

Presentation DS04

A Practical Exploration of SEND for CBER Submissions

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Introduction

March 2023

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- What is CBER and when will it affect SEND?
 - Requirement date -> 15 March 2023
 - CBER are accepting these data endpoints now
- Why should we start preparing sooner rather than later?
 - Connections and networks with the CBER team are not yet established
 - Current data collection systems designed with SEND in mind
 - Current implementation guidance could be improved

What Challenges Did I Face?



- Lack of knowledge and understanding of the data
- Need to learn new domain structures
- Inconsistent and poorly organised raw data format

What Have I Learned?



- Domain specifications and Controlled Terminology
- Background of the science
 - Helped mapping correct Tests, Test Details, Categories, etc.
- Knowledge of SDTMIG
 - Information here transferable to CBER data endpoints

What Recommendations Do I Have?



- Changes to implementation guides
 - Changes are needed to the current SENDIG v3.1
 - SENDIG v3.2 on the CDISC Wiki does address some changes
 - More concepts from the SDTMIG could be introduced to the SENDIG
- Changes could include:
 - Additional Variables within Domains
 - Additional Domains
 - Additional Assumptions and Examples of domains in SENDIG

Domain Examples: MI

Modelling Immunohistochemistry data:

- Currently no examples in the SENDIG
- Modelled using SDTMIG v3.4 and SDTM Terminology
- Key findings:
 - MITEST and MITESTCD terminology was extended
 - MITSTDTL (Microscopic Examination Detail) was utilized
 - Differences in how SDTMIG handle MISPEC and MILOC

Row	STUDYID	DOMAIN	USUBJID	MISEQ	MITESTCD	MITEST	MITSTDTL	MIORRES	MISTRESC	MIRESCAT	MISPEC	MILOC	MIMETHOD	MIDTC	MIDY
1	ABC	MI	ABC-001	1	HNCAM	hNCAM	STAINING INTENSITY	0	0	NEGATIVE	TISSUE	BRAIN	IHC	2020-02-26	29
2	ABC	MI	ABC-001	2	KI67	Ki-67	STAINING INTENSITY	1+	1+	POSITIVE	TISSUE	BRAIN	IHC	2020-02-26	29
3	ABC	MI	ABC-001	3	KU80	KU80	STAINING INTENSITY	2+	2+	POSITIVE	TISSUE	BRAIN	IHC	2020-02-28	29
4	ABC	MI	ABC-002	4	HNCAM	hNCAM	STAINING INTENSITY	4+	4+	POSITIVE	TISSUE	BRAIN	IHC	2020-07-22	183
5	ABC	MI	ABC-002	5	KI67	Ki-67	STAINING INTENSITY	3+	3+	POSITIVE	TISSUE	BRAIN	IHC	2020-07-29	183
6	ABC	MI	ABC-002	5	KU80	KU80	STAINING INTENSITY	3+	3+	POSITIVE	TISSUE	BRAIN	IHC	2020-07-29	183

Domain Examples: EX

Modelling Stereotactic Intra-Striatal dosing data:

- CBER Submitted studies introduce new dosing methods
- Modelled using SENDIG v3.1
- Key findings:
 - UNIT codelist extended for EXDOSU
 - EXTRT used to represent different levels HESC-PC was spiked with HESC

Row	STUDYID	DOMAIN	USUBJID	EXSEQ	EXTRT	EXDOSE	EXDOSU	EXDOSFRM	EXDOSFRQ	EXROUTE	EXLOT	EXLOC	EXMETHOD
1	ABC	EX	ABC-001	1	HESC-PC	0	10^5 cells	SUSPENSION	ONCE	INTRACEREBRAL		Right Striatum	INTRAstriatal INJECTION
2	ABC	EX	ABC-002	2	HESC-PC	7	10^5 cells	SUSPENSION	ONCE	INTRACEREBRAL	ABC1	Right Striatum	INTRAstriatal INJECTION
3	ABC	EX	ABC-003	3	100% HESC	7	10^5 cells	SUSPENSION	ONCE	INTRACEREBRAL	DEF1	Right Striatum	INTRAstriatal INJECTION
4	ABC	EX	ABC-004	4	HESC-PC 0.001% HESC	7	10^5 cells	SUSPENSION	ONCE	INTRACEREBRAL	ABCD1	Right Striatum	INTRAstriatal INJECTION
5	ABC	EX	ABC-005	5	HESC-PC 0.1% HESC	7	10^5 cells	SUSPENSION	ONCE	INTRACEREBRAL	ABCD2	Right Striatum	INTRAstriatal INJECTION
6	ABC	EX	ABC-006	6	HESC-PC 1% HESC	7	10^5 cells	SUSPENSION	ONCE	INTRACEREBRAL	ABCD3	Right Striatum	INTRAstriatal INJECTION

Domain Examples: CP

Modelling Immunophenotyping data:

- Modelled using SENDIG v3.2 (CDISC Wiki) + SDTM terminology
- Key findings:
 - Terminology extended for Test code and Test Name
 - Much research was needed in the background of the data
 - Understanding how the Tests relate to marker strings
 - Understanding how subset cell populations are represented
 - Communication with scientists was key

Row	STUDYID	DOMAIN	USUBJID	CPSEQ	CPTSTCD	CPTST	CPCELSTA	CPCSMRKS	CPMRKSTR	CPCAT	CPORRES	CPORRESU	CPRESTYP
8	ABC	CP	ABC-001	8	TLSTLY	TLym Sub/TLym	ACTIVATED	CD69+	CD3+CD69+	IMMUNOPHENOTYPING	1.7	%	NUMBER FRACTION
9	ABC	CP	ABC-001	9	TLYCE	T-Lymphocytes			CD3+	IMMUNOPHENOTYPING	3.4	10^9/L	NUMBER CONCENTRATION
11	ABC	CP	ABC-001	11	TLYH	TLym Help			CD3+CD4+CD8-	IMMUNOPHENOTYPING	2.1	10^9/L	NUMBER CONCENTRATION
12	ABC	CP	ABC-001	12	TLYHSTLY	TLym Help Sub/TLym Help	ACTIVATED	CD69+	CD3+CD4+CD8-CD69+	IMMUNOPHENOTYPING	1	%	NUMBER FRACTION
13	ABC	CP	ABC-001	13	TLYHTLY	TLym Help/TLym			CD3+CD4+CD8-	IMMUNOPHENOTYPING	62.4	%	NUMBER FRACTION
15	ABC	CP	ABC-001	15	TLYLY	TLym/Lym			CD3+	IMMUNOPHENOTYPING	68.4	%	NUMBER FRACTION

Domain Examples: IS

Modelling Antidrug Antibody and Neutralizing Binding Antidrug Antibodies data:

- Modelled using SENDIG v3.2 (CDISC Wiki)
- Key findings:
 - Previously modelled ADA data in LB domain
 - Now better suited to IS domain
 - Data not provided in a desirable format

Row	STUDYID	DOMAIN	USUBJID	ISSEQ	ISTESTCD	ISTEST	ISBDAGNT	ISTSTDTL	ISCAT	ISSCAT	ISORRES	ISORRESU
1	ABC	IS	ABC-001	1	ADA_NAB	Neutralizing Binding Antidrug Antibody	AAV VirusA	NEUTRALIZING TITER 50%	IMMUNOGENICITY	HUMORAL IMMUNITY	1 in 135	titer
2	ABC	IS	ABC-002	2	ADA_NAB	Neutralizing Binding Antidrug Antibody	AAV VirusA	NEUTRALIZING TITER 50%	IMMUNOGENICITY	HUMORAL IMMUNITY	1 in 405	titer

Domain Examples: PC

Modelling Quantitative Polymerase Chain Reaction data:

- Currently no examples in SENDIG v3.1, SENDIG v3.2 or SDTMIG v3.4
- Key findings:
 - Not quite right in PC domain
 - Additional variables would be useful (--LAT, --ANTREG and --DIR)
 - Needed to extend specimen codelist
 - Test Detail variable would be useful (Instead of PCSCAT)
 - Introduce variable for “Lower limit of Detection”?
 - Should we consider the GF domain?

Row	STUDYID	DOMAIN	USUBJID	PCSEQ	PCTESTCD	PCTEST	PCCAT	PCSCAT	PCORRES	PCORRESU	PCSTRESC	PCSTRESN	PCSTRESU	PCSPEC	PCMETHOD
1	ABC	PC	ABC-001	1	VIRUSAVG	VirusA vector genome	Adeno-Associated Virus	Shedding Sample Results	N/D	DNA copies/ug	N/D		DNA copies/ug	FECES	Quantitative polymerase chain reaction
12	ABC	PC	ABC-001	12	VIRUSAVG	VirusA vector genome	Adeno-Associated Virus	Tissue Sample Results	37000	DNA copies/ug	37000	37000	DNA copies/ug	LIVER, LEFT MEDIAN LOBE LOWER HALF	Quantitative polymerase chain reaction
13	ABC	PC	ABC-001	13	VIRUSAVG	VirusA vector genome	Adeno-Associated Virus	Tissue Sample Results	700000	DNA copies/ug	700000	700000	DNA copies/ug	LIVER, RIGHT MEDIAN LOBE UPPER HALF	Quantitative polymerase chain reaction
16	ABC	PC	ABC-001	16	VIRUSAVG	VirusA vector genome	Adeno-Associated Virus	Tissue Sample Results	<=LOD	DNA copies/ug	<=LOD		DNA copies/ug	URINARY BLADDER	Quantitative polymerase chain reaction

Future Domain Examples



- Future data to explore:
 - T Cell Dependent Antibody Response (TDAR)
 - Delayed-Type Hypersensitivity Studies
 - Host Resistance Studies
 - Hypersensitivity Studies
 - Autoimmunity Studies
- May not be in scope for SEND 3.2
- Could be included as supportive data endpoints
 - Precedent to investigate and explore this data

Conclusion

CALL TO ACTION!

Update future SEND implementation guides with CBER in mind

Work with scientists and system operators to update processes and collection systems

Educate ourselves on the new domains, new terminology and new data types

References

- [SEND Implementation Guide v3.2, available on the CDISC Wiki](#)
- [CDISC SENDIG v3.1](#)
- [CDISC SDTMIG v3.4](#)

Thank you for listening!

Any Questions?

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