foundational model, consistent implementations of clinical and nonclinical concepts in a study can be delivered. Additionally, SDTM and SEND have Implementation Guides (SDTMIG and SENDIG) that

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provides guidance on these concepts. The importance of understanding these standards will aid the FDA Reviewers to discover common trends between the Common Technical Document (CTD) Nonclinical Module 4 and Clinical Module 5. By implementing the use of standards, the regulatory agencies reduce the review time by improving data review and analysis using tools that use standardized study data. This paper will discuss some of the critical concept similarities and differences between these standards.

AGENCY DELIVERABLES REQUIRED FOR SUBMISSION

The International Conference on Harmonization (ICH) Multi-disciplinary Group 2 (M2) Expert Working Group (EWG) was established in 1994. The EWG provided the recommendation to have requirements for Electronic Standards for the Transfer of Regulatory Information (ESTRI). The CTD is an internationally agreed upon format and structure for the preparation of investigational and new drug applications. The CTD became the mandatory format for new drug application submissions in US, EU, and Japan in 2003 with additional regions accepting submission in CTD format.

As technology and data standards advanced, agency acceptance of electronic submissions and Study Data expanded the requirements for submission. The table below represents the FDA and PMDA required study data documents when clinical and nonclinical study data are submitted to the agency based on the current versions of FDA Data Standards Catalog v5.0 and PMDA Data Standards Catalog vMarch 03, 2017. The implementations of SDTM and SEND should consider guidances based on the current version of FDA Study Data TSC v4.1, March 2018 and PMDA Study Data TSC vAugust 2016. Refer to the latest version of the agency's DSC for additional information on the version of the standard being accepted.

Table 1: FDA and PMDA deliverables for clinical and nonclinical

FDA	PMDA
CLINICAL: • SDTM Datasets v3.1.2, v3.1.3, v3.2 • Define XML 2.0 • aCRF.pdf • Study Data Reviewer's Guide (cSDRG) • ADaM Datasets v1.0, v1.1 • Define XML 2.0 • Analysis Data Reviewer's Guide (ADRG) NONCLINICAL: • SEND Datasets • Define XML 2.0 • Study Data Reviewer's Guide (nSDRG) • No ADaM datasets are required	CLINICAL • SDTM Datasets v3.2 • Define XML 2.0 • aCRF.pdf • Study Data Reviewer's Guide (cSDRG) • ADaM Datasets 1.0 • Define XML 2.0 • Analysis Data Reviewer's Guide (ADRG) NONCLINICAL: • SEND is not required

STUDY DATA STANDARDIZATION PLAN (SDSP):

FDA CDER-CBER has recommended sponsors to draft a Study Data Standardization Plan (SDSP) describing the submission of standardized study data to FDA for Clinical and Nonclinical studies within the development program. This assists the FDA in identifying potential data standardization issues early in the development program. Sponsors can initiate discussions at the pre-IND stage. For INDs, the SDSP should be located in the general investigational plan. Currently Pharmaceutical Users Software Exchange (PhUSE) has developed a SDSP template (available on the PhUSE Wiki site) by sponsors. The current version of FDA's Study Data TCG V4.1 suggests updates to the SDSP when the development program expands and additional studies are planned. The cover letter should describe the extent to which the latest version of the SDSP was executed. SDSP Appendix should be completed for submissions to CBER no later than end of Phase 2 meeting.

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SIMILARITIES AND DIFFERENCES:

There are various resources available to understand each CDISC foundational standard for nonclinical (SEND) and clinical (SDTM) studies. When using these standards in nonclinical and clinical studies, there are several factors that should be considered. The following factors are considered when starting a clinical trial:

- Process and Tools
- Controlled Terminology
- Domain Structure
- Trial Design
- Validation Checks

PROCESSES AND TOOLS:

The processes and tools used to deliver SDTM datasets for clinical studies and the roles and responsibilities are different from how the nonclinical studies are performed. For data collection, electronic data capture systems are used for both clinical and nonclinical studies.

In clinical studies, electronic data capture (EDC) databases are used to enter subject data which is then cleaned, reconciled, and then tabulated for analysis. When developing the EDC data capture screens, Clinical Data Acquisition Standards Harmonization (CDASH) concepts and CDISC Controlled Terminology are used to design them. This information along with external data is mapped to SDTM, and later to ADaM for analysis in submission. The collected data is saved in one electronic database that is tabulated and analyzed. To confirm conformance to the standard, CROs run the validation checks on SDTM and ADaM datasets for the creation of the clinical Study Data Reviewers Guide (cSDRG) and Analysis Data Reviewers Guide (ADRG). The below figure shows one of the implementations, stakeholders and roles and responsibilities for SDTM and ADaM deliverables

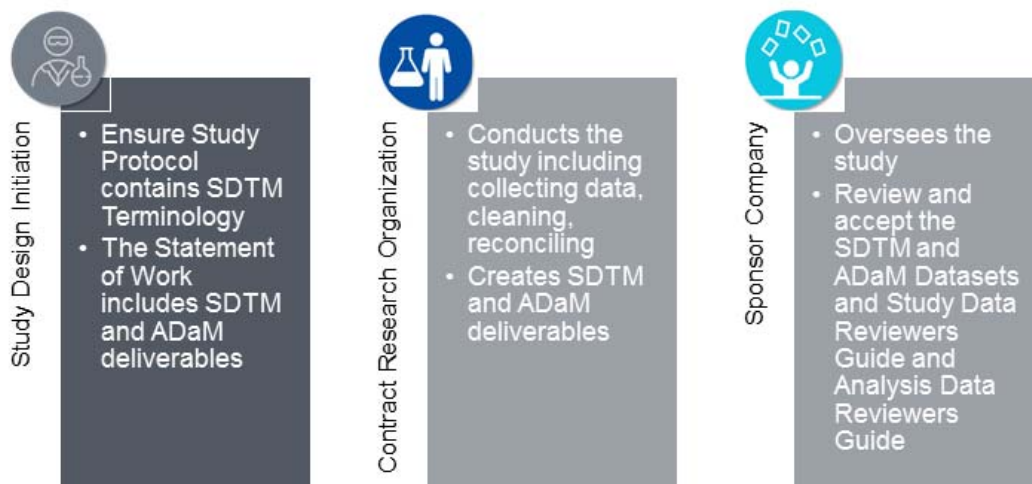


FIG: 1- ROLES AND RESPONSIBILITIES OF CLINICAL RESEARCH

In nonclinical, in-life electronic data record systems capture the macroscopic and microscopic clinical observations. The systems create reports and generate data tables. Most of these nonclinical systems have the capabilities to export the data in SAS export (XPT) format. There may be multiple data sources that have to be aggregated by the SEND data system. The Trial Summary dataset gets created by the main site for the study. In various instances, there may be multi-site study conduct, which then requires various domains to be provided and incorporated into the SEND dataset package. The SEND requirement has introduced new challenges to the industry. Organizations have engaged expertise (SEND vendor) to confirm the conformance to the standard by running the validation checks and creation of the nonclinical Study Data Reviewers Guide (nSDRG).

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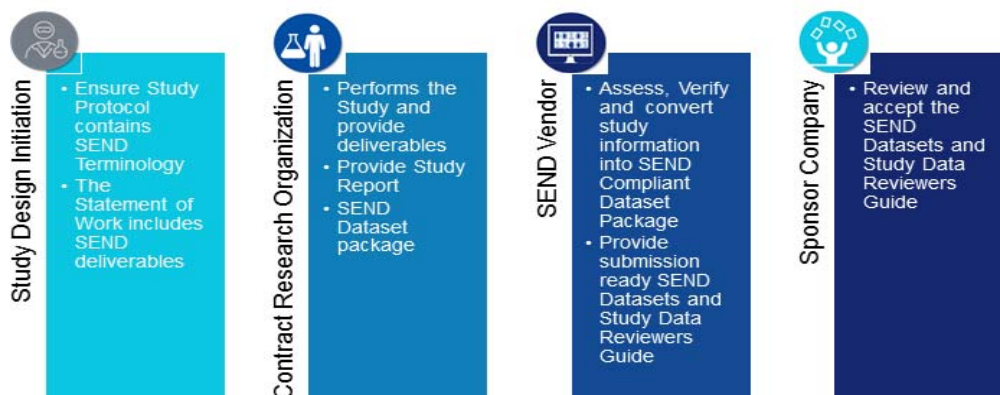


FIG: 2- ROLES AND RESPONSIBILITIES OF NONCLINICAL RESEARCH

CONTROLLED TERMINOLOGY:

Clinical Data Interchange Standards Consortium (CDISC) is a global, nonprofit charitable organization that develops data standards to streamline clinical research and enable connections to healthcare. NCI CDISC Controlled Terminology is the set of standard expressions (values) used with data items within CDISC-defined datasets and is used throughout the clinical research lifecycle, from data collection through analysis and submission.

International Harmonization of Nomenclature and Diagnostic Criteria (INHAND) is an international organization composed of toxicological pathology societies across the world. INHAND is developing terminologies by providing a standardized nomenclature for the findings in the nonclinical studies.

For nonclinical, a combination of both CDISC SEND Terminology and terminology developed by INHAND are used. For clinical studies, the protocol drafted and the Electronic Case Report Forms (eCRF) are aligned to the CDISC SDTM Terminology.

Using common terminology across clinical and nonclinical studies (Modules 4 and 5) will help to compare and visualize the data, although the published CDISC terminology is not always consistent between the two. For example, "Country" Codelist was available in the SDTM and has been retired but it still exists in SEND Terminology. There are also SEND and SDTM-specific needs that are represented as separate codelists and codelist terms.

For example when comparing the SDTM Controlled Terminology v2018-03-30 to SEND Controlled Terminology v2018-03-30:

- 34 codelists are common between SDTM V3.2 and SEND 3.1
- 18 codelists have similar codelist names but the code terms are specific to each standard

Table 2: Example of Common Codelist between SDTMv3.2 and SEND 3.1

Common Code	SDTM Codelist Name	SEND Codelist Name
C128683	PK Units of Measure - Weight kg	PK Units of Measure - Weight kg
C128684	PK Units of Measure - Weight g	PK Units of Measure - Weight g
C128685	PK Units of Measure - Dose mg	PK Units of Measure - Dose mg
C128686	PK Units of Measure - Dose ug	PK Units of Measure - Dose ug
C65047	Laboratory Test Code	Laboratory Test Code
C67154	Laboratory Test Name	Laboratory Test Name

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Table 3: Example of Different Codelists with similar codelist names between SDTMv3.2 and SEND 3.1

SEND Code	SDTM Code	SDTM Codelist Name	SEND Codelist Name
C120532	C101847	Cardiovascular Test Code	SEND Cardiovascular Test Code
C120533	C101846	Cardiovascular Test Name	SEND Cardiovascular Test Name
C111113	C66734	SDTM Domain Abbreviation	SEND Domain Abbreviation
C89974	C132263	SDTM Microscopic Findings Test Code	SEND Microscopic Findings Test Code
C89973	C132262	SDTM Microscopic Findings Test Name	SEND Microscopic Findings Test Name
C120534	C111106	Respiratory Test Code	SEND Respiratory Test Code
C120535	C111107	Respiratory Test Name	SEND Respiratory Test Name

DOMAINS STRUCTURE:

The SDTM is a standard structure for study data tabulations which are submitted as part of an investigational or marketing application to a regulatory authority. The SDTM supports multiple implementation guides (IG) such as SDTMIG and SENDIG. Currently, the implementation guides of SDTM and SEND are supported by different versions of the SDTM.

The development of the Implementation Guides over a period of time starting from the release of SDTMIG v3.2 is shown in Figure 3. It is worthwhile to note that SDTMIG-AP (Associated Persons) is based on SDTM 1.4. For the development of SDTMIG-MD (medical devices) most of the SDTM structure has been used in addition to creating the new special purpose domain, Device Identifier (DI) and new variables to support these concepts. As much as possible, the CDISC SDS teams take into account future needs before releasing the SDTM. For example as SEND 3.1 needed new variables, a new version of SDTM v1.5 was released (Figure 4). The SDTMIG-PGx (Pharmacogenomics) uses this model. For the development of therapeutic area standards, each user guide used SDTM and its implementations that were available at the time. Each user guide has a section "Relation to Other Standards" section that describes the SDTM and implementation guides used.

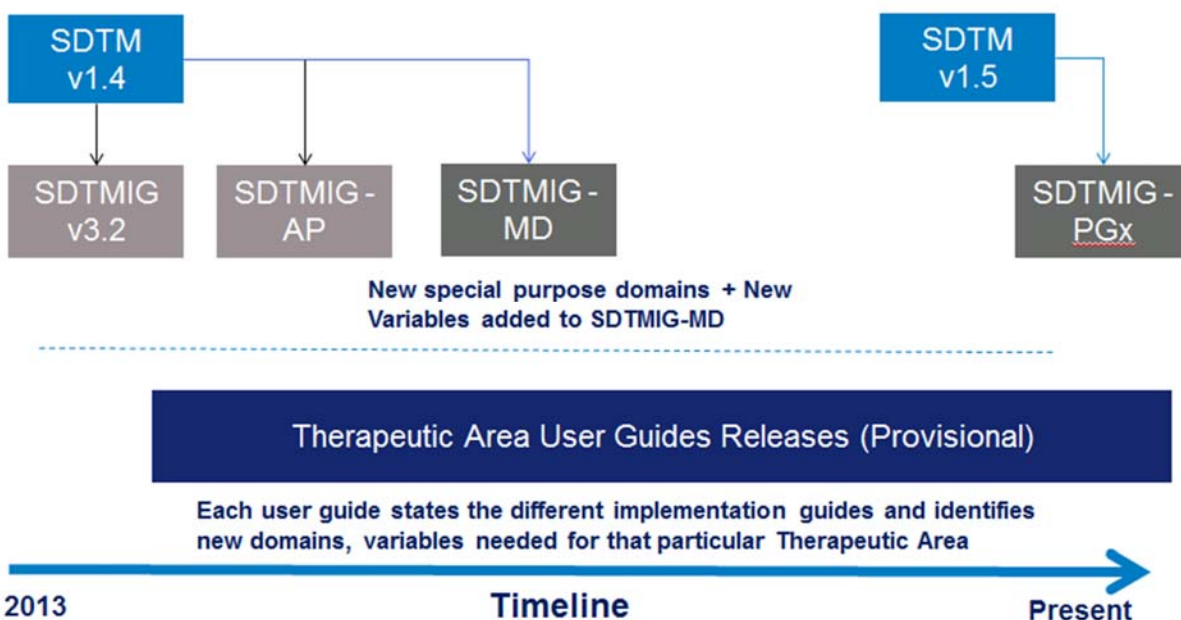


FIG 3: SDTMIG IMPLEMENTATION

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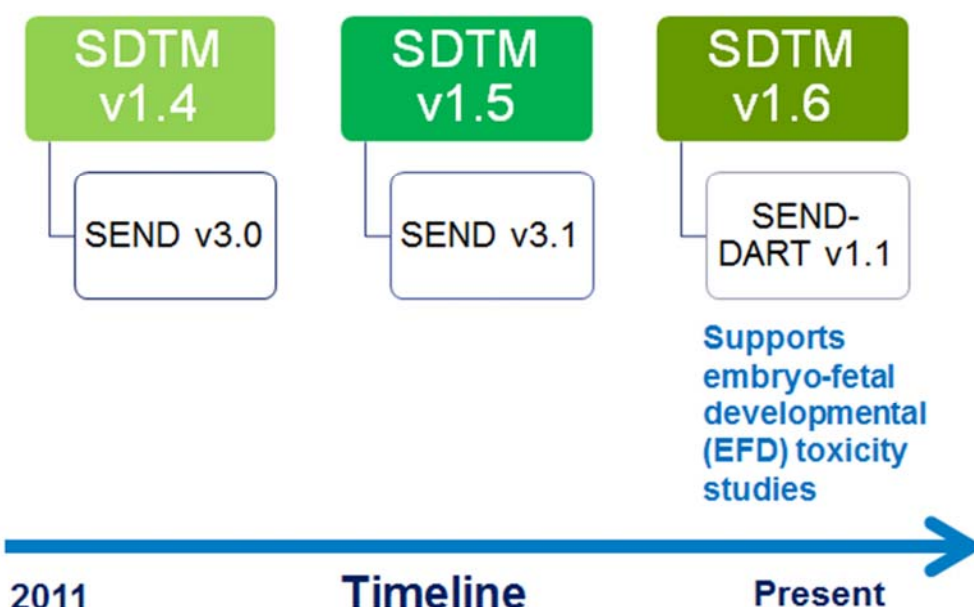


FIG 4: SEND IMPLEMENTATION

The SDTM and SEND implementations support different trial designs for clinical and nonclinical studies. For clinical trials, within a therapeutic area, CDISC has developed therapeutic area user guides that have added new new specific datasets as well as encompasses other datasets identified in the SDTMIG for the foundational standard, Medical Devices, Associated Persons and Pharmacogenomics . For nonclinical studies SEND is a way to collect and present data in a consistent way.

The inter-relational aspects of the two types of trials – clinical and nonclinical have an impact to the SDTM Model as the data representations are different. The nonclinical studies datasets identified for SEND v3.0 was based on the SDTM Model v1.4. As part of SEND 3.1, Safety Pharmacology studies needed new domains for Cardiovascular and Respiratory along with new domain variables that are based on the SDTM Model v1.5. The requirement for SEND continues to expand. Developmental and Reproductive Toxicology (DART) studies introduced new concepts and study data based on reproductive study phase and events. As new domains became required, a new implementation was released. The SENDIG-DART is based on and should be used in conjunction with SENDIG 3.1. The SENDIG-DART is in provisional phase as the implementatoin will depend on a future publication and release of SDTM.

Below is a brief description of the changes made to the SDTM Model v1.5. These variables are noted if they are not used for clinical-trials data (noted with an “N”), when unlikely (noted with an “U”), and others when it is potentially applicable to clinical as well as nonclinical data (noted with an “P”).

Table 4: List of New variables in SDTM v1.5

SDTM Table	Variable and Label	Used in Clinical Trial
Interventions	--USCHFL Unscheduled Flag	N
Events	--USCHFL Unscheduled Flag	N
Findings	--ORREF Reference Result in Original Units	P
	--STREFC Reference Result in Standard Format	P
	--STREFN Numeric Reference Result in Std Units Label	P
	--IMPLBL Implantation Site	N
	--CHRON Chronicity of Finding	P
	--DISTR Distribution Pattern of Finding	P
	--LOBXFL Last Observation Before	P

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SDTM Table	Variable and Label	Used in Clinical Trial
	Exposure Flag	
	--USCHFL Unscheduled Flag	N
	--REPNUM Repetition Number	P
Identifiers for All Classes	APID Associated Persons Identifier	Y
	FETUSID Fetus Identifier	N
	FOCID Focus of Study Specific Interest	P
	--RECID Invariant Record Identifier	P
TimingVariables	--NOMDY Nominal Study Day for Tabulations	N
	--NOMLBL Label for Nominal Study Day	N
	MIDS Disease Milestone Instance Name	P
	RELMIDS Temporal Relation to Milestone Instance	P
	MIDSDTC Disease Milestone Instance Date/Time	P
Subject Disease Milestones (new table)	One record per disease milestone per subject	Y
Domain-Specific Variables for the General Observation Class	Added variables to EX, EG and IC	Y
Trial Disease Milestones (new table)	One record per disease milestone	Y

Comparing the Implementation Guides for SDTMIG 3.2 and SENDIG 3.1

The general observational class domains are compared between the SDTM and SEND models:

- For Interventions general observational class models, in clinical studies, the concepts of Exposure as collected, Concomitant Medications, Procedures and Substance Use are relevant. Based on the nonclinical studies performed, only Exposure is used in SEND. Exposure is the only interventions general observational class domain common between the two models
- For Events general observational class models, in clinical studies, the subjects enrolled are tracked for adverse events, medical history, protocol deviations, clinical events and disposition. In nonclinical studies, the only Events domain used is the disposition to track when the animals left the study.
- For Findings general observational class models, in clinical studies, the subjects are observed to track their wellbeing for safety and efficacy assessments. In nonclinical studies, the anatomical findings are evaluated and are represented in the Macroscopic and Microscopic findings domains. The findings general observational class domains that are common are Vital Signs, Laboratory Test Results, and Microscopic findings.
 - o Importantly, the Morphology domain was added in SDTM aligning to the concept established in SEND. After real-world experience, CDISC found this to be more challenging in SDTM, and now the proposal is to move away from Morphology in future versions of SDTM, mapping data to body-system specific domain.
 - o The clinical interpretations between SDTM and SEND are the same except for the following:
 - For this to happen, concepts in the standards must be defined unambiguously. An example of where there has been noted confusion in the SDTM and SDTMIG is the variable, --LOC (Location). In Findings domains, --LOC can represent either a target location or a result location. Looking at the data it is difficult to know if it is a target location (e.g., chest, as in an x-ray), and a result location to report an abnormality in the left lung. The SENDIG defines the --LOC variable as always being related to the test; the same applies to --LAT (Laterality), and --DIR (Directionality). If more detail is needed for results, additional variables will be created. Names such as --RESLOC (Result Location), --RESLAT (Result Laterality), and --RESDIR (Result Directionality) have been suggested, but no action has been taken for the SENDIG v3.1 or for the SDTM 1.5.
- For Special Purpose domains,
 - o The clinical studies use the Subject Visits (SV), Trial Visits (TV) domains that are not part of the SEND 3.1. There are timing variables used in SEND 3.1 such as --NOMDY (Nominal Study Day) that are used instead of using the --VISITDY.
 - o The POOLDEF table appears in the SENDIG 3.1 and not in the SDTMIG. The POOLDEF allows for

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- identifying the individual animals that contribute to data collected within a group
- o Trial Sets (TX) appears only in SENDIG 3.1 where it allows for subsets of animals within an Arm or grouping multiple arms. In clinical studies, Inclusion/Exclusion and subject Characteristics together can be used to group subjects within an arm.
- o Related Records are identified using RELREC. In SDTMIG, RELREC is used to represent relationships across two or more datasets. In SENDIG, the relationships are needed to relate the in-life observation to other findings such as macroscopic findings. In SEND, there is a need to use permissible variable of POOLID versus using USUBJID and VISIT in SDTMIG.

The below figure represents the comparison of the SDTM 3.2 domains with SEND 3.1 model:

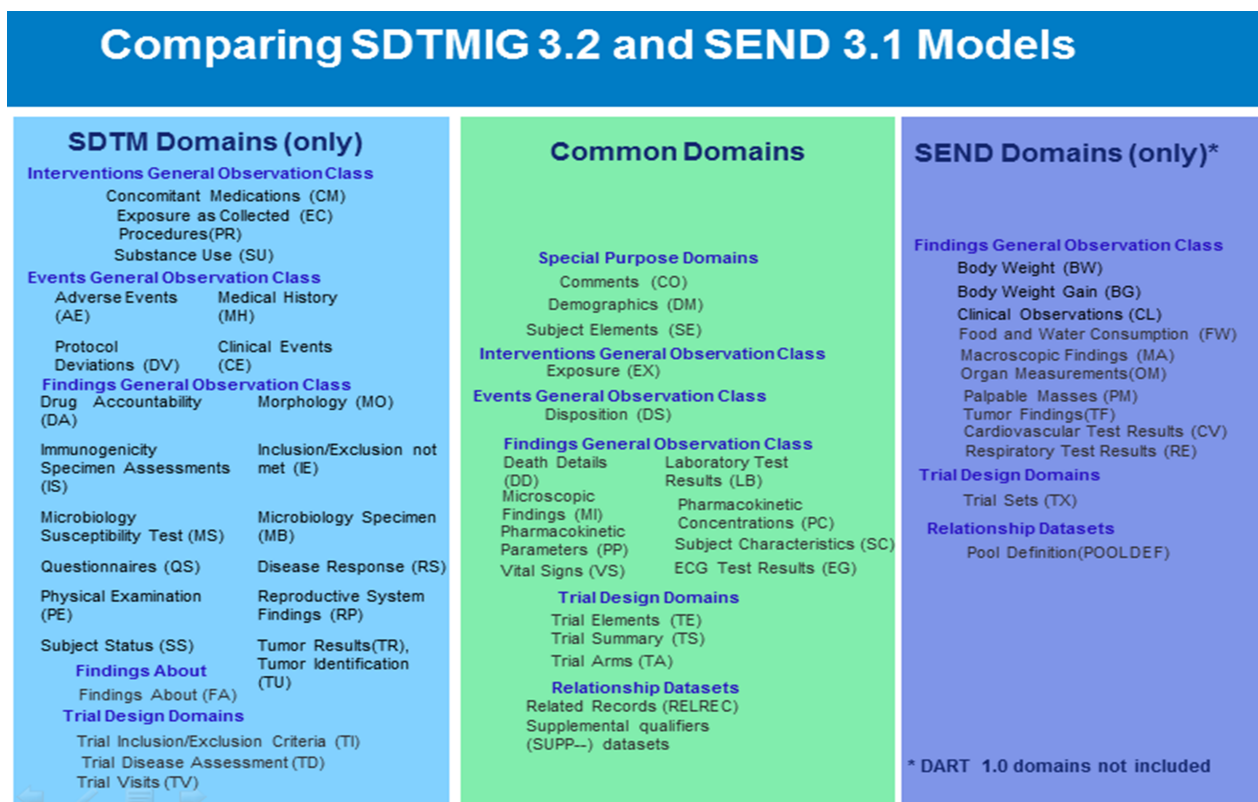


FIG 5: COMPARISON BETWEEN CDISC STANDARDS – SDTM AND SEND

TRIAL DESIGN:

For clinical studies, all the trial design domains are used except for Trial Sets (TX). SEND does not use the Trial Visits (TV), Trial Inclusion/Exclusion Criteria (TI) since the screening of animals requires the documentation of inclusion/exclusion exceptions and uses the Trial Arms (TA), Trial Elements (TE) and Trial Summary (TS) in the same way as SDTMIG.

The Trial Design Model includes Trial Arms (TA), Trial Elements (TE), Trial Visit (TV), Trial Inclusion/Exclusion Criteria (TI), Trial Summary (TS), and Trial Disease Assessment (TD). FDA has provided guidance in section 4.1.1.3 of the Study Data TCG V5.0 that states, "The Trial Summary (TS) dataset will be used to determine the time of study start. The requirement to submit using a particular study data standard is dependent on its support by FDA as listed in the Catalog at the time of study start. TSPARMCD = SSTDTC will allow the determination of the study start date and should be included in all SDTM submissions. Sponsors submitting legacy data (See section 8.3.2) should provide a TS dataset (ts.xpt) which includes the study start date in the form of SSTDTC (TSPARMCD = SSTDTC) and TSVAL= 'yyyy-mm-dd'."

This above statement from the FDA TCG V5.0 shows the TS domain is needed for all studies including the legacy studies for both Clinical and Nonclinical studies. FDA has also announced the addition of Technical Rejection Criteria to the existing eCTD validation criteria to ensure Study Data Conformance Validation. There are 4 primary checks run by the FDA's Technical Validation process. One of the eCTD Data validation checks is "Trial Summary (TS) dataset must be presented for each study in Module 4 or 5". Refer to [FDA Technical Rejection Criteria](#) for more information. The FDA does not wish to give Refuse to File (RTF)/Refuse to Receive (RTR) for this type of conformance issue. The Technical Rejection Category gives the FDA the ability to reject based on non-compliance to standards, and gives the sponsor the ability to correct and re-submit the data.

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VALIDATION CHECKS:

The validation checks defined check the conformance to the CDISC Model. The validator tools can be used to check compliance with a range of CDISC standards such as SDTM, SEND, ADaM, and Define.xml as well as any regulatory agency published business rules for submission data. A validation report generated produces the results of validation and is rendered in different formats and contains issue messages, descriptions, and details of data records that failed validation. Software companies such as Pinnacle21 and XML4Pharma implement these checks into their tools. Before sending the datasets to the Sponsor, the validator tool is executed and a validation report is generated. As a general rule, any validation findings should be explained in the Study Data Reviewers Guide.

FDA has released their updated Business Rules v1.2 in December 2017 that identifies specific rules for SENDIG 3.0 and SDTMIG 3.2. There are no rules identified for SENDIG 3.1 at this time.

PMDA has also released their Study Data Validation Rules in Nov 2015 that identifies rules specific to SDTM v3.2, ADaM 1.0 and Define 2.0. The validator tools implementing these rules can provide validation messages with statuses of "Error", "Warning" and "Reject". PMDA has also not published their Business and Validation Rules for SENDIG 3.1.

Software companies such as Pinnacle21 have validator tool that implements SEND validation checks are identified by Pinnacle21ID and FDA ID that are specific to SENDIG 3.0. The tool does not support SENDIG 3.1 yet and will have to be updated to support SENDIG 3.1.

The CDISC SDTM team has released conformance rules that are specific to SDTMIG v3.2. There are no validation tools available that implement these rules as yet. Sponsor companies or CROs will have to implement these in their environment to check for conformance. Currently CDISC SEND team has not published conformance rules defined for SENDIG. They are working to release a new set of conformance rules defined for SENDIG 3.0 and 3.1.

BEST PRACTICES:

Following are the best practice solutions that support implementing different standards and provide an integrated view:

- Keep track of the commonly released agency documents. This includes understanding what constitutes a requirement versus what is guidance.
- Volunteer in CDISC and/or PhUSE groups to learn and collaborate on how to handle such changes.
- Collaborate with groups or SMEs who support delivery of standardized data on clinical studies to understand the intricacies of the model and implementations.
- At Shire, we established a Data Standards Governance Model to provide a cross-functional forum for discussing some of the specific needs and how this can be handled.
- Keep track of the commonly released CDISC Implementation Guides (IGs) and related documents. This includes understanding the disease metadata and domains associated with it.
- Attend webinars to learn about the changes which are not always clear from an end-user's perspective. For example, a User Group webinar discussed the IGs for the CDISC SDTM (clinical) and SEND (nonclinical) standards are based on a common model, SDTM. The different IG documents are linked to distinct SDTM model documents as follows:
 - o Both the SDTMIG v3.2 and the CDISC non-clinical standard SENDIG v3.0 are associated with the SDTM Model, version 1.4.
 - o When the next version of nonclinical Standards SEND was developed (SENDIG v3.1), the SDTM model was extended, and released as version 1.5.
 - o Subsequently, the CDISC SEND DART was released (SENDIG-DART provisional), further extending the SDTM Model, and was released as version 1.6.
 - o The industry is waiting for the release of next version of SDTMIG 3.3, which will be anchored in the SDTM Model, version 1.7.
- We have found that having a Data Standards Governance Model helps to propagate throughout the organization some of the challenges discussed in industry forums (e.g., CDISC and PhUSE).
- Understand external CRO partner and vendor capability and how they affect the submission-ready packages creation. Ensure proper oversight capabilities are in place to ensure quality and timing of the deliverables.

FUTURE:

As mentioned earlier, FDA and PMDA are requiring sponsors to submit standardized data in electronic format. This requirement is communicated to the industry specifically in the Data Standards Catalog, as well as in the FDA's Study Data Technical Conformance Guide. The use of the standardized data for both Clinical and Nonclinical studies supports integrated data review using review tools within the agency environment. FDA is working to make the

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Technical Rejection Criteria required to validate the submitted standardized data. FDA has communicated their needs to the industry and provided the severity of these data conformance checks.

Legacy nonclinical studies have been submitting study reports as PDF. The legacy data is contained within the PDF. Converting legacy data into SEND format can be quite costly and challenging. Organizations continue to learn processes for creating standardized study data for nonclinical studies. A standard practice that should be expanded would be for clinical and nonclinical Subject Matter Experts (SMEs) to collaborate and align with common terminology, domains, and internal standards and practices.

With respect to the CDISC SDTM team, they are planning to release the next version of the SDTM 3.3 that uses the SDTM v1.7.

CONCLUSION:

This paper discusses items to consider when planning and creating a standardized data packages for clinical and nonclinical studies. Understanding the agency requirements for data standards helps facilitate the regulatory review which provides organizations to have efficient processes that support the submission of the electronic study data. Organizations face day to day challenges when there are no processes and personnel that support and understand the submission of electronic study data specifications and requirements. The changing landscape of CDISC, agency requirements, and internal company needs, along with having a robust Data Standards Governance process, supports overall standards development and helps to ensure quality data submissions.

As SEND is fairly new requirement to the industry and organizations have started to create new processes to support this requirement. It is helpful to collaborate with clinical teams as clinical teams have been submitting standardized study data (SDTM) since 2004. Understanding similarities and differences in processes, tools, controlled terminology, domain structure, trial designs and implementation guides between clinical standard (SDTM) and nonclinical (SEND) is beneficial to both clinical and nonclinical teams within organizations since the personnel with the knowledge of clinical standards can support/mentor teams that oversee the nonclinical deliverables. This collaboration also builds a supporting culture and platform to share questions and experiences on topics such as using controlled terminology, domain structure, implementation guides, validation reports and study data reviewers guide and understand the impact of changes due to CDISC and agency.

As additional regions such as Japan accept electronic submissions, regulatory authorities have data standards roadmap and strategy to reinforce their commitment to expand their knowledge and capabilities of accepting and evaluating electronic standardized study data. It is critical for organizations to build processes that are lean and adaptable to this changing landscape which can support global standardized study data submissions. Submission of electronic data allows reviewers to look for common trends and themes across various drugs. By having a consistent format and standard within the nonclinical and clinical modules, regulatory agencies could reduce the duration of their reviews.

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- Providing Regulatory Submissions in Electronic Format — Submissions Under Section 745A(a) of the Federal Food, Drug, and Cosmetic Act (December 2014)
<http://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/UCM384686.pdf>
- Providing Regulatory Submissions In Electronic Format — Standardized Study Data (December 2014)
<http://www.fda.gov/ucm/groups/fdagov-public/@fdagov-drugs-gen/documents/document/ucm292334.pdf>
- FDA Technical Rejection Criteria
<https://www.fda.gov/downloads/Drugs/DevelopmentApprovalProcess/FormsSubmissionRequirements/ElectronicSubmissions/UCM523539.pdf>
- PMDA –Office of Advanced Evaluation with Electronic Data <https://www.pmda.go.jp/english/review-services/reviews/advanced-efforts/0002.html>
- PMDA Data Standards Catalog (English) published March 03, 2017
<https://www.pmda.go.jp/files/000216763.zip>
- PMDA Study Data Technical Conformance Guide (English) PMDA/AREDPG Notification No. 0630001; published on June 30, 2016, Notification No. 0824001; published on August 24, 2016
<https://www.pmda.go.jp/files/000215100.pdf>
- PMDA Study Data Validation Rules published 18 Nov 2015 <https://www.pmda.go.jp/files/000208341.zip>

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