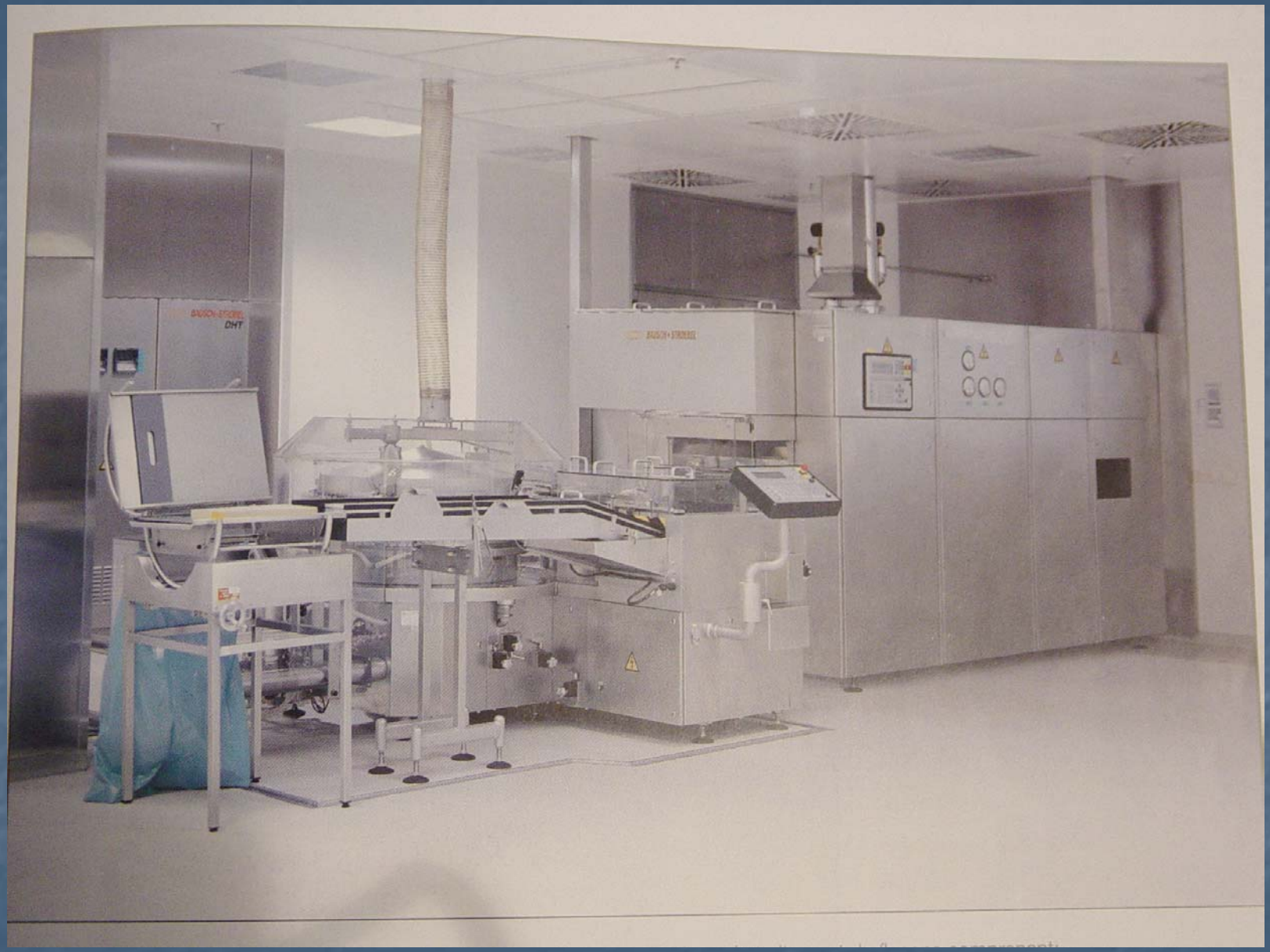
Pharmaceutical Facility Design

PhEn-602

J. Manfredi

Section 102 (Wed.)



Pharmaceutical Facility Design – PhEn 602
Syllabus

Term: 2009 Spring Semester

NJIT Course Title: Pharmaceutical Facility Design

NJIT Course Number: PhEn 602, Section 102 (Wed.)

Course Instructor: Joseph J. Manfredi
Adjunct Professor
New Jersey Institute of Technology
Department of Chemical Engineering
University Heights
Newark, NJ 07102-1982

Instructor's Telephone & Fax: Ph: (973) 575-4990 Fax: (973) 808-9201

Instructor's E-Mail Address: JJM1152@AOL.com

Instructor's Office Hours: As an adjunct faculty member, Prof. Manfredi does not maintain an office on campus. Students may contact him, preferably by email, to schedule a meeting, to pose questions, or to request clarifications regarding course materials. Responses will be handled as quickly as possible, subject to scheduling, travel and other prior commitments. Phone calls should be limited to emergencies only. Prof. Manfredi will generally be available prior to and after each class for discussion.

Grader/Assistant: None

Course Day and Time: Wed. (Sect. 102) 6:00 – 9:05 p.m.

Location: NJIT, Newark, NJ, Kupfrian Hall , Room 110

Course Prerequisites: Graduate Standing
PhEn-601 – Principles of Pharmaceutical Engineering
PhEn-603 – Pharmaceutical Processing and Manufacturing
Permission by the Instructor or the Program Director

Course Description: This course provides students with a basic understanding of the challenges faced by engineers and designers when designing a pharmaceutical manufacturing facility. The course will focus on the sterile manufacturing facility design model, although many of the principles discussed will apply to all other types of Pharmaceutical facilities. Pharmaceutical facilities are required to meet Good Manufacturing Practices (GMP) regulations, while at the same time, must be in compliance with all governing codes, laws and regulations. The main objective of the course is to provide students with a solid understanding of the key principles of facility design. The course blends practical applications, with the underlying theory behind basic concepts, so that the student obtains a balanced understanding of the topics. The course is intended to 1) teach students the basics of facility design, 2) highlight the major challenges faced by designers and engineers, 3) provide helpful "do's" and "don'ts" concerning design options, and 4) present important operational, testing and construction considerations that impact design decisions.

Course Requirements:

- Examination: Two exams, i.e. a midterm exam and a final exam
- Quizzes: Four quizzes as scheduled by instructor

Grading Policy:

- Midterm exam.....30%
- Final exam.....30%
- Quizzes.....40% (10% each quiz)

Course Final Grade: a tentative guideline for the assignment of final grades is provided below:

Cumulative Points	Overall Grade
90-100%	A
88-89%	B+
80-87%	B
78-79%	C+
70-77%	C
<69%	F

The grade of "D" is not assigned to students taking graduate courses.
Please remember that this is only a guideline designed to help the students understand how they are performing in the course.

Exams:

- A calendar of the exams is included in the Course Outline given below;
- All exams are typically 3 hours long unless otherwise stated;
- All exams are open book and open notes, unless otherwise announced;
- The final exam will include all material covered throughout the course (although the main emphasis of the exam may be on the material covered after the midterm exam);
- Make-up exams will only be given to students who cannot attend the regular exam time, **and** only under documented and extraordinary circumstances. In any case, no student will be allowed to a take a make-up exam unless he/she has the **prior** consent of the instructor. If a student fails to take an exam as scheduled, the exam grade will automatically be zero.

Quizzes:

- A calendar of the quizzes is included in the Course Outline below.
- Quizzes are typically 1 hour long unless otherwise stated.
- Quizzes may be open or closed book and notes. Format will be announced.
- Quizzes will typically cover material from immediately preceding classes.
- Make-up quizzes will only be given if approved in advance for documented and extraordinary circumstances.

Class Attendance: As for all graduate courses at NJIT, attendance is not mandatory, but strongly recommended. Experience shows that students who do not regularly attend class typically perform poorly in the course. In addition, discussions and material provided by any guest lecturers will not be covered in the notes. In any case, students are responsible for all material covered in class. Interwise access is anticipated for students unable to attend class in person due to travel or other business related activities. Details for accessing Interwise will be provided at the first class session.

Important Dates on the NJIT Calendar (Spring 2009) – visit NJIT's website

01/21/09	First Class PhEn-602 Section 102
02/02/09	Last Day for a Refund Based Upon A Partial Withdrawal
Ck. Registrar	Last Day for a Refund Based Upon a Complete Withdrawal
03/18/09	No Class – Spring Break
03/30/09	Last Day to Withdraw from Course(s) (No Refund)
04/29/09	Last Class-PhEn-602-102
05/06/09	Reading Day
05/13/09	Final Exam PhEn-601 (Finals 12/15-19/08)
05/14/09	Grades Due in Registrar's Office

PHARMACEUTICAL FACILITY DESIGN (PhEn-602)

Wk #1 (1/21) Introduction & Planning
- A) GMP's, CFR, FDA
- B) Project planning

Wk #2 (1/28) Design Considerations
- A) Regulations
- B) Building & Zoning Codes
- C) Support Utility Requirements
- D) Bldg. Materials & Finishes
- E) Safety

Wk #3 (2/04) Types of Manufacturing
- A) Sterile / Aseptic
- B) Non-Sterile
- C) Liquid vs Dry
- D) Cross-Contamination
- E) Cleaning
- F) Single vs Multiple Products

Quiz #1 (Tentative)

Wk #4 (2/11) Classified Spaces & Controlled Environments
- A) Clean Rooms
- B) ISO vs FSA
- C) Air Flow
- D) Exchange Rates

Wk #5 (2/18) Environmental Issues & Monitoring
- A) Microbial.
- B) Air & Liquid Discharge

Quiz #2 (Tentative)

Wk #6 (2/25) Architectural
- A) Materials & Finishes
- B) Service / Maintenance
  - a. Interstitial & Mech. Rooms

Wk #7 (03/04) Midterm Examination

Wk #8 (03/11) Heating & Ventilation
- A) Equipment
- B) Configuration

Wk #9 (03/25) Air Conditioning
- A) Equipment
- B) Configuration

Quiz #3 (Tentative)

Wk #10 (04/01) Moisture
- A) Humidification / Dehumidification
- B) Related Problems

Wk #11 (04/08) Utility Sizing
- A) Heating & Cooling Loads
- B) Psychometrics

Wk #12 (04/15) Critical Utilities
- A) Water
- B) Steam
- C) Gases

Quiz #4 (Tentative)

Wk #13 (04/22) Layout
- A) Adjacencies
- B) Materials Flow
- C) Personnel Flow

Wk #14 (04/29) Semester Review

Wk #15 (05/13) Final Examination

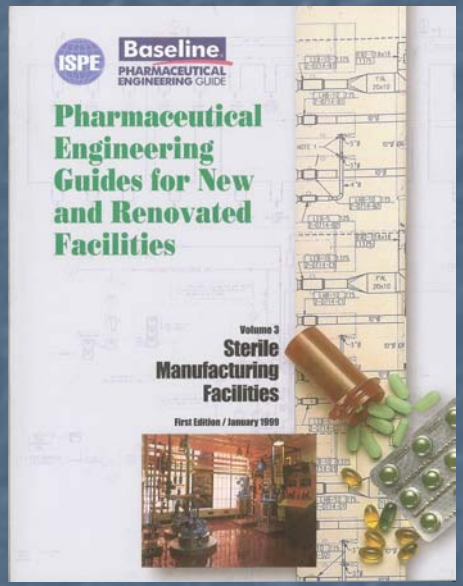
Course Notes, Textbooks, and Other Reference Material:

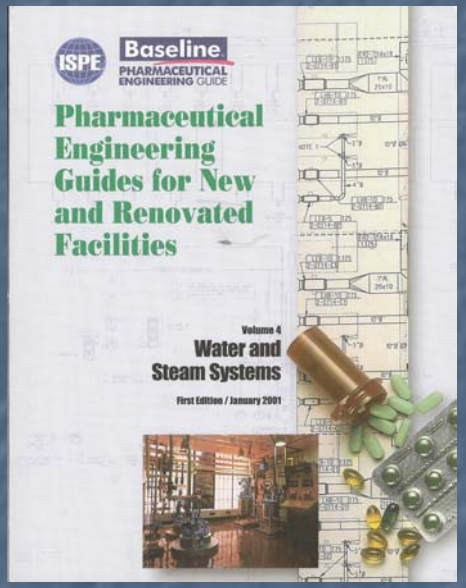
- **Notes**: *Pharmaceutical Facility Design Course Notes*. These notes are duplications of the presentations used in class. The *Notes* will be posted on the NJIT website:
  http://web.njit.edu/~armenant/PhEn602-102
- **Textbook**: (Optional)
  International Society for Pharmaceutical Engineering,; Pharmaceutical Engineering Guides for New and Renovated Facilities, Volume 3, "Sterile Manufacturing Facilities". Additional reference books are listed under "references".

Reference material:

1. International Society for Pharmaceutical Engineering, Pharmaceutical Engineering Guides for New and Renovated Facilities, Volume 3, *Sterile Manufacturing Facilities*, (textbook).
2. "Sterile Product Facility Design and Project Management", 2nd edition, Jeffery N. Odum, CRC Press.
3. "Good Design Practices for GMP Pharmaceutical Facilities", Andrew Signore and Terry Jacobs, Taylor and Francis
4. "Aseptic Pharmaceutical Manufacturing, Applications for the 1990's", Groves and Murty, Interpharm Press
5. "Validation of Pharmaceutical Processes", Carlton and Agalloco, Marcell Dekker, Inc.
6. "Cleanroom Technology, Fundamentals of Design, Testing and Operation", Whyte, John Wiley
7. "Cleanroom Microbiology for the Non-Microbiologist", Carlberg, Interpharm Press
8. International Society for Pharmaceutical Engineering; Pharmaceutical Engineering Guides for New and Renovated Facilities, Volume 4, "Water and Steam Systems"
9. International Society for Pharmaceutical Engineering; Pharmaceutical Engineering Guides for New and Renovated Facilities, Volume 5, "Commissioning and Qualification"

ISPE Guides


ISPE
Baseline
PHARMACEUTICAL ENGINEERING GUIDE
Pharmaceutical Engineering Guides for New and Renovated Facilities
Volume 3
Sterile Manufacturing Facilities
First Edition / January 1999


ISPE
Baseline
PHARMACEUTICAL ENGINEERING GUIDE
Pharmaceutical Engineering Guides for New and Renovated Facilities
Volume 4
Water and Steam Systems
First Edition / January 2001


Pharmaceutical Engineering Guides for New and Renovated Facilities

ISPE

- Excellent Resource
  - Publications: Guides, PE, JPI
  - Networking
  - COP's (Community of Practice)
  - Educational Programs
  - Student Programs

Class Notes

Notes can be found at:

http://web.njit.edu/~armenant/PhEn602-102

THIS ADDRESS IS CASE SENSITIVE

Housekeeping

- The email address listed with the official class roster will be used as needed to communicate with the class. Check this regularly, especially during periods of inclement weather
- Guest lecturers &/or tours may be scheduled as available and class schedule adjusted accordingly.
  - Novartis Tour 2/25/09
- Text is optional and will not impact performance
- 30 Minute Policy for instructor absence
- Class Breaks will be discussed and a format selected, however this will remain at the instructor's discretion.

Library Research

- http://www.library.njit.edu/staff-folders/slutsky/PharmTutorial/Pharmtutorial.html
- **Important Announcement for Users of Scifinder Scholar - The Web version became available to NJIT on January 20, 2009**

INTERPHEX2009™

March 17-19, 2009

(Spring Break)

Jacob K. Javits Center

New York, NY

PhEn-602
Pharmaceutical Facility Design

Week 1

GMP's

Project Approach

Design and Validation

Pharmaceutical Facility Design

Good Manufacturing Practice (GMP's)

Food, Drug and Cosmetic act gives FDA authority to enforce legal requirements in manufacturing, processing, packing and holding of drugs.

- These requirements are found in

  21CFR Part 211

  Subpart C relates to "Buildings and Facilities"

Pharmaceutical Facility Design
21 CFR Part 211 - Subpart C-Buildings and Facilities

§ § 211.42 Design and construction features.

(a) Any building or buildings used in the manufacture, processing, packing, or holding of a drug product shall be of **suitable size**, construction and location to facilitate cleaning, maintenance, and proper operations.

(b) Any such building shall have **adequate space** for the orderly placement of equipment and materials to prevent mixups between different components, drug product containers, closures, labeling, in-process materials, or drug products, and to prevent contamination.

The flow of components, drug product containers, closures, labeling, in-process materials, and drug products through the building or buildings shall be **designed to prevent contamination**.

(c) Operations shall be performed within specifically defined **areas of adequate size**.

Pharmaceutical Facility Design
21 CFR Part 211 - Subpart C-Buildings and Facilities

§ § 211.42 Design and construction features.

There shall be **separate or defined areas for the firm's operations to prevent contamination or mixups** during:

(1) Receipt, identification, storage, and withholding from use of components, drug product containers, closures, and labeling, pending the appropriate sampling, testing, or examination by the quality control unit before release for manufacturing or packaging;

(2) Holding rejected components, drug product containers, closures, and labeling before disposition:

(3) Storage of released components, drug product containers, closures, and labeling;

(4) Storage of in-process materials;

(5) Manufacturing and processing operations;

(6) Packaging and labeling operations;

Pharmaceutical Facility Design
21 CFR Part 211 - Subpart C-Buildings and Facilities

§ § 211.42 Design and construction features (cont).

(7) Quarantine storage before release of drug products;

(8) Storage of drug products after release;

(9) Control and laboratory operations;

(10) Aseptic processing, which includes as appropriate:

(i) Floors, walls, and ceilings of smooth, hard surfaces that are easily cleanable;

(ii) Temperature and humidity controls;

(iii) An air supply filtered through high-efficiency particulate air filters under positive pressure, regardless of whether flow is laminar or nonlaminar;

(iv) A system for monitoring environmental conditions;

(v) A system for cleaning and disinfecting the room and equipment to produce aseptic conditions;

(vi) A system for maintaining any equipment used to control the aseptic conditions.

Pharmaceutical Facility Design
21 CFR Part 211 - Subpart C-Buildings and Facilities

§ § 211.42 Design and construction features.

(d) Operations relating to the manufacture, processing, and packing of penicillin shall be performed in facilities separate from those used for other drug products for human use

Pharmaceutical Facility Design

Note:

The GMP Regulations specify what a particular requirement is (i.e. what is to be controlled), not ***how*** that requirement is to be achieved.

What does FDA look for in a facility?

Buildings and Facilities

1) Is the facility suitable for the operations being carried out?
2) Is the facility readily cleanable?
3) Are there proper controls against cross-contamination?
4) Is there adequate ventilation while still keeping out sources of contamination?
5) Are there adequate sanitary facilities?
6) Are there operational areas separate to prevent mix-ups and cross-contamination?
7) What is the source of the water supply?
8) Are there adequate systems for the handling and disposal of waste?

What does FDA look for in a facility?

Materials handling and storage

1) Is there proper segregation between incoming and released components?
2) Are environmental factors, such as temperature and humidity, monitored and controlled properly?
3) Is there adequate storage space under the required environmental conditions?
4) Are in-process materials properly stored?
5) Are containers suitable for raw materials and intermediate product?

What does FDA look for in a facility?

Equipment

1) Is the facility equipment suitable for its intended use?
2) Is equipment designed to facilitate cleaning?
3) Are there proper filtration systems adequately designed and properly functioning?
4) Does equipment design prevent contamination from external sources?
5) Is equipment clearly and uniquely identified?

Pharmaceutical Facility Design

Pharmaceutical Facility Project Sequence

Design

Good Engineering Practice

Validation

Pharmaceutical Facility Design

There must be a compelling reason for pursuing a new or renovated facility.

- ***Sales of existing products have surpassed the capabilities of the current facility and an expansion is necessary.***
- ***New products have been identified which require different types of facilities.***
- ***Existing facility does not meet current regulatory requirements (e.g. FDA, EPA or other agency)***

From J. Odum, Sterile Product Facility Design and Project Management

Pharmaceutical Facility Design

There must be a compelling reason for pursuing a new or renovated facility.

- ***Economic or business advantage associated with relocation to a new or existing site.***
  - ***Improved labor pool***
  - ***Cost of upgrade, renovation, or change***
  - ***Cost of manufacturing and/or shipping***
  - ***Tax incentive***
  - ***Lower labor rate***
  - ***Reduced cost of employee benefits***

Not From J. Odum, Sterile Product Facility Design and Project Management

Pharmaceutical Facility Design

- ***Establish Goals***
- ***Prepare the Business Case***
  - ***From the business case we develop a plan for manufacturing, and then proceed into the Facility Planning stage***

Facility Planning is Critical

"Exceptional facilities don't just happen…they are planned to be functional, efficient, cost effective, and compliant to all regulations. They are planned to meet market demands for product…to be environmentally pleasing to those that work in them on a daily basis…and they are planned to be safe, protecting the workers and the outside environment."

From J. Odum, Sterile Product Facility Design and Project Management.

Facility Planning is Critical

Proper planning is the key…..having a sound project management process is crucial

In order to properly plan the facility, a significant amount of information is needed, such as project goals and objectives, product volumes, schedule, budget costs, utility requirements, safety requirements, etc., etc.
This information is typically gathered during the facility programming portion of the conceptual design phase.

Pharmaceutical Facility Design

Project Approach – 9 stages

1. Conceptual Study
2. Functional Design/Preliminary Engineering
3. Request for Funds Approved
4. Detailed Engineering
5. Procurement/Bidding
6. Construction
7. Commissioning
8. Validation/Qualification
9. Turnover to Owner

Pharmaceutical Facility Design

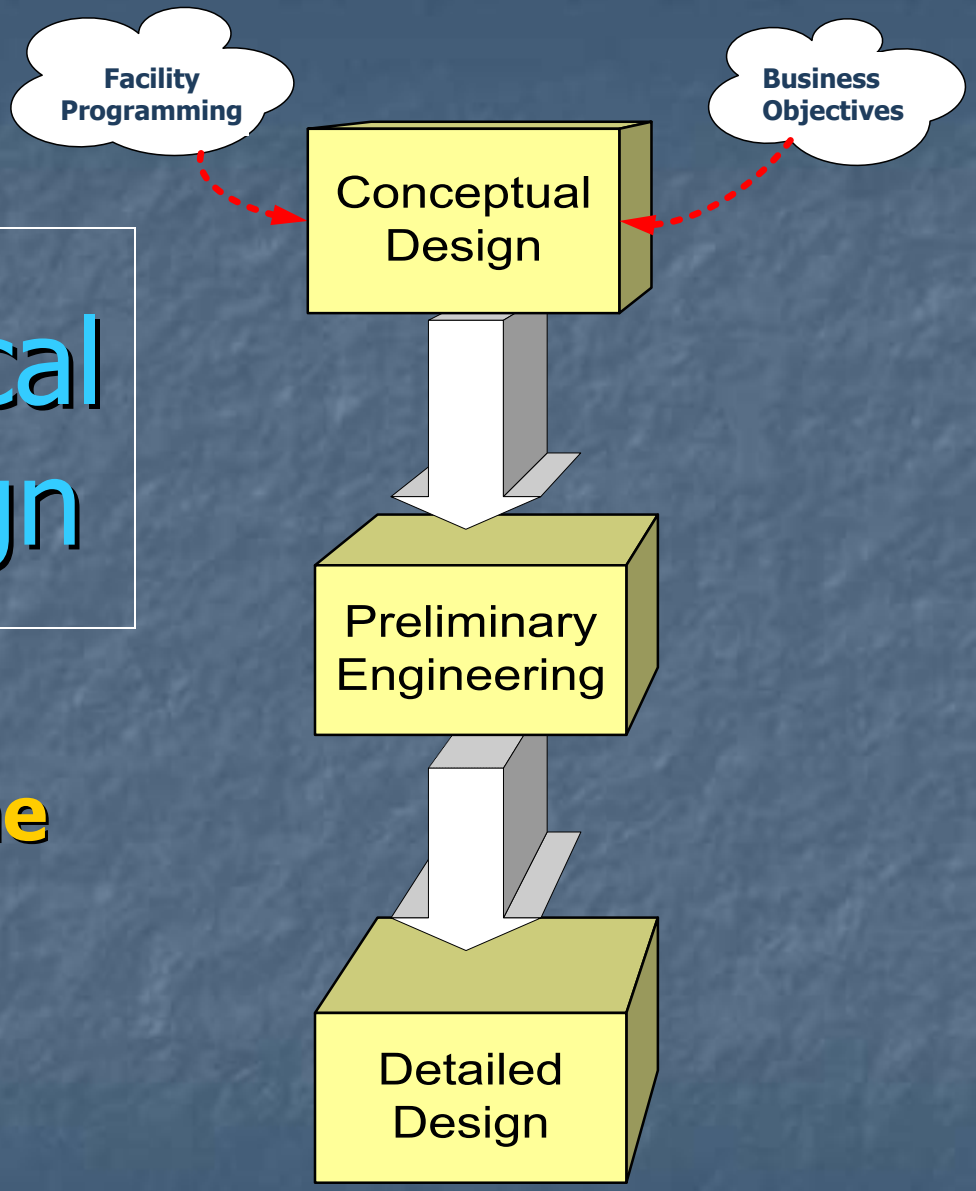
PhEn-602 will focus on:

- **Design (1,2 & 4)**
- **Commissioning, Validation/Qualification(7 & 8)**

1. **Conceptual Study**
2. **Functional Design/Preliminary Engineering**
3. Request for Funds Approved
4. **Detailed Engineering**
5. Procurement
6. Construction
7. **Commissioning**
8. **Validation/Qualification**
9. Turnover to Owner

Pharmaceutical Facility Design

Three phases to the Design Process



Conceptual Design-Basic Elements

- Establish goals and objectives, and discuss how GMP requirements will be met
- Conduct facility programming, with extensive data gathering - Very important!
- Conceptual layout and Accommodation Schedule
- Prepare "Basis of Design" (statement of criteria)
- Establish design philosophy: e.g. state-of-the-art or leading edge?
- Heating, Ventilation and Air-Conditioning philosophy
- Major equipment list
- Budget estimate (often prepared for management review)

Conceptual Design – Facility Programming

Process	Company Z	- Laboratory
Packaging		
	Preliminary Program	- Office / Amenities
	Single Level Manuf./Pkg. Facility with Mezzanine	- General Support

Functional Unit Title/ Space Description	Unit Area Net SF	2008 No. of Units	2008 Total Area Net SF	2013 No. of Units	2013 Total Area Net SF	Remarks
PROCESS						
Manufacturing						
Pharmacy	120	4	480	6	720	
Drying	400	3	1,200	4	1,600	
Blending	300	9	2,700	10	3,000	
Compression	480	13	6,240	13	6,240	
Encapsulation	480	2	960	2	960	
Coating	400	5	2,000	6	2,400	
Dirty Equipment Staging	600	1	600	1	600	
Equipment Wash	600	1	600	1	600	
Clean Equipment Storage	1,200	1	1,200	1	1,200	
Turret/Tooling Maintenance	600	1	600	1	600	
Tool Storage	400	1	400	1	400	
Tool Inspection	400	1	400	1	400	
Instrumentation Shop	300	1	300	1	300	
In-Process Test	250	1	250	1	250	
Solution Prep	450	1	450	1	450	
QA Sampling	120	1	120	1	120	
Men's Lockers	12	80	960	100	1,200	Includes toilets, sinks and showers. Based on two shifts.
Women's Lockers	12	80	960	100	1,200	Includes toilets, sinks and showers. Based on two shifts.
Manufacturing Process SUBTOTAL - NSF			**20,420**		**22,240**	

Manufacturing Admin

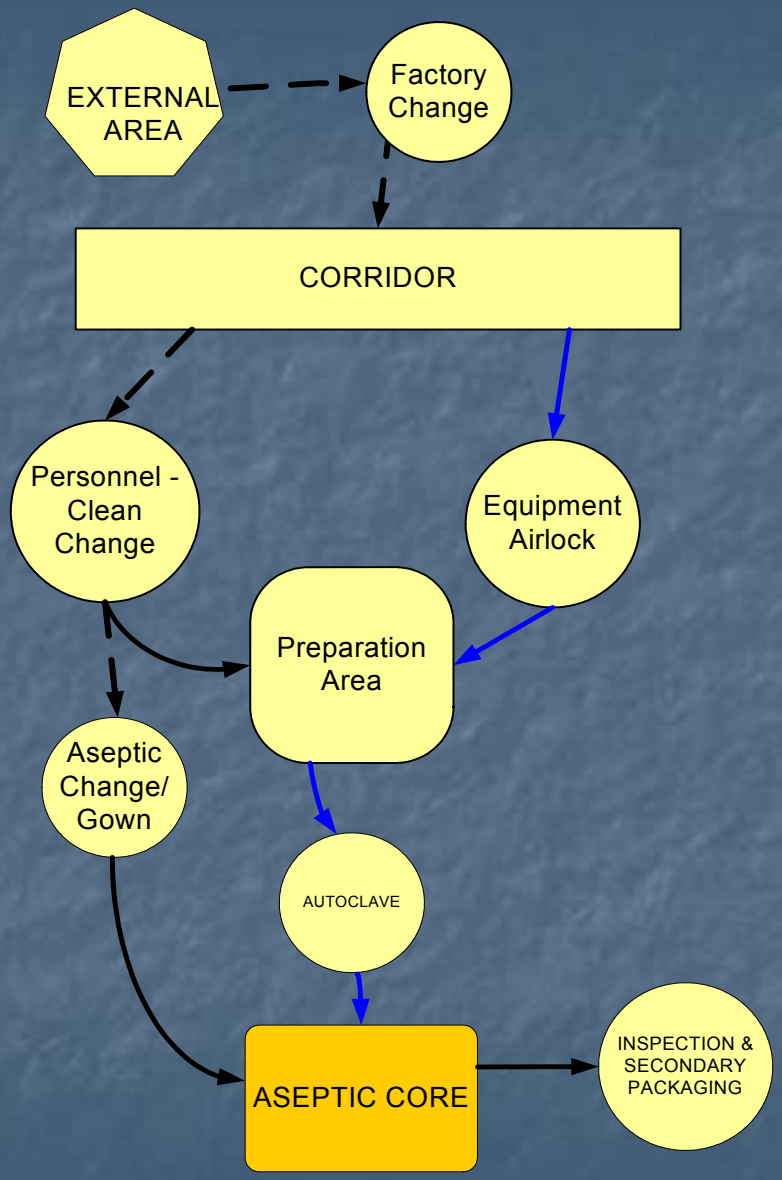
General Admin - Office	120	5	600	8	960	
General Admin - Workstation	64	3	192	4	256	
Engineering - Office	120	10	1,200	16	1,920	
Engineering - Workstation	64	20	1,280	30	1,920	
Purchasing - Office	120	3	360	4	480	
Purchasing - Workstation	64	3	192	4	256	
Health, Safety & Environ. - Office	120	2	240	2	240	
Maintenance - Office	120	6	720	10	1,200	
Production Planning - Office	120	3	360	4	480	
Support Areas	150	55	8,250	82	12,300	Includes break areas, conference rooms, storage rooms, etc.
Manufacturing Admin SUBTOTAL - NSF			**8,250**		**12,300**	

General Support - Manufacturing

Warehouse - Unreleased Material	6.00	1168	7,008	1756	10,536	
Warehouse - Released Material	6.00	1067	6,402	1604	9,624	
Warehouse - Manufacturing WIP	6.00	718	4,308	1080	6,480	
Technical Services	5,927	1	5,927	1	5,927	
Maintenance Shop	5,000	1	5,000	1	5,000	
Consumable Storage	1,200	1	1,200	1	1,200	
Filter Storage	1,200	1	1,200	1	1,200	
Chemical Dispensing	450	1	450	1	450	
Waste Drum Storage	200	1	200	1	200	

Conceptual Design Basic Elements:

1) "Accommodation Schedule" also called "Bubble Diagram"
2) Defines adjacencies and high level flow of material and personnel
3) Performed prior to layout of area



Functional Design– Basic Elements

Also called: "Preliminary Engineering", "Front-end Design", "Design Development"

- Establish a basis for detailed design
  - Prepare Basis of Design (BOD)
- Layout of production lines, location of equipt., building services/utilities defined
- Create process specifications, process flow diagrams, and P&ID's (Process and Instrumentation Diagrams)
- Detailed cost estimate is generated
- Develop User Requirements Specifications (URS)

Detailed Design

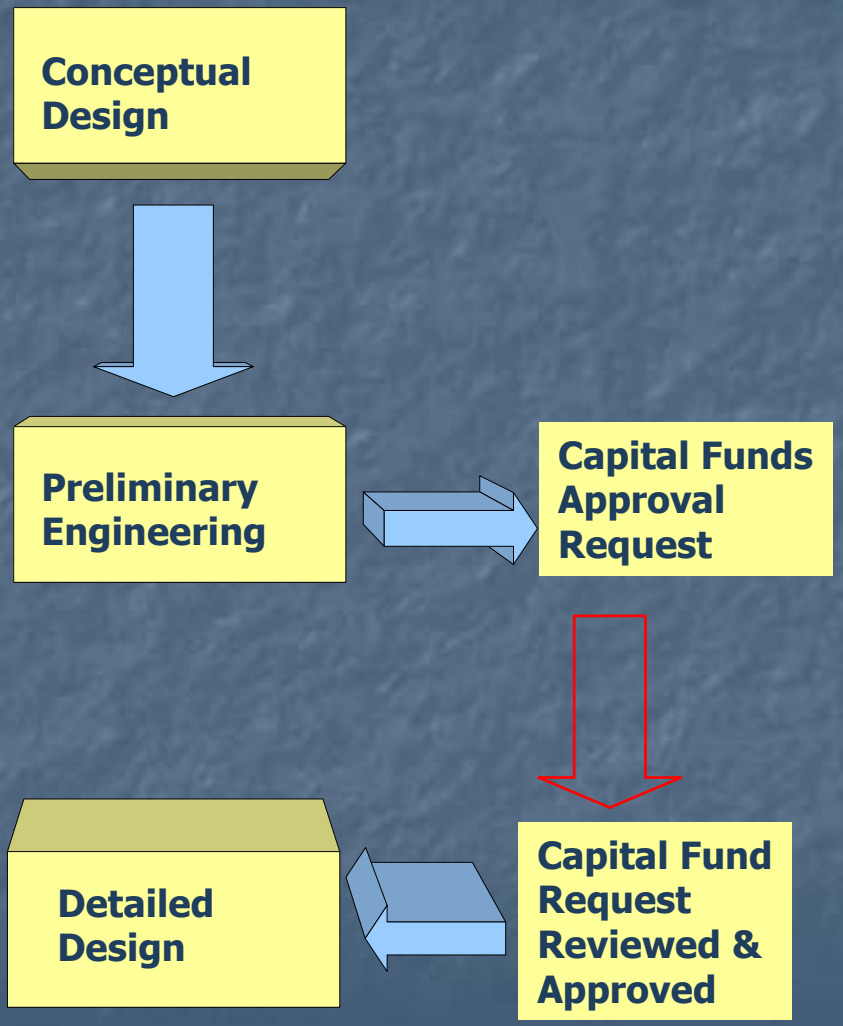
- Prepare detailed engineering drawings to be issued for construction
- Create detailed equipments lists and instrument lists
- Develop construction strategy
- Set the basis for the Installation Qualification (IQ)
- Finalize layouts, size and routing of utilities

Pharmaceutical Facility Design

Note: A more developed design produces a more accurate estimate!

Too often projects are estimated at the conceptual design stage….

Tip: If possible finish the functional design (preliminary engineering) before requesting funds to minimize submission of budget revisions.



Good Engineering Practice

"Established engineering methods and standards that are applied throughout the project lifecycle to deliver appropriate cost-effective solutions"…including:

- **Professional and competent project management**
- **Professional and competent engineering design, procurement, construction and commissioning**
- **Full consideration of applicable safety, health and environmental statutory requirements**
- **Full consideration of operation and maintenance requirements**
- **Full consideration of recognized standards and guidance**
- **Appropriate documentation for ongoing operation and maintenance, and to demonstrate compliance with applicable regulations and codes**

Commissioning

"A well planned, documented and managed engineering approach to the start-up and turnover of facilities, systems, and equipment to the End-User that results in a safe and functional environment that meets established design requirements and stakeholder expectations."

Commissioning Plan

- Prepared and approved by Commissioning Team
- Approvers include Construction, Design, Quality, Validation and User Department Representatives.
- Includes list of systems and equipment to be commissioned, including process equipment and utilities.
- Can include schedule/timeline for the commissioning activities
- Often precedes validation
- ETOP (Engineering Turn-Over Package) is often a deliverable.

Commissioning Benefits

- Can streamline the validation, since thorough up-front testing is done to eliminate bugs
- Improved documentation in place prior to IQ can reduce IQ execution effort
- Provides a formal structured approach to testing and owner acceptance, ensuring a minimum level of acceptable documentation
- Provides a formal structured approach to testing and acceptance, for those systems that are not validated (non-GMP).

Validation – An Essential Part of GMP

Validation is the scientific study of a system:

- To prove that the facility system/equipment is consistently doing what it is supposed to do

  (i.e., that the process is under control)
- To determine the process variables and acceptable limits for these variables, and to set-up appropriate in-process controls.

Validation as defined by FDA:

"Establishing documented evidence which provides a high degree of assurance that a specific process will consistently produce a product meeting its predetermined specifications and quality attributes."

Validation Execution-*Three* primary elements

DQ – Design Qualification

Verifies the design is suitable/appropriate and will work

IQ - Installation Qualification

Verifies the system/equipment is supplied and installed correctly

OQ – Operational Qualification

Verifies that the system/equipment ***operates*** as specified, intended throughout all anticipated ranges

PQ – Performance Qualification

Verifies that the system/equipment performs as intended meeting predetermined acceptance criteria

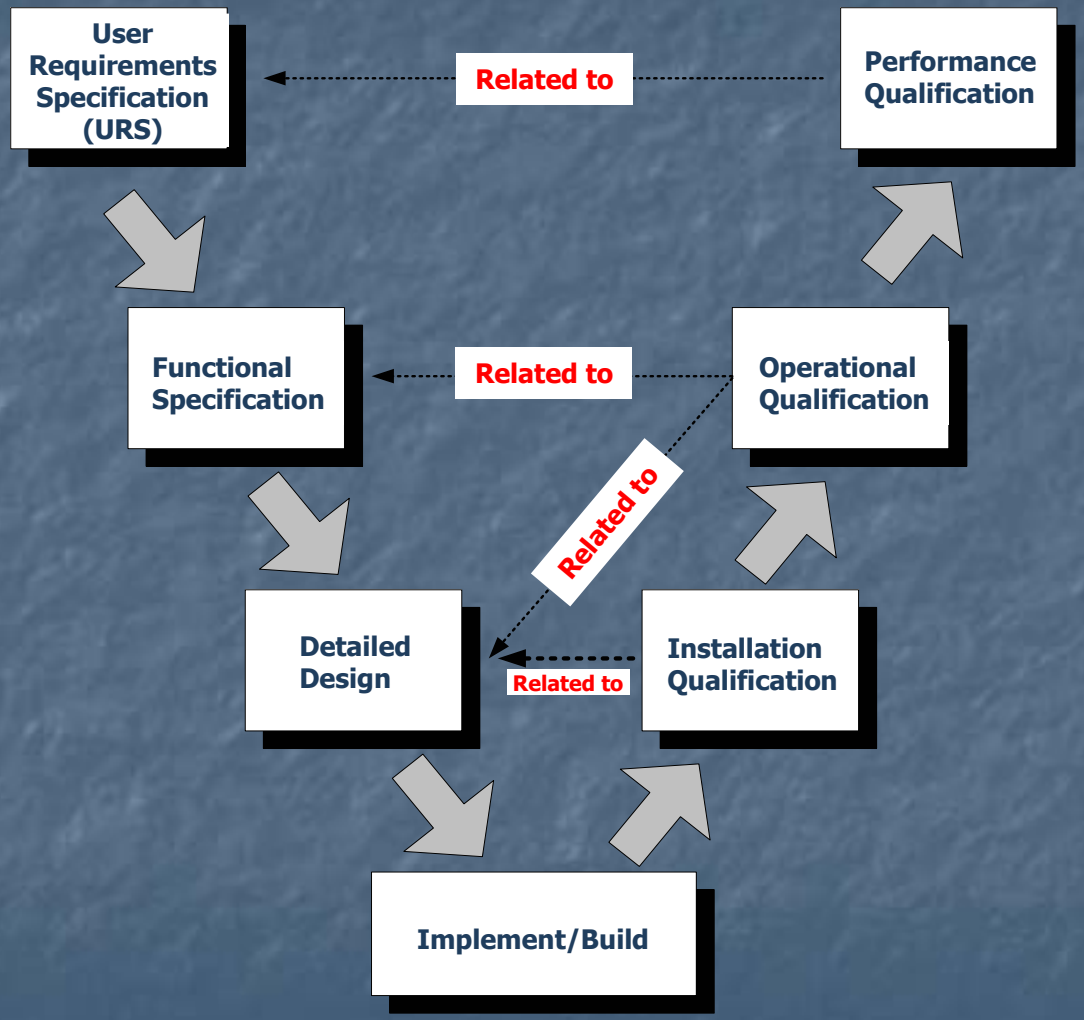
When to begin planning?

- Validation needs must be incorporated in earliest stages of the project (DQ?)
- Should be considered during the design phase (DQ?)
- Validation cannot be thought of as the last hurdle.
- Ignoring validation early in the project **will** be disastrous!

Project Validation Plan

- Defines overall validation approach
- Defines validation activities to be performed; at a high level
- Defines roles and responsibilities
- Describes the phases to the validation effort
- Provides estimated timelines
- Must be approved by cross-functional team, with final approval by QA

The V-Model



Us
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User Requirements Specification (URS)

- Also called "User Requirement Brief"
- Describes what the system or equipment is supposed to do.
- Often sent to suppliers as part of the vendor solicitation process.
- Includes essential requirements (*musts*) as well as desirable requirements (*wants*)
- Normally written by user department, or engineer

Functional Specification (FS)

- Often written by supplier
- Describes what the system will do.
- Detailed functions are described.
- Links to an OQ, which tests all functions specified.
- The FS is a design output.

Detailed Design Specifications (DDS)

- Documents how the system will be built
- Like FS, is a design output
- Links to both IQ and OQ
- Based upon the detail design documents

Quality Plan

- A document setting out the specific quality practices, resources, and sequence of activities relevant to a particular product or process. It defines the general distribution of responsibilities for quality related tasks and the implementation of the Quality System elements

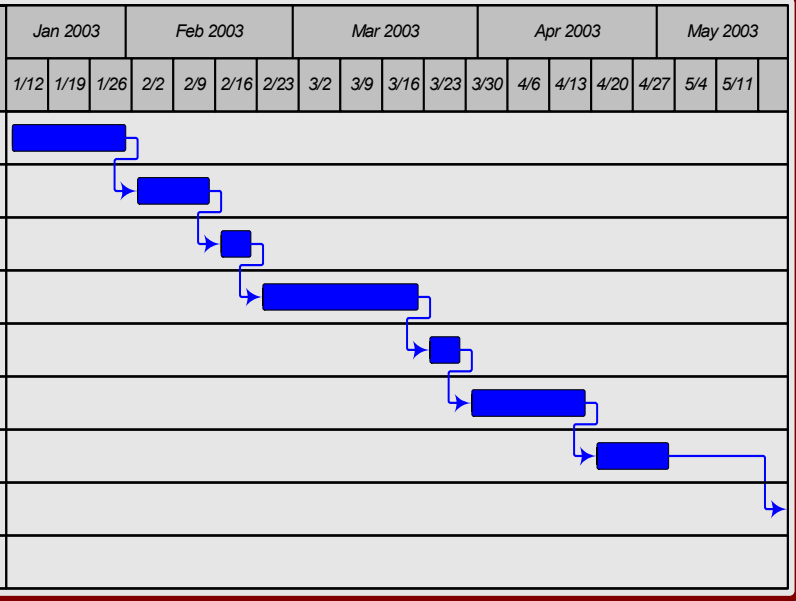
Project Planning & Schedule

Agreed by team members

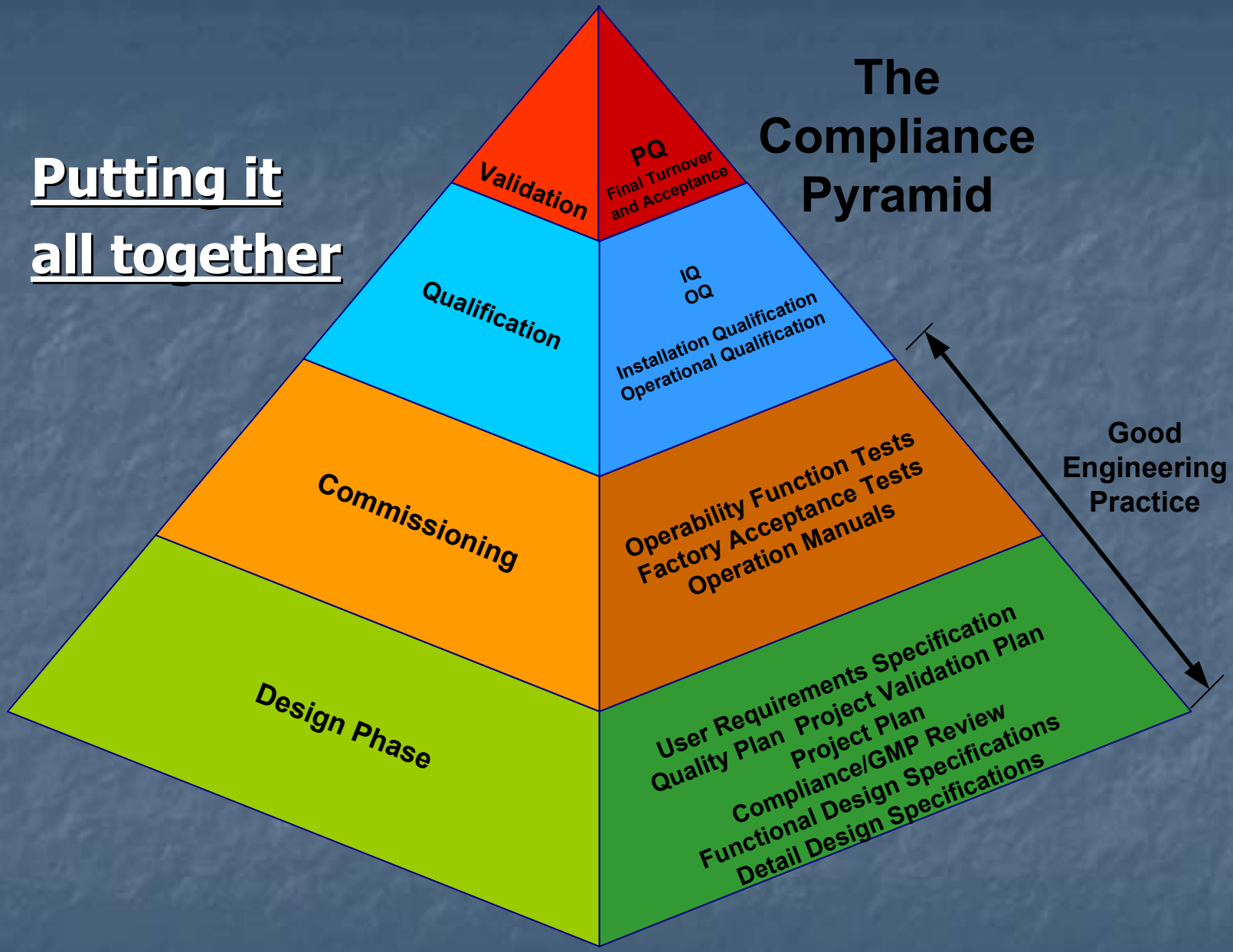
Details phases, activities, and milestones

Gantt Chart most commonly used

ID	Task Name	Start	Finish	Duration
1	Design	1/13/03	1/31/03	15d
2	Prepare Quality Plan	2/3/03	2/14/03	10d
3	Prepare URS	2/17/03	2/21/03	5d
4	Prepare Project Justification Document	2/24/03	3/21/03	20d
5	Obtain Funding	3/24/03	3/28/03	5d
6	Construct	3/31/03	4/18/03	15d
7	Commission	4/21/03	5/2/03	10d
8	Validate	5/23/03	6/5/03	10d
9	Turnover - Project Complete	6/6/03	6/6/03	1d



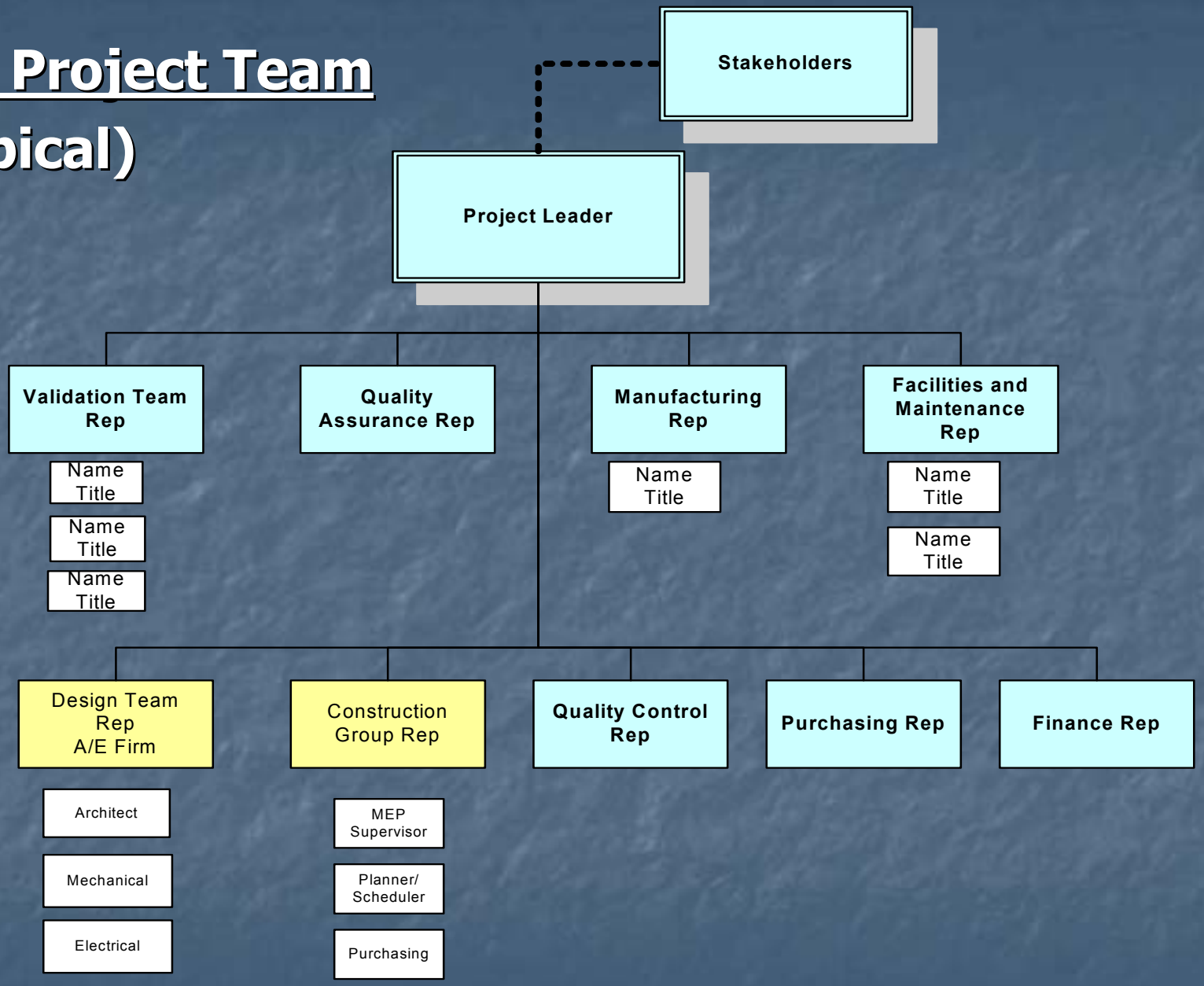
Putting it all together



Project Life Cycle Discussion

- Who are the players that make everything happen?

The Project Team (Typical)



Pharmaceutical Facility Design

Some unique aspects of Pharmaceutical Facility Projects

- Plants are very expensive to build, as compared to other industries.
- Procurement costs for process equipment are astronomical…can be 30% of overall project cost.
- Validation costs are very high…,in some cases 15-20% of overall project cost.
- Very long timelines from start to finish, often due to two major issues:
  - **Specialty equipment lead-time**
  - **Validation is extensive…up to 1 – 3 years in some cases, depending on size of project .**

Pharmaceutical Facility Design
Summary:

- A structured project approach is required for successful implementation of Pharmaceutical Facility Projects
- A phased approach to the design is often used
- Good Engineering Practice and Commissioning play a key role in the project life-cycle
- Validation is an essential part of the facility system and must be considered at the earliest part of the project; during the design phase.

Documentation "Golden" Rules

- If there is no documentation; the job wasn't done
- That which is written remains

Six Phases of a Project:

- 1) Enthusiasm
- 2) Disillusionment
- 3) Panic
- 4) Search for the guilty
- 5) Punishment of the innocent
- 6) Praise and honors for non-participants


Change Order
YAMAHA


Change Order
YAMAHA


YAMAHA