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

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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**

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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

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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

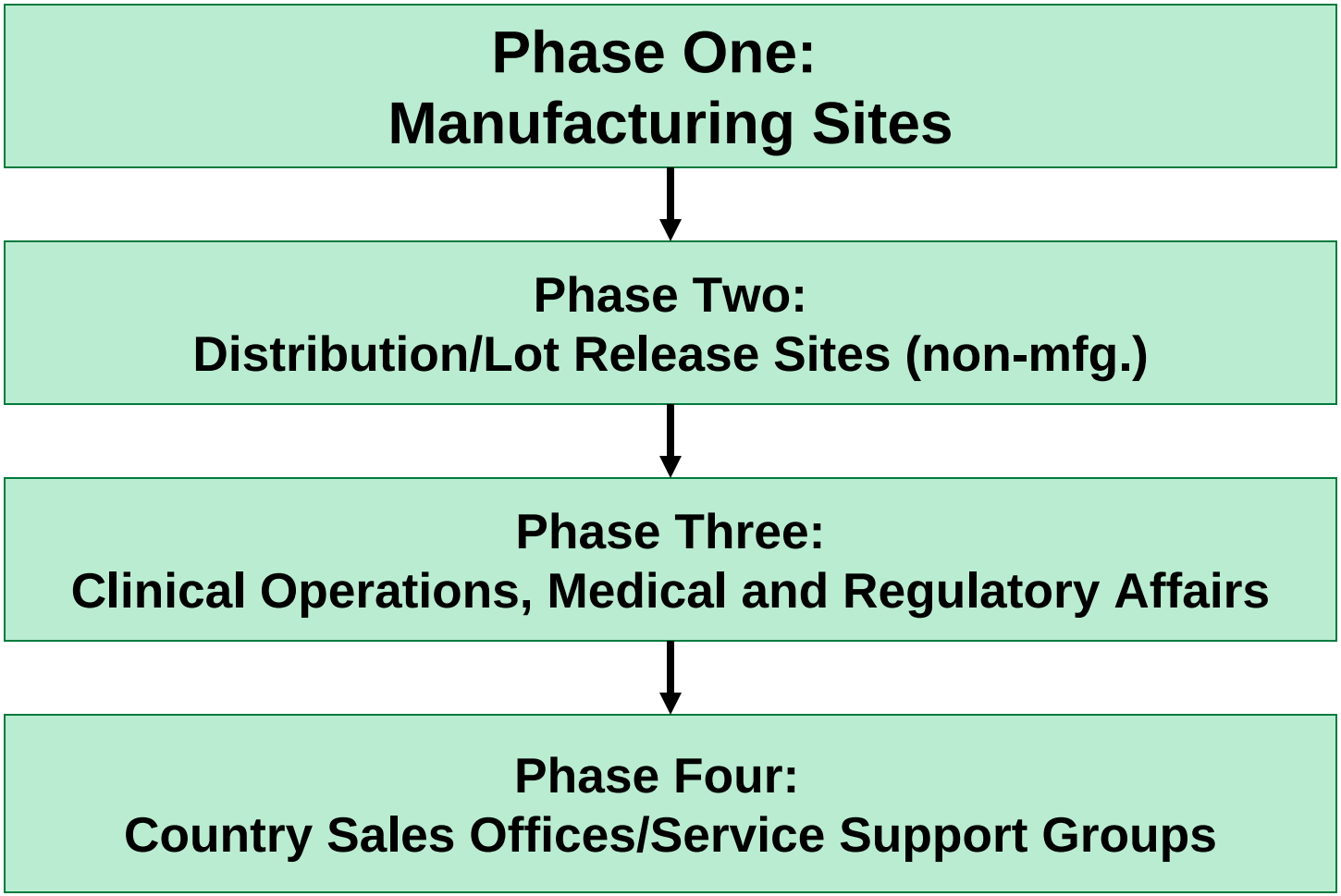
Score	Maturity Level
1	No approach in place
2	Missing level 3 elements and/or insufficient approach and/or missing evidence of deployment
3	Genzyme target maturity level for compliance – required for all participating sites
4	Best practice – local management decision to pursue
5	Best Practice – local management decision to pursue

5-Star Quality Criteria … Initial Phase

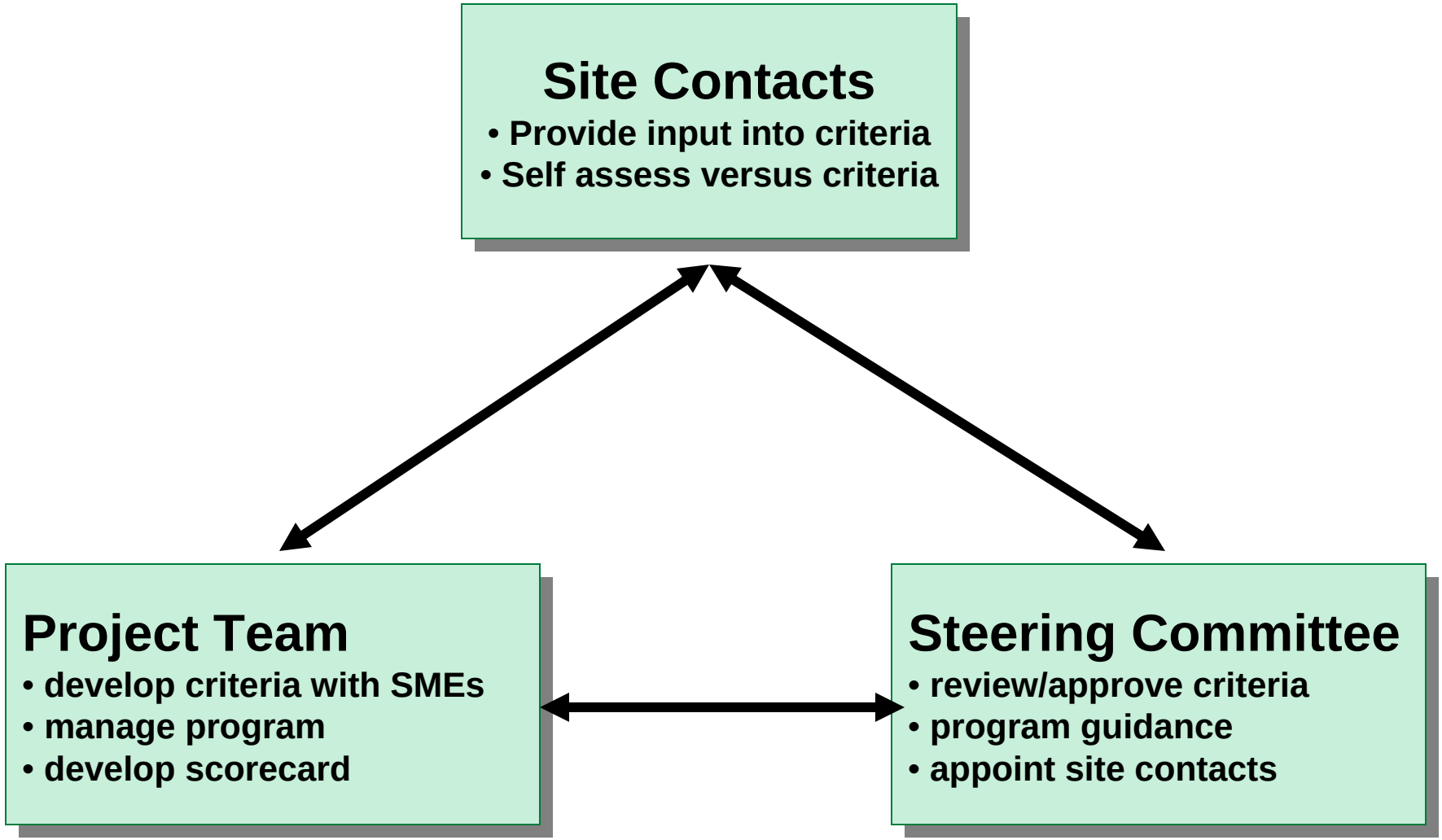
Selection Process: Criteria that are applicable to all manufacturing sites and can have a single interpretation:

- 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



5-Star Teams/Committee Structure



5-Star Criteria … Equipment Validation Example

Equipment and Utilities Validation Criteria			
Rating	Description	Evidence of Approach	Evidence of Deployment
1-star	**Limited or no approach in place.**		
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	Documented process or standard operating procedure (SOP)	Master list system, equipment list, etc.
	Utilize a scheduling and planning process for validation activities	Documented process or standard operating procedure (SOP)	Resources dedicated to project, project schedule, validation master plan, etc.
	Follow concurrent, retrospective or prospective validation approach to equipment and utilities as appropriate	Documented process or standard operating procedure (SOP)	Validation reports, summaries, etc. illustrating various approaches
	Follow a validation approach that conforms to applicable regulations and standards	Documented process or standard operating procedure (SOP) with reference to applicable regulations and standards	Availability of relevant regulations and standards
	Establish protocols that include acceptance criteria for applicable equipment and utilities	Documented process or standard operating procedure (SOP)	Validation reports supporting protocols; sample of data that feeds reports
	Document/summarize validation activities via validation reports	Documented process or standard operating procedure (SOP)	Validation reports
	Assess the need for re-validation and follow a re-validation approach where applicable	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 decribes 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

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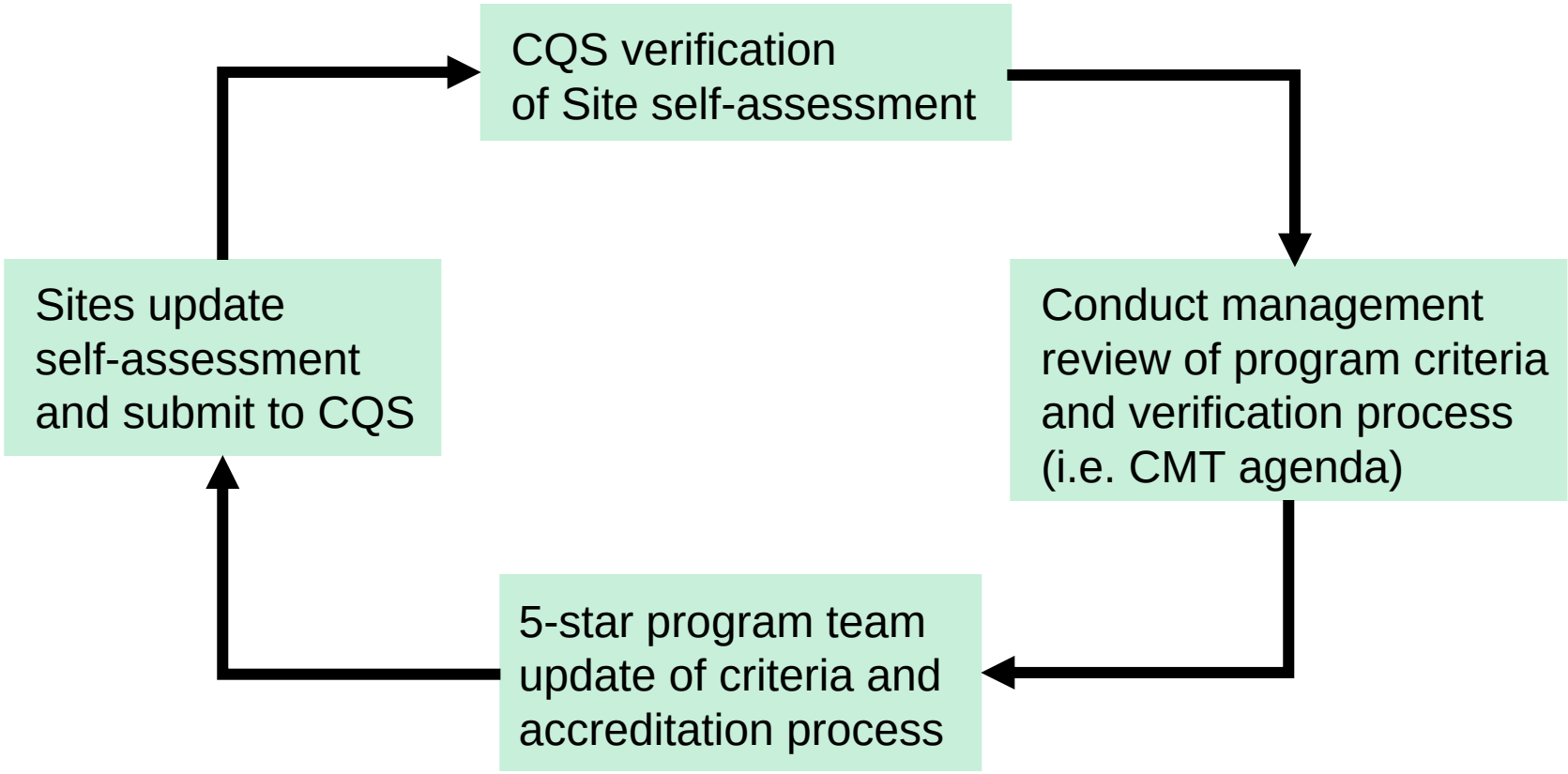
Level 4 & 5 Key Themes

Key Theme	Applicable Criteria
Electronic System Usage	Documentation, CAPA, Training, Material Control
Statistical Process Control	Equipment Validation, Process Validation, Process Control
Cost of Quality	CAPA, Maintenance, Nonconforming Product
Performance Monitoring	Inspection/Test, Computer Validation, Management Review, Metrology, Equipment/Process Validation, Process Control
Deployment Beyond Quality	Management Review, Internal Audit, Records, Training
Miscellaneous Themes	Computer Validation, Material Control, Metrology, Management Review

5-Star Quality Annual Cycle



5-Star Quality Corporate Scorecard

Criteria	Site 1	Site 2	Site 3	Site 4	Site 5	Site 6	Site 7	Site 8	Site 9	Site 10	Site11	Average Criteria Score
CAPA	2	3	3	3	2	2	2	2	4	2	2	2.5
Computer Validation	3	3	4	3	2	2	5	2	3	3	2	2.9
Documentation	3	3	3	3	2	3	3	3	4	3	3	3.0
Equipment Validation	4	3	3	3	3	3	3	3	4	4	3	3.3
Inspection/Test	3	3	3	3	2	3	3	3	3	5	3	3.1
Internal Audit	4	3	3	3	2	3	3	3	3	3	3	3.0
Maintenance	3	3	3	3	3	3	3	3	3	3	2	2.9
Management Review	2	3	3	4	4	2	2	4	4	2	2	2.9
Materials Control	3	3	3	3	3	3	3	3	4	3	3	3.1
Metrology	3	3	2	3	2	3	3	2	3	3	3	2.7
Non-conforming Product	3	3	3	3	3	3	3	3	4	3	2	3.0
Process Control	3	3	3	3	3	3	3	3	3	4	3	3.1
Process Validation	4	3	3	3	3	3	3	3	5	4	3	3.4
Records	3	3	3	2	2	3	3	3	4	3	2	2.8
Training	3	3	3	3	3	2	3	3	4	3	2	2.9

* Note: Scorecard data for example only; not actual data

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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.**

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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

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Questions