

West Coast Chapter PDA



May 19th Dinner Meeting



Integrating
Quality

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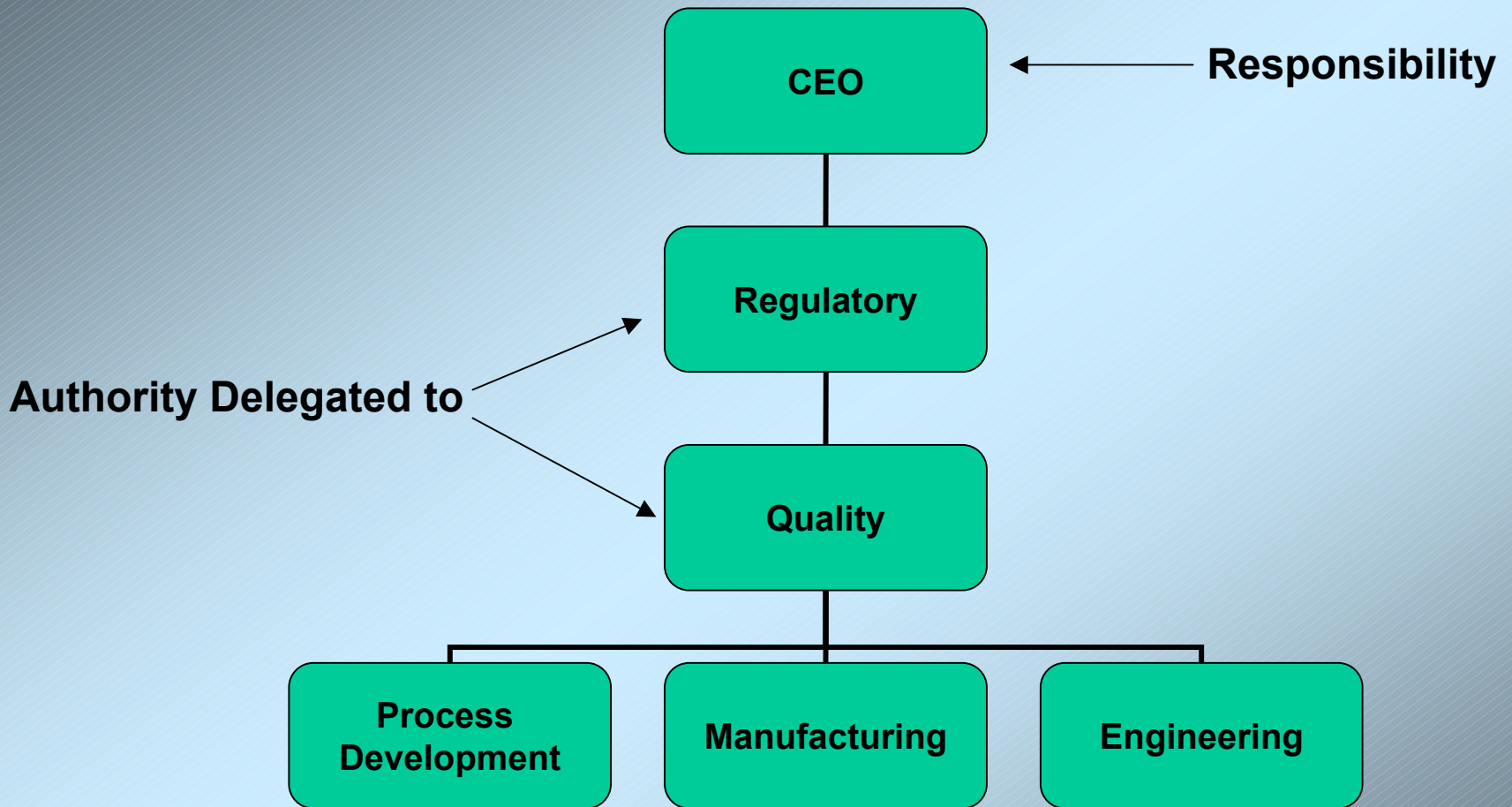
Managing Quality Oversight

The timely introduction of Quality Management.
Quality Participation to Quality Control.

Overview

- Responsible for Quality
- Product and Cost Considerations
- Operations
- Facility Examples
- Closing Points

Responsible for Quality



GMP/QSR Requirements

Drugs

- 211.22(a) There shall be a Quality Control unit that shall have the responsibility and authority to approve or reject all components, drug product containers, closure, in-process materials, packaging material, labeling and drug products...

Medical Device QSRs

- 820.20(a) Management with executive responsibility shall establish its policy and objective for, and commitment to, quality. Management with executive responsibility shall ensure that the policy is understood, implemented, and maintained at all levels of the organization.

FDA Guidance for API

Q7A Good Manufacturing Practice Guidance for API

- Quality should be the responsibility of all persons involved in manufacturing. Each manufacturer should establish, document, and implement an effective system for managing quality that involves the active participation of management and appropriate personnel.

Food Drug and Cosmetic Act

“The FD&C Act is a strict liability statute, which requires anyone in a position of responsibility, with the authority and power to prevent the violation to exercise the necessary care to prevent the violation. It is a felony to intentionally offer misleading information that results in a violation of the FD&C Act.

Strict Liability

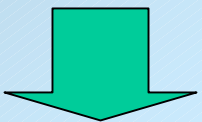
- No Knowledge
- No Intent



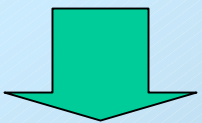
FDA Inspection

← **FDA 483**

← **Warning Letter**



OCI



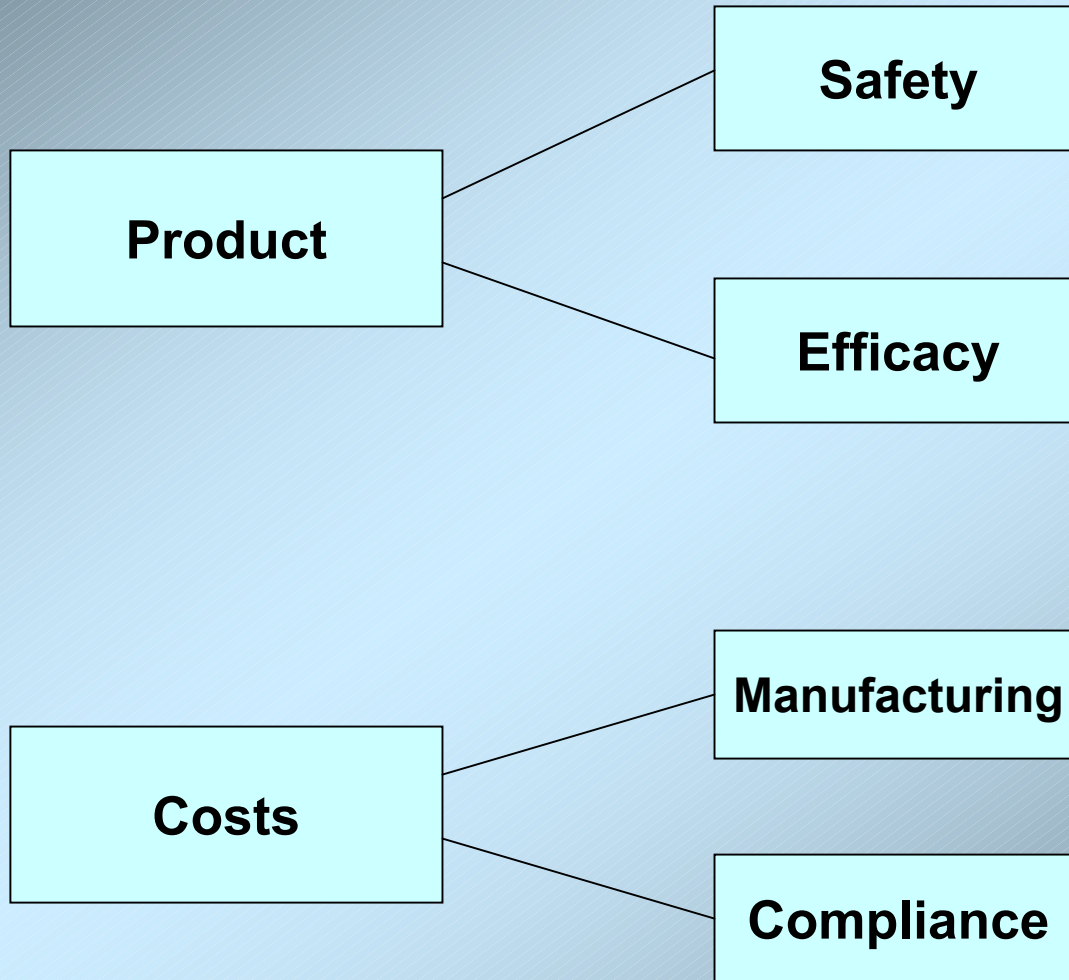
DOJ



Quality Managers

“Things to Consider”

- Product
- Costs



Cost

- The cost of drug development to market - \$897 million
- The cost of drug development to market in 1991 was \$318 million

May 2003 Report, Tufts Center for the Study of Drug Development

Develop a Quality Management Oversight Strategy...

...that does not diminish your firms ability to comply...

...but is flexible...

General Operations

OPERATIONS

R&D

Facilities/Equipment

Supporting Programs

Manufacturing Process

Product Release

“Risk” Assessment



Regulatory Intelligence

“Know your product/market”

- Regulatory Laws.
- Regulatory Guidance.
- Current Industry Compliance Trends/Strategies
 - Qualification Strategies
 - Validation Strategies
- Memberships/participation in professional organizations such as – PDA, ISPE, RAPS,

FDA Risk Assessment Guidance Documents (March 24, 2005)

- Premarketing Risk Assessment
- Development and use of Risk Minimizations Action Plans
- Good Pharmacovigilance and Pharmacoepidemiologic Assessment

Top 10 Drug Observations Identified in Turbo EIR FY 04

National

1. Process Control (416)
2. QC Responsibilities (369)
3. Lack of Procedures (259)
4. Lack of SOPs (254)
5. Batch Records (254)
6. Testing & Release (246)
7. Lack of Controls (232)
8. Employee Training (227)
9. Calibration of Equip (198)
10. Lack of QC (198)

Pacific Region

- LOS, SAN, SEA
LOS, SAN, SEA

SEA, SAN
SEA, LOS
SEA, LOS
LOS
SEA, SAN
SEA, SAN
SEA

“The FDA 483” by Carl Anderson, Immel Report, March April 2005 Vol 1. No 3



Top 10 Device Observations Identified in Turbo EIR FY 04

National

1. Complaint Handling (357)
2. Procedures - CAPA (348)
3. Lack of MDRs proc (348)
4. Quality Audits conducted (290)
5. CAPA Documented (278)
6. Mgmt Responsibility (269)
7. Process Validation (265)
8. Quality Audit procedures (228)
9. Design Control Proc. (206)
10. Design Changes (205)

Regional

- LOS, SAN, SEA
LOS, SAN, SEA
LOS, SAN, SEA
LOS, SAN, SEA
SAN, SEA
SAN, LOS
LOS
SAN
SEA

“The FDA 483” by Carl Anderson, Immel Report, March April 2005 Vol 1. No 3

FDA “direct”

Marcia Madrigal

21 years with FDA, 16 years as an Inspector, 6years SBR

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(510) 637-3980

**Covering: AK, AZ, CA, HI, ID, MT, NV,
OR, WA**

OPERATIONS

Control

Quality Oversight

**Acceptance
Criteria**

R&D

Least

Participation

General

Supporting Programs

**Facilities/Equipment
Commissioning**

**Facilities/Equipment
Qualification**

Manufacturing Process

Product Release

Most

Control

Specific

Costs

- The cost of drug development to market - \$897 million
 - New Facility Construction
 - 2 - 20 million
 - 8%-12% initial facility qualification or approximately 160K – 2.4 million dollars

*“For Reference Only
Not used to make Process Decisions”*

New Facility Construction

- New facilities constructions provide an excellent opportunity to develop and implement an equipment and systems qualification strategy that will support future conformance lot production and validation efforts.

New Facility

Quality's New Role

Quality's Past Participation

Design

Build

Commission

Qualify

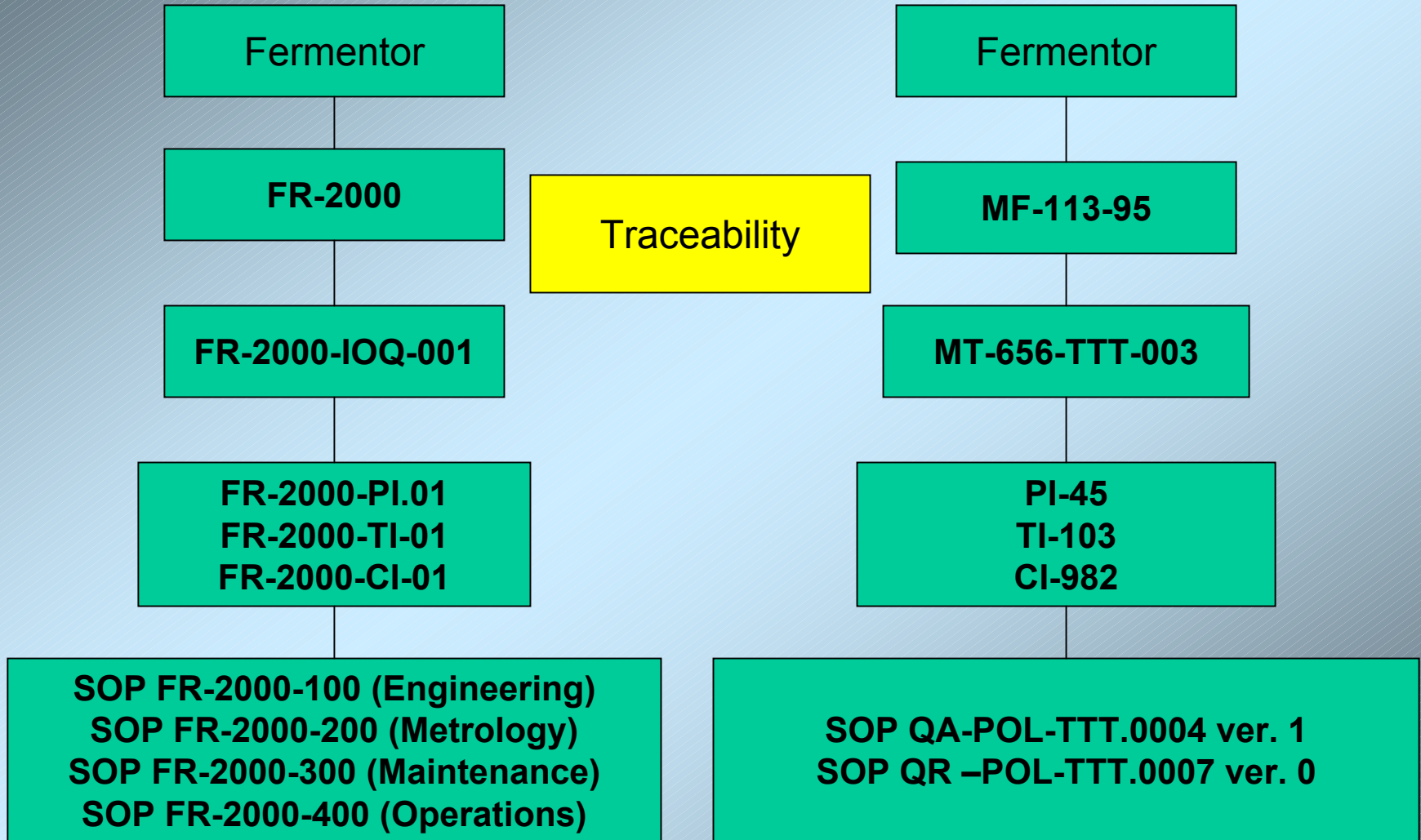
**Information
Management
System**

QU

**Information
Management
System**

QU

IMS –Document Control



**Banging your head against a wall
burns 150 calories an hour.**

New Facility Qualification

- Quality Participation.
- Document Control .

“Integrated Approach” - Developed to...

- Integrate new facility/systems construction and installation activities with GMP requirements.

New Facility

**Acceptance
Criteria**

Design

General

Build

Commission

Qualify

Specific

End User

**Process
Suitability**

Benefits...

- Elimination of redundant system testing.
- Establishes early on in the process standards of document integrity that will support GMP requirements.
- Centralizes information facilitating regulatory inspections.
- Facilitates Change Control
- Establishes and demonstrates to Regulatory Agencies Control.

Examples – New Facilities

Managed Quality Oversight

Performance Teams

Strategy

Design/Build

Document System Testing during startup in a manner consistent with cGMP documentation requirements

Collate and Retain System Information

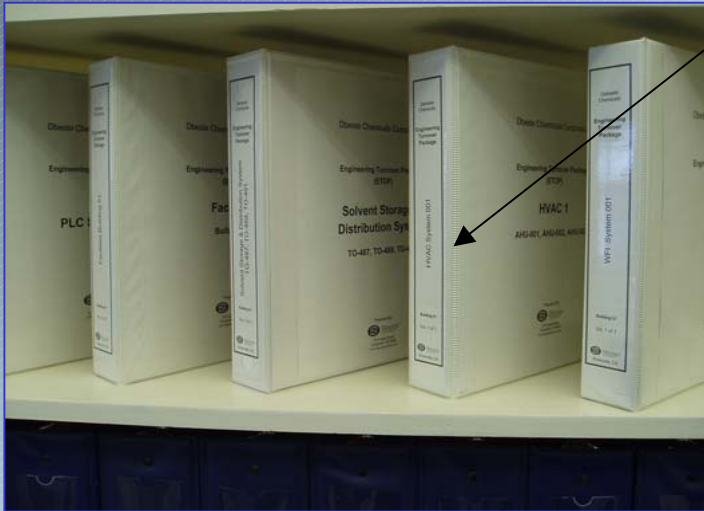
Complete System Qualification Process





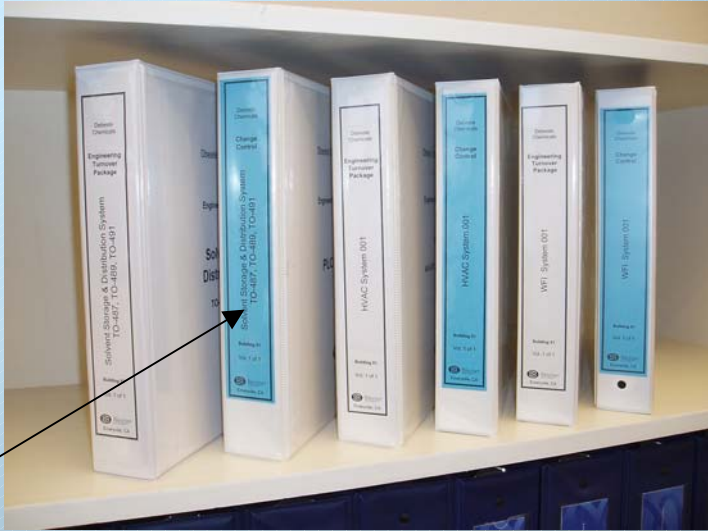
**Aerojet Fine Chemicals Facility,
Rancho Cordova, California**

Controlled Document



Turn Over Packages

Change Control History



Controlled Document



**Large Scale Biology - Plant- Made Biopharmaceutical Facility
Owensboro, Kentucky**



**Chiron Facility - Multi-drug
Rosia, Italy**



**Human Genome Sciences,
Gaithersburg, Maryland**

Summary

- Manage Quality Oversight
 - Know your product/market
 - Regulations/Guidance/Regional Challenges
 - Assess Risk/Operations
 - Be timely and flexible in managing quality.
 - Develop a “Participate to Control Strategy”.

Closing Points

- Senior Management/Operations Management need to be GMP aware.
- Periodically utilize third party auditors/reviewers to assess your firms compliance position.
- Do not maintain “baggage” procedures/policies and programs because they are to “difficult to change”.

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THANK YOU