Regulatory Education for Industry (REdI): Focus on CGMPs & FDA Inspections

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Production and Process Controls: Overview of CGMP Regulations and Regulatory Expectations

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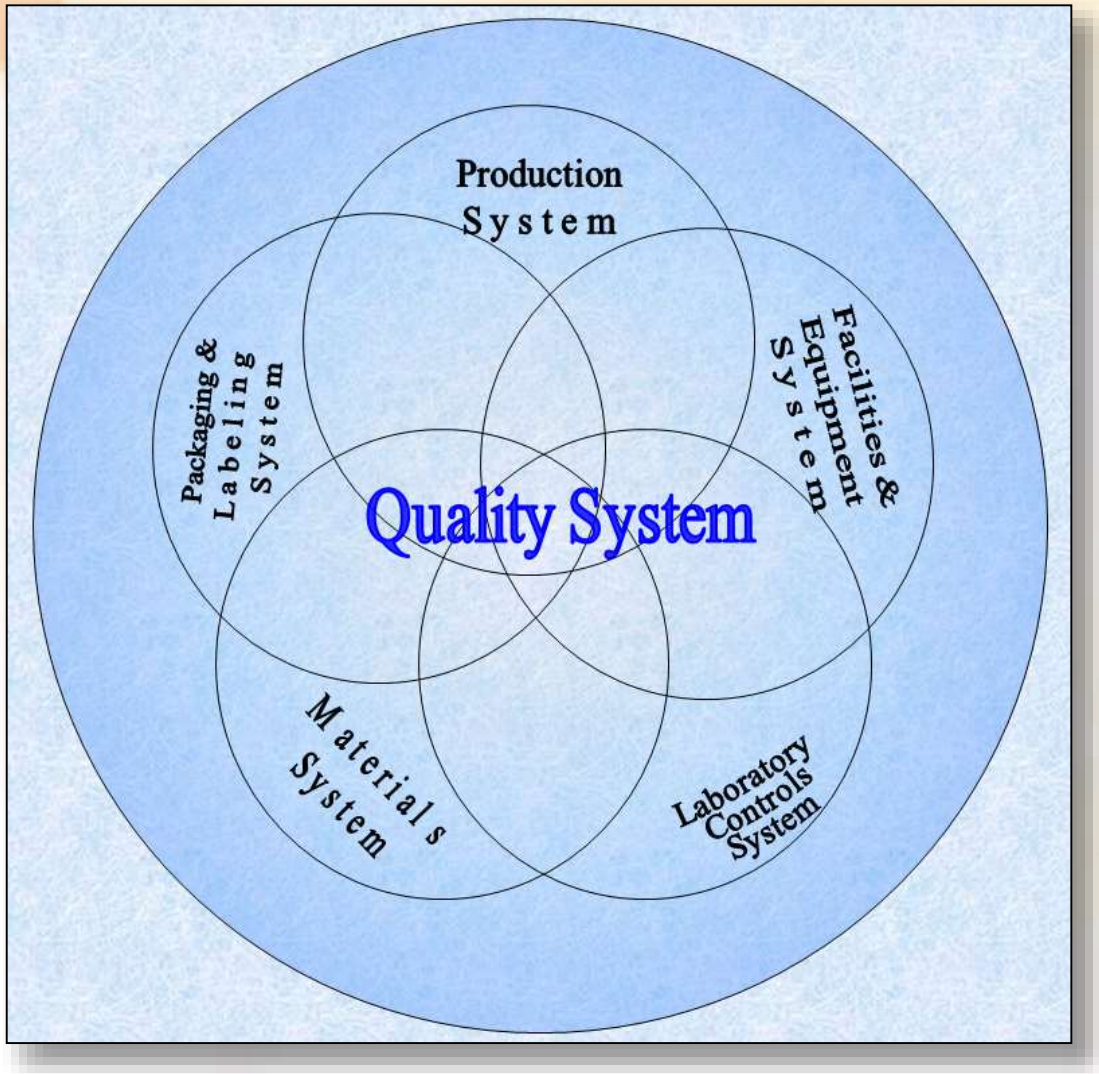
The Six Components

- Quality
- Production
- Laboratory
- Materials
- Facilities & Equipment
- Packaging & Labeling



Overview

- Public Health and Product Quality Expectations
- Pharmaceutical Manufacturing Operation
- Production Relevant CGMP Regulations
- Regulatory Tools for Compliance
- Regulatory Expectations
- Summary
- Questions

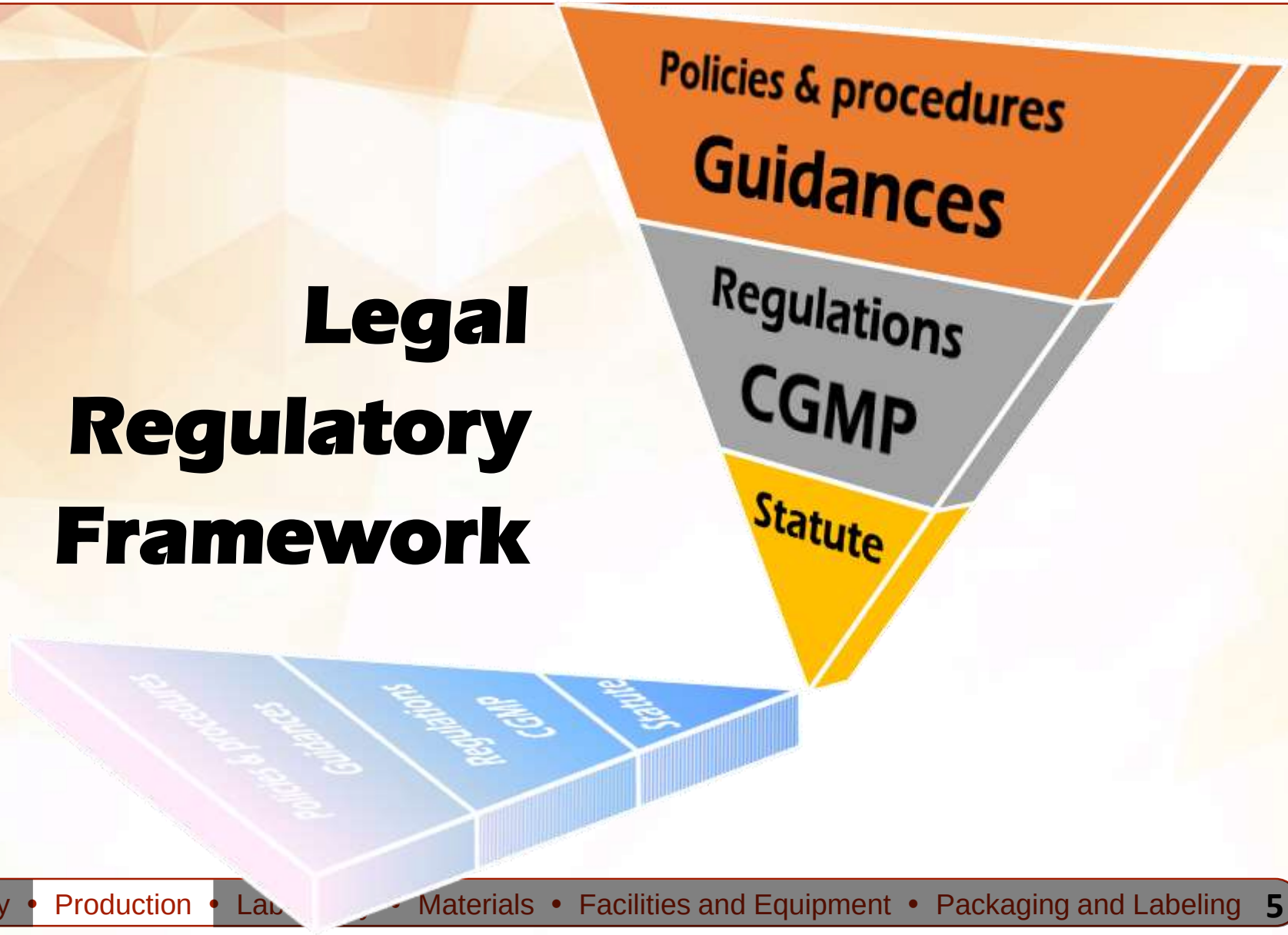
Public Health - Expectations

Public Health Care System - Stakeholders

- **Patients/Consumers**
  - Expects reliable access to safe, efficacious, stable and affordable high quality pharmaceuticals
- **Manufacturers**
  - Manage reliable and secure supply chain
  - Maintain risk mitigated, reliable, and efficient manufacturing operations
  - Provide safe, efficacious, and defect-free high quality drug products
- **Regulators**
  - Stand in for the consumer (patient) to ensure quality
    - Exercise risk-commensurate regulatory oversight

Drug Regulation Framework

Legal Regulatory Framework



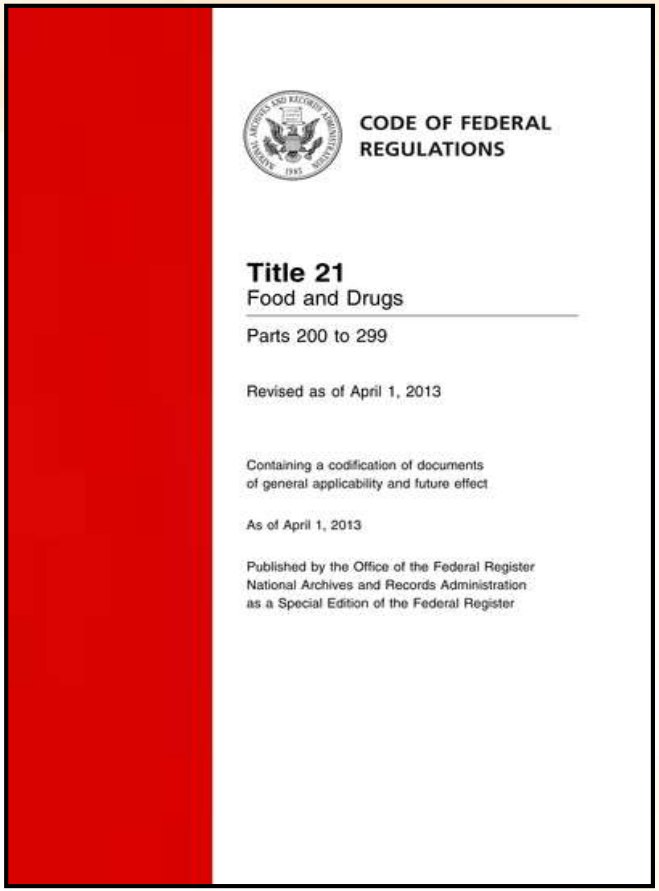
Statute

FD&C Act Section 501(a)(2)(B)

"A drug shall be deemed to be **adulterated** if the **methods** used in, or the **facilities** or **controls** used for, its ***manufacture, processing, packing,* or *holding*** do not conform to or are not operated or administered in conformity with **current good manufacturing practice** to assure that such drug meets the requirements of this Act as to ***safety*** and has the ***identity*** and ***strength***, and meets the ***quality*** and ***purity*** characteristics, which it purports or is represented to possess."

Current Good Manufacturing Practice (CGMP) Legal Basis

- **FD&C Act Sec. 501(a)(2)(B)** – requires conformity with Current Good Manufacturing Practice (**CGMP**) for manufacture of drugs
  - No **distinction** between API, excipients and finished pharmaceuticals
- **CGMP regulations** - Agency's interpretation of the statute for compliance



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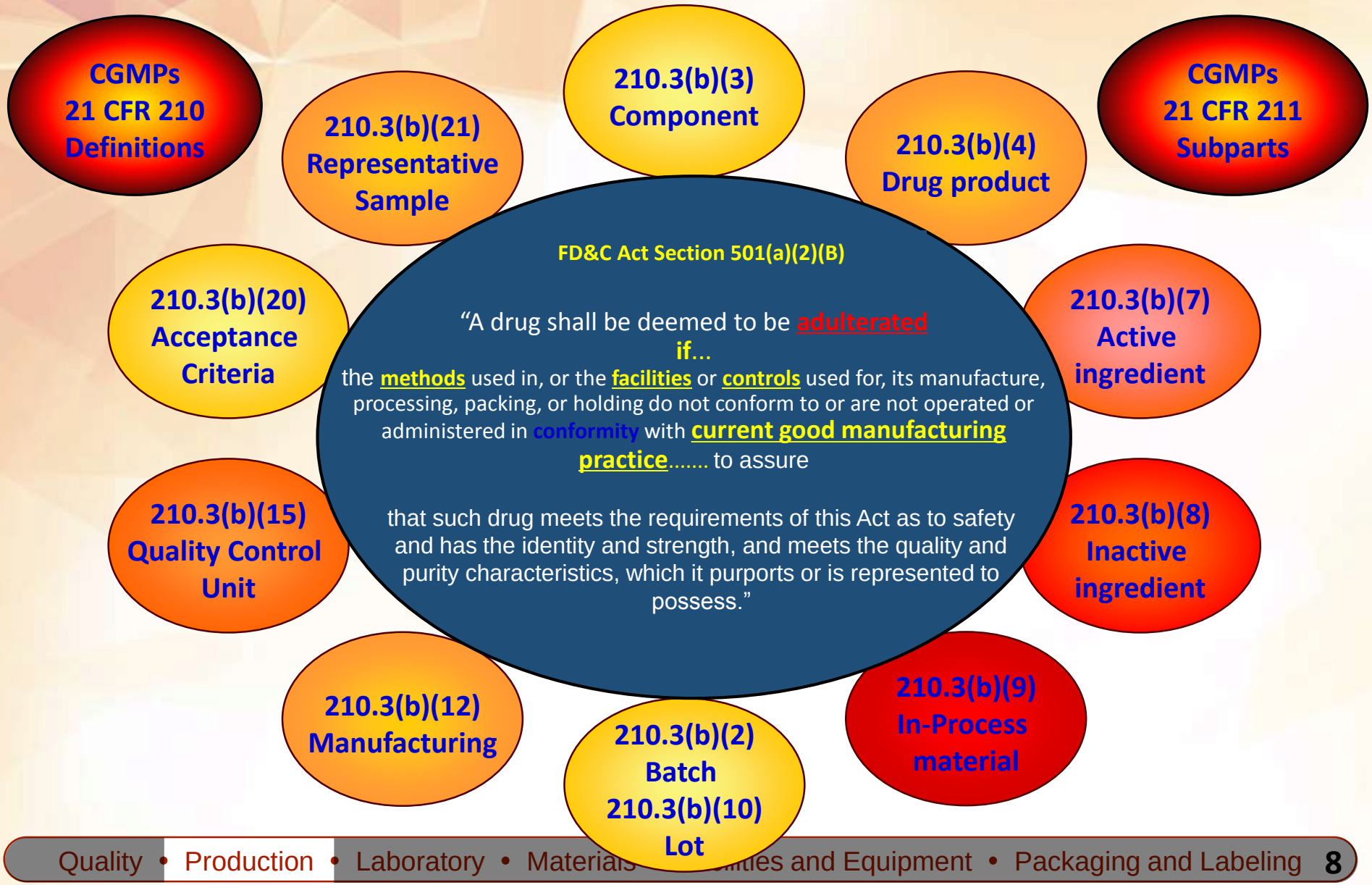
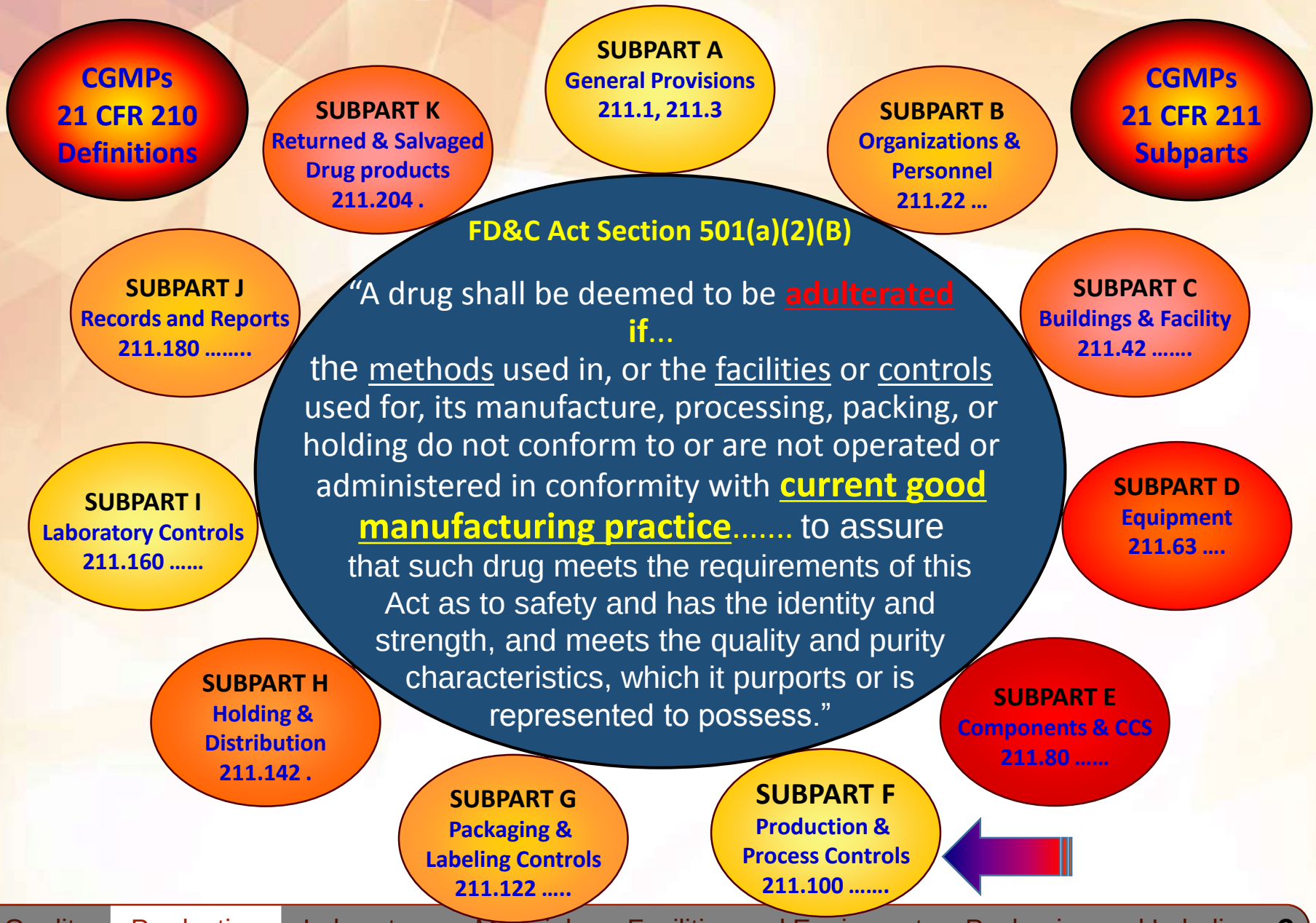
CGMP Regulations : Law of the Land



CGMP Regulations : Law of the Land



CGMP Regulations: Production System

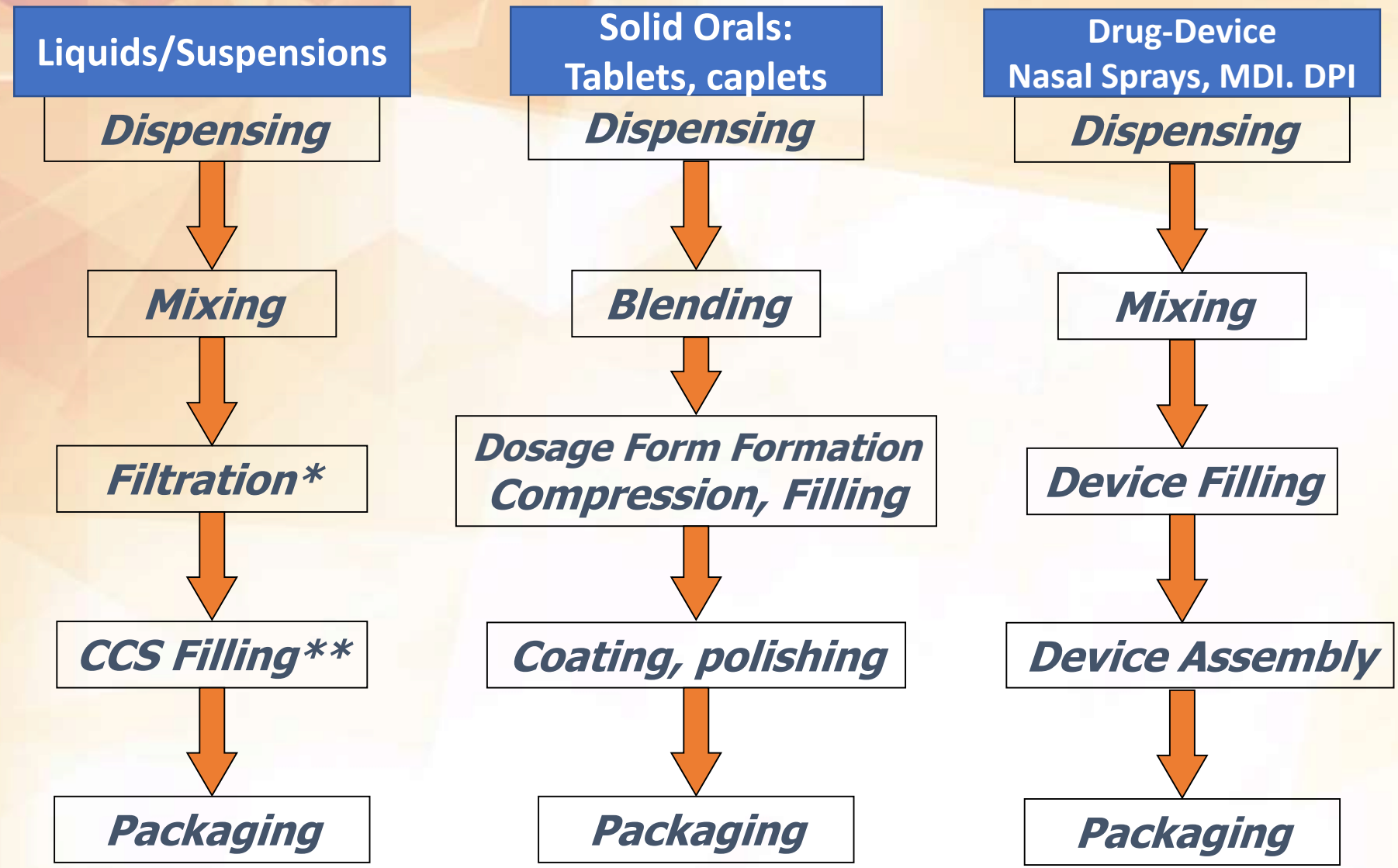
21 CFR 211 Subpart F
Production and Process Controls

- **Applies to Finished drug products**
  - Prescription drug products (Rx)
    - NDA, ANDA, BLAs
  - Over-The-Counter drug products (OTC)
  - Unapproved drugs
  - Compounded drugs (under Sec. 503B of the Act)
  - Any type of Method of Manufacture
    - Batch, Semi-continuous, Continuous
    - Aseptic, Sterile, Biotechnology

Production System

- Production System includes
  - measures and activities to control the manufacture of in-process materials and drug products including
    - batch compounding
    - dosage form production
    - in-process sampling and testing and
    - process validation
  - establishing, following, and documenting performance of approved manufacturing procedures
- See 21 CFR 211 Subparts B, F, I, and J

Typical Pharmaceutical Manufacturing Operations



21 CFR 211 Subpart F

Production and Process Controls

§ 211.100 - Written procedures; deviations

§ 211.101 - Charge-in of components

§ 211.103 - Calculation of yield

§ 211.105 - Equipment identification

§ 211.110 - Sampling and testing of in-process materials and drug products

§ 211.111 - Time limitations on production.

§ 211.113 - Control of microbiological contamination

§ 211.115 - Reprocessing

Subpart I - Laboratory Controls: § 211.160(b)(2)(3) - Sampling procedures for in-process materials and finished drug products

Subpart J - Records and Reports: § 211.180(e)(2)(3) - Annual Product Review

§ 211.192 – Production Record Review, Deviation and investigation

§ 21 CFR 211.100
Written procedures; deviations – Key points

(a) Requires **written procedures** for production and process control

- designed to **assure** that the drug products have the ***identity, strength, quality,* and *purity*** they purport or represent to possess.
- shall include all requirements in this Subpart F
- Responsibility of the appropriate organizational units to draft the procedures including any changes, review, and approve
- Responsibility of the **quality control unit to** review and approve

(b) The written PPC procedures shall be

- followed in the execution of the various production and process control (PPC) functions
- documented at the time of performance
- any **deviation** from the written procedures shall be recorded and justified

§ 21 CFR 211.101
Charge-in of components – Key points

Written PPC procedures shall include the following:

(a) The batch shall be ***formulated*** with the intent to provide ***not less than 100 percent*** of the labeled or established amount of active ingredient

(b) Components for drug product manufacturing shall be ***weighed, measured, or subdivided*** as appropriate.

- If a component is removed from the original container to another, the new container shall be identified with the following information:
  - (1) Component name or item code;
  - (2) Receiving or control number;
  - (3) Weight or measure in new container;
  - (4) Batch for which component was dispensed, including its product name, strength, and lot number.

§ 21 CFR 211.101
Charge-in of Components – Key points

Written PPC procedures shall include the following:

(c) ***Weighing, measuring, or subdividing & dispensing of components***

Manual operation:

- Requires adequate **supervision** by a **second**
- Second person must ***examine*** and ***assure***
  - (1) release of the components to Mfg. by the **quality control unit (QCU)**
  - (2) the weight/measure matches the **Batch Production Records (BPRs)**
  - (3) proper identification of the containers

Automated equipment Operation (211.68):

- Requires only **one person** to verify theses operations and assure (c)(1)-(3)

(d) **Component addition:** (e.g., order of addition)

- Manual Operation: Require one person to add and a second to verify
- Automated equipment Addition(211.68): Require one person to verify

§ 21 CFR 211.103
Calculation of yield – Key points

- Requires determination of actual yields and % theoretical yield
  - at the conclusion of each appropriate phase of manufacturing, processing, packaging, or holding of the drug product.
- Yield calculations
  - performed by one person
  - independently verified by a second person
- Yield calculations by automated equipment (211.68)
  - independently verified by one person

21 CFR 211.105
Equipment identification – Key points

(a) Requires proper ***identification*** (**ID**) of all equipment at all times during production

- compounding and storage containers
- processing lines
- major equipment
  - to indicate their contents
  - to indicate the phase of processing of the batch when necessary

(b) Requires **identification** and **recording** of a **major equipment** by a distinctive ID number or code in the batch production record

- to show the use of a specific equipment for manufacture of each DP batch
- ID by equipment name allowed in lieu of a distinctive ID number or code
  - if only one of a particular type of equipment exists in a facility

§ 21 CFR 211.110 - Sampling & testing of in-process materials & drug products – Key points

(a) Requires establishing and following **written procedures**

- To *assure* **batch uniformity** and **integrity** of drug products
- That *describe* the **in-process controls**, and **tests**, or **examinations** to be conducted on
  - appropriate samples of in-process materials of each batch
- To *monitor* the **output** and *validate* the **performance** of those manufacturing processes
  - responsible for **causing variability** in the characteristics of in-process material and the drug product

§ 21 CFR 211.110 - Sampling & testing of in-process materials & drug products - Key points

(a) Requires establishing and following **written procedures**

- Such control procedures shall include, but are not limited to, the following (characteristics), where appropriate:
  - (1) Tablet or capsule weight variation
  - (2) Disintegration time
  - (3) Adequacy of mixing to assure uniformity and homogeneity
  - (4) Dissolution time and rate
  - (5) Clarity, completeness, or pH of solutions
  - (6) Bioburden testing

§ 21 CFR 211.110 - Sampling & testing of in-process materials & drug products - Key points

(b) Requires establishing **valid** **in-process specifications** for such characteristics

- shall be consistent with drug product final specifications
- shall be derived from previous acceptable process average and process variability estimates where possible
- determined by the application of suitable statistical procedures where appropriate.
- Examination and testing of samples shall assure that the drug product and in-process material conform to specifications.

§ 21 CFR 211.110 - Sampling & testing of in-process materials & drug products - Key points

(c) Requires *testing* of in-process materials for **identity**, **strength**, **quality**, and **purity** as appropriate

Requires the **quality control unit** to ***approve*** or ***reject*** the in-process materials during the production process, e.g.,

- at commencement or completion of significant phases
- or after storage for long periods

(d) Requires identification and control of the **rejected in-process materials** under a quarantine system

- designed to prevent their use in manufacturing or processing operations for which they are unsuitable

§ 21 CFR 211.111
Time limitations on production- Key points

- Requires to establish **time limits** for the completion of each phase of production when appropriate
  - to assure the quality of the drug product.
- Any **deviation** from established time limits may be acceptable
  - if such deviation does not compromise the quality of the drug product.
- Such deviation shall be justified and documented.

§ 21 CFR 211.113
Control of microbiological contamination

(a) Appropriate written procedures, designed to prevent objectionable microorganisms in drug products not required to be sterile, shall be established and followed.

(b) Appropriate written procedures, designed to prevent microbiological contamination of drug products purporting to be sterile, shall be established and followed. Such procedures shall include validation of all aseptic and sterilization processes.

Dr. Pawar will cover these aspects in his presentation

§ 21 CFR 211.115
Reprocessing - Key Points

(a) Requires establishing and following procedures

- Prescribing a system for reprocessing batches that do not conform to standards or specifications
- Steps to insure that the reprocessed batches will conform with all established standards, specifications, and characteristics

(b) Reprocessing shall not be performed <u>without the review and approval</u> of the quality control unit.

Sec. 21 CFR 211.160 (b)
General requirements - Key Points

In-process Materials:

(2) Requires determination of conformance to

- written specifications and sampling and testing procedures
- samples shall be representative and properly identified

Drug Products:

(3) Requires determination of conformance to

- written descriptions of sampling procedures and appropriate specifications for drug products.
- samples shall be representative and properly identified

Sec. 21 CFR 211.180 (e)
General requirements – Key Points

(e) **Requires maintaining and evaluating written records and data at least annually**

- to evaluate the quality standards of each drug product
- to determine the need for changes in drug product specifications or manufacturing or control procedures

Requires establishing and following procedures for such evaluations and include provisions for:

(1) A review of a representative number of batches, whether approved or rejected, and, where applicable, records associated with the batch.

(2) A review of complaints, recalls, returned or salvaged drug products, and investigations conducted under 211.192 for each drug product

Sec. 21 CFR 211.192
Production Record Review- Key Points

- Requires thorough investigation of any unexplained discrepancy whether or not the batch has already been distributed
  - exceeding the maximum or minimum of a theoretical yield established in master production and control records
  - failure of a batch or any of its components to meet any of its specifications
- Requires to extend investigation to other batches
  - same drug product and other drug products that may have been associated with the specific failure or discrepancy
- Requires a written record of the investigation with conclusions and follow-up

Regulatory Tools for Compliance

Guidances

Pharmaceutical Development → Technology Transfer → Commercial Manufacturing → Product Discontinuation

CGMP

Product Design

Process Design

Manufacturing

Process Monitoring, Control & Continuous Process Verification

ICH Q8(R2) - Pharmaceutical Development (PD)

FDA's Process Analytical Technology (PAT) Guidance

ICH Q9 – Quality Risk Management (QRM)

FDA's Quality Systems Guidance & ICH Q10 Pharmaceutical Quality Systems (PQS)

ICH Q11 – Development and Manufacture of Drug Substances

FDA's Process Validation (PV) Guidance

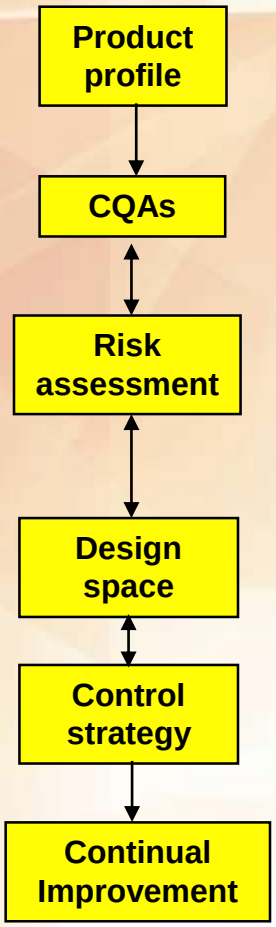
PAT, QbD and Process Validation (PV)
A robust Commercial Process

- Ultimate goal of QbD and PAT is to ***design*** and ***deliver*** an efficient commercial process by
  - Establishing scientific foundation for technology transfer from lab, pilot, and sub-commercial scale manufacturing activities
- Goal of process validation is to demonstrate with sufficiently rigorous scientific evidence and statistical measures that the designed commercial process
  - works as intended
  - remains under state of control (validated) all the time
  - capable of delivering quality product reliably
  - product and process deviations can be explained scientifically with identifiable root causes
  - proactive rather than reactive Change Control Management
  - provides mechanism for continuous process verification and continual improvement over lifecycle

PAT Framework - Central Thesis

- Quality cannot be tested into products; it should be built-in (i.e., by design) and verified during the process to the extent possible rather than relying alone on end product testing
- Source(s) and range(s) of variability in raw materials (attributes), in-process materials (attributes), and process parameters need to be identified; impact of such variability on product quality needs to be understood and their acceptable ranges be controlled
- Timely measurement and management of such variability through process understanding, monitoring and risk-mitigating control strategies can
  - facilitate **Real Time Release**
  - improve quality and productivity throughout product's lifecycle

QbD Approach Example (Q8R)



- Define **Quality Target Product Profile** (QTPP)
  - Relating to quality, safety and efficacy and
  - route of administration, dosage form, bioavailability, strength, and stability
- Determine **critical quality attributes** (**CQAs**) for an API, excipients, in-process materials and the drug product
  - having an impact on product quality
- Select an appropriate manufacturing process
- Link **material attributes** and **process parameters** to **CQAs** and perform risk assessment
- Develop a **design space**
- Define, design and implement a **control strategy**
  - Real-time release testing
- Manage product lifecycle, including continual improvement

Process Validation - A lifecycle approach

- ***Stage 1, Process Design:***
  - Lab, pilot, small scale and commercial scale studies to establish process; process/product development
- ***Stage 2, Process Performance Qualification (PPQ)*:**
  - Facility, utilities and equipment
  - Performance Qualification (confirm commercial process design)
- ***Stage 3, Continued Process Verification (CPV):***
  - Monitor, collect information, assess during commercialization
  - Maintenance, continuous verification, process improvement
- **Requires Statistical Quality Control criteria for**
  - Appropriate acceptance or rejection levels

Process validation - A lifecycle approach

Stage 1: Process Design

- The goal of this stage is to **design** a process
  - suitable for routine commercial manufacturing that can consistently deliver a product that meets its critical quality attributes
  - important to understand the degree to which models represent the commercial process
- Control of the process through operational limits and in-process monitoring is essential
  - where the product attribute is not readily measurable due to limitations of sampling or detectability (e.g., viral clearance or microbial contamination), or
  - when intermediates and products cannot be highly characterized and well-defined quality attributes cannot be identified.
- Use of Process Analytical Technology (PAT) is encouraged

Process validation - A lifecycle approach

Stage 2: Process Qualification

- Two elements:
  - Design of the *facility* and qualification of the *equipment* and *utilities*
  - Process Performance Qualification confirming the commercial process design
- Accumulation of enough data and knowledge about the commercial production process is expected
  - must follow CGMP-compliant procedures
  - to support post-approval commercial distribution successful completion of PPQ necessary
- Products manufactured during this stage, if acceptable, can be released under certain situations

Stage 3: Continued Process Verification

- The goal of the third validation stage is to continually ***assure*** that the process remains in a **state of control** (the validated state) during commercial manufacture
- Recommends continued monitoring and/or sampling
  - at the level established during the PPQ stage until sufficient data is available to generate significant variability estimates
  - Once the **variability** is known, sampling and/or monitoring should be adjusted to a statistically appropriate and representative level
- Process variability should be periodically assessed and sampling and/or monitoring adjusted accordingly
- Requires Statistical Quality Control criteria for
  - Appropriate acceptance or rejection levels

CGMP Compliance Programs

Pre-approval Inspection:

- 7346.832: Pre-Approval Inspections/Investigations
  - Readiness for Commercial Manufacturing
  - Conformance to Application
  - Data Integrity Audit

Post-Approval Inspection:

- 7346.843: Post-Approval Audit Inspections
- 7356.002: Drug Process Inspections (sub-programs follow…)
  - 7356.002A: Sterile Drug Process Inspections
  - 7356.002B: Drug Repackers and relabelers
  - 7356.002C: Radioactive Drugs
  - 7356.002E: Compressed Medical Gases
  - 7356.002F: Active Pharmaceutical Ingredients Process Inspections
  - 7356.002M: Inspections of Licensed Biological Therapeutic DPs
  - 7356.002P: Positron Emission Tomography

CGMP Inspection Coverage Examples

- Actual conditions and practices
- Raw Material Quality
- State of maintenance of equipment, and facilities
- Personnel -- Actual Operations, Procedures, Training
- Changes in manufacturing and laboratory
- Adequacy of design (discussed 18x in CGMP regulations)
- Latest stability data
- Process Implementation and experience
  - Process Validation, lifecycle improvements
  - Batch trends: latest in-process control data
- Complaints, returns, deviations, failures, OOS and CAPA
- Reporting requirements met for Field Alerts, APRs, ADEs, BPDRs, CMC Phase 4 Commitments

Regulatory Expectations

- Leverage the scientific knowledge derived from
  - the product/process development and scale-up studies
  - designed systematically by utilizing well established material science, (process) control systems engineering and quality risk management principles
- In developing a well-controlled, validated and robust commercial manufacturing process,
  - ready to deliver product of intended quality reliably over the product's lifecycle

Summary: Quality Assurance Under CMC & GMP

Summary: Quality Assurance Under CMC & CGMP

In theory, there is no difference between theory and practice. **But**, in practice, there is.

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Microbiological overview of Biopharmaceutical Production & Process

Presenter:

Vinayak Pawar, Ph.D. Senior Review Microbiologist

Office of Process and Facilities, OPQ, CDER

The Components for Discussion

- **Overview of Production & Process Control** **21 CFR 211**
  Subpart F – Production & Process Control **211.113 Microbial Quality**
- **Objectionable Microorganisms & Products at Risk**
- **I. Non-Sterile II. Multi-dose Products**
- **III. Sterile Products –**
  - **A. Terminally sterilized or**
  - **B. Aseptically Filled**
- **A. Terminally Sterilized Products – Regulatory requirements & parametric release**
- **B. Aseptically Filled Products – Regulatory Requirements and Control of Aseptic manufacturing process & Environment.**

Overview of Production and Process Controls

- **General - 21 CFR 211 - Subpart F** Production & Process Control

  - Procedures for production and process control designed to assure that the drug products have the identity, strength, quality, and purity they purport to possess.
  - Such procedures shall include all requirements in this subpart. 21 CFR 211 110(a)
  - Any Deviation from the written procedures shall be recorded and justified. 21 CFR 211 110(b)

- **Microbial Quality – 21 CFR 211.113** Control of microbiological contamination

  (a) Appropriate written procedures, designed to prevent objectionable microorganisms in drug products not required to be sterile, shall be established and followed.

  (b) Appropriate written procedures, designed to prevent microbiological contamination of drug products purporting to be sterile, shall be established and followed. Such procedures shall include validation of any sterilization process.

Objectionable Microrganims & Products at Risk

Objectionable microorganisms:

- Potential to cause infection when a drug product is used as per label directions
- Capable of growth in a drug product
- Cause spoilage/reduce efficacy of a drug product
- Many organisms can be objectionable under right circumstances

Type of Products at Risk:

- By route of administration – Injectables, ophthalmic, oral or topical
- Dosage forms – Liquids, suspensions, solid oral dosage forms

Ophthalmic (eyewashes, solutions - required to be sterile per 21 CFR 200.50(a)(1))

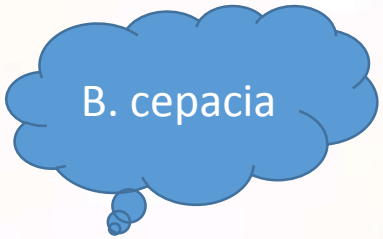
Oral Inhalation (aqueous-based required to be sterile under 21 CFR 200.51)

Combinations products (a drug and a device)

Microbiological Requirements for Non-Sterile Products

I. Non-Sterile Products: Must comply with relevant harmonized acceptance criteria for microbiological quality. 21 CFR 211.113 (a) USP <1111>

Drug Type	Harmonized Criteria
Non-Aqueous Oral	• TAMC 10^3 CFU/g/mL • TYMC 10^2 CFU/g/mL • E. coli absent 1g/mL
Aqueous Oral	• TAMC 10^2 CFU/g/mL • TYMC 10^1 CFU/g/mL • E. coli absent 1g/mL
Rectal Use	• TAMC 10^3 CFU/g/mL • TYMC 10^2 CFU/g/mL
Vaginal	• TAMC 10^2 CFU/g/mL • TYMC 10^1 CFU/g/mL • S. aureus, C.albicans, P. aeruginosa absent 1g/mL
Transdermal Patch	• TAMC 10^2 CFU/g/mL • TYMC 10^1 CFU/g/mL • S. aureus, P. aeruginosa absent 1g/mL



Microbiological Requirements - Multidose Products

II. Multidose Products

- Must comply with preservative efficacy test and acceptance criteria (pharmacopoeial tests not yet harmonized) USP/BP/Ph. Eur.
- Take home lesson from Harmonized Pharmacopoeial chapters is:
- The list of specified organisms is not necessarily exhaustive.
- May be necessary to test for other microrganisms depending on process and nature of materials.

Microbiological Requirements - Sterile Products

III. Sterile Products:

- **Must comply with Sterility (harmonized pharmacopoeial tests) USP <71>**
- **Must Comply, where applicable with Bacterial Endotoxins Test (harmonized pharmacopoeial tests) USP <51>**

Two categories of sterile products

- **those that can be sterilized in final container (terminally sterilized).**
- **those that cannot be terminally sterilized but filtered through a sterile 0.22µm (or less) sterilizing grade membrane filter into a previously sterilized container in an aseptic environment (Aseptic Fill).**

Microbiological Requirements - Terminally Sterilized Products

A. Terminally Sterilized Products

- Model is using kill/heat penetration on a resistant spore former (e.g. Stearothermophilus) organism. Validation + Historical data is more reliable than sterility test. Can lead to parametric release – no sterility test performed.
- Regulatory requirements to be aware of:
- Provide pre-sterilization bioburden limit.
- Provide initial qualification and most recent requalification studies PPQ & MPQ.
- Validate extended hold times for bulk product prior to terminal sterilization.
- Validation of Maximum load and Minimum load configurations.
- Provide validation if changes to sterilization load size or configuration has occurred.

(The Agency recommends that if possible the products be terminally sterilized)

Microbiological Requirements – Sterile Filtered, Aseptically Filled Products

B. Sterile Filtered products:

- Model is using small organism to determine filterability and reliance on Microbial challenge and filter integrity and supported by media fill to assure 1:1000 chance for sterility failure.
- Assumption: Filters are absolute. Not pore size dependent. Reproducibly remove test organisms from process stream, producing a sterile filtrate.
- Requires: Control of the manufacturing environment , “Aseptic Fill” is critical.

Microbiological Requirements – Sterile Filtered, Aseptically Filled Products

B. Sterile Filtered products (contd.):

- **Control of Aseptic Manufacturing Process & Environment**: (Aseptic Processing Guidance 2004)

  a. Procedures that expose product to the manufacturing environment

  b. Process Simulation and Media Fills Validation

  c. Filtration Efficacy – Filter Validation (PDA TR 26, ASTM F838-05)

  d. Sterilization of Equipment, Containers & Closures.

Microbiological Requirements – Sterile Filtered, Aseptically Filled Products

B. Sterile Filtered products (contd.):

a. Procedures that expose product to the manufacturing environment:

- Should be performed under Class 100 (ISO 5) conditions, Isolators included.
- Critical areas should be surrounded by Class 10,000 (ISO 7) or better environment
  - Environmental monitoring should be performed during operations
  - Surface monitoring should be performed at the end of operations
  - Personnel monitoring should be performed in association with operations
  - Alert and action levels should be defined. Response to deviations from alert & action levels must be addressed.
  - 21 CFR 211.42 & 211.113

Microbiological Requirements – Sterile Filtered, Aseptically Filled Products

B. Sterile Filtered products:

b. Process Simulation and Media Fills Validation

i. Process simulation studies covering steps preceding filling and sealing should:

- **Be designed to incorporate all conditions, product manipulations, and interventions that could impact the sterility of the product.**
- **Demonstrate that controls are adequate to protect the product during manufacturing**
- **Incorporate all product manipulations, additions, and procedures involving exposure of product and product contact surfaces to the environment**
- **Include worse-case conditions**
- **Include storage of sterile bulk drug substance or product if it is part of the process, bulk vessel integrity, hold times**

Microbiological Requirements – Sterile Filtered, Aseptically Filled Products

B. Sterile Filtered products:

b. Process Simulation and Media Fills Validation

i. Process simulation studies covering steps preceding filling and sealing should (contd.):

- **Simulation studies for the formulation stage to be performed at least twice**
- **Where possible, for cell therapy and some cell-derived products, that cannot be sterile filtered must undergo aseptic manipulation throughout the manufacturing process preferably through a closed system where possible.**

ii. Process simulation - Media fills

- **Three consecutive media fills –units filled, units rejected, units incubated and units positive.**

Microbiological Requirements – Sterile Filtered, Aseptically Filled Products

B. Sterile Filtered products:

c. Filtration Efficacy – Filter Validation

- **Filter Qualification (Filter Manufacturer) Filter compatibility Bacterial retention study**
- **Filter Validation – (Filter User) (1) verify the flow rates required for pharmaceutical process (2) sized to provide flow rates volumes adequate to keep pace with filling machines (3) throughput adequate to support complete batch without interruption**

[PDA TR 26, ASTM F838-05 Standard technical manual]

Microbiological Requirements – Sterile Filtered, Aseptically Filled Products

B. Sterile Filtered products:

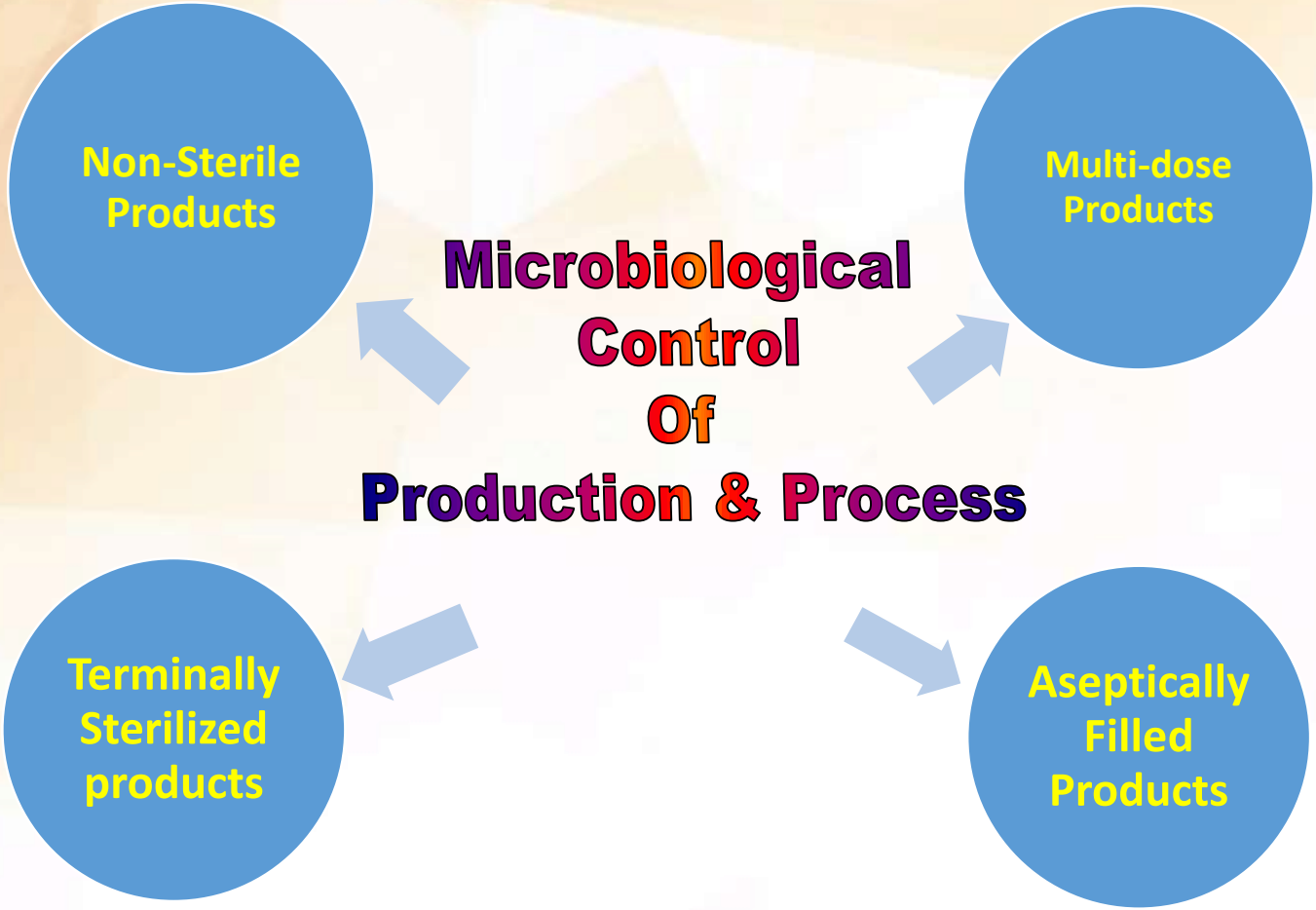
d. Sterilization of Equipment, Containers & Closures.

It is as important in aseptic processing to validate the processes used to sterilize such critical equipment as it is to validate processes used to sterilize the drug product and its container and closure. (2004 Aseptic Processing Guidance)

Qualification and Validation of:

- **SIP**
- **Washers**
- **Autoclaves**
- **Depyrogenation Ovens, Tunnels**
- **Lyophilizers when applicable**

Summary


Non-Sterile Products
Multi-dose Products
Microbiological Control Of Production & Process
Terminally Sterilized products
Aseptically Filled Products

Questions?

Evaluation: surveymonkey.com/r/GDF-D1S3