Actionable Metrics to Improve Study Efficiency & Collaboration

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Actionable Metrics to Improve Study Efficiency and Collaboration

Veeva Clinical Roundtable
September 26, 2013
Philadelphia, PA
• Standardized Performance Metrics
  – What they are and how to use them
• eTMF Systems and Performance Metrics
• How to Get Started
  – Process Maturity Model, Metrics and eTMF
• Q&A
“What gets measured, gets managed.”
— Peter Drucker

Performance metrics establish where you expect to go and whether you got where you intended.

**Lessons Learned:** Organizations need to understand the purpose of performance metrics before utilizing them to assess and manage clinical trials.
Performance Metrics Should Be Paired to Ensure Performance Improvement

TIME
(“CT” cycle time metrics)
(“T” timeliness metrics)

QUALITY
(“Q” metrics)

COST/EFFICIENCY
(“E” metrics)

Measuring/improving only time can lead to degradations in quality or efficiency

Study Performance
Key Questions to Consider When Defining Performance Metrics

- **What are you measuring? Why?**
  - Process?
  - Relationship?
  - CT, T, Q, E?

- **How and when will it be measured?**
  - Definition
  - Formula
  - Target
  - Frequency

- **Who will track & report metric?**
  - Sponsor?
  - CRO/Core Lab?
  - Other?

- **Who’s performance is being measured?**
  - Sponsor?
  - CRO/Core Lab?
  - Sites?

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eTMF can provide important data
### Anatomy of a MCC Performance Metric

<table>
<thead>
<tr>
<th>Metric #</th>
<th>Metric Type</th>
<th>Metric Title</th>
<th>Category</th>
<th>Metric Indicator</th>
<th>Part of Study</th>
</tr>
</thead>
<tbody>
<tr>
<td>CT, T, Q or E</td>
<td></td>
<td></td>
<td>Business Operations, Clinical Operations, Data Management, etc.</td>
<td>LEADING or LAGGING Indicator</td>
<td>Study Startup, Conduct and Close-Out</td>
</tr>
</tbody>
</table>

#### Definition (see Wiki for detailed definitions)

**Formula / Example**

- **Formula:**
- **Example:**

<table>
<thead>
<tr>
<th>Definition (see Wiki for detailed definitions)</th>
<th>Formula / Example</th>
<th>Reporting Detail</th>
</tr>
</thead>
<tbody>
<tr>
<td>Formula:</td>
<td></td>
<td>Site / Country / Study / Therapeutic Area / Portfolio levels</td>
</tr>
<tr>
<td>Example:</td>
<td></td>
<td>Unit of Measure</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Calendar days, % etc.</td>
</tr>
</tbody>
</table>

#### Business Driver(s) / Benefit Statement

Statement about why this metric is important / the reason for utilizing metric. Who / what / why…

#### Additional Analysis on a "for cause" basis

List of “drill down” metrics that should be reviewed when the metric is not within established target

#### Reporting Frequency

- Monthly, Quarterly, etc.

#### Threshold Target

- Threshold target or acceptable range.
- Exceeding target triggers additional analysis on a “for cause” basis.

#### Companion Metrics

The term “companion metrics” refers to the concept that many MCC metrics should be examined in combination with other MCC metrics … together they give you a more complete picture of performance.
Performance Metrics Should Be Designed Around the Process

Quality Assurance: Project & site quality oversight

Program Management: Project oversight; Manage timelines, budget, staffing

- Start
- Write & optimize protocol
- Find sites
- Ship drug & initiate sites
- Monitor sites (CRFs, GCP, deviations, AEs/SAEs, etc.) & retrieve data
- Enroll subjects
- Sites execute protocol
- Enter data
- Close out sites
- Lock database
- Generate & resolve queries, safety data, etc.
- Run safety & efficacy analyses
- Generate reports
- End

Business Operations: Contract negotiation, management, scope control, support processes

Finance: Budget oversight
**Performance Metrics Should Be Designed Around the Process**

**Quality Assurance: Project & site quality oversight**

**Program Management: Project oversight; Manage timelines, budget, staffing**

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**eTMF can support the process**

- **Start**
  - Write & optimize protocol
  - Find sites
  - Ship drug & initiate sites
- **Develop & test statistical analyses**
- **Run safety & efficacy analyses**
- **Generate reports**
  - Lock database
- **Enter data**
  - Monitor sites (CRFs, GCP, deviations, AEs/SAEs, etc.) & retrieve data
- **Generate & resolve queries, safety data, etc.**
  - Sites execute protocol
  - Close out sites
- **End**

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**Business Operations: Contract negotiation, management, scope control, support processes**

**Finance: Budget oversight**

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Driving improvement Through Collaborative Use of Standardized Metrics
MCC Clinical Trial Performance Metrics
v 1.2 [Oct 2012]

Quality Assurance: Project & site quality oversight

Program Management: Project oversight; Manage timelines, budget, staffing

- Cycle Time
- Timeliness
- Quality
- Efficiency / Cost

Start
- Write & optimize protocol
  - 1
  - 2
  - 3

Find sites
- 5
- 6
- 7

Ship drug & initiate sites
- 8
- 9
- 12
- 13

Monitor sites (CRFs, GCP, deviations, AEs/SAEs, etc.) & retrieve data
- 10
- 20
- 21
- 22
- 23

Develop & test statistical analyses

Run safety & efficacy analyses

Lock database

Generate reports

Generate & resolve queries, safety data, etc.

Enter data
- 24
- 25
- 26
- E4
- 33
- 34

Sites execute protocol
- 18
- 19

Close out sites
- 49
- 50
- 51
- 52
- 53
- 54

End

- 27
- 28
- 29
- 37
- 38
- 39
- 40
- 41
- 42
- 43
- 44
- 45
- 46
- 47
- 48
- E1
- E2
- E3

Program Management: Project oversight; Manage timelines, budget, staffing

- 30
- 31
- 32
- 35
- 36

Business Operations: Contract negotiation, management, scope control, support processes

- 4
- 15

Finance: Budget oversight

- 16
- 17

eTMF/document handling system can provide more accurate metrics
## eTMF metrics supporting Study Start-Up

<table>
<thead>
<tr>
<th>Metric</th>
<th>Metric Title</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Protocol Feasibility (CT)</td>
</tr>
<tr>
<td>2</td>
<td>Protocol Versions (Q)</td>
</tr>
<tr>
<td>4</td>
<td>Contract execution timeliness for non functional outsourcing models (CT)</td>
</tr>
<tr>
<td>6</td>
<td>Regulatory Authority Package Approval Rate (Q)</td>
</tr>
<tr>
<td>8 - EDC</td>
<td>Final Approved Protocol to Final Approved eCRF – EDC (CT)</td>
</tr>
<tr>
<td>9 - paper</td>
<td>Final Approved Protocol to Final Approved CRF – paper (CT)</td>
</tr>
<tr>
<td>10</td>
<td>Monitoring Plan Availability (Q)</td>
</tr>
</tbody>
</table>
**Example: Study Start-Up Protocol Metrics**

**How many days does it take to develop a protocol (CT)?**

**How many versions were created prior to approval (Q)?**

**Was the protocol approved before completing quality checks??**

New metrics that organizations are interested in collecting …

**How many “avoidable amendments”* prior to site activation (Q)?**

**How many “avoidable amendments”* prior to FPFV (Q)?**

* As defined in the TCSDD protocol amendment study
## eTMF metrics supporting Study Conduct

<table>
<thead>
<tr>
<th>Metric</th>
<th>Metric Title</th>
</tr>
</thead>
<tbody>
<tr>
<td>15</td>
<td>Change Order execution (CT)</td>
</tr>
<tr>
<td>20</td>
<td>Monitoring Visit Frequency (Q)</td>
</tr>
<tr>
<td>21</td>
<td>Monitoring Visit Report Completion (Q)</td>
</tr>
<tr>
<td>22</td>
<td>Documented Monitoring Visit Report Review (CT)</td>
</tr>
<tr>
<td>23</td>
<td>Monitoring Follow-Up Letter Completion (CT)</td>
</tr>
<tr>
<td>32</td>
<td>Protocol Amendments (Q)</td>
</tr>
<tr>
<td>33</td>
<td>Protocol Deviations (Q)</td>
</tr>
<tr>
<td>35</td>
<td>Audit Findings per Site (Q)</td>
</tr>
<tr>
<td>36</td>
<td>Issue identification, management and criticality (Q)</td>
</tr>
</tbody>
</table>
# eTMF metrics supporting Pharmacovigilance

<table>
<thead>
<tr>
<th>Metric</th>
<th>Metric Title</th>
</tr>
</thead>
<tbody>
<tr>
<td>46</td>
<td>SAE submitted by sites within protocol window (T)</td>
</tr>
<tr>
<td>47</td>
<td>Unresolved SAE queries &gt; 30 calendar days (Q)</td>
</tr>
<tr>
<td>48</td>
<td>SUSARs reported to regulatory authorities on time (T)</td>
</tr>
<tr>
<td>49</td>
<td>AEs reported per dosed subject (Q)</td>
</tr>
<tr>
<td>50</td>
<td>Study drug-related AEs reported per dosed subject (Q)</td>
</tr>
<tr>
<td>51</td>
<td>SAEs reported per dosed subject (Q)</td>
</tr>
<tr>
<td>52</td>
<td>Study drug-related SAEs reported per dosed subject (Q)</td>
</tr>
<tr>
<td>53</td>
<td>Subject Death Reporting per dosed subject (Q)</td>
</tr>
<tr>
<td>54</td>
<td>Subject Death Reporting (study drug-related) per dosed subject (Q)</td>
</tr>
</tbody>
</table>
eTMF metrics supporting Study Close-out

<table>
<thead>
<tr>
<th>Metric</th>
<th>Metric Title</th>
</tr>
</thead>
<tbody>
<tr>
<td>39</td>
<td>DBL (Database Lock) to final TLG/TFL (Tables, Listings and Graphs/Table Figure Listing)</td>
</tr>
<tr>
<td>40</td>
<td>Final TLGs to First Draft CSR complete (CT)</td>
</tr>
<tr>
<td>41</td>
<td>DBL (Data Base Lock) to Final CSR Complete (CT)</td>
</tr>
<tr>
<td>43</td>
<td>Deviation of final TLGs delivered from final agreed target date (T)</td>
</tr>
</tbody>
</table>
How Many and What Types of Documents Don’t Meet Quality Standards?

<table>
<thead>
<tr>
<th>Document Type</th>
<th>Inaccurate Cont</th>
<th>Expired</th>
<th>Duplicate</th>
<th>Incomplete Meta</th>
<th>Signature Not P</th>
<th>Missing</th>
<th>Misclassified</th>
</tr>
</thead>
<tbody>
<tr>
<td>Central Trial Documents</td>
<td>7</td>
<td>9</td>
<td>2</td>
<td>18</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Centralized Testing</td>
<td>4</td>
<td>8</td>
<td>3</td>
<td>17</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Data Management</td>
<td>2</td>
<td>16</td>
<td>2</td>
<td>22</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>IP and Trial Supplies</td>
<td>4</td>
<td>19</td>
<td>4</td>
<td>31</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>IRB/IEC and other Approvals</td>
<td>8</td>
<td>12</td>
<td>1</td>
<td>21</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Regulatory</td>
<td>6</td>
<td>7</td>
<td>13</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Safety Reporting</td>
<td>2</td>
<td>6</td>
<td>9</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Site Management</td>
<td>4</td>
<td>20</td>
<td>16</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Statistics</td>
<td>4</td>
<td>15</td>
<td>2</td>
<td>23</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Third parties</td>
<td>1</td>
<td>5</td>
<td>2</td>
<td>9</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Trial Management</td>
<td>1</td>
<td>10</td>
<td>4</td>
<td>22</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Source: Vault eTMF demo dashboard

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<table>
<thead>
<tr>
<th>Document Name</th>
<th>Document Number</th>
<th>Document Status</th>
<th>Owner</th>
<th>Auditor</th>
<th>QC Start Date</th>
</tr>
</thead>
<tbody>
<tr>
<td>AVEG 027 Independent Data Monitoring Committee Charter (v0.1)</td>
<td>eTMF-VPX-00007</td>
<td>Planned</td>
<td>Tom Frattarola</td>
<td>AVEG 027 Sponsor Study Team Auditor</td>
<td>8/19/13</td>
</tr>
<tr>
<td>Trial Manager CV (v1.0)</td>
<td>eTMF-VPX-00882</td>
<td>Approved</td>
<td>Ann-Marie Gardner</td>
<td>AVEG 027 Sponsor Study Team Auditor</td>
<td>8/19/13</td>
</tr>
<tr>
<td>Plan 1 (v0.1)</td>
<td>eTMF-VPX-00999</td>
<td>In Progress (In House)</td>
<td>Jason Methia</td>
<td>AVEG 027 Sponsor Study Team Auditor</td>
<td></td>
</tr>
<tr>
<td>Kick-off Meeting Minutes (v1.0)</td>
<td>eTMF-VPX-00848</td>
<td>Approved</td>
<td>Ann-Marie Gardner</td>
<td>AVEG 027 Sponsor Study Team Auditor</td>
<td>8/19/13</td>
</tr>
</tbody>
</table>

Source: Vault eTMF demo dashboard
<table>
<thead>
<tr>
<th>Area</th>
<th>KPI</th>
<th>Metric/Data</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Trial Management</strong></td>
<td>Site/CRO Quality</td>
<td>% of documents completed accurately the first time</td>
</tr>
<tr>
<td></td>
<td></td>
<td># of QC cycles before document is approved</td>
</tr>
<tr>
<td></td>
<td>Site/CRO Responsiveness</td>
<td># of days to complete a document</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Compare site performance across sites/countries</td>
</tr>
<tr>
<td><strong>TMF Management</strong></td>
<td>Study Closeout Readiness</td>
<td>% missing or late documents</td>
</tr>
<tr>
<td></td>
<td></td>
<td>% complete TMF</td>
</tr>
<tr>
<td><strong>Remote or Central Monitoring</strong></td>
<td>Site Risk</td>
<td>Trend in document turnaround times for a site</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Trend in audit issues from Site Monitoring Reports</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Trend in site quality metrics</td>
</tr>
<tr>
<td><strong>Inspection “Readiness”</strong></td>
<td>Quality Assurance</td>
<td>Status per site</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Status by functional area</td>
</tr>
</tbody>
</table>
Inspection readiness metrics

Source: Vault eTMF demo dashboard
Inspection readiness metrics

Source: Vault eTMF demo dashboard
• Which metrics should my company be collecting and utilizing?
  IT DEPENDS …

• Where are you starting from?
  – Do you have a poorly defined, adhoc process or a documented, standardized, proactive process?

• What are you trying to achieve?
Process Maturity Model

Level 1
Initial

Ad hoc, undefined, unpredictable

Level 2
Repeatable

Processes characterized, repeatable, typically reactive

Level 3
Defined

Documented, standardized, often proactive

Level 4
Managed

Measured & controlled, high quality

Level 5
Optimized

Continuously improving
Process Maturity Model

**Level 2:** Processes characterized, repeatable, typically reactive
- Track limited number of metrics

**Level 3:** Documented, standardized, often proactive process
- Standardize metrics and add new metrics that look at quality aspects

**Level 4:** Measured & controlled, high quality
Process Workflow Metrics

Site Exchange Cycles per Type

<table>
<thead>
<tr>
<th>Classification</th>
<th>Site Exchange Cycles Started</th>
</tr>
</thead>
<tbody>
<tr>
<td>Acceptance of Investigator Brochure</td>
<td>1</td>
</tr>
<tr>
<td>Clinical Trial Agreement</td>
<td>1</td>
</tr>
<tr>
<td>Confidentiality Agreement</td>
<td>1</td>
</tr>
<tr>
<td>Data Privacy Agreement</td>
<td>1</td>
</tr>
<tr>
<td>Feasibility Document</td>
<td>1</td>
</tr>
<tr>
<td>Financial Disclosure Form</td>
<td>1</td>
</tr>
<tr>
<td>Form FDA 1572</td>
<td>1</td>
</tr>
<tr>
<td>IND Identity</td>
<td>1</td>
</tr>
<tr>
<td>Investigator Regulatory Agreement</td>
<td>1</td>
</tr>
<tr>
<td>Investigators Agreement (Device)</td>
<td>1</td>
</tr>
<tr>
<td>Other Curriculum Vitae</td>
<td>1</td>
</tr>
<tr>
<td>Principal Investigator Curriculum</td>
<td>1</td>
</tr>
<tr>
<td>Protocol Signature Page</td>
<td>1</td>
</tr>
<tr>
<td>Site Contact Details</td>
<td>2</td>
</tr>
<tr>
<td>Site and Staff Qualification Support</td>
<td>3</td>
</tr>
<tr>
<td>Sub-Investigator Curriculum Vitae</td>
<td>1</td>
</tr>
<tr>
<td>Trial Initiation Monitoring Report</td>
<td>2</td>
</tr>
</tbody>
</table>

Legend:
- 101
- 102
- 103
- 104
- 105
- 106
- 107
- 109
- None
• Define document handling processes
• Speed up the process – easier to locate and track documents study startup & site startup
• Increase in transparency and better access to metrics can *create sentinel effect*
• Easier to identify missing documents, incomplete documents – *able to generate new quality metrics*
• Able to produce Inspection readiness metrics
• Reduces rework by identifying problems early
• Common performance metrics language and definitions are critical to success
• Metrics should drive desired behaviour and minimize undesired short-sighted behaviour
• Understand the *purpose* of performance metrics before utilizing them to assess and manage clinical trials
Questions?