Successful SEND Compliance for Pharmaceutical Companies

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Introduction

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- In our company (AKP), we collaborated with CRO and/or SEND Solution Provider to create SEND Datasets
- Needless to say, we as a sponsor is responsible to the quality of SEND Datasets
- We successfully passed FDA SEND Trail Submission together with partner CRO and Solution Provider
- In this presentation, I would like to introduce about our experience of FDA SEND Trial Submission and its key points

SEND Trial of AKP

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- 3-Month Study of Compound X in Rats
  - Study A: Once-Weekly s.c. Dose Study
  - Study B: Daily s.c. Dose Study
  - Study C: Twice-Weekly s.c. Dose Study
- INA (CRO: Test facility) conducted above studies on behalf of AKP
- AKP asked INA and PDS (SEND solution provider) to create SEND Datasets

Today, I would like to introduce about Study B

Deliverables

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- SEND data files
  - SEND Datasets (XPT)
  - Define Files (XML & PDF)
  - SDRG (MS-Word)

- Others
  - Validation Report from PDS
  - Validation Report from FDA

SEND Datasets Creation Process (INA)

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- In-life data were collected using Provantis (Instem) with the exception of clinical observations, which were collected onto Excel spreadsheets
- Postmortem data were transferred to PathData (PDS)
- Bioanalytical and pharmacokinetic data (TK Test Site) were collected onto Excel spreadsheets
- Trial Design data were transferred to Excel templates

SEND Datasets Creation Process (PDS)

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- Study data were mapped to CT, integrated, and transformed to SEND 3.0 with TranSEND™ (PDS)

- All of the SEND domains were processed by TranSEND to produce an integrated SEND dataset that includes submission ready XPT SEND files and Define XML and PDF files

Quality Process for SEND Datasets (PDS)

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- Each TranSEND dataset export includes a full set of TXT files that correspond to each XPT file or SEND domain in the export
- To QC individual SEND files, each of these TXT files was saved to Excel, and the “track changes” feature was activated to record any findings
- Upon finding resolution with the project SEND Specialist, the SEND file(s) were corrected, re-exported by TranSEND, and subjected to another QC review to verify correction
  - Manually created SEND domains or domains that required a large amount of manual mapping underwent 100% QC
  - All of the other domains underwent 10% - 75% QC review

List of SEND Datasets: Study B (1/2)

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Dataset	Dataset Label	Observation Class
TA	Trial Arms	Trial Design
TE	Trial Elements	Trial Design
TS	Trial Summary	Trial Design
TX	Trial Sets	Trial Design
DM	Demographics	Special Purpose
SE	Subject Elements	Special Purpose
EX	Exposure	Interventions
DS	Disposition	Events
BW	Body Weight	Findings
CL	Clinical Observation	Findings

List of SEND Datasets: Study B (2/2)

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Dataset	Dataset Label	Observation Class
FW	Food & Water Consumption	Findings
LB	Laboratory Test	Findings
MA	Macroscopic Findings	Findings
DD	Death Diagnosis	Findings
PC	Pharmacokinetics Concentrations	Findings
PP	Pharmacokinetics Parameters	Findings
SC	Subject Characteristics	Findings
POOL DEF	Pooled Definition	Relationship

SEND Dataset Verification (PDS)

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- Compliance with SEND 3.0 was determined by TranSEND programming, accurate SEND mapping by a team of SEND specialists with extensive toxicology experience, and validation against SENDIG 3.0 using the Pinnacle 21 (Version 2.0.1)
- Of a total of 30,806 records, there were no errors and 1,807 warnings resulting from published FDA validation rules
- None of the warnings were relevant to this SEND submission for the reasons shown below

Warnings: Study B (1/2)

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FDA Rule	Message	Domain	Count	Explanation in SDRG
FDAN212	Duplicate records	FW	1347	The validation rule is incorrectly applied because it does not take FWORRES into consideration.
FDAN154	Missing value for LBORRESU when LBORRES is provided	LB	79	The value for LBORRES is albumin / globulin ratio, which is not associated with units. Accordingly, LBORRESU should not be populated, and the validation rule is incorrectly applied.
FDAN169	Missing value for LBSTRESU when LBSTRESC is provided	LB	79	The value for LBSTRESC is albumin / globulin ratio, which is not associated with units. Accordingly, LBSTRESU should not be populated, and the validation rule is incorrectly applied.

Warnings: Study B (2/2)

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FDA Rule	Message	Domain	Count	Explanation in SDRG
FDAN033	SEND/dataset variable label mismatch	LB	1	The variable in question is LBSTNRC (Reference Range for Character Result-Standard Unit), and it was used in the LB dataset in accord with SENDIG 3.0. Accordingly, the validation rule was incorrectly applied.
FDAN341	PCORRESU and PCSTRESU values not found in Unit extensible codelist	PC	276	The PCORRESU and PCSTRESU values in question are pg/mL. The correct CT codelist for these variables is PKUNIT and not Unit. The validation rule is therefore incorrectly configured and does not apply here.
FDAN212	Duplicate records	PP	25	The validation rule is incorrectly applied because it does not take PPORRES into consideration.

Final QC Review (INA)

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- SEND Datasets
  - To QC individual SEND files, each of these TXT files was saved to Excel using the Viewer.
  - All the domains underwent 100% QC review
- Define.pdf and SDRG
  - Printouts were fully checked

AKP inspected the QC records

FDA Trial Submission

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- Completing the final confirmation (INA), PDS conducted “Trial submission” of Study B on behalf of AKP (August 2015)
- Study B was passed successfully with no error (November 2015)

Pinnacle 21 (v.2.0.1) vs FDA's validator

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- We used Pinnacle 21 (v2.0.1) at that time
  - It includes FDA SEND validation rules (v.2.0)
  - There were 1,807 warnings
- On the other hand, FDA used DSIMS™ (PointCross) at that time
  - It includes FDA SEND validation rules (v.2.1)
  - There were 15,028 warnings

AKP's SEND Trial is in Progress

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- Recently, we have created SEND Datasets for Studies A & C
  - We revised the SEND Datasets for Study B to have consistency among 3 studies
- "Trial submission" again for 3 studies (May 2016)
- E-mail from FDA (June 2016)
  - We received a lot of new SEND sample submission recently and there are some backlogs
  - Since your submissions are pretty similar, we will only validate one study
- AKP is waiting for FDA's validation (as of 27 July 2016)

Key Points

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- Pharmaceutical company as a sponsor is responsible to the quality of SEND Datasets
- SEND Datasets have not been officially categorized as GLP data at present
- However, I think GLP level of quality is required because it will be used for the new drug evaluation
- In order to achieve the targeted quality, we should learn more about SEND and the necessary procedures

Thank you for your attention