July 25, 2019The CDISC[1] Standard for Exchange of Nonclinical Data for the Center for Biologics Evaluation and Research (SEND for CBER) Working Group is requesting from the public, realistic toxicology study examples to support conducting a Proof-Of-Concept (POC) for implementation of SEND for submissions to FDA CBER offices. The purpose of the POC is to familiarize FDA CBER reviewers with complete studies in SENDIG v3.1 format and allow them to explore ways of reviewing data in this format, using tools in development at FDA. For example, reviewers could use the POC datasets to view and analyze aspects of study review in SAS JMP, or technicians at FDA can determine how the datasets will be loaded into FDA databases or other tools. The participating offices from CBER are:

- Office of Vaccine Research & Review
- Office of Blood Research & Review
- Office of Tissues and Advanced Therapies
- Office of Director
- Office of Biostatistics & Epidemiology

Reviewers from each of these offices would like to see study data for repeat dose toxicology for products in their scope of review. A single dose, with a study period of observations is also useful. Generally, all offices are flexible in seeing data from studies in either small and/or large animals, incorporating one or more dose levels and treatment groups. The various safety assessments conducted in these studies may be product-specific and not applicable to all offices detailed above. However, it would be ideal to receive as much information as possible from each study to include the following as feasible:

- Clinical observations
- Mortality
- Ophthalmoscopy
- Food and water consumption
- Body weight
- Pharmacokinetics/Toxicokinetics: plasma activity and antigen levels[2]
- Immunogenicity/Antibody development[3]
- Clinical pathology – standard hematology to include coagulation parameters
- Clinical chemistry - standard
- Urinalysis – standard
- Local tolerance
- Terminal procedures: comprehensive macroscopic and microscopic evaluation; organ weight
- Body temperature (should always be included in vaccine toxicology studies)
- Cardiovascular function – electrocardiogram, heart rate, blood pressure, etc.
- Respiratory function
- Specifically noted for Vaccines: C-reactive protein (in rabbits) or Alpha 2 macroglobulin (in rats)

A maximum of data from 10 useable studies will be accepted. All study data donated should be shareable with the public. Studies can be "anonymized" by the Sponsor, if desired. No study data submitted for the POC will be used for commercial regulatory review by FDA. There is no cut-off to when the team will accept a study data donation, but prefer to have the studies by the end of October 2019. The team is flexible on formats, but need a study report (.pdf) and computable electronic data in (.xpt, .csv, .xlsx). Ideally, the study data will be in SEND format, but not required.

Sponsor representatives who provide study data examples are welcome to join the SEND for CBER Team, if not already participating, to engage with FDA reviewers on their experiences and feedback on SEND for studies typically seen by CBER. As a result of the POC, the SEND for CBER team will make a

recommendation to CDISC on how to ensure SEND meets CBER needsand to FDA on how to implement a SEND requirement for CBER.

To ask a question or to offer a donated study, please contact:

Lisa Lin, Co-lead SEND for CBER Team

Office of Director

Center for Biologics Evaluation and Research (CBER)

U.S. Food and Drug Administration

301-796-5059

wei.lin@fda.hhs.gov

Details of the process for companies to submit a report and data files for this POC has been developed by FDA. Once a company contacts Lisa Lin with their intent to donate a study, details for the method of data submission will be provided to the donor company.

Thank you for your consideration,

Susan

Susan DeHaven, Co-lead SEND for CBER Team

Director, Data Standards and Business Applications

Sanofi US, Inc.

Bridgewater, NJ

908-338-1983

susan.dehaven@sanofi.com

[1] CDISC: Clinical Data Interchange Standards Consortium

[2] For studies conducted using recombinant coagulation factors. The activity and levels of these proteins are typically measured to assess exposure to the test article.

[3] Antibodies can develop against a human product that is being administered into animals. Antibody development and any subsequent in vivo clearance of the product can provide additional information such as exposure to product.