Planning for Data Reporting Processes for Submission - Key Considerations

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Drug Approval: Necessary and sufficient evidence of drug safety, efficacy, and pharmacovigilence.

Clinical Trial Data: Trial-1, Trial-2, Trial-3, Trial-4

Data Analysis, Tabulation, And Reporting

Regulatory Submission
Regulatory Submission - Factors Causing Pressure

- Patent Life Restriction
- Regulatory Efforts - Fast track approvals
- Fierce Competition

Uncertainties about drug performance
Generic Drug Players
Uncertainties about market adoption

Regulatory Submissions Process

Drugs in Market
Regulatory Submission - Data Reporting Process

Cohort based planning for data pooling and defining analysis methods and specs through analysis plan → Analysis datasets and data reports (tables, listings and graphs) generation process → Statistical review of data reports and analysis results → Clinical Review of Data reports and approvals

Medical writer’s review of reports and their inclusion into medical reports → Regulatory review of submission package → Regulatory submission
Regulatory Submission - Data Reporting Complexities: Overlap of Timelines

Trial -A: Progression

SDTM data → Safety Review → BDR Data → Blinded Data Review → Analysis Data → CSR

Draft SAP along with LoT and Table Shells

Initial Cohorts based on BDR data → First version or Draft TLGs → Revised SAP → Future Cohorts based on final data → Finalized TLGs

Progression of Reporting Based on Pooled Data

Trial -B: Progression

SDTM data → Safety Review → BDR Data → Blinded Data Review → Analysis Data → CSR
Regulatory Submission - Data Reporting Complexities: Overlap of Timelines

- Significant data issues causing re-opening of locked database
- Inclusion of additional analyses, parameters or even data into the trial level CSR reporting.
- Amendment of data reporting based on trial level CSR reviews

Risk Factors caused by overlap of timelines of trial level reporting with submission of pooled data

Impact of these risk factors

Lack of consistency between analysis results from trial level data and pooled data.
- Number of serious adverse events
- Number of discontinued patients
- Reporting of significant and key safety findings
- Efficacy reporting results
Regulatory Submission - Data Reporting Complexities - Data Standards Differences

Trial-1: CRO-A
- SDTM data
- ADaM Data

Trial-2: CRO-A
- SDTM data
- ADaM Data

Trial-3: CRO-B
- SDTM data
- ADaM Data

Mapping and Integration Issues

Trial-3: CRO-B
Data Mapped to ensure consistency of SDTM variables and ADaM methodology

Pooled Data
Regulatory Submission - Data Reporting Complexities - Iterative Nature of Data Analysis

- Initial Version of analysis plan
- Initial SAS Code
- Amendments in methodologies based on changing data properties
- Changes in needs of data representation
  - Combining tables
  - Splitting them apart
  - Adding or removing columns
- Changes in analyses needs based on clinical and medical reviews
- Additional exploratory analyses and data reporting

Assess impact
Modify the code
Re-run Program
Revise Algorithm
Quality Check
Modification For Program
Regulatory Submission - Data Reporting Complexities - Iterative Nature of Data Analysis

Initial Version of analysis plan

Amendments in methodologies based on changing data properties

Changes in needs of data representation
  • Combining tables
  • Splitting them apart
  • Adding or removing columns

Changes in analyses needs based on clinical and medical reviews

Additional exploratory analyses and data reporting

Initial SAS Code

Process Revision-1

Process Revision-2

Process Revision-3

Process Revision-4
If you don’t assess these factors in advance, don’t blame the technology.
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.
.
blame yourself!!!!
.
.
if you can!
Continued availability of individuals with strong knowledge of data and analysis methodologies used for the data analysis and reporting of a drug.
Regulatory Submission - Data Reporting: Other Reporting Aspects

- Reporting of PK/PD and Biomarker Data
- Outcomes Research Assessments (in case of sNDA)
- Planning for Advisory Committee meeting
- Reporting of other data not part of database
Different Submission Types

- Drug approved by one regulatory authority and submitted to another one.
- Drug approved for one indication and submitted for another indication for approval from same regulatory authority
- Biologic product vs new drug application
- Co-licensed drug application
Conclusion

• Effective submission execution should have necessary elements of:

  - **Cante** (Well defined roles and responsibilities)
  - **Toque** (Fit to position of Resources)
  - **Baile** (Effective Execution)
  - **Jaleo** (Quality assessment And Compliance)
  - **Palmas** (Effective timeline Planning)
  - **Pitos** (Necessary Agility in Processes)

Well……..there is always room for some Tapas (improvement)!
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Questions?