Washington Group International

Integrated Engineering, Construction, and Management Solutions

The Extra Work that goes into Building a Manufacturing Facility when it is FDA-Regulated

Jorge Ferreira

Director of Aseptic Processing and Fill/ Finish Technologies

Our Questions…

Extra Work???… what extra work?…

"The Extra Work that goes into Building a Manufacturing Facility when it is FDA Regulated…"

Who is this?…

Why do they regulate facilities?…

How do they regulate facilities?…

U. S. Food and Drug Administration

Excerpt from the FDA Mission Statement…

"…the FDA is responsible for ***protecting the public health*** by assuring the ***safety***, ***efficacy***, and ***security*** of human and veterinary drugs, biological product, medical devices…"

emphasis added…

Who is the FDA?

U. S. Food and Drug Administration

Some little known FDA factoids…

- FDA monitors the manufacture, import, transport, storage, and sale of about ***$1 trillion worth of products*** annually
- FDA regulates more than ***150,000 medical products***
- Regulated products account for ***25 cents of every dollar*** spent by consumers
- 9,000 employees/ conduct 16,000 facility visits
- Cost to taxpayers less than $0.02 per day per person

For more information go to www.fda.gov

Who is the FDA?

Historical milestones of the FDA

- **1862**- PRESIDENT LINCOLN appoints a chemist to serve in the Bureau of Chemistry, the predecessor of the Food and Drug Administration.
- **1820**- Eleven physicians establish U.S. PHARMACOPEIA, the first compendium of standard drugs for the United States.
- **1906**- The original FOOD AND DRUGS ACT is passed by Congress
- **1938**- The FEDERAL FOOD, DRUG, AND COSMETIC (FDC) ACT is passed by Congress
- **1949**- FDA publishes GUIDANCE TO INDUSTRY for the first time.

Who is the FDA?

FDA Regulation

The purpose of FDA regulation…

- **Safety**- ensure products are safe to use…
  - Product Review and Approvals
  - Products are monitored for continued safety after they are in use
- **Efficacy**- ensure products work in the manner they claim…
  - Accurate labels and product information
  - Demonstrated effectiveness
- **FDA evaluates "Benefit vs. Risk"**

Why do they regulate facilities?…

FDA Regulation

Compliance is ***not*** optional…

- Federal Regulation
- All products (prescription and over-the-counter) that are available for use in the U.S. must be produced according to the FDA's cGMP regulations.

cGMP Regulations

- "current Good Manufacturing Practice"
- Dynamic set of requirements intended to protect product:
  - Identity
  - Strength
  - Quality
  - Purity

Why do they regulate facilities?…

FDA Regulation

How are FDA regulations enforced…

- Federal Regulations establish cGMPs…
  - To ensure Product Quality
  - To ensure Consistent Production
- FDA enforces cGMPs…
  - Inspection
  - Enforcement

U.S. Food and Drug Administration
OFFICE OF REGULATORY AFFAIRS

For more information go to www.fda.gov/ora

How do they regulate facilities?…

FDA Regulation

Code of Federal Regulations
Title 21- Food and Drugs- Parts 1 to 1405

Regulations applicable to the pharmaceutical industry:

- **21 CFR Parts 210 and 211**- Human Pharmaceutical Products and Veterinary Products
- **21 CFR Part 600 and 620**- Biologically Derived Products
- **21 CFR Part 820**- Quality System Regulation for Medical Devices
- **21 CFR Part 11**- Electronic Records

What regulations does the FDA enforce?…

Quality Control

cGMP Regulations establish Quality Control requirements for all operations including:

- Approval and rejection of product
- Audits

How do we establish Quality?

- PDA/ ISPE- Validation
- ASQ- Quality Audit

Quality Control

Validation-

Establishing ***documented evidence*** which provides a ***high degree of assurance*** that a ***specific process*** will ***consistently produce*** a ***product*** which meets it's ***pre-determined specifications*** and quality attributes.

ISPE Definition…

For more information go to www.ispe.org

Quality Control

Quality Audit-

A quality audit is a ***systematic***, ***independent inspection*** and ***examination*** of a ***process*** or quality system to ***ensure compliance*** to requirements.

ASQ Definition…

For more information go to www.asq.org

FDA Inspection/ Enforcement

GMP Compliance requires documented evidence…

- Must demonstrate that all operations comply with requirements and specifications…
  - Product
  - Process
  - Facility
- Quality Control- ensure products are produced in a manner that demonstrates that they meet all requirements
  - Maintain “state of control”
  - Maintain “unadulterated” status…
- This “quality effort” is unique to FDA regulated facilities
  - Hence, the “Extra Work”…

GMP Compliance - Extra Work…

A great deal of “Extra Work” can be required throughout the life of a project…

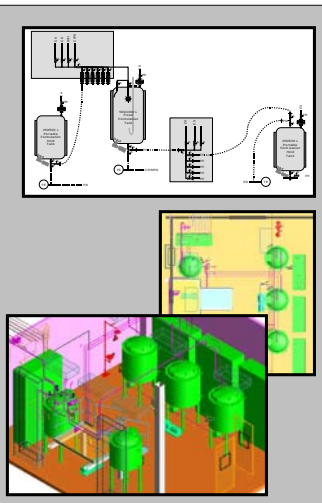
- Design and Engineering
- Construction
- Commissioning
- Validation
- Operation

The goal is GMP Compliance…

GMP Compliance - Extra Work…

Design and Engineering Phase…

- GMP Design Reviews
  - Establish design criteria to be verified during Qualification efforts…
  - Identify "Direct Impact" Systems/ components to be validated
  - FDA Pre-Reviews
- Vendor Data Requirements
  - Establish documentation requirements up front which will support downstream efforts…
- User Requirement Specifications
  - Establish documentation of project specific performance requirements



GMP Compliance - Extra Work…

Construction Phase…

- cGMP Training for Trades/ Craft workers
  - Training records
- Construction Quality
  - Weld Records
  - Witnessing and documentation of test results
  - Engineering Turn-over Packages
- Clean Construction Techniques
  - Ductwork
  - Piping
  - Installation Sequence for Facility and Equipment

GMP Compliance - Extra Work…

Commissioning and Start-up Phase…

- Integrated C & Q Approach
  - Record of commissioning activities become part of qualification record
  - Need to be properly documented
- Testing and Documentation
  - Capacity
- Cleaning and Passivation
  - Clean Piping
- Testing and Balancing
  - HVAC Systems
- Start-up Sequence
  - Major Utilities/ Clean Utilities/ Equipment

GMP Compliance - Extra Work…

Validation Phase…

- Installation/ Operational Qualification
  - P+ID system walk-down
  - Loop Checks
  - Temperature Mapping
- FAT/ SAT
- Performance Qualification
  - Environmental Monitoring
  - HEPA Filter Aerosol Challenge (DOP)
  - Clean Utility USP Testing
- Process Validation
  - Product testing

GMP Compliance - Extra Work…

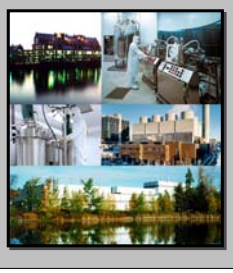
Operation Phase…

- cGMP Training for Production Personnel
  - Training Records
- Batch Records
  - Documentation of each significant production step
  - Equipment used
  - Samples
  - Label Control
  - Other requirements
- QC Release
  - In-process testing
  - QC Release
  - Other requirements

Future Trends in Regulation…

Pharmaceutical cGMPs for 21st Century-
A Risk Based Approach

- FDA Strategic Initiative currently underway
  - Science-based, efficient risk management
  - Existing GMPs have not been updated in 25 years…
- Final Report issued September 2004

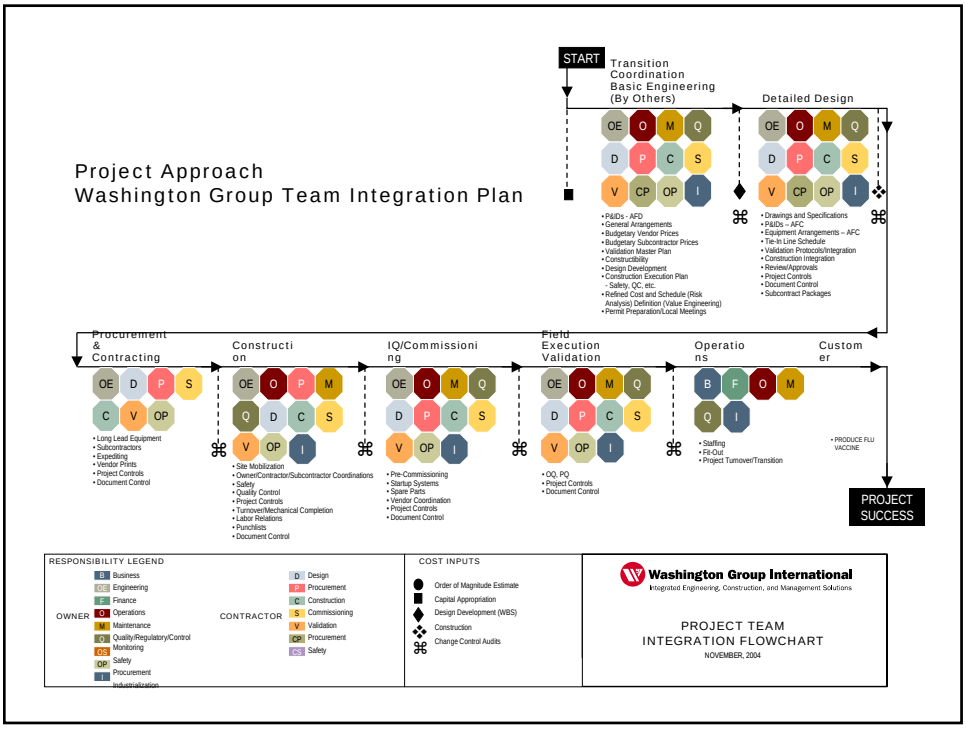


Answers…

GMP Compliance is…

- not “Extra Work”…
- It is a mandatory level of Quality…
- A diligent response to industry requirements to do our part to help ensure public health and safety; which impacts:
  - Design
  - Construction
  - Qualification
  - Operation

Did we get our Answers?…



Questions/ Discussions

- Thanks to our Hosts!!!
  - New England Chapter of the PDA
  - Boston Chapter of the ASQ
- Thanks to our Sponsors!!!
  - Commissioning Agents, Inc
  - Masy Systems, Inc.
  - Washington Group International
- Thank You for your attention!!!…