Show and Tell session

TT12

“towards a harmonized data transfer agreement (DTA) feedback and recommendation from EBF TT 12”

Introduction

EBF 9th Open Symposium
16-18 November 2016
Barcelona

Preparation team:

- José Groenboom-Nieuwenhuijzen (PRA HS, team lead)
- Bernd Matthes (Celerion)
- Martina Wein (Boehringer-Ingelheim)
- Richard Abbott (Bayer Pharma AG)
- Regine de Gier (PRA HS)
- Rebecca Sleigh (LGC)
- Susanne Globig (Actelion)
- Tsvetelina Ivanova (Comac Medical)
- Philip Timmerman (Sponsor, on behalf of EBF)

EBF TT-12 : Overview

- Previously worked on a Generic Lab Manual
  - Ideas and survey presented in BCN in 2013
  - Initial Lab Manual drafted by small subteam
  - Follow up workshop in Brussels in Feb 2014
    - With input from clinical as well as bioanalysis
  - Draft Lab Manual refined and finalised June 2014
  - Published on Bioanalysis zone and in Clinical Investigations
  - http://www.bioanalysis-zone.com/2015/10/30/development-of-a-generic-laboratory-manual-for-biological-sample-logistics-in-clinical-pharmacokinetic-studies/

EBF TT-12 : Overview

- New topic : Generic Data Transfer Agreement
  - Ideas and survey presented in BCN in 2015
  - Workshop in Limelette in March 2016 (input from CRO and industry, both bioanalysts and DM, as well as QA)
  - Final version September 2016
  - Presenting at BCN 2016
  - Looking for opportunities to publish on Bioanalysis Zone and in datamanagement magazine
  - And: start using the DTA!

Towards a harmonized DTA

- Bioanalysts and data managers have different functions and follow different procedures
- Often they do not really understand each other
- They have different interests :
  - BA : interested in the quality of the data
  - DM : interested in the format of the data
- CDISC/SEND : important DM languages typically not used and understood by bioanalysts
- **Regulatory requirement (end of this year required by FDA!)**

Generic Data Transfer Agreement

- Why needed?
- Some of the issues we encounter on a daily basis:
  - Data Reconciliation
  - Lacking (business) Relationships between Central Labs and Clinical sites
  - Variation in data formats, number and types of standard fields
  - Filename of data file
  - Number and types of data transfer

Use and preparation of data transfer agreements - Summary

Bioanalysts	yes		**Data managers**	yes
Provided with specs in time?	36%		Use specs?	84%
Transfer agreement in place?	44%		Let review?	72%
Input possible?	51%			
Made aware of changes?	46%			

Bioanalysts: What would be the minimal criteria for a generic DTA?

- Timelines
- Who should receive the data
- How to transfer the data
- File format
- Column headers
- Contents of the columns
- Which samples should be reported
- Any abbreviations to be used
- Blinded/Unblinded
- Sign off Vendor and receiver

Show and Tell session

TT12

Generic Data Transfer Agreement Document

Introduction

EBF 9th Open Symposium
16-18 November 2016
Barcelona

Generic Data Transfer Agreement

- Generic DTA is a .....

Template

- Therefore can be changed as required
- DTA covers both Clinical and Non-Clinical Data

Generic Data Transfer Agreement

Sponsor/Company:	
Protocol No:	
Bioanalytical Project Id:	
Version Date:	
Version Number:	
Expected data base lock	

Type of Transfer	**Description of Transfer (including timelines, (un)blinded))**	**Who will receive the transfer?**	**Contact details**
Test Transfer:	<Describe the frequency of test transfers here. Be sure to be precise. For example, "the first Monday of every month.", or provide planned date of each transfer.>	Company Name	Email Phone
Interim Transfer	<Describe the frequency of interim data transfers here, include if the data is blinded or not, describe who is allowed to receive the unblinded files.>		Email Phone
Reconciliation transfer	<Describe the frequency of reconciliation transfers, does it contain concentrations? All received/analyzed samples/ including placebo samples>		Email Phone
Final data transfer	<Describe the date of final data transfer, unblinded, describe that unblinded data should not be sent before a specific date, or only after approval has been given, by whom>		Email Phone

Generic Data Transfer Agreement

Data format:	<Describe source data format here (i.e. ASCII, SAS, Excel, including delimiter (.csv,…)>
File name interim:	<Describe naming of file, e.g. ProtocolNumber_Vendor number_Contents_Version_Status_Date._Time> Status can be QC-ed, QA-ed, interim Date_Time is when the file is saved
Transfer type:	☐ Incremental, specify: ☐ Cumulative
Which samples/subjects are included?	☐ All samples received in the lab ☐ All samples analyzed ☐ Other (e.g. including placebo subjects), specify:
Analytes	<Describe analyte names, describe how they should be reported>
Matrix	<In case of different matrices, describe if these should be reported separately>

Generic Data Transfer Agreement

5.0 Approvals <delete whichever is not applicable>

Name of Sponsor Representative/Title:	<Print Name/Title>
Signature of Sponsor Representative/Date:	<Signature/Date>

Name of BA Representative/Title:	<Print Name/Title>
Signature of BA Representative/Date:	<Signature/Date>

Name of (Lead) Data Manager /Title:	<Print Name/Title>
Signature of (Lead) Data Manager/Date:	<Signature/Date>

Name of Programmer /Title:	<Print Name/Title>
Signature of Programmer/Date:	<Signature/Date>

Generic Data Transfer Agreement

Starter Questions

- Who is using a DTA?
- Who would be willing to implement a Generic DTA in their company?

Show and Tell session

TT12

CDISC
Introduction for the Bioanalyst

EBF 9th Open Symposium
16-18 November 2016
Barcelona

Some definitions

CDISC = Clinical Data Interchange Standards Consortium

- ✓ CDISC is a global, open, multidisciplinary, non-profit organization that has established standards to support the acquisition, exchange, submission and archive of clinical research data and metadata
- ✓ The CDISC mission is to develop and support global, platform-independent data standards that enable information system interoperability to improve medical research and related areas of healthcare

SDTM = Study Data Tabulation Model for clinical trials

- ✓ Recommended for FDA regulatory submissions since 2004
- ✓ Submissions of trials with a start date after 17 Dec 2016 are expected to conform to this format

SEND = Standard for Exchange of Non-clinical Data

- ✓ Accepted in 2011
- ✓ Submissions of studies with a start date after 17 Dec 2016 have to conform to this format

Why Standards?

- ✓Facilitate the data management activities
- ✓Enable more efficient data review
- ✓Facilitate the regulatory submission process
- ✓Ensure data mining across different studies

How to implement the standards?

SDTM Implementation Guide:

- ✓ Available at www.cdisc.org / standards
- ✓ Provides specifications, defines domains and variables, and offers examples with study data
- ✓ New Draft Content SDTMIG v3.3 Batch 3 Now Available for Public Review – Comments Due 21 October 2016

SEND Implementation Guide:

- ✓ Available at www.cdisc.org / standards
- ✓ SENDIG (Implementation Guide) v3.1 is now available
- ✓ DISC SEND Implementation Guide: Developmental and Reproductive Toxicology (SENDIG-DART) v1.0 is now available

How to read the standards?

Domain structure:

- ✓ Variable Name
- ✓ Variable Label: Describes the meaning of the variable
- ✓ Type: Character or numeric
- ✓ Controlled terminology: Indicates whether code lists or certain formats are to be used
- ✓ Three categories of variables are available:

Requested (Req) - variable must be included and cannot be null
Expected (Exp) – column for this variable must be included, but may contain some null values
Permissible (Per) – variable should be included if data was collected or derived, columns which only contain null values might be omitted

Laboratory Results are organized in three domains – PC (Pharmacokinetic Data), LB (Pharmacodynamics Data) and IS (Immunogenicity Data)

PC domain

Variable Name	Label	Format	Required/ Expected/ Permissible
STUDYID	Study Identifier	Char	Req
DOMAIN	Domain Abbreviation	Char	Req
USUBJID	Unique Subject Identifier	Char	Req
PCSEQ	Sequence Number	Num	Req
PCGRPID	Group ID	Char	Perm
PCREFID	Reference ID	Char	Perm
PCSPID	Sponsor-Defined Identifier	Char	Perm
PCTESTCD	Pharmacokinetic Test Short Name	Char	Req
PCTEST	Pharmacokinetic Test Name	Char	Req
PCCAT	Test Category	Char	Perm
PCSCAT	Test Subcategory	Char	Perm
PCORRES	Result or Finding in Original Units	Char	Exp
PCORRESU	Original Units	Char	Exp
PCSTRESC	Character Result/Finding in Std Format	Char	Exp
PCSTRESN	Numeric Result/Finding in Standard Units	Num	Exp
PCSTRESU	Standard Units	Char	Exp
PCSTAT	Completion Status	Char	Perm
PCREASND	Reason Test Not Done	Char	Perm
PCNAM	Vendor Name	Char	Exp
PCSPEC	Specimen Material Type	Char	Req /Exp[3)]
PCSPCCND	Specimen Condition	Char	Perm
PCMETHOD	Method of Test or Examination	Char	Perm

PC domain (cont.)

PCFAST	Fasting Status	Char	Perm
PCDRVFL	Derived Flag	Char	Perm
PCLLOQ	Lower Limit of Quantification	Num	Exp
PCULOQ[2)]	Uppper Limit of Quantification	Num	Perm
VISITNUM	Visit Number	Num	Exp
VISIT	Visit Name	Char	Perm
VISITDY	Planned Study Day of Visit	Num	Perm
PCDTC	Date/Time of Specimen Collection	Char	Exp
PCENDTC	End Date/Time of Specimen Collection	Char	Perm
PCDY	Actual Study Day of Specimen Collection	Num	Perm
PCTPT	Planned Time Point Name	Char	Perm
PCTPTNUM	Planned Time Point Number	Num	Perm
PCELTM	Planned Elapsed Time from Time Point Ref	Char	Perm
PCTPTREF	Time Point Reference	Char	Perm
PCRFTDTC	Date/Time of Reference Point	Char	Perm
PCEVLINT	Evaluation Interval	Char	Perm

LB domain

Variable Name	Label	Format	Required/ Expected/ Permissible
STUDYID	Study Identifier	Char	Req
DOMAIN	Domain Abbreviation	Char	Req
USUBJID	Unique Subject Identifier	Char	Req
LBSEQ	Sequence Number	Num	Req
LBGRPID	Group ID	Char	Perm
LBREFID	Reference ID	Char	Perm
LBSPID	Sponsor-Defined Identifier	Char	Perm
LBTESTCD	Lab Test or Examination Short Name	Char	Req
LBTEST	Lab Test or Examination Name	Char	Req
LBCAT	Category for Lab Test	Char	Exp
LBSCAT	Subcategory for Lab Test	Char	Perm
LBORRES	Result or Finding in Original Units	Char	Exp
LBORRESU	Original Units	Char	Exp
LBORNRLO	Reference Range Lower Limit in Orig Unit	Char	Exp
LBORNRHI	Reference Range Upper Limit in Orig Unit	Char	Exp
LBSTRESC	Character Result/Finding in Std Format	Char	Exp
LBSTRESN	Numeric Result/Finding in Standard Units	Num	Exp
LBSTRESU	Standard Units	Char	Exp
LBSTNRLO	Reference Range Lower Limit - Std Units	Num	Exp
LBSTNRHI	Reference Range Upper Limit - Std Units	Num	Exp
LBSTNRC	Reference Range for Char Rslt-Std Units	Char	Perm
LBNRIND	Reference Range Indicator	Char	Exp
LBSTAT	Completion Status	Char	Perm
LREASND	Reason Test Not Done	Char	Perm
LBNAM	Vendor Name	Char	Perm
LBLOINC	LOINC Code	Char	Perm
LBSPEC	Specimen Type	Char	Perm
LBSPCCND	Specimen Condition	Char	Perm
LBMETHOD	Method of Test or Examination	Char	Perm

LB domain (cont.)

LBBLFL	Baseline Flag	Char	Exp
LBFAST	Fasting Status	Char	Perm
LBDRVFL	Derived Flag	Char	Perm
LBTOX	Toxicity	Char	Perm
LBTOXGR	Standard Toxicity Grade	Char	Perm
VISITNUM	Visit Number	Num	Exp
VISIT	Visit Name	Char	Perm
VISITDY	Planned Study Day of Visit	Num	Perm
LBDTC	Date/Time of Specimen Collection	Char	Exp
LBENDTC	End Date/Time of Specimen Collection	Char	Perm
LBDY	Study Day of Specimen Collection	Num	Perm
LBTPT	Planned Time Point Name	Char	Perm
LBTPTNUM	Planned Time Point Number	Num	Perm
LBELTM	Planned Elapsed Time from Time Point Ref	Char	Perm
LBTPTREF	Time Point Reference	Char	Perm
LBRFTDTC	Date/Time of Reference Time Point	Char	Perm

IS domain

Variable Name	Label	Format	Required/ Expected/ Permissible
STUDYID	Study Identifier	Char	Req
DOMAIN	Domain Abbreviation	Char	Req
USUBJID	Unique Subject Identifier	Char	Req
ISSEQ	Sequence Number	Char	Req
ISGRPID	Group ID	Num	Perm
ISREFID	Reference ID	Char	Perm
ISSPID	Sponsor-Defined Identifier	Char	Perm
IETESTCD	Immunogenicity Test/Exam Short Name	Char	Req
ISTEST	Immunogenicity Test or Examination Name	Char	Req
ISCAT	Category for Immunogenicity Test	Char	Perm
ISSCAT	Subcategory for Immunogenicity Test	Char	Perm
ISORRES	Result or Finding in Original Units	Char	Exp
ISORRESU	Original Units	Char	Exp
ISSTRESC	Character Result/Finding in Std Format	Char	Exp
ISSTRESN	Numeric Result/Finding in Standard Units	Num	Exp
ISSTRESU	Standard Units	Char	Exp
ISSTAT	Completion Status	Char	Exp
ISREASND	Reason Not Done	Char	Perm
ISNAM	Vendor Name	Char	Perm
ISSPEC	Specimen Type	Char	Perm
ISMETHOD	Method of Test or Examination	Char	PPerm

IS domain (cont.)

ISBLFL	Baseline Flag	Char	Perm
ISLLOQ	Lower Limit of Quantification	Num	Exp
VISITNUM	Visit Number	Num	Exp
VISIT	Visit Name	Char	Perm
VISITDY	Planned Study Day of Visit	Num	Perm
ISDTC	Date/Time of Collection	Char	Exp
ISDY	Study Day of Visit/Collection/Exacm	Num	Perm

Conclusion

Regulatory requirements for standardization of data exchange trigger the need for standardization of Data Transfer Agreements