Assessing Quality Performance at Genzyme Manufacturing Sites

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Agenda

- Past Product Regulatory Compliance Challenges
- Why Introduce Metrics?
- Applying Metrics to Corporate Policies and Compliance Audits
  - 5-Star Quality Program
- Questions
Past Product Regulatory Compliance Challenges

- Senior understanding of compliance performance compliance
  - Attention to audit reports
  - Detailed information without overall perspective

- Deployment of compliance policies
  - Interpretation
  - Responsibility for compliance
  - Quality function pushing other functional groups

- Consistency of compliance requirements
  - Among auditors
  - Between auditors and sites

- Audit Process
  - ‘Hide and seek’

- Lack of compliance performance visibility
  - Key risk areas
  - Best practices
  - Site performance
Why Introduce Compliance Metrics?

- Establish compliance performance visibility
  - Capture and maintain senior attention
  - Ensure site follow-up
  - Visibility of best practices
  - Ability to view cross-corporate compliance trends

- Increase accountability ‘transparency’
  - Encourage the development and/or clarify applicable requirements
    - Site/functional group attention to requirements

- Establish a baseline and gauge for future compliance improvement activities
Why Introduce Compliance Metrics?

“If we can observe it, we can measure it.”

“If we can measure it, we can improve it.”

Juran
Measuring Policies and Audits: Expectations

- “Tell me where my organization is with quality”
- Minimize regulatory risk
- Set a baseline across company
- Leverage best ‘quality’ practices
- Identify key cross corporate improvement areas
- Create a maturity measurement
Measuring Policies and Audits: 5-Star Quality Program

- An assessment process for Genzyme manufacturing sites to assess themselves across key quality elements; a consistent approach for corporate audit evaluations
  - List of 15 criteria (manufacturing)
  - Each criteria contain ‘factors’ at Level 3, 4, and 5 ratings
  - Level 3 closely represents gmp and ISO
  - Level 4/5 represents performance beyond ‘compliance’
  - Level 3 is the corporate target maturity level; Level 4/5 attainment is determined by local management

- A common and objective reference point for Genzyme corporate quality levels

- A mechanism for identifying Genzyme regulatory compliance risk areas and best practices
### 5-Star Quality Framework

<table>
<thead>
<tr>
<th>Score</th>
<th>Maturity Level</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>No approach in place</td>
</tr>
<tr>
<td>2</td>
<td>Missing level 3 elements and/or insufficient approach and/or missing evidence of deployment</td>
</tr>
<tr>
<td>3</td>
<td>Genzyme target maturity level for compliance – required for all participating sites</td>
</tr>
<tr>
<td>4</td>
<td>Best practice – local management decision to pursue</td>
</tr>
<tr>
<td>5</td>
<td>Best Practice – local management decision to pursue</td>
</tr>
</tbody>
</table>
5-Star Quality Criteria … Initial Phase

Selection Process: Criteria that are applicable to all manufacturing sites and can have a single interpretation:

- Nonconforming Material
- Process Validation
- Equipment/Utilities Validation
- Computer Validation
- Process Control
- Maintenance
- Metrology
- Training
- Internal Audits
- Documentation
- Materials Control
- Records
- Corrective Action/Preventive Action
- Management Review
- Inspection and Test
Original Program Phases

Phase One: Manufacturing Sites

Phase Two: Distribution/Lot Release Sites (non-mfg.)

Phase Three: Clinical Operations, Medical and Regulatory Affairs

Phase Four: Country Sales Offices/Service Support Groups
5-Star Teams/Committee Structure

**Site Contacts**
- Provide input into criteria
- Self assess versus criteria

**Project Team**
- develop criteria with SMEs
- manage program
- develop scorecard

**Steering Committee**
- review/approve criteria
- program guidance
- appoint site contacts
## 5-Star Criteria … Equipment Validation Example

### Equipment and Utilities Validation Criteria

<table>
<thead>
<tr>
<th>Rating</th>
<th>Description</th>
<th>Evidence of Approach</th>
<th>Evidence of Deployment</th>
</tr>
</thead>
<tbody>
<tr>
<td>1-star</td>
<td>Limited or no approach in place.</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
| 2-star | Level 3 approach in place with one or more of the following situations:  
One or more Level 3 factors not addressed  
Insufficient evidence for factors  
Incomplete implementation |              |                        |
| 3-star | Approach in place that completely and consistently addresses the following factor(s) **AND** implemented to all site equipment and utilities requiring validation:  
Define equipment and utilities to be validated  
Utilize a scheduling and planning process for validation activities  
Follow concurrent, retrospective or prospective validation approach to equipment and utilities requiring validation  
Follow a validation approach that conforms to applicable regulations and standards  
Establish protocols that include acceptance criteria for applicable equipment and utilities  
Document/summarize validation activities via validation reports  
Assess the need for re-validation and follow a re-validation approach where applicable | Documented process or standard operating procedure (SOP) | Master list system, equipment list, etc. |
|         |              | Documented process or standard operating procedure (SOP) | Resources dedicated to project, project schedule, validation master plan, etc. |
|         |              | Documented process or standard operating procedure (SOP) | Validation reports, summaries, etc. illustrating various approaches |
|         |              | Documented process or standard operating procedure (SOP) with reference to applicable regulations and standards | Availability of relevant regulations and standards |
|         |              | Documented process or standard operating procedure (SOP) | Validation reports supporting protocols; sample of data that feeds reports |
|         |              | Documented process or standard operating procedure (SOP) | Validation reports |
|         |              | Documented process or standard operating procedure (SOP) | Validation reports, summaries, etc. illustrating various approaches |
| 4-star | Meets all of Level 3 criteria **AND** the following factors:  
Documented approach which describes how the site identifies, prioritizes, and implements additional monitoring and measurement beyond validation protocols | Documented process or standard operating procedure (SOP) | List of critical areas to be monitored beyond validation protocols; examples of measurement and monitoring as specified within approach |
| 5-star | Meets all of Level 4 criteria **AND** the following factors:  
Documented approach which describes how the site applies Statistical Process Control (SPC) to monitor high impact areas | Documented process or standard operating procedure (SOP) | Evidence of control charts for high impact areas |
## Level 4 & 5 Key Themes

<table>
<thead>
<tr>
<th>Key Theme</th>
<th>Applicable Criteria</th>
</tr>
</thead>
<tbody>
<tr>
<td>Electronic System Usage</td>
<td>Documentation, CAPA, Training, Material Control</td>
</tr>
<tr>
<td>Statistical Process Control</td>
<td>Equipment Validation, Process Validation, Process Control</td>
</tr>
<tr>
<td>Cost of Quality</td>
<td>CAPA, Maintenance, Nonconforming Product</td>
</tr>
<tr>
<td>Performance Monitoring</td>
<td>Inspection/Test, Computer Validation, Management Review, Metrology, Equipment/Process Validation, Process Control</td>
</tr>
<tr>
<td>Deployment Beyond Quality</td>
<td>Management Review, Internal Audit, Records, Training</td>
</tr>
<tr>
<td>Miscellaneous Themes</td>
<td>Computer Validation, Material Control, Metrology, Management Review</td>
</tr>
</tbody>
</table>
5-Star Quality Annual Cycle

- CQS verification of Site self-assessment
- Sites update self-assessment and submit to CQS
- Conduct management review of program criteria and verification process (i.e. CMT agenda)
- 5-star program team update of criteria and accreditation process
# 5-Star Quality Corporate Scorecard

*Note: Scorecard data for example only; not actual data*
Site Response to 5-Star Quality

Some Comments ….

- Criteria were clearly defined
- Good tone for the program (i.e. promote honesty)
- Was not as burdensome on the site as expected
- Questions meaningful around approach and deployment
- Helps us understand where we are compliant and where to establish improvements
- Program promotes comparability and consistency; summarized the areas that the site needs to focus on; general idea of program that identifies areas for improvement across the corporation is good.
5-Star Quality Program Current Activities

- Program Expansion – Develop unique criteria
  - Biomedical Operations
  - Clinical Operations
  - Medical Affairs
  - Regulatory Affairs
  - Sales Offices (International)
  - Genetic Testing Sites

- Senior Management Review
  - Quarterly Compliance Management Team Meetings
    - Program Plan
    - Review of Results
  - Annual Global Quality Meeting
    - Best Practice Sharing
  - CEO Expanded Management Meeting
Lessons Learned

- **Steering Committee Support**
  - Agree on policies, measurement, and interpretation
  - Occasional ‘arbitration’
  - Management review mechanisms
  - Committees aligned to existing functions/councils

- **Include the ‘subject matter experts’ from various sites in the development of the criteria**

- **Auditor training and consistency**

- **Site input**
  - Criteria
  - Auditing of program
Questions