



DEVELOPING SEND FOR CBER UPDATE

– COLLABORATIVE WORKSTREAM INITIATIVE

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March 10, 2020



FDA Disclaimer

The views and opinions presented here represent those of the speaker and should not be considered to represent advice or guidance on behalf of the U.S. Food and Drug Administration.

Collaborating to Achieve Intent

“The Center for Biologics Evaluation and Research (CBER) intends to receive SEND datasets in future submissions.” ¹

Today....

Future....

Use	Data Exchange Standard	Supported Implementation Guide Version	FDA Center(s)
Animal study datasets	Standard for Exchange of Nonclinical Data (SEND)		
Animal study datasets	SEND	3.1	CDER, CBER



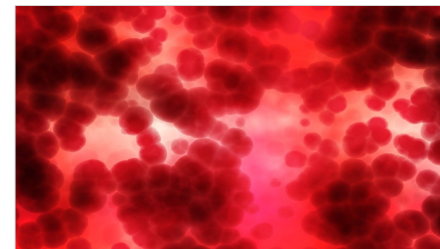
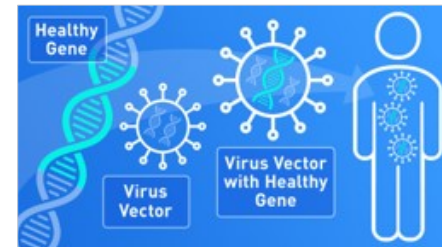
We are on the way!
Assessing, Analyzing, Recommending, Piloting



¹ Developing SEND for CBER – Collaborative Workstream Initiative

How can SEND have impact for CBER

- **Office of Vaccine Research and Review (OVRR)**
- **Office of Tissues and Advanced Therapies (OTAT)**
- **Office of Blood Research and Review (OBRR)**



CBER Offices Conducting Animal Review

- **Office of Vaccine Research and Review (OVRR)**

- ❖ **Products Reviewed**

- Vaccines for prevention or treatment of infectious disease indications only
 - Allergens
 - Miscellaneous biologics:
 - Fecal microbiota transplants
 - Probiotics
 - Phage products



- ❖ **Nonclinical Studies**

- Single and repeat dose toxicology
 - Developmental and reproductive toxicology (DART)
 - Genotoxicity, safety pharmacology (allergens)
 - Immunogenicity
 - Proof-of-concept, efficacy
 - Biodistribution
 - No chronic toxicity or carcinogenicity

- ❖ **Data Consideration**

- Timing of endpoints following vaccinations
 - Draize Scoring
 - Body temperature
 - Acute phase reactants
 - Immunogenicity/Serology Assays
 - Injection site histology

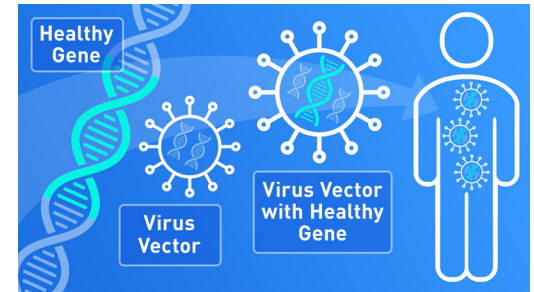
*Study and data
types well aligned
with SEND
roadmap*

CBER Offices Conducting Animal Review

- **Office of Tissues and Advanced Therapies (OTAT)**

- ❖ **Products Reviewed**

- Stem cell and stem-cell-derived products
- Somatic cell products
- Xenotransplantation products
- Certain devices and combination products
- Therapeutic vaccines
- Recombinant or plasma derived proteins
- Wound healing products
- Gene therapy



- ❖ **Nonclinical Studies**

- **Proof-of-concept/safety/toxicity**
- Cell-fate/biodistribution, typically no PK studies
- Differentiation/integration capacity
- Tumorigenicity: required for stem cell therapy
- Biocompatibility (implantable scaffolds)
- **Immunogenicity (therapeutic vaccines)**

- ❖ **Data Consideration**

- Animal model of disease/injury
- Hybrid safety and activity studies
- Distribution/biodistribution assessments
- Biocompatibility of devices

*SEND for CBER Team
will be working
closely with CDISC on
developing IS Domain
for Nonclinical
Immunogenicity Data*

CDER Offices Conducting Animal Review

- **Office of Blood Research and Review (OBRR)**

- ❖ **Products Reviewed**

- Modified blood components
 - Hemoglobin-based oxygen carriers
 - Container-closure systems
 - Process-related impurities
 - Excipients
 - Pathogen reduction systems

- ❖ **Nonclinical Studies**

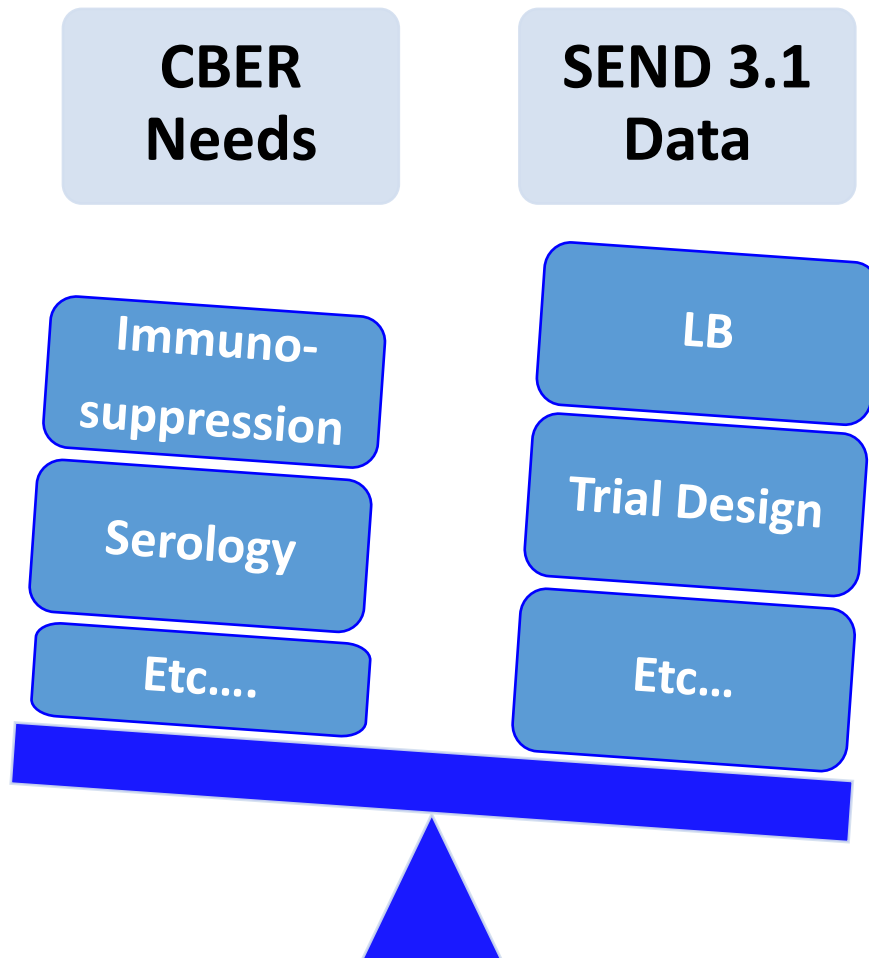
- Focuses on biocompatibility
 - Extractables and leachables testing
 - Container closure systems
 - Occasionally see developmental or embryo-fetal toxicology for replacement proteins
 - Proof-of-concept
 - Carcinogenicity

- ❖ **Data Consideration**

- **GLP-compliant toxicology studies only requested on a case-by-case**
 - Most nonclinical studies are not amenable to SEND data
 - Systemic toxicity (biocompatibility, hemoglobin-based oxygen carriers),
 - Mutagenicity (impurities, extractables, leachables)

Most Nonclinical studies are not amenable to SEND data

Workstream Mission: Assess & Analyze for CBER



- Is SEND 3.1 sufficient?

➔ Comparing needs to the published and developing Standard Domains

- What knowledge is needed?

➔ Assuring expertise and information sharing

- What are the gaps?

➔ Publishing gap identification & analysis results

- How to mitigate the gaps?

➔ Developing recommendation to CDISC for evolving SEND based on Proof of Concept Pilot for SEND 3.1 submission to CBER

Team Operations & Accomplishments

- Biweekly Workstream Teleconferences
 - Working meetings with Domain reviews, data samples and IG review
 - Open to new participants!
- Published Work Products on CDISC WIKI
 - CBER Study Types and Endpoints by Office Inventory
 - Developing GAP Analysis

PROGRESS: DOMAIN REVIEW AND GAP IDENTIFICATION

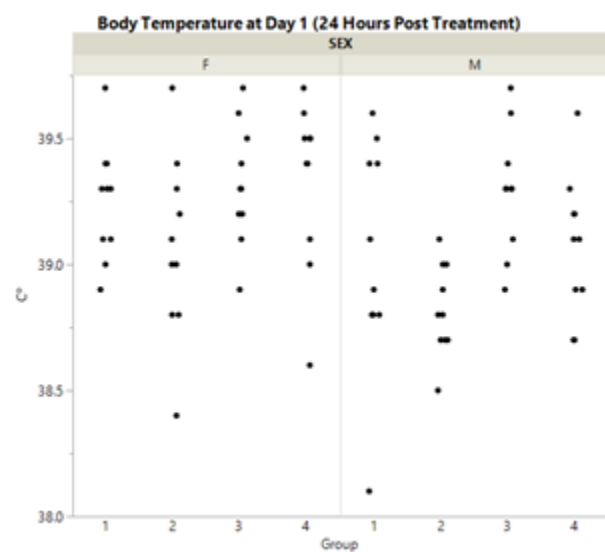
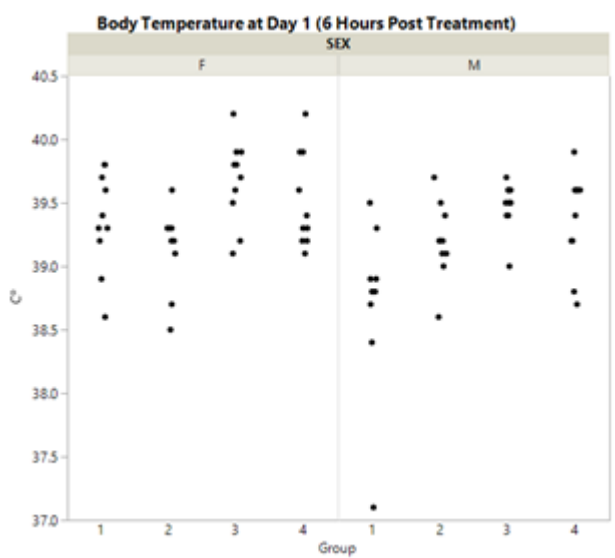
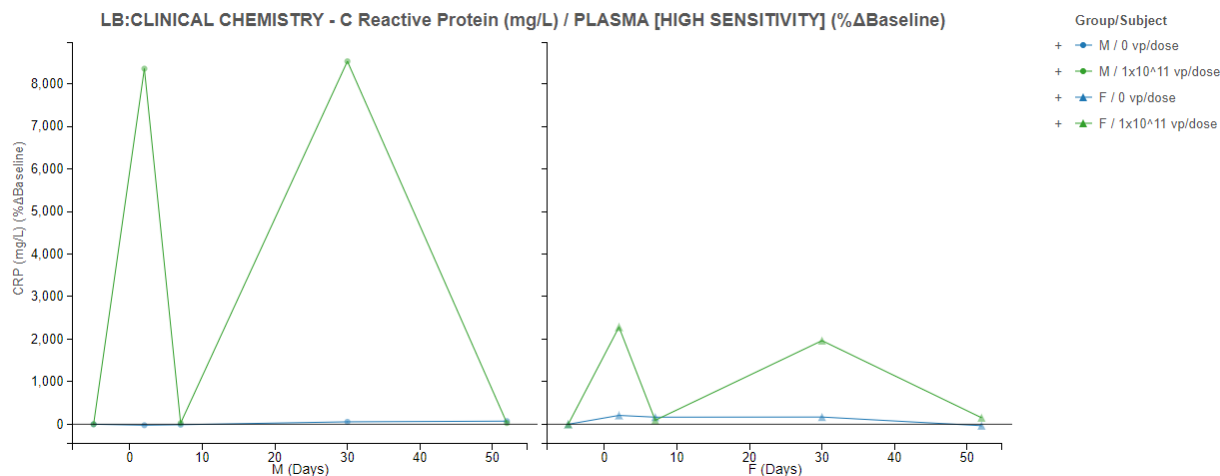
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Preparing for Future Implementation Tools & Training



- Provide Training for Reviewers
 - CDISC study data standards
 - Analysis tools including JMP, JMP Clinical, SEND Explorer
- Provide consultation service to CBER reviewers on reviewing SEND data
- Help Reviewers to use tool for visualizing SEND data

Preparing for Future Implementation Tools & Training



Preparing for Future Implementation

Submission Standards



- Conduct Proof-of-Concept Pilot starting the end of 2019
 - Received 4 valid POC studies to CBER
 - Going through data standards validation check
 - Currently under review with CBER Reviewers
 - Exploring data by using tools and evaluating define.xml and non-clinical study data reviewers guide
- CBER will announce support for SEND in the future when time is ready, normally via Federal Register Notice

Conclusion

- Achieve a robust assessment of SENDIG 3.1 for implementation use on CBER submissions
- Proof of Concept Pilot is ongoing
- Additional activities for CDISC workstreams will be defined
- Continue maintain a close relationship with CDISC SEND team

For Your Reference

- FDA Data Standards Catalog
<https://www.fda.gov/forindustry/datastandards/studydatastandards/default.htm>
- FDA Data Standards Program Action Plan
<https://www.fda.gov/media/135231/download>
- Confirmed Data Endpoints for Exchange (CoDEx) for SENDIG v3.1
<https://wiki.cdisc.org/display/SENDCODEX/CoDEx+for+SENDIG+Compiled>
- SEND for CBER wiki site
<https://wiki.cdisc.org/display/SEND/SEND+for+CBER>

Any Questions ?



THANK YOU!

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And at anytime, you can send questions to CBER: cber-edata@fda.hhs.gov