

SEND Datasets from Studies Conducted at Multiple Organizations:

An Update based on Current Practices

Interorganizational SEND

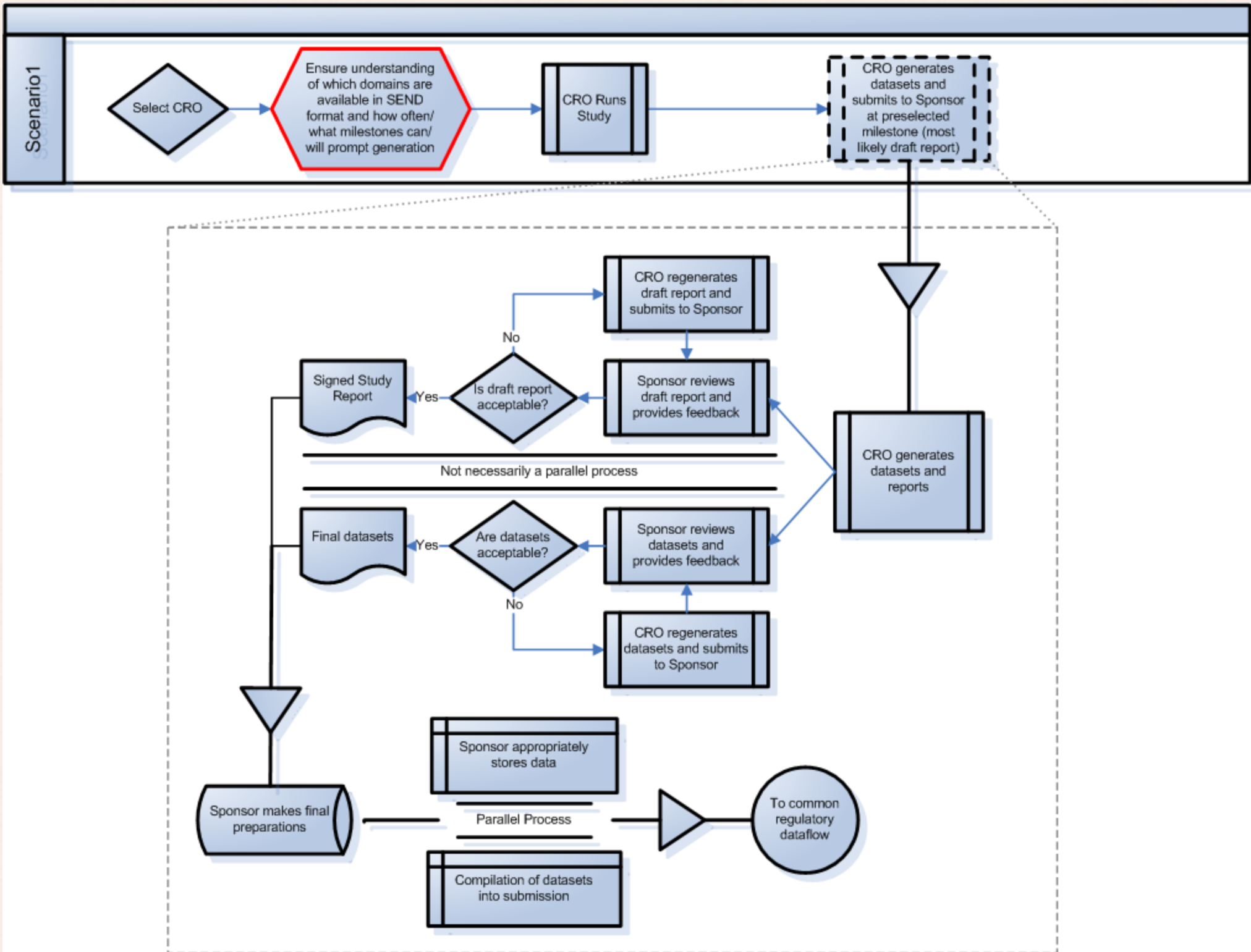
Introduction

The FDA is expected to finalize guidance 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 Interorganizational SEND project (I-SEND) within Working Group 6 (Nonclinical Roadmap and Impacts on Implementation) 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 (i.e. sponsors and CRO(s)) to meet the pending regulatory requirement.

Initially (2013 PhUSE Computational Science Symposium), the I-SEND developed 3 use-case scenarios incorporating data and process flows identified through collaborative sessions among representatives from CROs, Sponsors and Informatics/Data Management Vendors. These scenarios were developed with ‘best practices’ in mind. In the past 12 months, informal surveys regarding how SEND files are actually generated were conducted, with the scenarios being updated to reflect the processes as they currently occur, versus the more ideal processes described previously. These updated scenarios demonstrate where sponsors and CROs need to actively work through the fine details for minimizing delays and developing SEND files that are suitable for submission and for interim uses.

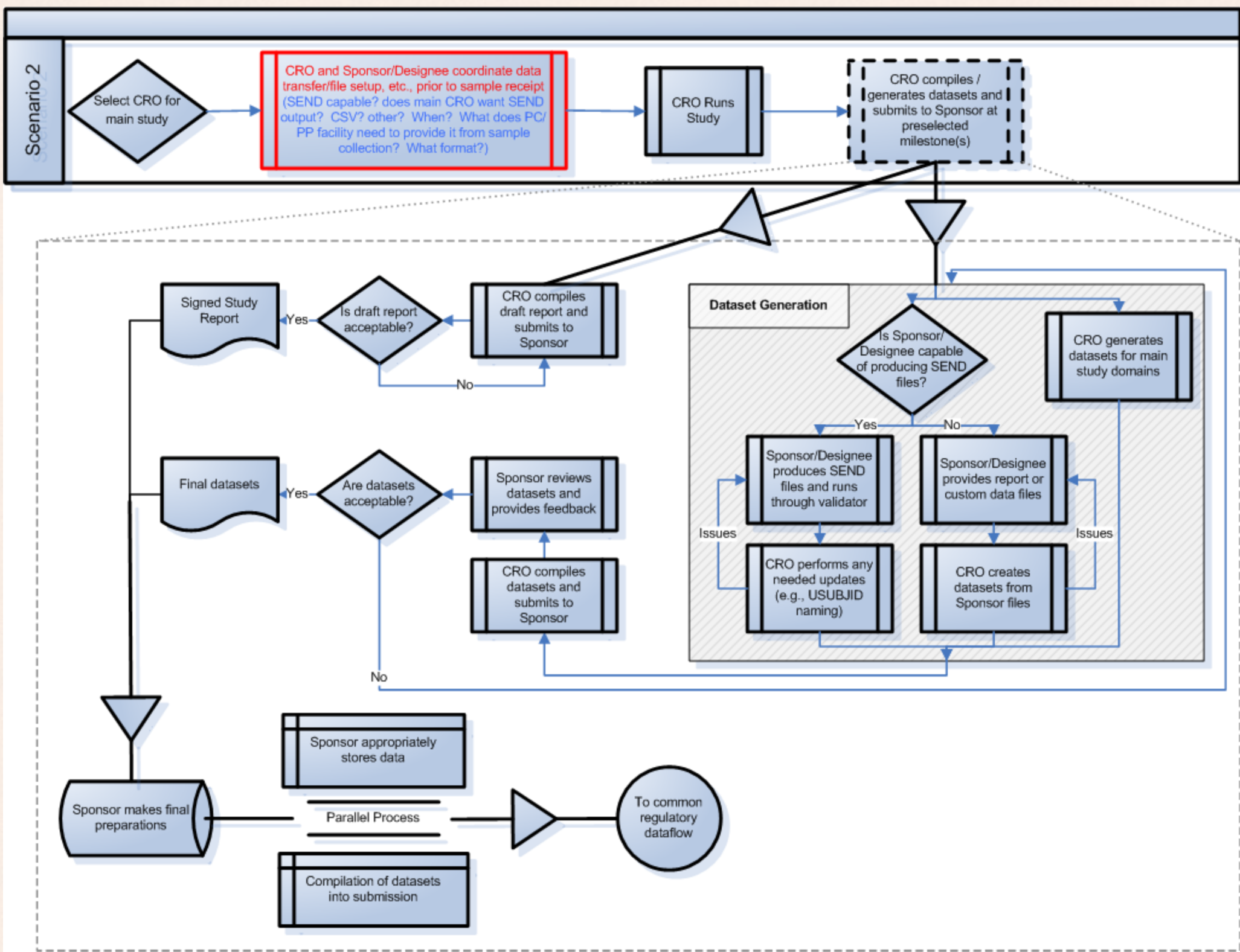
Scenario 1: CRO Study with SEND Dataset Fully Assembled by CRO

- A clear understanding of deliverables, limitations, milestones, and timing should be established before study initiation.
- Important discoveries:
 - Challenges with interim data files, with incomplete data or some domains missing
 - Study setup information is important to define ahead of time (e.g., TS and DM)
 - Previously, a step for generation of final data sets after review was included, which does not occur in reality, as the reviewed datasets will be used
 - In reality, the draft report and SEND data set flows do not always happen in parallel



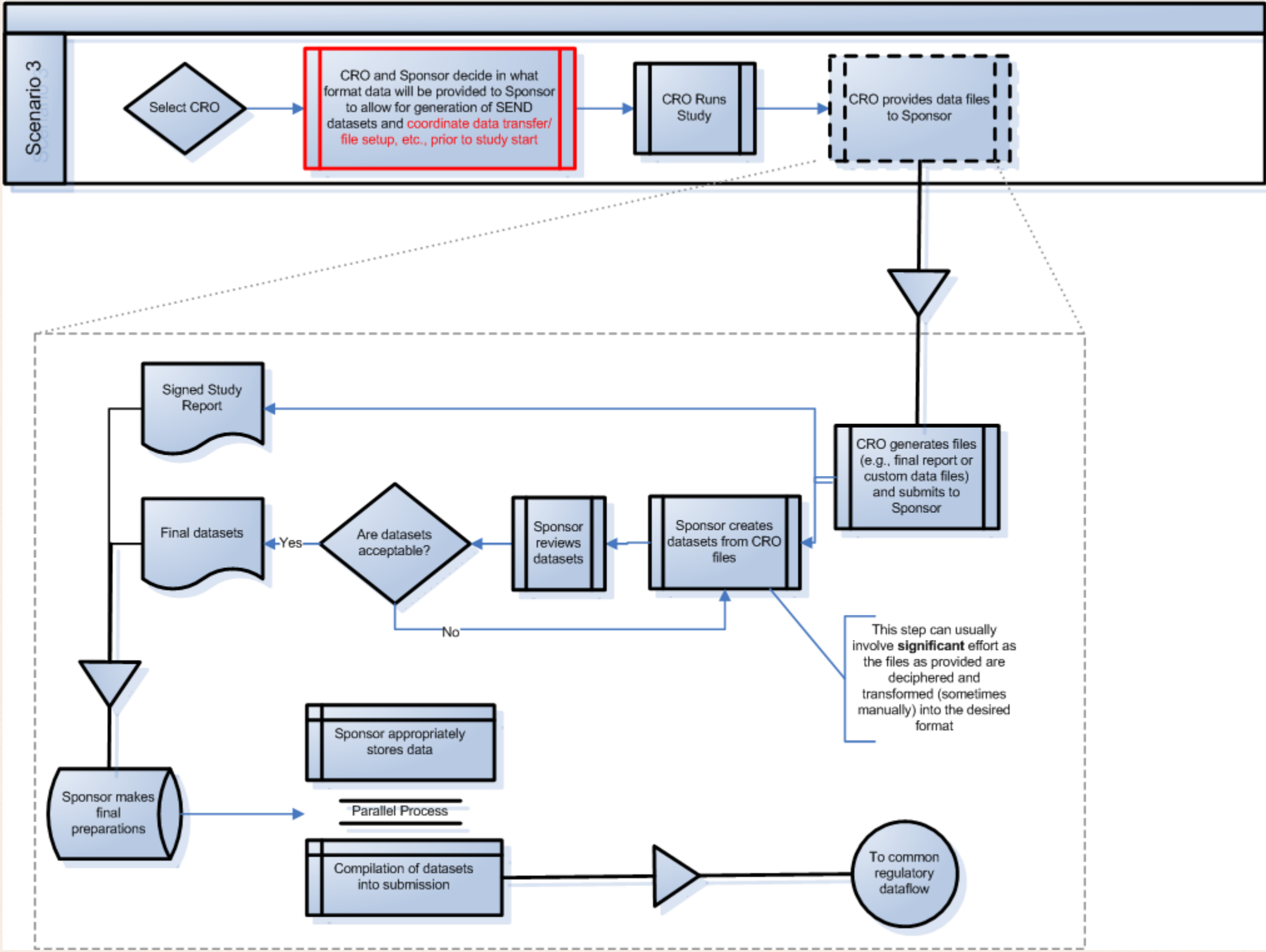
Scenario 2: A CRO generating SEND datasets for a study with the Sponsor or its designee providing PK/TK data

- In addition to topics identified under Scenario 1, this scenario introduces further considerations, ideally discussed prior to study initiation.
- Important discoveries:
 - Third party often used for PK/TK, with files (non-SEND) passed to CRO for SEND PC/PP generation
 - Significant effort in generation of datasets from third party files



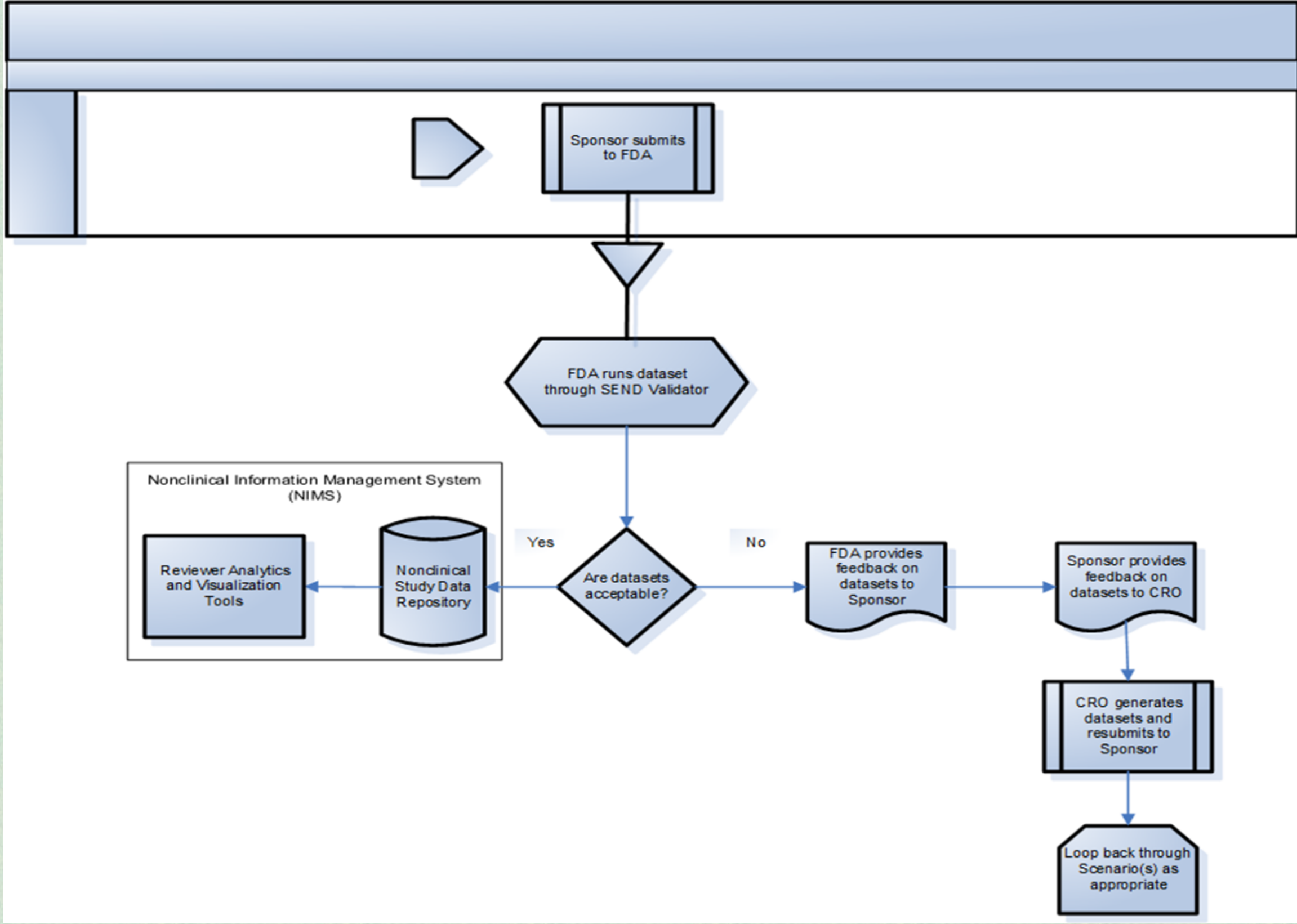
Scenario 3: CRO Study with SEND Dataset Fully Assembled by Sponsor

- This scenario builds on topics identified under Scenario 1 with additional considerations that should be discussed prior to study initiation.
- Important discoveries:
 - Most common occurrence is for finalized studies that the Sponsor wants to warehouse
 - Involves significant effort and QC working with final PDF or OCR'd reports and legacy data capture systems
 - No review loops with CRO in that the final data files are used
 - Not generally for regulatory submission
 - Some domains and variables that support regulatory submissions may be omitted



Common Regulatory Data Flow for All Scenarios

- Steps involved in processing SEND datasets may differ by FDA Division.
- No significant changes noted in regulatory flow.



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 use case scenarios developed collaboratively with inputs from various stakeholders have played 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. Results of the I-SEND internal survey and continuing discussions amongst I-SEND team members have demonstrated that individual organizations are approaching SEND implementation differently. Notable observations from the survey and team discussions over the last year include:

- Adoption of the use of SEND varies across primary CROs.
- Third party CROs utilized by sponsors for activities such as bioanalytical analysis and PK/TK characterization lag behind primary CROs conducting the main studies. This will result in the Sponsor, or more likely the main CRO, creating PC and PP files at more expense to the sponsor.
- SEND or SEND-like files for interim data for ongoing studies are a challenge for CROs as they will be incomplete and require early development of TS, TX and DM files.
- SEND file delivery is less likely to occur in parallel with draft report authoring and delivery.
- Creating SEND files from legacy data (i.e. data from previously completed studies) presents a significant resource challenge.

Use cases 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. This collaborative work is expected to continue to contribute valuable and practical knowledge that can be widely used by the pharmaceutical 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 interorganizational setting to drive productivity and scientific gains.

Acknowledgements: Troy Smyrnios, Zoetis, Kalamazoo, MI; Jeff Foy, Celgene, Summit, NJ; William Houser, Bristol Myers Squibb, Mt Vernon, IN; Debra Oetzman, Covance Laboratories, Inc, Madison, WI; Kathryn Brown, Sanofi US, INC, Bridgewater, NJ; Lynda Sands, GlaxoSmithKline, King of Prussia, PA; Peggy Zorn, INDS, Inc, Ann Arbor, MI; Gerald Randolph, Roche TCRC, Inc., New York, NY; Isaac Hatzell, Janssen Research & Development, Springhouse, PA

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