

Scenarios for Generating SEND Datasets from Nonclinical Safety Studies Conducted across Multiple Organizations

Introduction

The FDA is expected to issue draft guidance in 2013 that addresses standardized submissions of nonclinical data in SEND (Standard for the Exchange of Nonclinical Data) format as part of pharmaceutical drug applications. The SEND standard is published by CDISC in the SEND Implementation Guide version 3.0 (SENDIGv3; <http://www.cdisc.org/send>). The FDA may provide additional expectations in its Study Data Specifications guide for electronic submissions. The Interorganizational SEND project (I-SEND) within Working Group 6 (Nonclinical Roadmap and Impacts on Implementation) of the FDA/PhUSE collaboration has focused its efforts since March 2012 on identifying needs for the assembly and flow of information exchange to generate CDISC SEND datasets across organizations to meet the pending regulatory requirement.

Addressing these needs in a precompetitive, collaborative manner is important given the increased trend towards nonclinical study outsourcing by sponsors and the prevalence of studies where different organizations conduct different parts of a study. This multi-organizational execution of inter-related parts of a study leads to challenges in data stewardship and the exchange of data destined for SEND submissions. The I-SEND project approached these challenges by developing use-case scenarios incorporating data and process flows identified through collaborative sessions among representatives from CROs, Sponsors and Informatics/Data Management Vendors.

Use Case Scenarios

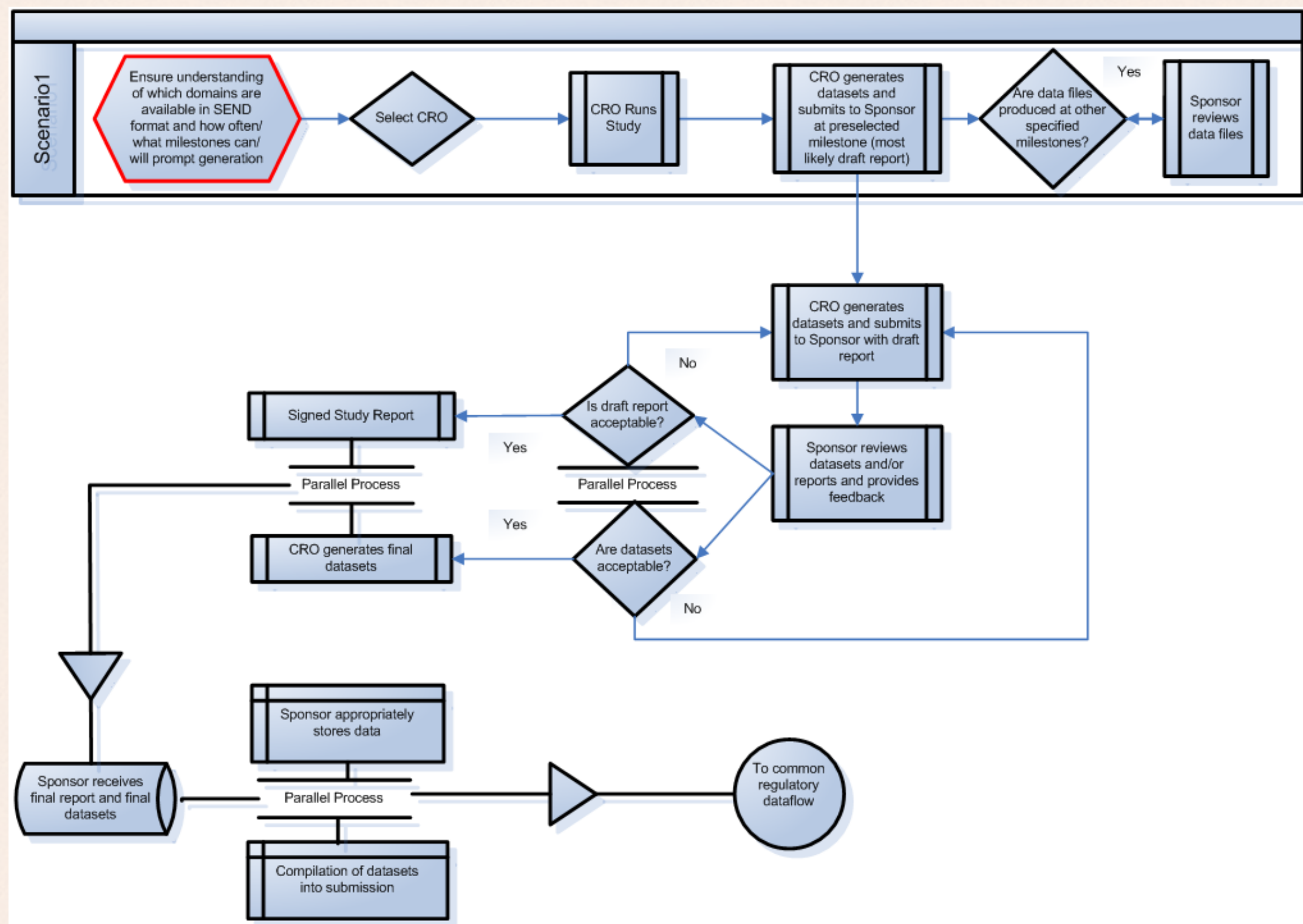
One of the first tasks for the I-SEND group was to develop a framework for describing, classifying and prioritizing scenarios for aggregating data across multiple sources. Secondly, to drill down into details of practical workflows, it was necessary to select a few example scenarios. Three such use case scenarios likely to occur in practice were selected for further definition and are shown in the flow charts below. For each scenario, data flows and processes showing inter-organizational transfer of control and the chain of data custody were identified as shown. All the scenarios culminate in a common regulatory data flow to the FDA and back to the Sponsor/CRO where necessary. Each scenario is depicted as a process diagram summarizing the likely sequence of activities including study start-up, data flows within an organization and between organizations, reviews, and decision gates. At each of these gates, options are indicated for both success and failure conditions. Each scenario is accompanied by assumptions, as well as recommendations on topics and questions that participating organizations may wish to clarify during study initiation and across its lifecycle. It is important to point out that the inter-organizational workflows described are examples of how specific activities might occur in practice, and are not intended to be prescriptive. It will be up to each sponsor and CRO to define their specific use cases, and consider additional controls and steps that they may wish to implement.

Scenario 1: CRO Study with SEND Dataset Fully Assembled by CRO

➤ A clear understanding of deliverables, limitations, milestones, and timing should be established before study initiation including:

- Impacts on the Study Data Plan
- Final and Interim Domains
- SEND Validation Status
- Which version of the SENDIG
- Which version of the Controlled Terminology (CT)
- The SEND Validator to be used
- Will data be provided at multiple milestones? How often and in what format
- Will the Define file be created by CRO or by Sponsor
- Will final signoffs be done by the Study Director

- Consider GLP and systems validation controls for quality assurance of datasets, especially:
 - at ownership-transfer points
 - if it is a legacy data conversion

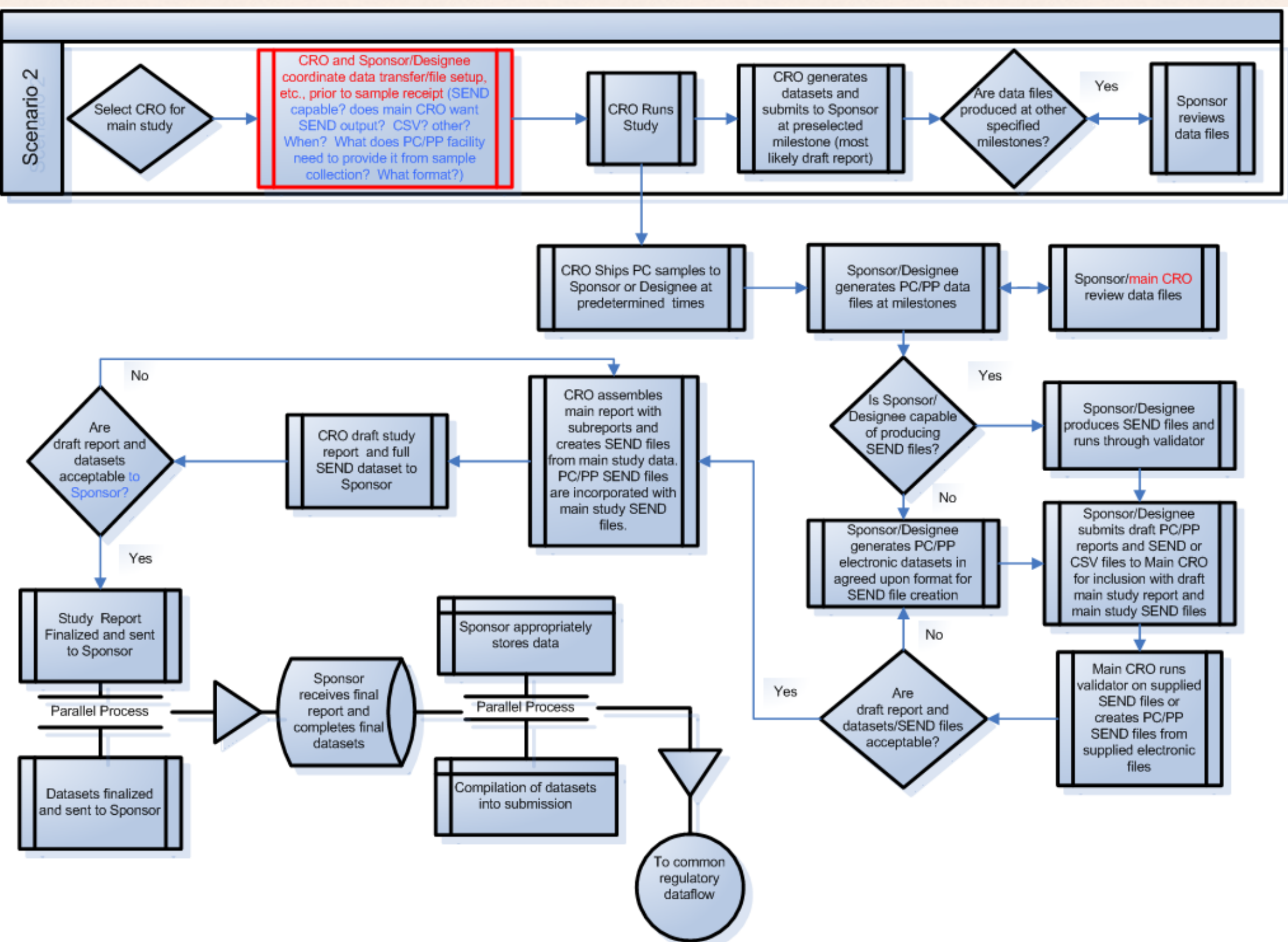


Scenario 2: A CRO generating SEND datasets for a study with the Sponsor or its designee providing PK/TK data

➤ In addition to topics identified under Scenario 1, the following items relating to data transfer should be considered prior to study initiation:

- File formats to be supplied to main CRO (SEND, ASCII, Excel, XML, ...)
- Metadata that the main CRO must provide for designee(s) to complete study set up and SEND file creation
- Multiple SEND validation steps needed for 2nd CRO SEND files
- Who will signoff on the datasets and at what point in the process

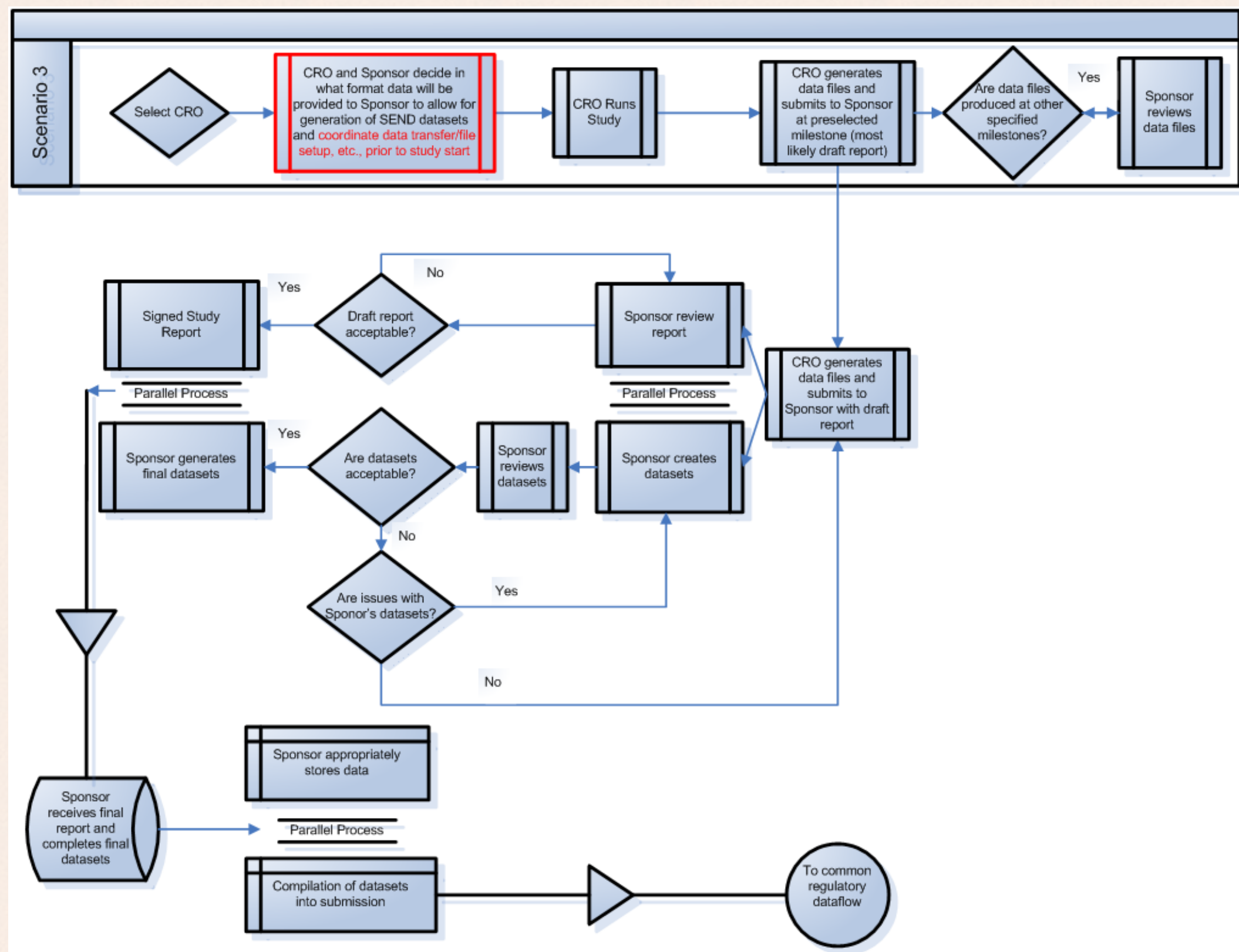
- The Process flow will repeat for each source supplying data



Scenario 3: CRO Study with SEND Dataset Fully Assembled by Sponsor

➤ In addition to topics identified under Scenario 1, the following items relating to data transfer should be considered prior to study initiation:

- File formats the CRO will use to transmit data (SEND, ASCII, Excel, XML, ...)
- Metadata that the CRO provides the Sponsor to complete Study setup and SEND file creation
- Who will signoff on the final package



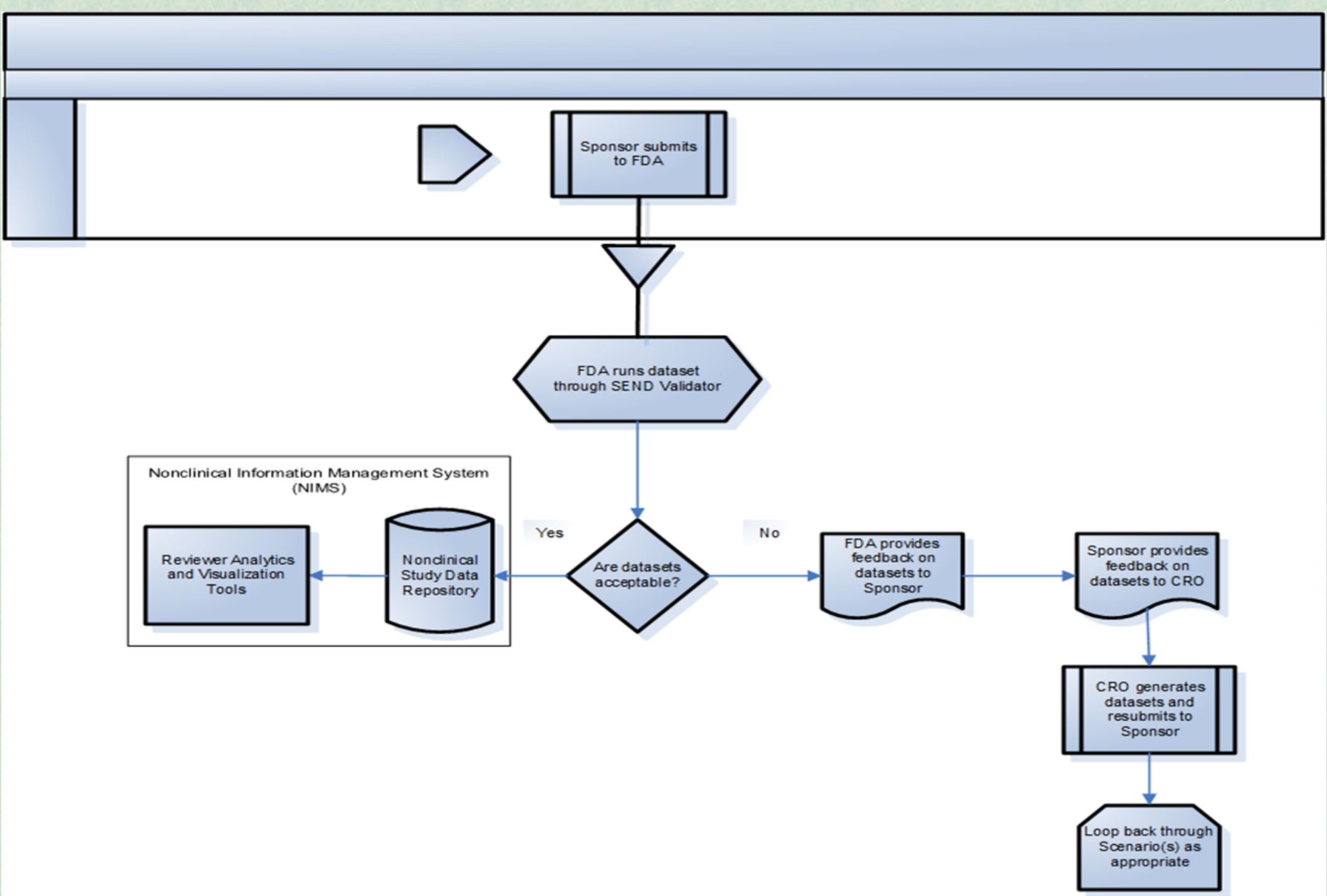
Common Regulatory Data Flow for All Scenarios

➤ Steps involved in processing SEND datasets may differ by FDA Division. The following steps are anticipated:

- Datasets will be validated for conformance with SEND and Study Data Specifications upon receipt by FDA..
- Submissions that pass SEND validation are released for use by assigned FDA reviewers

- Error correction will be performed by the organization responsible for creation of the original datasets and will trigger recycling through steps for dataset creation, review and resubmission as needed.

- For CDER submissions, a test submission process is available to “pre-validate” datasets before regulatory submission



Note: The flow diagram depicted in this figure applies to CDER e-data submissions which flow into the Agency's NIMS environment consisting of a repository, analytics and visualization tools.

Summary and Conclusions

The I-SEND team has been successful in recruiting participation from CROs, Sponsors and informatics vendors that represent a broad spectrum of expertise and experience, and that have forged an effective collaboration over the past year.

The results of the work conducted by the I-SEND team suggest that data flow and process modeling through real world use case scenarios are a powerful way to identify common issues and responsibilities for multiple organizations participating in the conduct of a study and in the preparation of submission ready datasets. Use case scenarios developed collaboratively with inputs from various stakeholders can play an important role in developing a common understanding of data management, business process management and review needs, and help uncover new requirements for SEND implementation solutions. Interactions among the I-SEND participants clearly demonstrated that individual organizations may approach a SEND implementation differently. Use cases can help identify key issues that must be addressed prior to launching a study or implementing SEND solutions particularly when multiple organizations are involved in conducting parts of a study, and in generating and assembling associated datasets.

The I-SEND subgroup anticipates that future collaboration will focus on testing of the use cases presented herein with role playing by CROs and Sponsors jointly preparing real datasets. We also anticipate that this effort will expand into scenario modeling and testing of other, more complex data assembly and exchange situations involving multiple CROs and a Sponsor. This collaborative work is expected to contribute valuable and practical knowledge that can be widely used by the Biopharma industry impacted by the upcoming FDA mandates for SEND submissions, and by organizations looking to implement solutions for effective exchange of nonclinical study data generated in an inter-organizational setting to drive productivity and scientific gains.

Acknowledgements: Shree Nath, PointCross Life Sciences, Inc, Foster City, CA; William Houser, Bristol Myers Squibb, Mt Vernon, IN; Debra Oetzman, Covance Laboratories, Inc, Madison, WI; Kathryn Brown, Sanofi US, INC, Bridgewater, NJ; Jeff Foy, Celgene, Summit, NJ; Lynda Sands, GlaxoSmithKline, King of Prussia, PA; Troy Smyrniotis, MPI Research, Mattawan, MI; Peggy Zorn, INDS, Inc, Ann Arbor, MI; Jyotsna Kasturi, Janssen Pharmaceutical Companies of Johnson & Johnson, Raritan, NJ; Susan DeHaven, Sanofi US, INC, Bridgewater, NJ

Note: The opinions expressed in this poster are those of the authors and do not necessarily represent the opinions of their respective companies.