Introduction to SEND

What is SEND?
CDISC SEND is the Clinical Data Interchange Standards Consortium Standard for Exchange of Nonclinical Data, an FDA standard data format/terminology that will soon be required for submission of preclinical study data to the FDA.

Scope of SEND
SEND is defined in the SEND Implementation Guide (SENDIG) and supports single-dose general toxicology, repeat-dose general toxicology, and carcinogenicity studies. At this time, safety pharmacology and reproductive toxicology study data is exempt from SEND 3.0, but will be included in future mandates.

What Does SEND 3.0 Encompass?
The SENDIG is intended to guide the industry about the structure, organization, and format of standard nonclinical tabulation datasets for exchange between organizations (e.g., sponsors and CROs) and for submission to the FDA. The SENDIG is based on the CDISC Study Data Tabulation Model (SDTM) for clinical data.

The goal of SEND
SEND seeks to increase efficiency and the quality of scientific review by the Center for Drug Evaluation and Research (CDER) pharmacologists and toxicologists, and to improve communication between the US Food and Drug Administration (FDA) and the industry. The ultimate goal is to phase out paper submissions.
What does SEND 3.0 cover?

**Datasets**

- Body weight (BW)
- Body weight gain (BG)
- Clinical observations (CL)
- Comments (CO)
- Death diagnosis (DD)
- Demographics
- Disposition (DS)
- ECG test results (EG)
- Exposure (EX)
- Food and water consumption (FW)
- Laboratory test results (LB)
- Macroscopic findings (MA)
- Microscopic findings (MI)
- Organ measurement (OM)
- Palpable masses (PM)
- Pharmacokinetic concentrations (PC)
- Pharmacokinetic parameters (PP)
- POOLDEF
- RELREC
- Subject characteristics
- Subject elements
- SUPP—
- Trial arms (TA)
- Trial elements (TE)
- Trial sets (TX)
- Trial summary (TS)
- Tumor findings (TF)
- Vital Signs (VS)
What does SEND look like?

How extensive is SEND data?
A six-month study in rats with four weeks of recovery: The LB (clinpath) domain contains approximately 18 columns and 36,000 rows of data. The graphic displays an example of what the “Body Weight” domain may look like.
Benefits of SEND

As an evolving standard – and one with several challenges to address before the industry can fully meet requirements – it may take some time for both the FDA and the industry to fully realize SEND benefits. There are no promises, but the SEND Consortium hopes to achieve:

**FDA**
- Standard mechanism for review of data
- Comparative and more in-depth analysis of data
- Harmonized terminology

**Industry**
- Standard format and delivery mechanism
- Efficient interactions with both vendors and regulators
- Faster time to market; for a blockbuster drug, this could be significant
“For many years sponsors and applicants have been submitting electronically using the electronic common technical document format and have included electronic study data in both legacy and standardized formats.

For some sponsors and applicants there may be new costs, including capital costs or operating and maintenance costs, which would result from the requirements under FDASIA and guidance, because some sponsors and applicants would have to change from submissions that have included legacy (non-standard) study data to submissions in compliance with the final guidance.”

The FDA estimates that the costs for some sponsors and applicants may be as follows:

- **Training**: $100,000-$250,000
- **Initial data management operations**: $500,000-$1,000,000
- **Data management (hardware/software)**: $350,000-$1,000,000

Excerpt from Final Guidance
The Prescription Drug User Fee Act (PDUFA) V Timeline for SEND 3.0 Compliance

- **February, 2014**: Publish Draft Guidance
- **May, 2014**: Public Comment Period (90 days)
- **December 17, 2014**: Final Guidance Published
- **Studies starting on or after December 18, 2016**: NDA/ANDA and Certain BLA Submissions MUST Comply
- **Studies starting on or after December 18, 2017**: IND Submissions MUST Comply
Industry Challenges

This is new to the industry.

Any extensive process change requires support, and companies facing the new SEND requirements have varying levels of knowledge. It will take time as they adapt to system modifications, process changes, new lexicons, and the increase in electronic data collection.

SEND software is in its infancy

As technology advances, new versions will continue to evolve at a rapid pace in order to ensure customers are compliant when the deadline hits.

Merging data from several sources

Merging data from multiple sources can be a challenge, especially when tools to do so are only starting to come on the market. Vendors differ in their ability to produce SEND files, making it difficult for companies to select a provider that meets their needs.

SEND is an evolving standard

Current SEND requirements are extensive, and still evolving. As future versions are developed, we can anticipate the inclusion of reproductive toxicology (embryo-fetal development) and safety pharmacology data in this new standard.
Creating SEND Files

The process of creating SEND files presents its own challenges. Data generated from several internal and vendor-based sources can vary in quality, completeness and readiness for submission.

This is compounded if gaps exist in the population of the original data source. In addition, the current lack of automation tools for some datasets requires the manual population of data, which can be a time-consuming process. In the future, the introduction of new technologies will continue to address these difficulties.
Summary

SEND data will be required of all studies within scope in 2016/2017.

All sponsor companies are ultimately responsible for the submission of SEND datasets. Submission of the SEND datasets to the FDA cannot be performed by the CRO or any other external body. The sponsor should have the ability to receive, review, submit and archive the SEND data; yet, pharmaceutical companies vary in their readiness to meet these mandates.

This new standard will require much effort to adopt, but once SEND becomes mainstream, its benefits will become apparent. The initial investment in SEND technologies and training promise to deliver long-term benefits to the industry as a whole, offering an improved FDA approval process.

With decades of experience and a commitment to providing comprehensive regulatory support, Charles River has made such an investment, and will continue to do so. Our involvement with the SEND initiative dates back to 2007, and has only grown since then.

Most recently, Charles River completed the validation of our SEND suite to produce SEND data for all in-scope studies conducted using our global data capture system. Throughout the course of this validation, we have been piloting SEND data with our sponsors to test the datasets and processes. As we move forward, Charles River clients can continue to rely on our regulatory expertise and guidance through ever-changing requirements.
Resources

Click on the links below for additional resources and contact information.

- SEND Implementation Guide (IG)
- CDISC Controlled Terminology
- FDA Study Data Standards Resources
- FDA Federal Register Notice
- Study Data Standards for Submission to CDER
- PhUSE - Non-Clinical Road-map and Impacts on Implementation
- PhUSE - SEND Implementation Wiki
- Questions and General Information Regarding Preparation of Submissions - CDER
- Questions and General Information Regarding Preparation of Submissions - CBER
- Questions Regarding Submission of Datasets to CDER
- FDA Electronic Regulatory Submission and Review