How to Improve Efficiency and Productivity of Statistical Output

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Introduction

- Statistical output is often a product of individual practice and reflects individual preference. However, as an early stage contract research organization (CRO) in the pharmaceutical industry serving many clients with one ultimate goal (product to market), delivering of statistical output with efficiency and productivity is the key to business success.
- Standardization in appropriate areas leads the path to improved efficiency and productivity.

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Opportunities for Standardization

- Common data from study to study
  - Adverse events
  - Other safety data - clinical laboratory tests, ECG, vitals
  - Demographic data
  - Subject disposition data
  - Screening and compliance data
- Data handled according to regulatory guidelines
  - Statistical analysis for specific study types – BA/BE, TQT
  - Submission data – CDISC standards for SDTM and ADaM
- Common documents
  - Study plans
  - Study reports
  - CRF and Data submission documents

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Standard Templates for Documents

- Standard contents to consistently provide information and directions needed to work with study data
- Standard verbiage to provide clear description of information and methods
- Standardize by type of study and/or sponsor requirements
- Documents include:
  - Statistical Analysis Plan (SAP)
  - Edit Check Plan
  - Data Management Plan
  - Reports (statistical, top-line, ICH, eCTD)
  - Other technical documents

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Standard Templates for Documents

Statistical Analysis Plan Template as an Example

- Required elements
  - Study design and endpoints
  - Treatment description
  - Analysis populations
  - Handling of early withdrawal, missing data, rechecks, and BLQ values, calculations of baseline and analysis variables
  - Specify dictionary used for coding
  - Interim analysis requirements
  - Statistical assumptions and methods
  - Use of decimal points and significant digits
- Standard verbiage and formula to provide clear and consistent description of information and methods, provide SAS codes if applicable

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Standard Templates for Documents

Statistical Analysis Plan Template as an Example (cont.)

- Include details for programmer to make SAP a programming guide
- Follow ICH report structure to make incorporation of statistical results seamless
- Get end-user approval before execution
- Specialty Templates - Standard template for specific type of studies to ensure required analysis are performed according to specific regulatory agency guidance
  - Thorough QT studies
    - QT correction methods (QTcB, QTcF, others)
    - ANCOVA of time-matched baseline for central tendency and assay sensitivity
    - Outliers and morphological changes
  - Bioequivalence studies

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Standard SAS Codes

- Same codes for the same algorithm and calculation to derive variables
- Same procedure codes for the same statistical analyses given study design, such as ANOVA, Regression.
- Same statistical method for the same testing, such as normality, homogeneous variance, outlier testing, bioequivalence, dose proportionality, steady state, etc.

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Standard Input

- Consistent database design to provide consistent input structure
  - Use of CDISC compliant data structure
    - CDASH for data collection
    - SDTM for individual subject data presentations
    - ADaM for analyses, summary tables and figures

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Standard Output

- Same layout for same data type in listings, tables, and figures to utilize standard macros
  - Pharmacokinetic concentration and parameter tables
  - Subject disposition listing and table
  - Adverse event listing and tables
  - Shift tables for results with normal ranges
  - Statistical comparison tables for bioequivalence/bioavailability studies, non-inferiority tables, ECG tables for TQT studies, etc.
  - Figures for observations over time
  - Correlation figures, spaghetti plots

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Benefits of Standardization (Improved Efficiency and Productivity)

- Consistent output quality
- Staff training
- QC and Review
- Operation procedures and timelines
- Documentation of compliance
- Submission ready
- More time and attention for study specific issues
- Systematic approaches are reproducible

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Questions?

Please contact info@celerion.com