



Boston
Section

The Global Voice of Quality™

ISO 9001 and 21 CFR 210 211

“Working Together for Quality”

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Agenda



- ◆ What Requirements in ISO 9001:2008 can be used to enhance your existing cGMP quality system?
- ◆ If you are ISO 9001:2008 registered what additional requirements are needed to management comply with 21 CFR 210?

Agenda

- Background Information on Standards
 - ◆ ISO 9001:2008
 - ◆ Voluntary Standard
 - ◆ FDA Quality Systems
 - ◆ Law
 - ◆ Guidance Documents Available
 - ◆ Discuss Additional Requirements

Companies Here Today??

- Medical Device
 - ◆ 21 CFR 820
 - ◆ ISO 13485:
- Biotech/Pharma
 - ◆ 21 CFR 210, 211
 - ◆ ICH Q7
- Other????



Quality Management Systems

- ISO 9001 first published 1987
- Then.....1994
- ISO 9001: 2000 **Technical Revision**
- **15 November 2008 is an Amendment-**
 - ◆ Clarify points in the text
 - ◆ Enhance compatibility with ISO 14001:2004
 - ◆ 700,000 worldwide certified
 - ◆ 50,000 North America certified

ISO Quality Management System

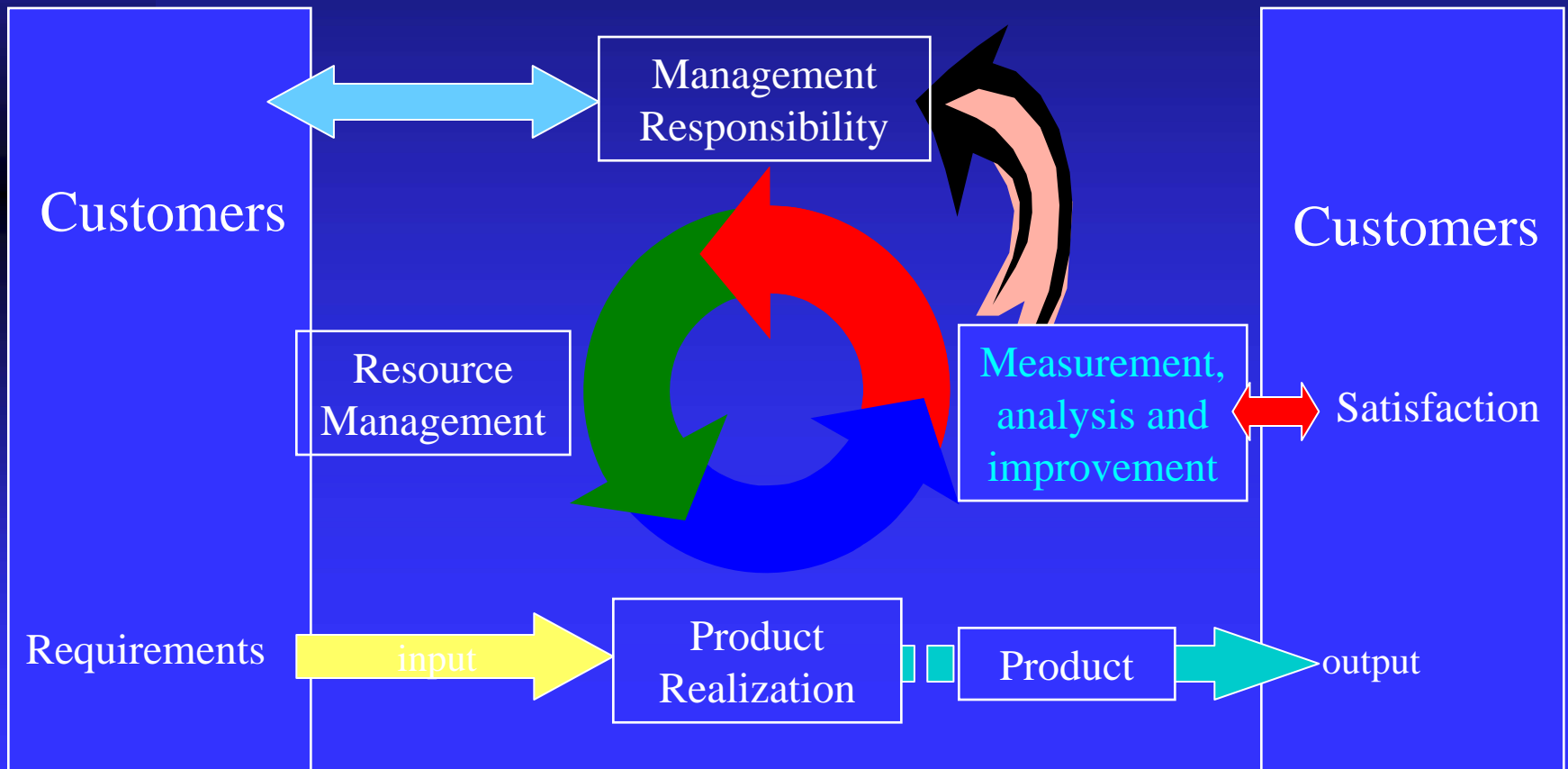
Management Review



Corrective and
Preventive Action

Internal Audit

ISO 9001 Quality Management System



ISO 9001:2008

- No legal requirement to comply with cGMP
 - ◆ Voluntary Standard
 - ◆ Registered
 - ◆ Minimize Customer Audits
- Unless.....Device Companies – Europe
 - ◆ Technical File
 - ◆ CE Marking???



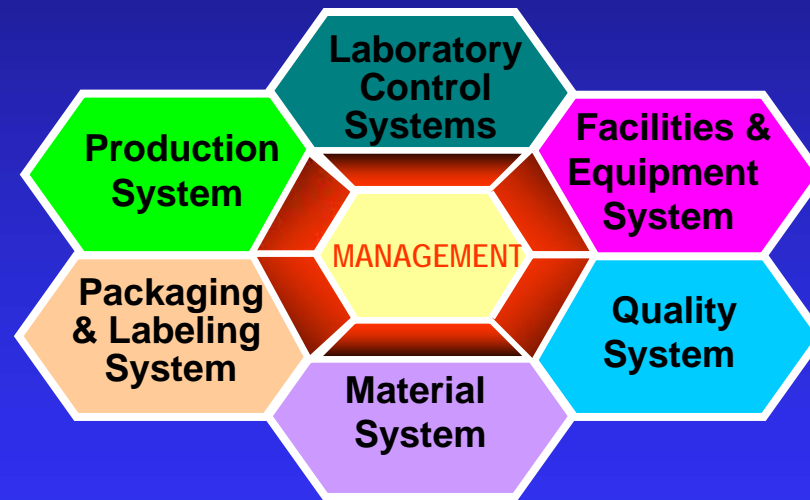
ISO 9001

- ◆ 4.0 Quality System
- ◆ 5.0 Management Responsibility
- ◆ 6.0 Resources
- ◆ 7.0 Product Realization
- ◆ 8.0 Measurement, Analysis and Improvement

Note: Configuration Management
AS9100, ISO13485, ISO14000, IPEC –GMP Guide

- ◆ ISO Eyesoh=Equal

FDA Drug Mfg Inspection Systems



cGood Manufacturing Practices

- Legally Required to comply with cGMP
- Regulations Enforceable by Law
- Enforced by the FDA
- Register with FDA annually



FDA

- When publishing the Guidance for Industry "Quality System Approach to Pharmaceutical cGMP" on 29 September 2004, the FDA took requirements from the ISO 9001 document on "Quality Management Systems" into account in the field of pharmaceutical manufacture
- **Guide on Quality Systems Model**
 - ◆ Management Responsibilities
 - ◆ Resources
 - ◆ Manufacturing Operations
 - ◆ Evaluation Activities

ICH Q 10

- International Council on Harmonization
 - ◆ “Pharmaceutical Quality Systems”
 - ◆ Guidance Model for Implementing Effective Quality Management System
 - ◆ Harmonization Effort
 - ◆ European Union
 - ◆ Japan
 - ◆ United States
 - ◆ Augment Rather than Replace Current Regulations
 - ◆ Harmonize with the Regional Guidance
 - ◆ ICH Q7

CGMP More Detailed Validation Requirements

- Equipment
- Facilities
- Methods
- Cleaning
- Software
- Electronic Systems
 - ◆ 21 CFR Part 11



ISO 9001 Process Based

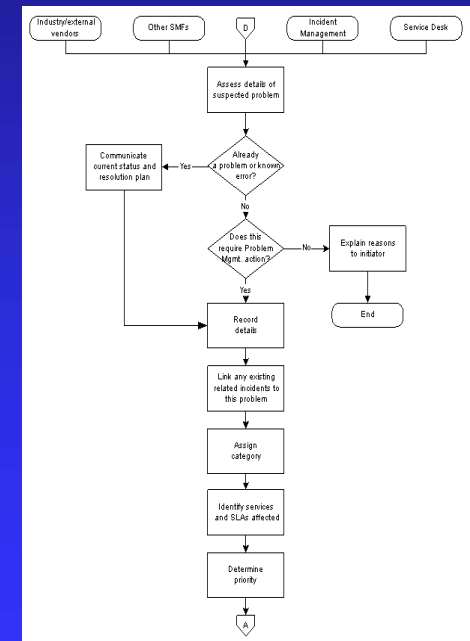
■ Identify Processes

◆ Process

- ◆ Input
- ◆ Output
- ◆ Phases
- ◆ Gates/Reviews
- ◆ C₂Q
- ◆ M&M

Core

Support

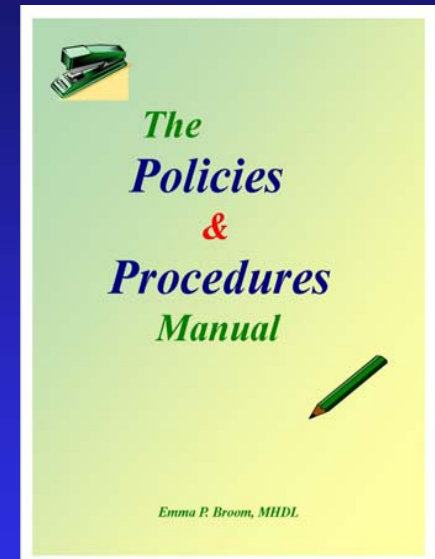


ISO 9001 Control of Documents

- While reviewing Records in ISO 9001:2008 System
 - ◆ cGMP Documentation Practices
 - ◆ Are there complete mfg instructions
 - ◆ Raw Material
 - ◆ Equipment
 - ◆ Steps: Performed By: **Verified By:**
 - ◆ **Documents that impact product quality reviewed by and approved by Quality (independent)**
 - ◆ Operating Parameters
 - (more than 6 SOPs required)

Adding ISO 9001 to a GMP System

- Develop a Quality Manual
- Develop a Quality Policy
 - ◆ Communicate
 - ◆ How do you Contribute?
 - ◆ Continually **Improve** the Effectiveness of the QMS
 - ◆ ISO 13485- Maintain



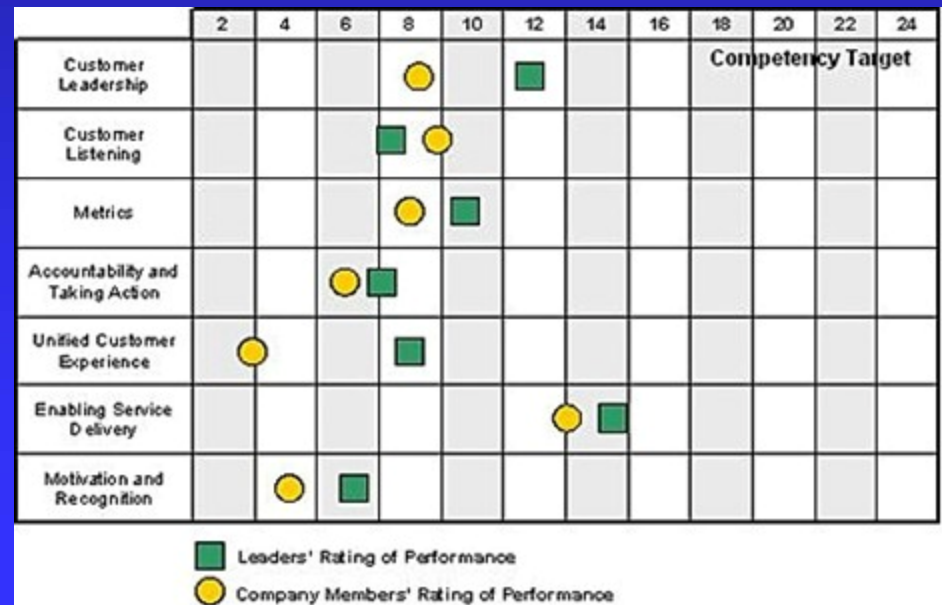
Customer Focus

- ISO – How are customer requirements determined and translated into the Quality System?
- GMP- **S I S P Q**
 - ◆ Safety
 - ◆ Identity
 - ◆ Strength
 - ◆ Purity
 - ◆ Quality

Planning

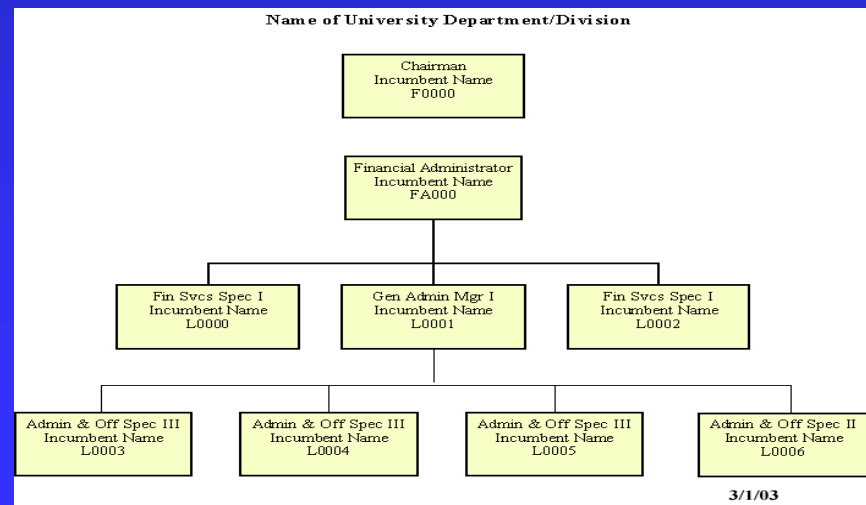
- Top Management shall ensure that Quality Objectives are established

- ◆ Product
- ◆ Processes



Responsibility and Authority

- **GMP**
- Quality Unit??? – Independent Reporting Relationship Between Production and Quality Unit.



Management Responsibility

- **ISO** Management Representative
 - ◆ Appointed
 - ◆ Establish Processes
 - ◆ Report
 - ◆ Promote awareness of Customer Requirements

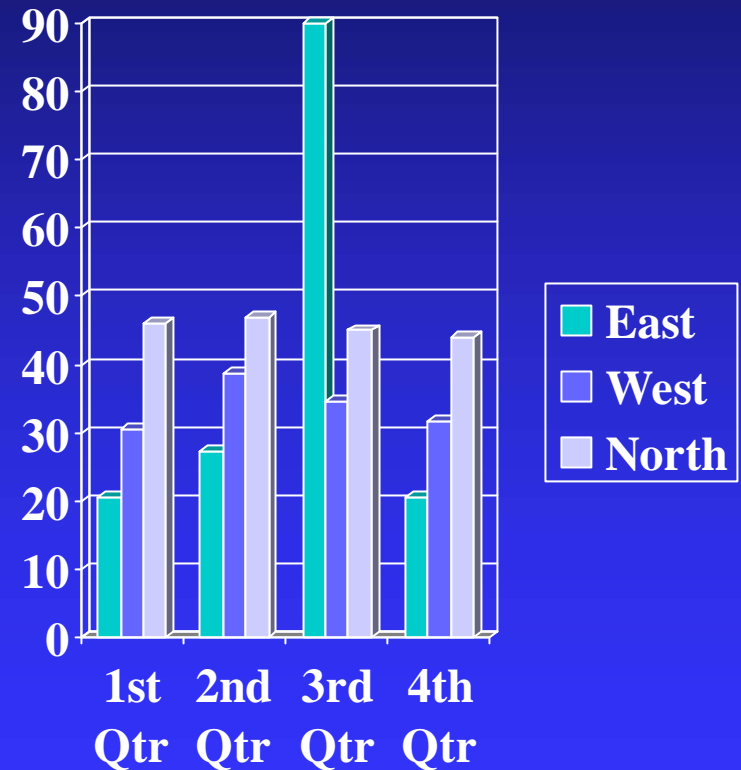


Management Review

■ Review Input

- ◆ Audits
- ◆ Customer Feedback
- ◆ Process Performance and Product Conformity
- ◆ Status of Preventive and Corrective Action
- ◆ Follow Up
- ◆ Changes that could affect qms
- ◆ Recommendation for Improving
- ◆ Note: 13485---Regulatory Requirements

Notes: **Quality Council**
 – Annual Product Review?? APR



cGMP Resources Needed in ISO 9001

- Section 6.0 ISO Standard Resource Management
 - ◆ 6.1 Provision of Resources

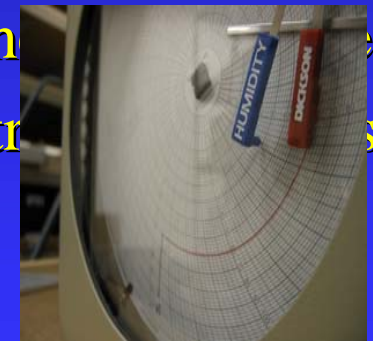
 - ◆ 6.2 Human Resources
 - ◆ Competence, Awareness and Training
 - **GMP training should be sufficient frequency to ensure employees remain familiar with GMP.**
 - ◆ **Personal Hygiene**

 - ◆ 6.3 Infrastructure
 - ◆ **Buildings and Facilities**
 - ◆ **Equipment - Commissioning**
 - **Construction – Contact Surfaces**
 - **Maintenance - SOP**
 - **Computer Systems – Access controls backup**
 - **Utilities – risk of contamination**
 - **Water –treatment and monitoring**

cGMP Resources Needed in ISO 9001

◆ **6.4 Work Environment** — shall determine and manage environment needed to achieve conformity to product.

- ◆ Air Handling – Recirculation
- ◆ Controlled Environment - Monitoring
- ◆ Cleaning and Sanitary Conditions – Schedule
- ◆ Pest Control – Free of Infestation, Control
- ◆ Lighting - Adequate
- ◆ Drainage - Adequate
- ◆ Washing and Toilet Facilities



7.0 Product Realization GMP Needs

- Planning of Product Realization
- Customer Related Processes
 - ◆ Customer Communication
- Design and Development – (defined point at which GMP applies in Mfg)
- Purchasing
 - ◆ Supply Chain Approach Changing
 - ◆ Quality Agreements
 - ◆ Heparin
 - ◆ BSE TSE



7.0 Product Realization GMP Needs

- Customer Property
 - ◆ Chain of Custody

- Preservation of Product
 - ◆ HSPPD –
 - ◆ **Temperature Mapping Warehouse**
 - ◆ **Pallets**
 - **ISO 9001???**

7.6 Calibration

- Out of Tolerance—OOT
 - ◆ Actions taken if found to be beyond
 - ◆ How is system documented?
 - ◆ Is there an SOP in ISO9001 or are Records required of the results?

8.0 Measurement Analysis and Improvement

■ M & M Processes

- ◆ Demonstrate conformity to **product**
 - ◆ 9001 and GMP
- ◆ Customer Satisfaction
 - ◆ “Customer Perception:
 - ◆ Methods for Obtaining Feedback



8.0 Measurement Analysis and Improvement



■ Analysis of Data

- ◆ Demonstrate Suitability and **Effectiveness** of QMS
 - ◆ Customer Satisfaction
 - ◆ Conformity to Product Requirements
 - ◆ Characteristics and Trends of Processes and Products
 - Opportunities for Preventive Action
 - ◆ Suppliers

8.2.2. Internal Audits

- Does 21 CFR 210, 211 call for Internal Audits?

Laboratory Controls

M&M of Product

- Procedures and Records
- Out of Specification Test Results
- Retained Samples
- Certificates of Analysis
- Impurities – Residual Solvents
- Stability

8.0 Measurement Analysis and Improvement

- Continual Improvement
- Corrective Action
 - ◆ Prevent **R**ecurrence
- Preventive Action
 - ◆ Prevent **O**ccurrence



Working Together for Quality

- Yes....Both Systems Need
 - ◆ Manpower
 - ◆ Methods
 - ◆ Measurements
 - ◆ Materials
 - ◆ Machines
 - Money?

Summary

■ ISO9001

- ◆ Create Quality Control Unit with More Responsibility and Authority than a Management Representative
- ◆ Create required systems and procedures required by GMP-Product Specific
- ◆ Trained and Aware of Legal Responsibilities inherent in GMP

Summary

- GMP need to Develop
 - ◆ Metrics and Procedures for Measuring the Effectiveness of QMS
 - ◆ Management Review Program
 - ◆ Program for Capturing Customer Satisfaction Data

Thank You for Your Participation

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- Note: Boscon Conference
 - ◆ Waltham Woods
 - ◆ April 11, 12
 - Asqbboston.org