Investigating Endpoint Modeling for SEND Datasets

A PhUSE project

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Introduction

A common challenge in Standard for Exchange of Nonclinical Data (SEND) implementation is determining the appropriate method for incorporation of endpoints not modeled in the SEND Implementation Guide (SENDIG). Best practices for the inclusion of these data are needed to ensure consistent methodology. To address this need, the Investigating Endpoint Modeling PhUSE project team authored a white paper outlining best practices for the inclusion of endpoints such as biomarker, anti-drug antibody (ADA) and immunophenotyping that are not modeled in the SENDIG. This poster presents the white paper* concepts and conclusions regarding the incorporation of unmodeled endpoints using biomarkers as an example.

"Unmodeled" Endpoints

Not every potential study type has been modeled in SEND yet, therefore encountering unmodeled endpoints is not an unusual experience. Before incorporating additional data, it is important to carefully consider the data to determine what endpoints and metadata are needed for accurate scientific interpretation.

Fortunately, the structures of the existing SEND domains are extremely flexible and can often handle the endpoint and associated metadata. An existing SEND domain should be utilized whenever possible. Predefined SEND domains have been thoroughly defined, tested, and verified to ensure the domain contains all of the variables needed to scientifically interpret data and conforms to standard reporting practices and validation checking tools.

If the endpoint and metadata cannot be incorporated into an existing SEND domain, the SENDIG allows for the addition of SDTM variables to an existing SEND domain or, beginning with SENDIG 3.1, the creation of a custom domain (Note that at the time this poster was created, version 3.1 of the SENDIG was not yet published). A custom domain must conform to the predefined set of SDTM variables. Custom domains are more likely to inadvertently omit variables needed to fully report or interpret the data.

The Investigating Endpoint Modeling PhUSE project team has developed methodology for the incorporation of these additional endpoints to assist in the determination of whether or not a custom domain is required.

Biomarkers

Biomarkers are anatomic, physiologic, biochemical, or molecular parameters associated with the presence and severity of specific disease states, medical conditions, or other biological characteristics. Biomarker data are detectable and measurable by a variety of methods including physical examination, microscopic examinations, laboratory assays, and medical imaging. In some cases, an endpoint assigned the role of biomarker is unique and not currently modeled in SEND. In other cases, an endpoint assigned the role of biomarker is already modeled in SEND. The study protocol and/or study report often highlight the special designation of an endpoint as a biomarker. The Investigating Endpoint Modeling PhUSE project team recommends that the designation of an endpoint as a biomarker be indicated in the SEND dataset and/or Study Data Reviewer's Guide. One method to accomplish this is populating the term "BIOMARKER" in the Subcategory (--SCAT) variable. An alternate method is including the information as a Supplemental Qualifier.

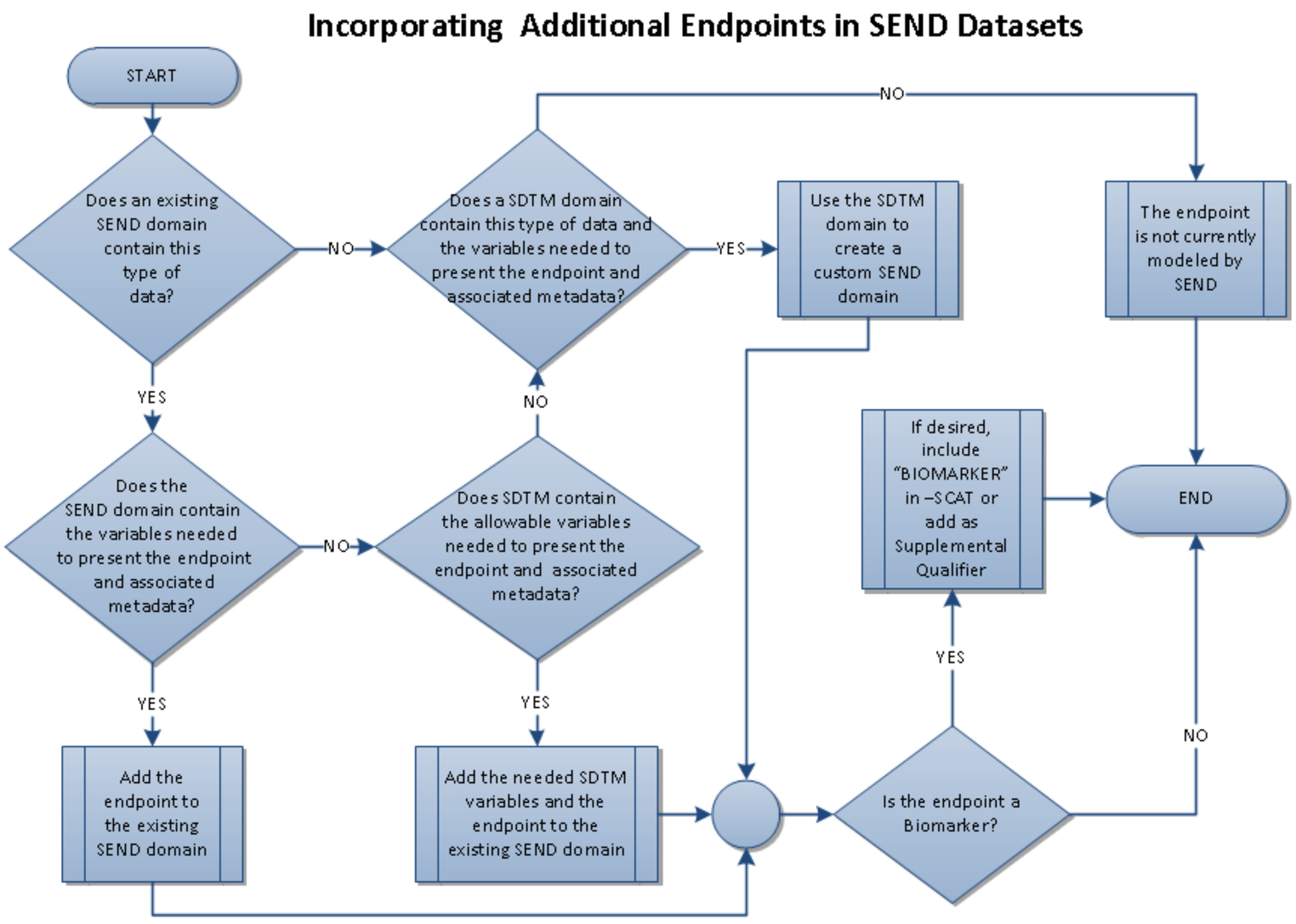
Methodology

Additional endpoints can be incorporated using one of three methods:

1. The endpoint and associated metadata are added to an existing SEND domain.
2. Additional allowable SDTM variables are added to an existing SEND domain to accommodate the addition of the endpoint and associated metadata.
3. The endpoint and associated metadata are added to an existing SDTM domain.

If the endpoint and associated metadata cannot be incorporated using one of the three methods listed above, the endpoint should be considered to be outside the current scope of SEND and not incorporated.

Determining the Appropriate Methodology for the Incorporation of an Additional Endpoint and Associated Metadata



Conclusion

Determining the appropriate method for incorporation of endpoints not modeled in the SENDIG is a common challenge encountered when implementing SEND. To address this need, the Investigating Endpoint Modeling PhUSE project team developed best practices to assist in selecting the correct methodology for the inclusion of additional endpoints such as biomarker, anti-drug antibody (ADA) and immunophenotyping. The team authored a white paper* detailing these recommendations and presented an overview of the recommendations in this poster using biomarkers as an example.

Additional endpoints can be incorporated by adding the endpoint and associated metadata into an existing SEND domain, adding allowable SDTM variables to an existing SEND domain, or utilizing an existing SDTM domain. If none of these three methods work, the endpoint should be considered outside the current scope of SEND and SDTM. The role of an endpoint as a biomarker can be designated by including "BIOMARKER" in the Subcategory (--SCAT) variable. This method allows for the inclusion of this important information in the SEND dataset as well as distinguishing the roles of endpoints that can be both routinely measured parameters and biomarkers. While several other options were explored, the team concluded that the use of the --SCAT variable, the Study Data Reviewer's Guide, or incorporating the information as a Supplemental Qualifier are the alternatives that offer the best alignment with current standards.

The flexibility of the current SEND model allows for the incorporation of many types of additional endpoints. The methodology presented in the white paper and poster provide recommendations for comprehensive, consistent methodologies that can be applied to all endpoints ensuring a consistent approach.

*The above-referenced white paper will be available on the PhUSE wiki.

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

References

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