Overview and feed-back from CDISC European Interchange 2008

(From April 21st to 25th, COPENHAGEN)

Groupe des Utilisateurs Francophones de CDISC
Bagneux - June 20th, 2008

Laurence Le Lann,

Hélène Savoye

sanofi aventis

L'essentiel c'est la santé.

Agenda

- SDTM Training
- ADaM Training
- Messages from SDTM & ADaM training
- Legacy Data Conversion Workshop
- General comments from that Interchange
- Useful WEB links
- Conclusion

SDTM Training - Content of 2 full days (1/2)

- Review the mains terms used by CDISC, their definition and the differences between some of them (SDTM vs AdaM…)
- Annotate the blank CRF with SDTM variables
- How to choose the correct model
- How to create a new domain (finding, intervention or event)
- Create the defines for SDTM
  - list of variables
  - name of variables ….
  - no use of derived variables (they should be kept in ADS)

SDTM Training - Content of 2 full days (2/2)

- Format for Date/Time variables
- Create few SUPPQUAL
- Create some Trial design define (Subject level data, Subject Elements and Subject visits)
- Create tables for “relationships”

ADaM Training - Content of 1 full day

- Background and introduction of CDISC and Standards, CDISC and the FDA
- Purpose of ADaM
- Basic principles of ADaM
- ADaM rules and variables
- ADaM Metadata
- ADSL
- ADaM Implementation guide - Draft

Messages from SDTM & ADaM training (1/7)

- **FDA according to CDISC presenter's experience**
  - **FDA wants to be able to replicate what the sponsor did so that they can trust them**
  - **First thing FDA statistician do**
    - **Recreate analyses datasets**
  - **Some tools at FDA only use SDTM**
    - **Some derived variables are needed in SDTM as well**
      - **ie "total score for a questionnaire"**
  - **FDA does not employ programmers**
    - **Statistical and Medical reviewers need ADaM**
  - **Traceability is of high importance**
    - **Traceability from p-value back to protocol**
    - **CDISC recommends to QC the transparency so that FDA understand easily what the sponsor did and how he did it**
  - **Keep in touch with FDA reviewer**
    - **to understand what they want**
    - **So that they understand what you did**

Messages from SDTM & ADaM training (2/7)

- Up to sponsor, but CDISC Recommendation
  - Use SDTM to build ADaM
- Separate submission of SDTM and ADaM
  - With corresponding define files
- No real recommendation from CDISC on derived variables to be in SDTM
  - “Include some derived as they seem natural to be in SDTM”

Messages from SDTM & ADaM training (3/7)

- Distinguish between what was observed and what was derived
- No imputation should be done in SDTM
  - If imputation needed, should be in ADaM
- Analysis Timing variables
  - Character variables (C) in SDTM
  - Numerical variables (N) in ADaM
    - if lots of imputation in (N) variable, keep (C) in ADaM as well

CDISC suggestion to FDA:

Minimum mandatory submission should include SDTM and ADSL from ADaM (still in discussion with FDA)

Messages from SDTM & ADaM training (4/7)

- **Specifications for organizing the datasets in eCTD**
  - **Contents of ECTD folders:**
    - **Folder Datasets/[study]/analysis => should contain analysis datasets and corresponding define files**
    - **Folder Datasets/[study]/tabulations => should contain data tabulation datasets, corresponding define files and blank annotated CRF**
      - **Annotated CRF recommended in data tabulation datasets folder with links in other directories (listing, analysis)**
      - **Recommendation is to not refer to annotated CRF in ADaM but to SDTM which themselves do refer to annotated CRF**

Messages from SDTM & ADaM training (5/7)

- If submission of SDTM, submission of subject profiles might not be needed
  - Need agreement with FDA at pre-NDA meeting
- Permissible variables
  - if information collected in CRF, variables must be submitted in SDTM
- (U?)SUBJID:
  - Recommendation from CDISC is
    - *The SUBJID uniquely identify each subject within a submission and ensure that the same person has the same number across studies*
  - However, Not always possible
    - Enough information might not be allowed to be collected to ensure same numbering across studies within submission
- Information on randomization (IVRS)
  - Might be recorded in sub-qualifier DM
  - However never discussed in SDTM WG
- Trial design domain
  - Not required but recommended for clinical trials

Messages from SDTM & ADaM training (6/7)

- Pilot ADaM submission
  - Not always what you are supposed to do!
- "Role" column in define
  - Was present in ADaM 2.0
  - Not included anymore in 2.1 since variables may have different roles within analyses
- "Reviewer guide"
  - Optional document presenting key decisions
  - Should add additional information compared to SAP
  - Not a CDISC document, no template exists
  - FDA's feedback in ADaM pilot: Felt as very Helpful
- ADaM 2.1 version just released for public consultation/review by September 5, 2008

Messages from SDTM & ADaM training (7/7)

- "one proc away" table
  - Dose not mean only one SAS proc to produce a given table
    - A table containing mixed information (baseline, value at time X, change from baseline and lsmeans estimates) OK
      - as long as information to produce this table available somewhere
      - even if you need 4 proc to produce the table
- Program codes
  - "Ensure program codes are well commented, easy to follow and well formed"
    - Provide code to help reviewer understand what you did (ie PROC MIXED with options)
    - FDA does not expect to run the code, just need to understand the options used

Legacy Data Conversion Workshop

- A ½ day workshop with 4 examples about the way to convert legacy data into SDTM data
- Very interesting workshop
  - Presentation of process to convert legacy data
    - Retrieve of all information needed
    - Harmonization of controlled terminology
    - CRF annotation
    - Mapping
    - QC
  - Demo of SAS ETL STUDIO used to do the mapping
- Link to WEB site will be given later?

General comments from that Interchange (1/3)

- Gray zones in SDTM definition on derived variables
  - Part of SDTM? SUPPQUAL? ADaM?
- Different approaches/interpretations of SDTM IG / ADAM but All the presentations report the data flow SDTM -> ADS
- Very wide profiles of participants (50% DM)
- A lot of new standards are under definition at CDSIC level, for Data management mainly
- Operational Data Model (ODM) trends to be a standard way to store data from EDC?
- Trend to integrate all kind of data used in research into 1 standard (public health as well)

General comments from that Interchange (2/3)

- Risks
  - Not follow-up the discussions and orientations
  - Not easy to understand all the initiatives: HL7, ODM etc ….
- Key words for 2008
  - TRANSPARENCY & INTEROPERABILITY
- Important focus on QC aspects, SDTM adherence checks
- Importance of metadata
- Ensure that FDA reviewers have complete & accurate information

General comments from that Interchange (3/3)

Training for all DM and PROG staff to SDTM is very important

(could be organized internally)

Training for all STAT staff to AdAM is also recommended

Useful WEB links

- **On FDA websites:**
  - **Checks performed by the FDA before any loading attempt in Data warehouse JANUS: http://www.fda.gov/oc/datacouncil/janus_sdtm_validation_specification_v1.pdf**
  - **Study data specifications: http://www.fda.gov/cder/regulatory/ersr/studydata.pdf**
- **On CDISC website:**
  - **Presentations from Congress part: http://www.cdisc.org/publications/interchange2008.html**

Conclusion

Very interesting congress & trainings

Recommended to EVERYBODY !