Meeting Minutes

CDISC-HL7 Stage I-B
June 5, 2008
11:00 am – 12:00 pm (EST)

Attendees / Affiliation

Jay Levine/CDISC (Co-Chair)
Julie Evans/CDISC
Patty Garvey/FDA (Facilitator)
Scott Getzin/Eli Lilly
Terry Hardin/IBM
Joyce Hernandez/Merck
Wayne Kubick/Lincoln Technologies
Mary Lenzen/Octagon
Diane Wold/GSK

Background

The Clinical Data Interchange Standards Consortium (CDISC) formed a Stage IB group to develop the requirements for the CDISC - Health Level 7 (HL7) Content to Message Project. It was agreed by FDA and CDISC to conduct a series of regular conference calls for sub-team members as the initial path forward on the CDISC-HL7 IB activities.

The purpose of this meeting is to review the "draft" Subject Data use cases from Jay Levine.

Discussion

- It was indicated that the Subject Data use cases presented describe what FDA's reviewers does with the data. The group thought that the use cases should describe what data should be submitted to the FDA for review. The use cases presented are all analysis cases.

- It was stated the use cases should be in a CDISC-HL7 message format. The context of the case should communicate what information is needed and not express what current information is not being submitted to the FDA.

- In reference to the Case Review #2 slide, the case does not indicated what data is needed and how it fit into the message. There was also a question regarding what adverse event for "severity" mean. Did the severity happen during the study or at a later date?

- In reference to the Case Review #3 slide, it was stated that the use case should be in a more structurally presented and not presented as a regulatory guidance.

- In reference to the Case Review #4 slide, it was stated the requirement specifics may be needed rather than a use case.

- At the next meeting, further discussion on these use cases will be needed and what determine the next steps.

Attachment: DRAFT Subject Data Use Cases (Jay Levine)

Drafted: PGarvey/7-31-2008
Approved:

Subject Data Use Cases

- Case Review
  - Diagnose AE in a subject
  - Evaluate AE for severity
  - Evaluate AE for causality
- Parameter Estimation
  - Estimate mean and variance of subject response in a study cell
  - Estimate survival time for subjects in a study cell
  - Estimate the baseline value of a subject response
  - Construct confidence intervals for estimates
- Hypothesis Testing
  - Analysis of covariance
  - MH Test

Case Review 1

- Diagnose adverse event in a subject
  - An drug that is marketed in Europe is being evaluated for marketing in the US. A consumer group claims that the drug is associated with a specific adverse event. A reviewer needs to evaluate patients that were treated with the product, and determine if they have experienced the adverse event. This will require the reviewer to evaluate patients that may not have been previously diagnosed as experiencing the adverse event.

Case Review 2

- Evaluate AE for severity
  - A product is known to cause a particular adverse event. Depending upon the severity of the adverse event, the effect of the adverse event on the patient can range from minor discomfort to disability or death. A reviewer needs to determine how many patients experienced the more severe manifestations of the adverse event.

Case Review 3

- Evaluate AE for causality
  - An drug that is marketed in Europe is being evaluated for marketing in the US. A consumer group claims that the drug causes a specific adverse event. A reviewer needs to evaluate patients that were treated with the product and experienced the adverse event, and determine if these adverse events can be reasonably explained by factors other than the drug, such as high fever, meningitis, treatment with drugs known to cause the adverse event, or pre-existing conditions. In order to determine causality, the reviewer plans to use reasoning similar to that described by Austin Bradford Hill in his paper “The Environment and Disease: Association or Causation (*Proceedings of the Royal Society of Medicine*, 58 (1965), 295-300.)

Case Review 4

- Determine if patients met inclusion criteria
  - A study is conducted in order to determine if a product is safe and effective in a sub-population of patients. The inclusion criteria are constructed so that only patients in the sub-population of interest are enrolled in the study. The reviewer wants to ensure that only patients who met the inclusion criteria were enrolled in the study.

Parameter Estimation 1

- Estimate mean and variance of subject response in a study cell, and functions of these means and variances.
  - A reviewer wishes to estimate the mean and variance of a continuous response variable (e.g. blood pressure) at one or more times (e.g. visit) in one or more study cells, and calculate functions of these means and variances.

Parameter Estimation 2

- Estimate mean survival time for subjects in a study cell
  - A reviewer needs to estimate the mean survival time to an event (e.g. heart transplant) in a study cell. In order to calculate the mean, the reviewer needs to know if the event happened, and if the happened, when the event happened.

Parameter Estimation 3

- Estimate the baseline value of a subject response
  - An analyst want to estimate the pretreatment value of a patient outcome (e.g. blood pressure). Estimation of this value will be based upon one or more values of the attribute in a study cell prior to the study cell containing study treatment, or from patient history data.

Hypothesis Testing 1

- Test that a function of the data in one or more study cells is equal to, less than, or greater than a constant.
  - Calculate an analysis of covariance for a continuous outcome measure for study cells in the second epoch of the study. The value at visit 3 is the response variable, and the sponsor-defined baseline score is the covariate.

Hypothesis Testing 2

- Test that a function of the data in one or more study cells is equal to, less than, or greater than a constant.
  - Calculate a Mantel-Haenszel test for study cells in the second epoch of the study. The response variable is categorical (e.g. presence or absence of an adverse event, seriousness of an adverse event). Stratification needs to be done by site, age, sex, and race.