SEND Challenges

Tabular Examples from Fit for Use

CDISC-SEND Fall F2F 2016

Elaine Thompson, Ph.D.
FDA Office of Computational Sciences

Disclaimer

The views expressed are those of the speaker and do not necessarily reflect the policies and practices of the FDA.

Data Standards Questions

- Some domains might benefit from standards improvement
- MI: 3.1 model should help
- CL
  - Multiple implementations permitted
  - Lack of clarity about what to put in CLSTRESC
  - What do we do with quantitative data?
- MA
  - Troubles with MASTRESC
  - IG may not have sufficient explanation for contents of SUPPMA
- PC: Hard to extract groupings & timings
- TF: Analysis business needs

CL, the "Wild West"

- SENDIG allows multiple implementations
- Three had mixtures of implementations within the dataset, one study with a confusing choice of CLCAT
- CLSTRESC was less detailed than the Study Report in three studies

Too Little in STRESC

CLTESTCD	CLTEST	CLCAT	CLSCAT	CLORRES	CLSTRESC	CLLOC
GEN	General	PHYSICAL EXAM	Veterinary Clinical Observations	body temperature, body temperature, 102	body temperature	
GEN	General	PHYSICAL EXAM	Veterinary Clinical Observations	body temperature, body temperature, 103	body temperature	
SK	Skin	CLINICAL SIGNS	Clinical Observations	abnormal color, muzzle, red	abnormal color	muzzle
SE	Secretion/ Excretion	CLINICAL SIGNS	Clinical Observations	feces, unformed	feces	
SE	Secretion/ Excretion	CLINICAL SIGNS	Clinical Observations	feces, watery	feces	

- Important information is not captured in CLSTRESC
- Cannot group on CLSTRESC and reproduce Study Report
- Prefer not to refer reviewers to CLORRES, cannot program on it
- Temperature is a numeric finding and perhaps should have been transmitted in VS?

Pure CLSTRESC Implementation

CLTESTCD	CLTEST	CLCAT	CLSCAT	CLORRES	CLSTRESC	CLLOC	CLSEV
CS	Clinical Signs	CLINICAL SIGNS	Toxicology Observations	Skin, Red, Pinna, Right	Skin, Red	Pinna, Right	
CS	Clinical Signs	OPHTHALMOLOGY		Cornea, Opacity, Diffuse, Left, 1 Very slight	Cornea, Opacity, Diffuse	Left	MINIMAL
CS	Clinical Signs	CLINICAL SIGNS	Signs of ill health or Reaction to Treatment/Cage Observations	Salivation, Slight	Salivation		MILD
CS	Clinical Signs	CLINICAL SIGNS	Signs of ill health or Reaction to Treatment/Cage Observations	Fur, Erected	Fur, Erected		
CS	Clinical Signs	CLINICAL SIGNS	Signs of ill health or Reaction to Treatment/Cage Observations	Swollen Soft, Mouth, Slight	Swollen Soft	Mouth	MILD

- Easiest style of implementation to use
- CLSTRESC and CLLOC contain all of the information
- All information in CLORRES is captured

CLTEST/CLSTRESC Implementation

CLTESTCD	CLTEST	CLCAT	CLSCAT	CLORRES	CLSTRESC	CLLOC	CLSEV
SKN	Skin	CLINICAL SIGNS	VIABILITY OBSERVATION	Bruise inner thigh(s), Left, Slight	Bruise inner thigh(s)	Left	SLIGHT
SKNABR	Skin Abrasion	CLINICAL SIGNS	VIABILITY OBSERVATION	Wet, Tail	Wet	Tail	
BHVR	Behavior	CLINICAL SIGNS	DOSE OBS	Decreased Activity	Decreased Activity		
VFC	Visual Food Consumption	VISUAL FOOD		4: 50 percent to most consumed	50 percent to most consumed		
DSITEID	Dose Site Identification	CLINICAL SIGNS	INJECTION SITE	Right Saphenous Vein	Right Saphenous Vein		
DSITEINF	Dose Site Information	CLINICAL SIGNS	INJECTION SITE	Dose site marked with indelible ink or tattoo	Dose site marked with indelible ink or tattoo		
EVENT	Event	CLINICAL SIGNS	VIABILITY	Animal out of cage	Animal out of cage		

- Extracting data VERY dependent on inclusion of CLTEST for some findings, but not for others
- Skin Abrasion is a finding, not a “test”
- Don’t injection sites belong in EX?
- Is “Animal out of cage” a finding?

Mixed Implementation

CLTESTCD	CLTEST	CLCAT	CLSCAT	CLORRES	CLSTRESC	CLLOC
SKINPLG	Skin/Pelage	CLINICAL SIGNS	Clinical Observations	thinning hair coat, dorsal cervical	thinning hair coat	dorsal cervical
DISCHARG	Discharge	CLINICAL SIGNS	Clinical Observations	oral, clear	oral	

- CLSTRESC of “oral” was our Fit for Use favorite for odd CL implementations
- Again, one field has useful info in CLSTRESC, the other essentially has the finding of “Discharge” in CLTEST
- Information in CLORRES is lost

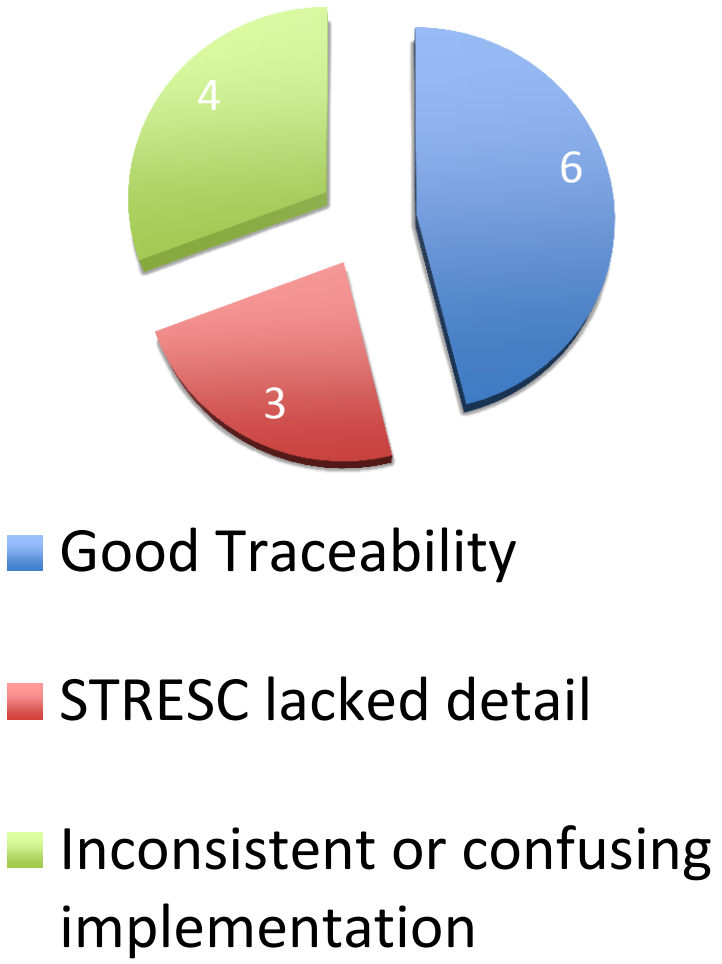
Quantitative Ophthalmology in CL

DOMAIN	CLTESTCD	CLSEQ	CLTEST	CLCAT	CLORRES	CLSTRESC	CLTPT	CLDTC
CL	IOP_OD	1	Intraocular Pressure OD	OPHTHALMOLOGY	16 mm/Hg	16 mm/Hg	S1	2015-01-01T00:00:00
CL	IOP_OS	2	Intraocular Pressure OS	OPHTHALMOLOGY	15 mm/Hg	15 mm/Hg	S1	2015-01-01T00:00:00
CL	HPD	3	Hour Post Dose	OPHTHALMOLOGY	0	0	S1	2015-01-01T00:00:00
CL	IOP_OD	4	Intraocular Pressure OD	OPHTHALMOLOGY	15 mm/Hg	15 mm/Hg	S2	2015-01-01T00:00:00
CL	IOP_OS	5	Intraocular Pressure OS	OPHTHALMOLOGY	14 mm/Hg	14 mm/Hg	S2	2015-01-01T00:00:00
CL	HPD	6	Hour Post Dose	OPHTHALMOLOGY	4	4	S2	2015-01-01T00:00:00

- SENDIG states that Ophthalmology belongs in CL
- CL does not support STRESN/STRESU pairs
- Summary statistics cannot be created without custom code
- Should I expect to have to program over timings like this? How?

Gross Pathology (MA)

- SENDIG seems to lack sufficient explanation of how to standardize STRESC
- Grouping by terms in STRESC should match the study report for good traceability
- Redundant “Present” in SUPPMA makes real modifiers hard to extract



Too little in STRESC

MAORRES	MASTRESC	MASPEC
LUNG : Area; apical lobe; pale : right	Area	LUNG
SKIN : Area; abdomen; ventral; dark : 40mm x 10mm	Area	SKIN
PANCREAS : Discolouration; pale	Discolouration	PANCREAS
LYMPH NODE : Discolouration; dark : thymic	Discolouration	LYMPH NODE

- AREA is too vague
- Can't rely on extracting the remainder from SUPPMA
- Discoloration is more meaningful, but the color was reported in the Study Report

More MA Standardization Issues

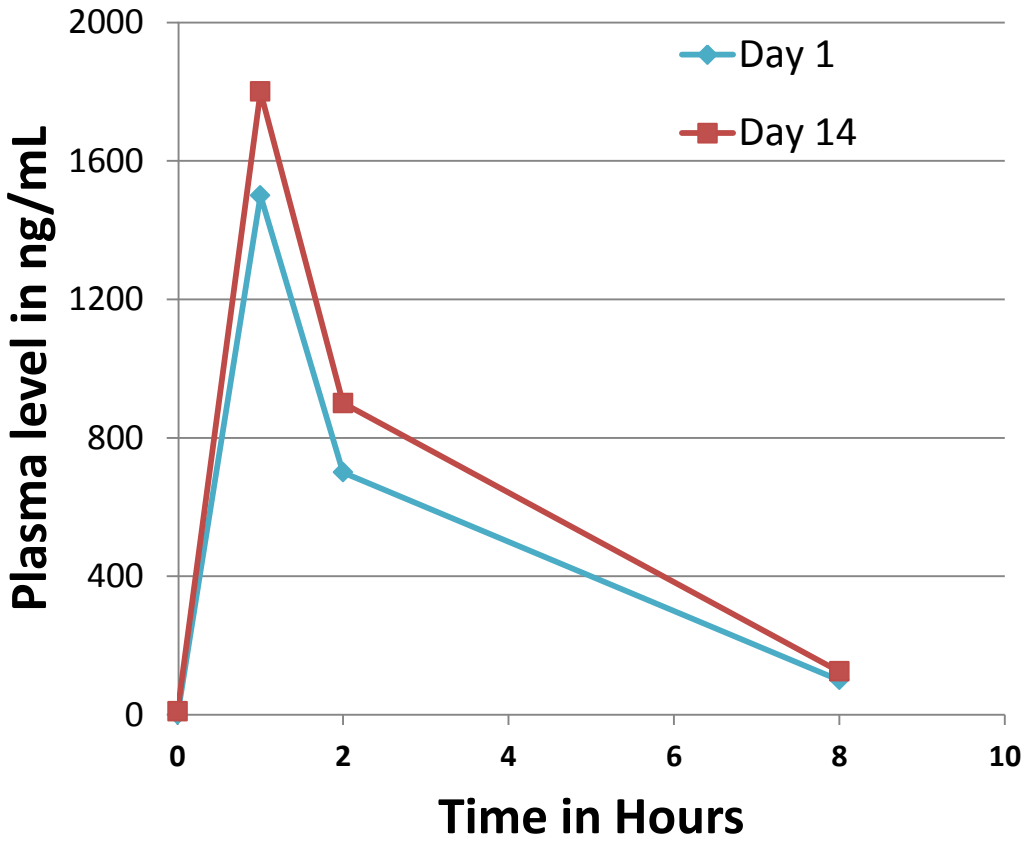
MAORRES	MASTRESC	MASPEC	SUPPMA
Dark area, multiple, right caudal lobe	DARK AREA	LUNG	MULTIPLE; RIGHT CAUDAL LOBE
Area dark-, multiple, right middle lobe	AREA DARK	LUNG	MULTIPLE; RIGHT MIDDLE LOBE
Discoloration, dark, left lobe	DISCOLORATION	LUNG	DARK; LEFT LOBE

PC Domain

Goal: pharmacokinetic graph to visualize and calculate PP

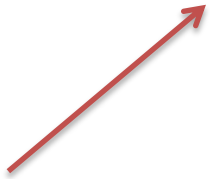
SEND challenges

1. Determining which sets of points should be grouped
2. Extracting numeric timings in hours without any string parsing
3. Short 24-hour series and weekly recovery in same study – possible to have IG example?

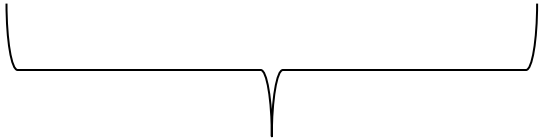


Example 1: Extracting hours is hard

STUDYID	PCSTRESN	PCSTRESU	VISITDY	PCDTC	PCDY	PCTPT	PCTPTNUM	PCELTM	PCTPTREF
FAKE1	1500	ng/mL	1	2016-05-12	1	D1 1h	3	PT1H	Day 1 Dose
FAKE1	700	ng/mL	1	2016-05-12	1	D1 2h	5	PT2H	Day 1 Dose
FAKE1	100	ng/mL	1	2016-05-12	1	D1 8h	7	PT8H	Day 1 Dose
FAKE1	10	ng/mL	14	2016-05-26	14	D14 predose	1		Day 14 Dose
FAKE1	1800	ng/mL	14	2016-05-26	14	D14 1h	9	PT1H	Day 14 Dose
FAKE1	900	ng/mL	14	2016-05-26	14	D14 2h	11	PT2H	Day 14 Dose
FAKE1	125	ng/mL	14	2016-05-26	14	D14 8h	13	PT8H	Day 14 Dose



Grouping Works



Hard to extract numeric hourly timings because of predose implementation

Example 2: Can't find groups

STUDYID	PCSTRESN	PCSTRESU	VISITDY	PCDTC	PCDY	PCTPT	PCTPTNUM
PDS2014	1350	ng/mL	1	2010-12-11T00:00:00	1	0.5H	0.5
PDS2014	1540	ng/mL	1	2010-12-11T00:00:00	1	1H	1
PDS2014	1480	ng/mL	1	2010-12-11T00:00:00	1	2H	2
PDS2014	1940	ng/mL	1	2010-12-11T00:00:00	1	4H	4
PDS2014	2230	ng/mL	1	2010-12-11T00:00:00	1	7H	7
PDS2014	2540	ng/mL	2	2010-12-12T00:00:00	2	24H	24
PDS2014	351	ng/mL	29	2011-01-08T00:00:00	29	0H	0
PDS2014	1690	ng/mL	29	2011-01-08T00:00:00	29	0.5H	0.5
PDS2014	2120	ng/mL	29	2011-01-08T00:00:00	29	1H	1
PDS2014	2160	ng/mL	29	2011-01-08T00:00:00	29	2H	2
PDS2014	2310	ng/mL	29	2011-01-08T00:00:00	29	4H	4
PDS2014	2000	ng/mL	29	2011-01-08T00:00:00	29	7H	7
PDS2014	351	ng/mL	30	2011-01-09T00:00:00	30	24H	24

Can't group PC sets on VISITDY

Hourly timings are useful

Example 3: Short and long series

PCSTRESN	PCSTRESU	VISITDY	PCDTC	PCDY	PCTPT	PCTPTNUM	PCELTM	PCTPTREF	PCRFTDTC
100	ng/mL	1	2016-01-01	1	Day 1 1H	101	PT1H	Day 1 Dose	2016-01-01
120	ng/mL	1	2016-01-01	1	Day 1 4H	104	PT4H	Day 1 Dose	2016-01-01
150	ng/mL	1	2016-01-01	1	Day 1 8H	108	PT8H	Day 1 Dose	2016-01-01
110	ng/mL	2	2016-02-01	2	Day 1 24H	124	PT24H	Day 1 Dose	2016-01-01
200	ng/mL	8	2016-01-14	14	Week 2 1H	1401	PT1H	Day 14 Dose	2016-01-14
210	ng/mL	8	2016-01-14	14	Week 2 4H	1404	PT4H	Day 14 Dose	2016-01-14
205	ng/mL	8	2016-01-14	14	Week 2 8H	1408	PT8H	Day 14 Dose	2016-01-14
190	ng/mL	8	2016-01-15	15	Week 2 24H	1424	PT24H	Day 14 Dose	2016-01-14
20	ng/mL	15	2016-01-21	21	Week 3 0H	2100	PT0H	Day 21 Dose	2016-01-14
10	ng/mL	22	2016-01-28	28	Week 4 0H	2800	PT0H	Day 28 Dose	2016-01-14
5	ng/mL	29	2016-02-04	35	Week 5 0H	3500	PT0H	Day 35 Dose	2016-01-14

PCDY and VISITDY don't match or group

TPTNUM requires special logic

ELTM at 0H in recovery period