Understanding the Importance of Data Consistency and Quality in SEND Submissions

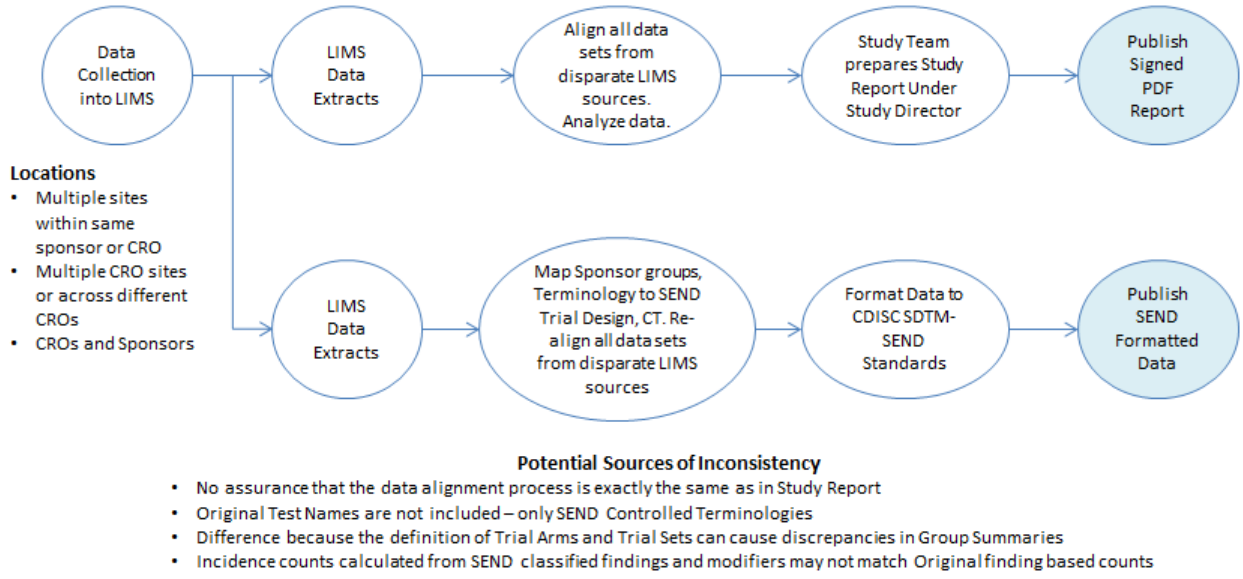
With the recent release of the FDA's binding guidance for electronic submission of nonclinical data, sponsor submissions will be required to include electronic datasets in SEND format in addition to the study report. With this new mandate, sponsors will have to ensure consistency and quality between the electronic datasets and the study reports. Any data discrepancies between the SEND datasets and the study report will impact not just the workflow for sponsors and CROs, but also for the FDA reviewers.

Impact on FDA Regulatory Reviewers

The main goal of providing study data in SEND format is to make the regulatory review process more efficient. When provided with SEND datasets, the reviewers will have access to subject level data in NIMS, the FDA's review system. Within NIMS the reviewers can use a number of analytical views to assess trends and potential areas of toxicity within a study. Reviewers will use the study report to confirm and compare any patterns or observations found in NIMS.
Any discrepancies found may result in data curation or data consistency checks through the Nonclinical JumpStart service. Data curation or consistency checks can result in delay of the study review and, in extreme cases, may result in the study being returned to the sponsor.

Impact on Sponsors

The current process for generating SEND datasets for sponsors is shown below. Data from LIMS extracts are carefully curated prior to being added to the study report. Similar processes will be applied when creating SEND datasets; however, without proper mechanisms in place this process can easily lead to discrepancies between the SEND datasets and study reports.
After having invested significant amounts of time and money to both develop the product and prepare the submission, the possibility of a delay for data inconsistency is a risk well worth avoiding.



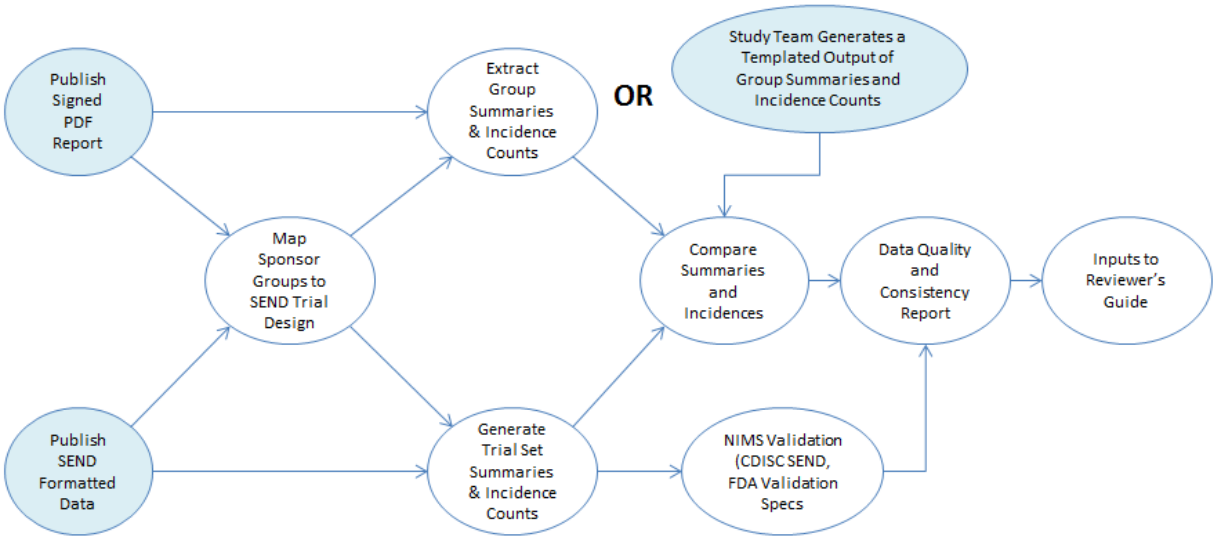
Sponsors can do a number of things to mitigate their risks:

1. Establish a team internally or contract with an organization to do the following:
    a. Model the study based on the Define.XML and the study report.
    b. Understanding the SEND standards and how to apply these to data.
    c. Compare SEND datasets to the study report.
    d. Provide inputs for the Study Data Reviewer's Guide.
    e. Provide recommendations to correct discrepancies between the SEND dataset and study report.
    f. Provide assurance that the SEND data will be ready for regulatory review with minimal or no risk.

This approach may be effective in cases where the reports are generated immediately after the study is completed, or where the source data comes from multiple CROs and coordinating the digitized SEND source datasets may be difficult.

2. Require that CROs provide group summary data in addition to the individual data. Ideally, the group summary data can then be used to:
    a. Create a map of the groups present in the SEND datasets to those given in the study report.
    b. Harmonize terminology in the LIMS systems and study reports to SEND controlled terminology.
    c. Map the standardized pathology findings to those given in the summary tables in the study report.
    d. Provide data quality and consistency reports and inputs for the Study Data Reviewer's Guide.

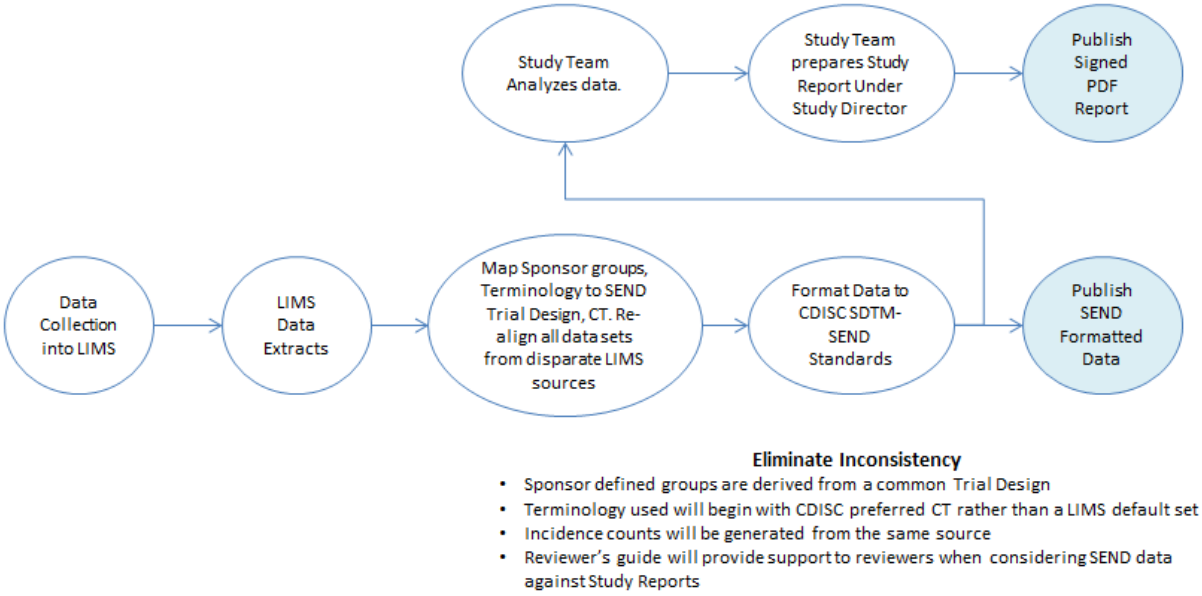
The above process is summarized in the below chart:



As the figure above shows, the comparison using the computed summary data into a template is far simpler than the effort of extracting the summaries from the PDF version of the study report.

3. Alternatively, the sponsor could create the SEND dataset and the study report concurrently. The following should be considered when implementing this process:
    a. Ensure that the SEND dataset is GLP compliant.
    b. The Study Director will need to certify the process and the end product of the SEND datasets as being true to the data collected in the study.
    c. A mapping of the LIMS terminology to the SEND Controlled Terminologies (CT) will need to be maintained.
    d. The study design will need to be harmonized between the SEND dataset and the study report.

A proposed modified workflow is shown in the below diagram:



This option would require vast changes to any existing workflow processes, but could serve as a stable long term solution.

Impact on CROs

CROs conduct studies according to their established protocols. However, they will now face the same requirements for generating SEND datasets as the sponsor. Sponsors and CROs will need to negotiate a process to ensure that the SEND datasets prepared by CROs match the data in the study reports.
The same options described above for sponsors could also help CROs ensure data consistency and quality.