Development of a Risk-Based Monitoring (RBM) Visualization Application Interface using JMP Scripting Language (JSL)

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Outline

• Background
• Objectives
• Application Interface - KRI Analyzer
• Demo
Traditional Monitoring Approach

- On-site monitoring
- Implemented by regular site visits
- Costly - multiple sites
- Negligible effect
RBM is a Risk-Based Approach

Application of Systematic Quality Risk Management to Clinical Trials
- Identification of risks
- Assessment of the risks represented by KRI
- Execution of monitoring and risk-mitigation plan
Centralized Monitoring is the Key to RBM

✓ Centralized monitoring is a remote evaluation carried out by sponsor personnel at a location other than the sites at which the clinical investigation is being conducted.

1. Provide many of the capabilities of on-site monitoring as well as additional capabilities
2. Reduce errors
3. Low cost – minimize the site visits
4. Helps in early identification and mitigation of data quality risk/issue(s)
# Guidelines on RBM

**The regulatory environment is changing**

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<table>
<thead>
<tr>
<th><strong>EUROPEAN MEDICINES AGENCY</strong></th>
<th><strong>ICH Guideline for GCP E6(R2)</strong></th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Reflection paper on risk based quality management in clinical trials</strong></td>
<td><strong>Revision of the 1996 GCP Scheduled for Approval in NOV16</strong></td>
</tr>
</tbody>
</table>

> “... Any analysis of trends should be done in relation to the overall impact on the scientific merits and usability of the generated data as established through **priority setting and identification of risks**.”

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<table>
<thead>
<tr>
<th><strong>Guidance for Industry (August 2013)</strong></th>
<th><strong>Introduces 3 new significant additions</strong></th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Oversight of Clinical Investigations — A Risk-Based Approach to Monitoring</strong></td>
<td><strong>Quality risk management</strong> <em>(Based on ICH Q9)</em></td>
</tr>
</tbody>
</table>

> “... certain data anomalies (e.g., fraud, including fabrication of data, and other non-random data distributions) may be more readily detected by **centralized monitoring techniques** than by on-site monitoring.”

**Oversight**:
The sponsor should develop a systematic, prioritized, risk-based approach to monitoring clinical trials

- Routine review of submitted data.
- Identification of missing data, inconsistent data, data outliers or unexpected lack of variability and protocol systematic or significant errors in data collection and reporting at a site or across sites, or may be indicative of potential data manipulation or data integrity problems.
- Using statistical analyses to identify data trends within and across sites.
- Analyzing site characteristics and performance metrics.
- Selection of sites and/or processes for targeted on-site monitoring.
JMP is an Interactive Visualization Tool to Evaluate Clinical Data

- Provide Interactive Tools to Create and Customize a Variety of Graphs to Explore Data
- Perform Statistical Analysis
- JMP Scripting Language (JSL) Customize, Repackage or Extend JMP Functionalities
- JSL Can Integrate with Powerful SAS, R Capabilities
Objectives

Use JSL to Create an Application Interface to

✓ Analyze and visualize ongoing data to identify the site at the risk in an efficient manner
  ▪ Allow access to the snapshots of multiple studies simultaneously
  ▪ Provide an interactive monitoring dashboard allowing for quick glimpse of the status of study sites
  ▪ Allow for drilldown to the detailed analysis of individual KRI
Risk Assessment

✓ Risk Identification - Key Risk Indicators
  • Based on the critical data and critical process
  • Subject Safety: Informed consent violation, AE underreporting
  • Data quality: missing primary end point data

✓ Risk analysis
✓ Risk evaluation
Application Interface
- Study Snapshots Selection
Dashboard Monitoring
  - Overview
Cell Plot of Site Risk Rank and KRI Fired
Dashboard Monitoring – KRI Trend
Dashboard Monitoring
- Site Profile

**Classification of KRI over Time**
▲ = fired
Dashboard Monitoring
– snapshot comparison

Note: Red = New Record
Yellow = Modified due to a change in KRI ranking
Blue = Stable indicating no change in the ranking
Green = Dropped
Dashboard Monitoring
– snapshot comparison

A.

B.
Analysis of Individual KRI
Analysis of Individual KRI

Dropout Rate by Site ID

Click to Order by
- Site ID
- Dropout Rate
- Site Overall Rank

Click a Button to View
- Data Table
- Dropout Rate at Study/Country Level
- More Dropout Rate Analysis

Select a Site then Click
- Show Site Ranking
- View Subjects at Site
- Cancel
- Help

Note: The dropout rate is defined as the number of subjects who discontinued from study divided by total exposure months at site.
Dropout Rate Analysis

- Plot 1: a scatter plot of Number of Dropouts and Patient Months in Site.
- Plot 2: a pie chart displaying proportions of disposition events (standard terms).
- Plot 3: a bar chart of Average Disposition Day for all sites in the study.
- Plot 4: a bar chart of monthly dropouts.
Dropout Rate Analysis

- Interactive Visualization

- Plot 1: a scatter plot of Number of Dropouts and Patient Months in Site.
- Plot 2: a pie chart displaying proportions of disposition events (standard terms)
- Plot 3: a bar chart of Average Disposition Day for all sites in the study
- Plot 4: a bar chart of monthly dropouts
## Dropout Rate Analysis

– Subject level data

### Disposition

<table>
<thead>
<tr>
<th>Study Identifier</th>
<th>Unique Subject Identifier</th>
<th>Subject Identifier for the Study</th>
<th>Study Site Identifier</th>
<th>Investigator Name</th>
<th>Country</th>
<th>Number of Subjects Treated in Site</th>
<th>Category for Disposition Event</th>
<th>Reported Term for the Disposition Event</th>
<th>Standardized Disposition Term</th>
<th>Start Date/Time of Disposition Event</th>
<th>Day of Disposition Event</th>
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</thead>
<tbody>
<tr>
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<td>XYZ0001-102-0001 000001</td>
<td>102</td>
<td>Dr. ABC</td>
<td>CZE</td>
<td>6</td>
<td>DISPOSITION EVENT</td>
<td>ADVERSE EVENT</td>
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<td>2018-01-29</td>
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<td>225</td>
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A JMP application is developed to enable an customized analysis of KRIIs for multiple studies

- Dashboard monitoring
- Drill down to the subject Level
- Interactive and automatic
- Easy-to-use buttons and list boxes to ensure that the analysis of complex KRI data be conducted in an efficient and effective way
Thanks!