GMP

Good manufacturing practice (**GMP**) is a system for ensuring that products are consistently produced and controlled according to quality standards. It is designed to minimize the risks involved in any pharmaceutical production that cannot be eliminated through testing the final product.

Principles of GMP

- The first **principle** of **GMP** is to develop detailed step-by-step procedures, in writing, that provide a "road map" for consistency in performance. ...

- Written Procedures.
- Following Procedures. ...
- Documentation. ...
- Validating Work. ...
- Audits

Principles of GMP

- Facilities and Equipment. ...
- Maintenance. ...
- Job Competence. ...
- Avoiding Contamination.
- Quality control

Importance of GMP

- Good Manufacturing Practices (GMPs) are systems created and mandated by the government to regulate production, verification and validation of drugs, food and/or medical devices, ensuring that finished products are effective and safe for market distribution.
- It's important to have GMPs because they are guidelines which are enacted to ensure food, drugs, cosmetics, medical devices and related products have no harmful substances. These regulations, enforced by the FDA, help reduce the instances of product recalls, harmful effects and eventual lawsuits that may arise from defective products.
- GMPs were first enacted in 1963 by the US Congress following the near-sale of thalidomide in the US, after it had resulted in over 10,000 birth defects and infant deformities in Europe.

Importance of GMP

- Today, GMPs are more commonly known as cGMPs, and have been established flexibly to permit every manufacturer to use their discretion in implementing the best controls for their own organization. This flexibility also allows manufacturers to make use of the latest and most innovative technologies to result in products of better/higher quality.
- The ‘current’ addition is also used to imply that the FDA expects companies to continuously stay up-to-date with regulations as they are altered to suit changing market and consumer needs. The reason for this is that systems, machines or equipment that were in use, say a few years ago, are not as efficient/effective today, and are hence inadequate in ensuring maximum consumer protection.

Difference between cGMP and GMP

- Both cGMP and GMP are put into place to certify quality assurance of products. GMP ensures that the product is exactly what the product claims to be and that it was created by the standard guideline set known as GMP.
- However, there is a little difference between cGMP and GMP. The “ c ” in cGMP is in place to certify that every step used in producing this product was done as the guidelines of GMP are stated , but they were finished in a more current manner . This means that as GMP rules and regulations are constantly improving , and increasing to better the production of new goods , the cleanliness of the process of creation, and neatness are also being improved and updated.

Difference between cGMP and GMP

- Another difference between cGMP and GMP is the cost. Since cGMP is mostly using new innovative technology the cost is usually more to implement than a regular GMP manufacturer. This is because new technology is expensive . When compared to the GMP goods, cGMP goods undergo remarkably more testing to prove the accuracy of it, compared to that of GMP . It has to undergo newer, and more in depth testing and requirements than that of FDA GMP so that the certification is accurate and proven to be effective.
- cGMP is also put into place to watch for the proper use of the new manufactured goods . cGMP goes above and beyond to ensure that the quality of the new pharmaceutical , and the assurance that it will be used for what it was created for, this is part of current standard regulation that is updated frequently so that pharmaceuticals are not being so commonly misused.

GMP

GMP

GMP - THE HISTORY

1960 **THALIDOMIDE** marketed in West Germany then Canada & Britain as sleeping tablet, treatment for colds, flu etc. *Pregnant women used for nausea.*

1961 Alarm at the sudden increase in the birth of deformed infants **ESTIMATED 10,000 INFANTS DEFORMED**

1961 Withdrawal of Thalidomide

DEMONSTRATED THAT SAFETY REQUIREMENTS OF NEW DRUGS HAD TO BE TIGHTENED

History of GMP

- The 1900s Early in this country's history, traveling medicine shows sold bottles of ointment or "miracle elixir" from the backs of wagons. Such medication was said to be good for aches and pains; for catarrh, rheumatism, and gout; of course it completely cured cancer — and it worked on horses too. In 1905, a book called The Jungle helped catalyze public opinion for change. The book was written by Upton Sinclair, a "muckraker" journalist and social reformer. He wrote about the Chicago meat packing industry: about the unsanitary conditions in which animals were slaughtered and processed and the practice of selling rotten or diseased meat to the public. He also reported that ground meat sometimes contained remains of poisoned rats and even unfortunate workers who fell into the machinery. Sinclair's main interest was in bringing attention to the miserable working conditions and the plight of the impoverished factory workers, many of whom were immigrants .

History of GMP

- In 1905, a book called The Jungle helped catalyze public opinion for change. The Jungle had a major impact on the American public. Congress passed the Pure Food and Drug Act in 1906, and for the first time it became illegal to sell contaminated (adulterated) food or meat. Also for the first time, labeling had to be truthful (no one could “promise the moon and the stars” on a label anymore). In the old days, syrup to calm “colicky” babies and “tonics” for adults often contained alcohol, opium, or morphine, which addicted many people who used them. So the 1906 Act also required selected dangerous ingredients to be labeled on all drugs. Inaccurate or false labeling was called misbranding, and that became illegal. Misbranded applies to statements, designs, or pictures in labeling that are false or misleading as well as to the failure to provide required information in labeling . Over the years, the word adulterated has been expanded to include products manufactured without following GMPs.

History of GMP

- The real reason the 1906 Act was passed is that Harvey Wiley and others had been pressing for such a law for 25 years. The act created one of the first government regulatory agencies, now known as FDA, and it also allowed for the seizure of illegal foods and drugs . Wiley later became chief chemist of the bureau given authority to enforce that act (the Bureau of Chemistry, U.S. Department of Agriculture), a forerunner of FDA . Biologic products were first regulated a few years before The Jungle, when at least 12 children died from a diphtheria antitoxin that was contaminated with live tetanus bacilli . Congress responded to that tragedy by passing the Biologics Control Act of 1902, which required inspections of manufacturers and sellers of biological products and testing of such products for purity and strength .

History of GMP

- A 1933 FDA exhibit of dangerous food, medicines, medical devices, and cosmetics illustrated the shortcomings of the 1906 law. Called “America’s Chamber of Horrors,” the famous exhibit included a womb supporter (also used as a contraceptive) that could puncture the uterus if inserted incorrectly; a weight-loss drug that caused death; a hair remover that caused baldness, even if not used on the head; lotions and creams that could cause mercury poisoning; hair dyes that could cause lead poisoning; and an eyelash dye that blinded women . Eleanor Roosevelt took that exhibit to the White House, asking Americans to campaign for stronger consumer protections. A tragedy was waiting around the corner that would make her case for her. The wrong raw material and an elixir of sulfanilamide.Sulfa drugs were introduced in 1935. Many manufacturers began making the new anti-infectives. One company used diethylene glycol, a poisonous solvent and chemical analog of antifreeze, in an oral “elixir of sulfanilamide.

History of GMP

- In response, Congress passed the Federal Food, Drug and Cosmetic (FD&C) Act of 1938. For the first time, companies were required to prove that their products were safe before marketing them.
- One tragedy in 1941 was not related to World War II. Nearly 300 people were killed or injured by one company's sulfathiazole tablets, a sulfa drug tainted with the sedative, phenobarbital. That incident caused FDA to revise manufacturing and quality control requirements drastically, leading to what would later be called GMPs . The Public Health Services Act, passed in 1944, covered a broad spectrum of concerns, including regulation of biological products and control of communicable diseases.

History of GMP

- The 1960s Thalidomide was marketed in Europe as a sleeping pill and to treat morning sickness. When regulatory agencies gave permission to sell the drug for that indication, they had no knowledge of its serious side effects. It turned out to be teratogenic: It caused serious deformities in developing fetuses. Children whose mothers took thalidomide in the first trimester were born with severely deformed arms and legs. An estimated 10,000 cases of infant deformities in Europe were linked to thalidomide use .

History of GMP

- The 1970s were a watershed for product regulation. GMPs for drugs (21 CFR Parts 210 and 211) and medical devices (21 CFR 820) were made final in 1978. They were intended to help ensure the safety and efficacy of all products: The regulations ... contain the minimum current good manufacturing practice for methods to be used in, and the facilities or controls to be used for, the manufacture, processing, packing, or holding of a drug to assure that such drug meets the requirements of the act as to safety, and has the identity and strength and meets the quality and purity characteristics that it purports or is represented to possess.

History of GMP

- Good Laboratory Practices (GLPs) were made final in 1979. They are defined as follows: ... good laboratory practices for conducting nonclinical laboratory studies that support or are intended to support applications for research or marketing permits for products regulated by the Food and Drug Administration, including food and color additives, animal food additives, human and animal drugs, medical devices for human use, biological products, and electronic products. Compliance with this part is intended to assure the quality and integrity of the safety data filed.

History of GMP

- Poisoned acetaminophen capsules. In 1982, 12-year-old Mary Kellerman told her parents that she felt like she had a cold. They gave her an extra-strength Tylenol acetaminophen capsule, and within a few hours she died. Six other people died in this tragic incident, including three members from one family (two brothers and one of their wives) and a woman who had just given birth to her fourth child . Johnson & Johnson announced a nationwide recall of 31 million bottles of Tylenol. Their investigation revealed that a criminal tamperer (who has never been found or prosecuted) had opened up and laced some capsules with cyanide. The company destroyed all 31 million bottles of the largest-selling over-thecounter (OTC) medicine in the country

History of GMP

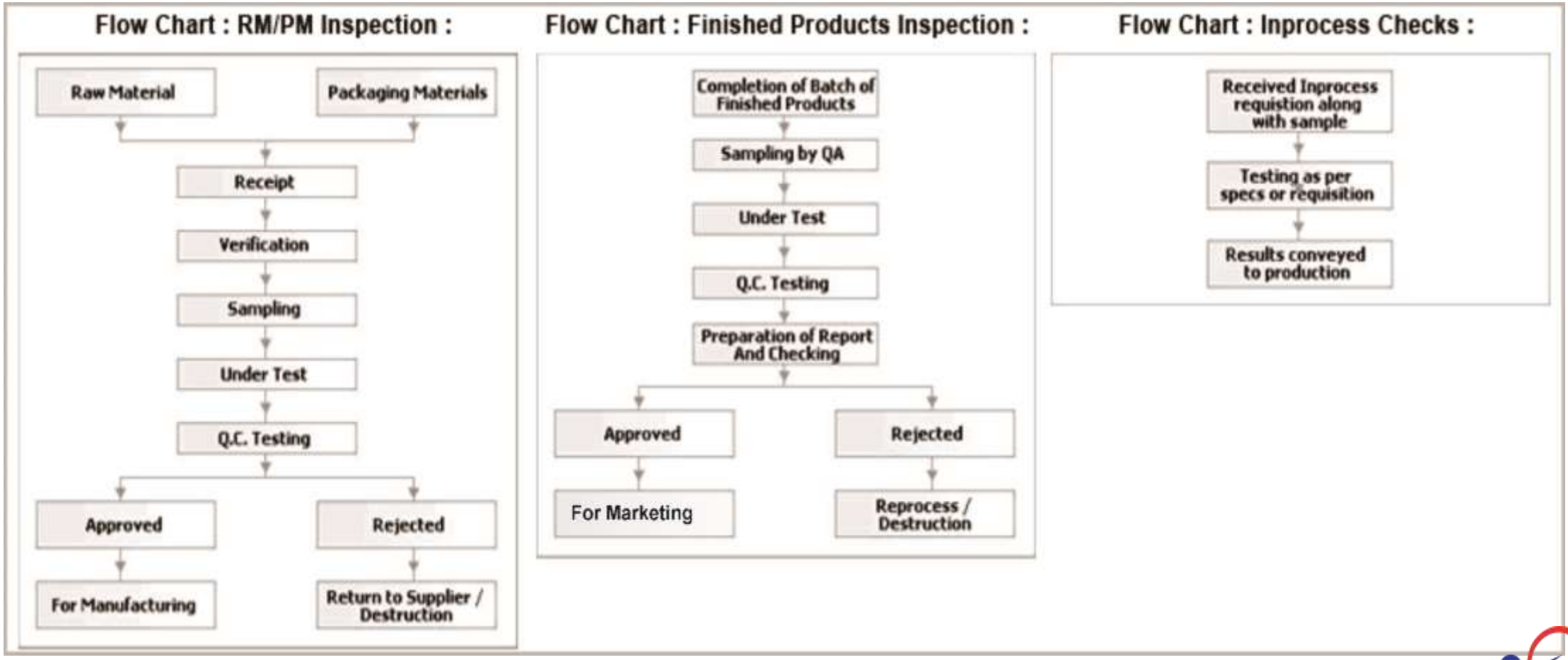
- Holding of Active Pharmaceutical Ingredients” was released in 1998 . Drug GMPs (21 CFR 210–211) are also considered to apply to the manufacture of APIs
- The International Conference on Harmonization (ICH) is a consortium of individuals from Europe, North America, and Japan working on a number of quality, safety, and effectiveness documents. As those documents are adopted or made final by ICH, they become “industry practice” in all participating countries

Flow Process in Pharma company

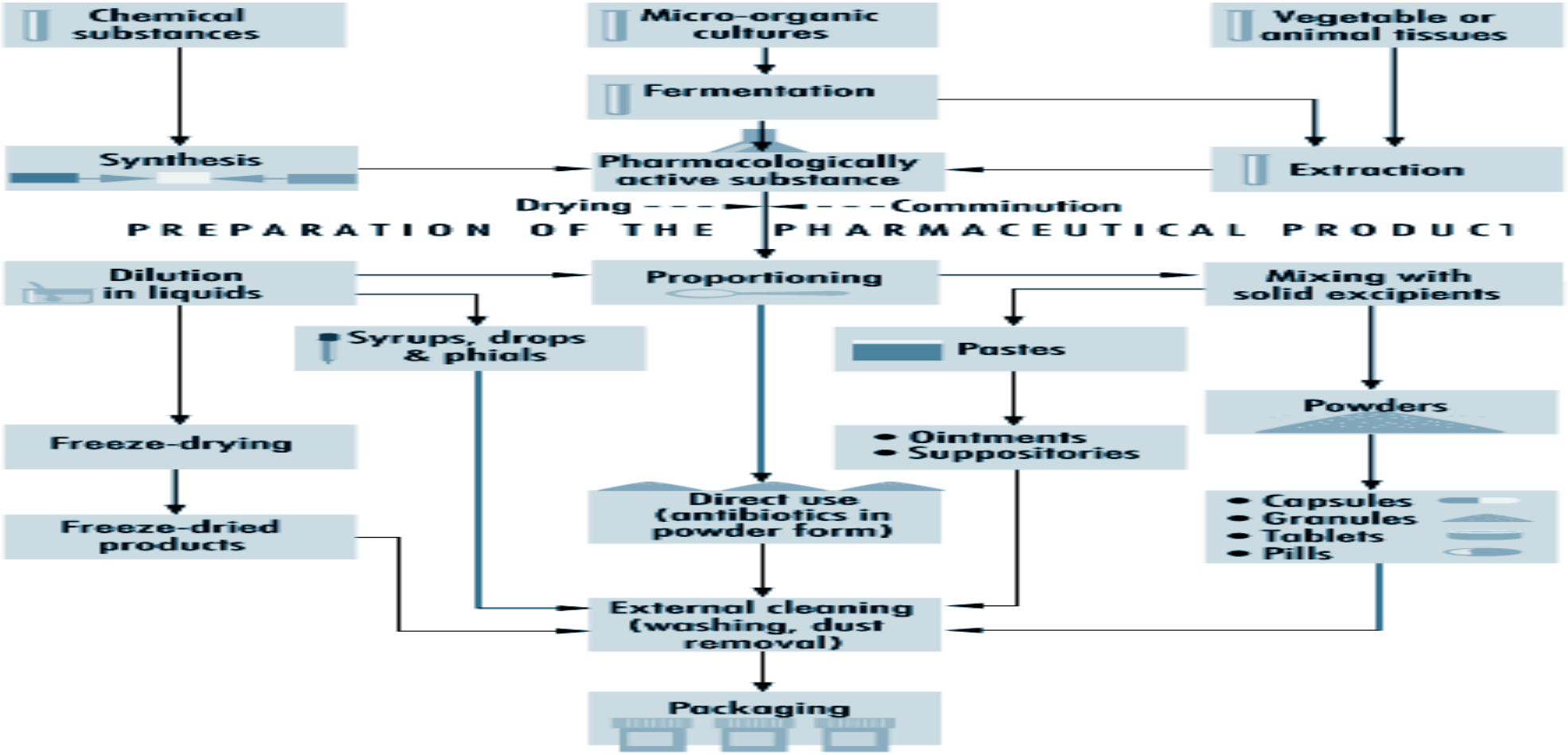
The six components

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

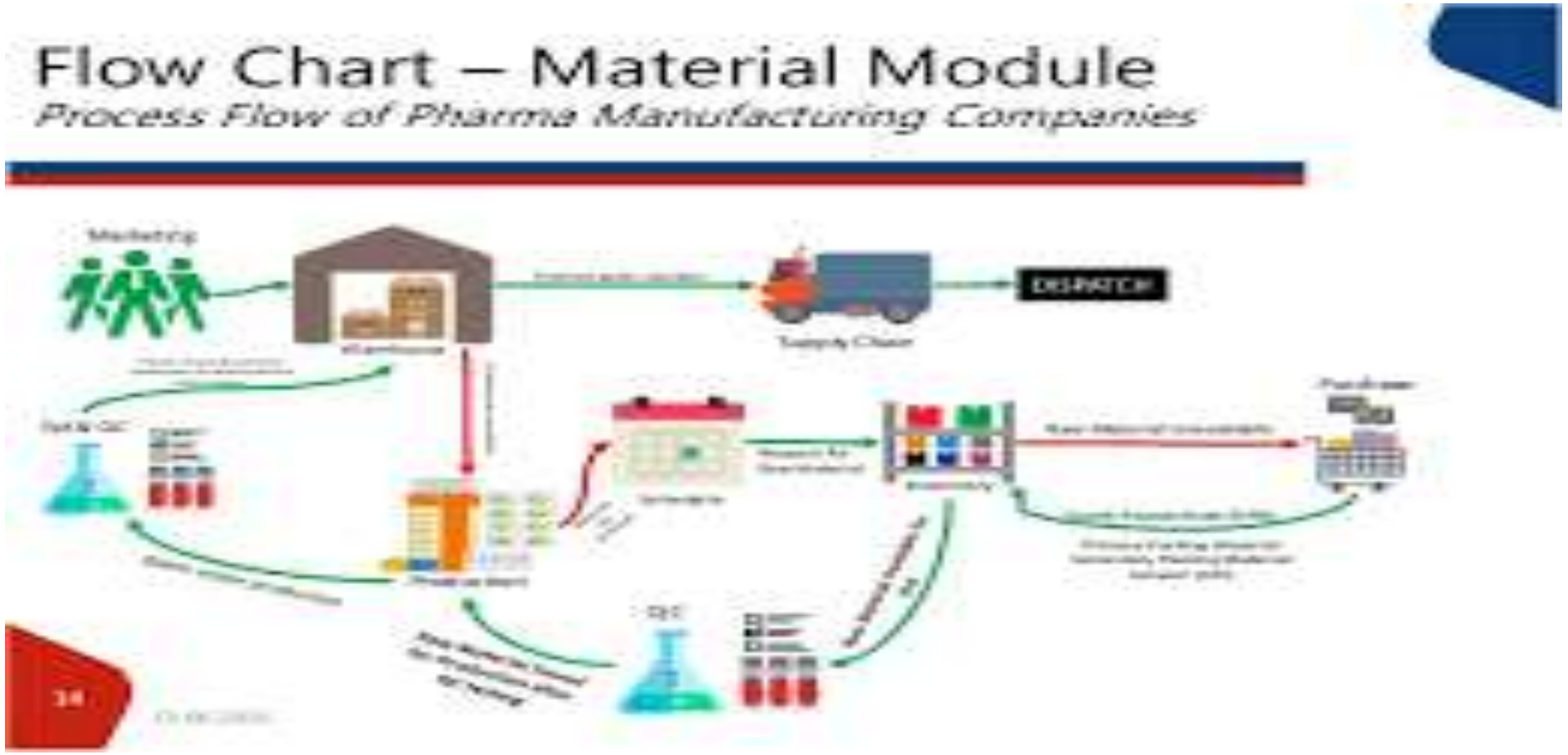
Quality



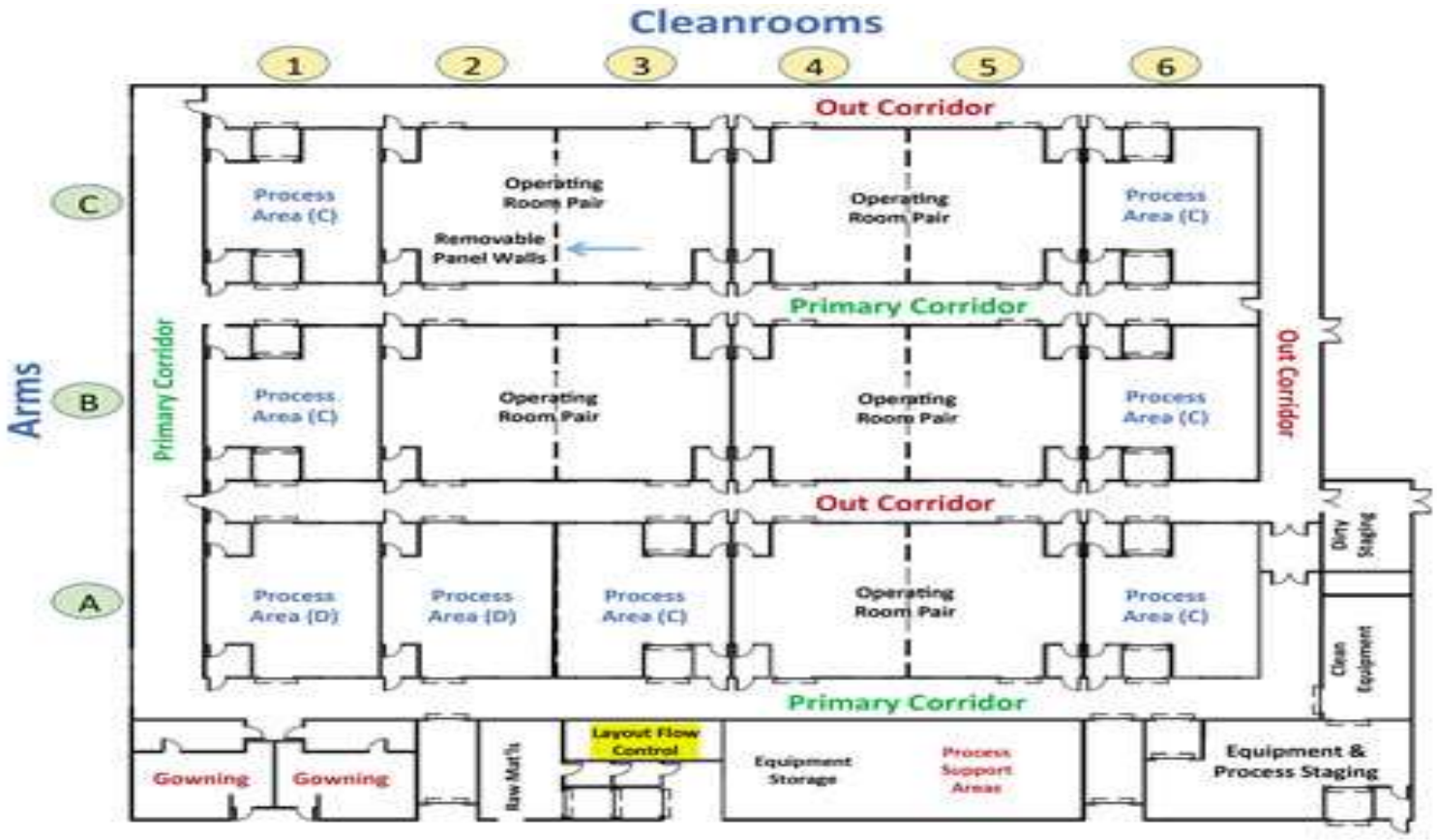
Production



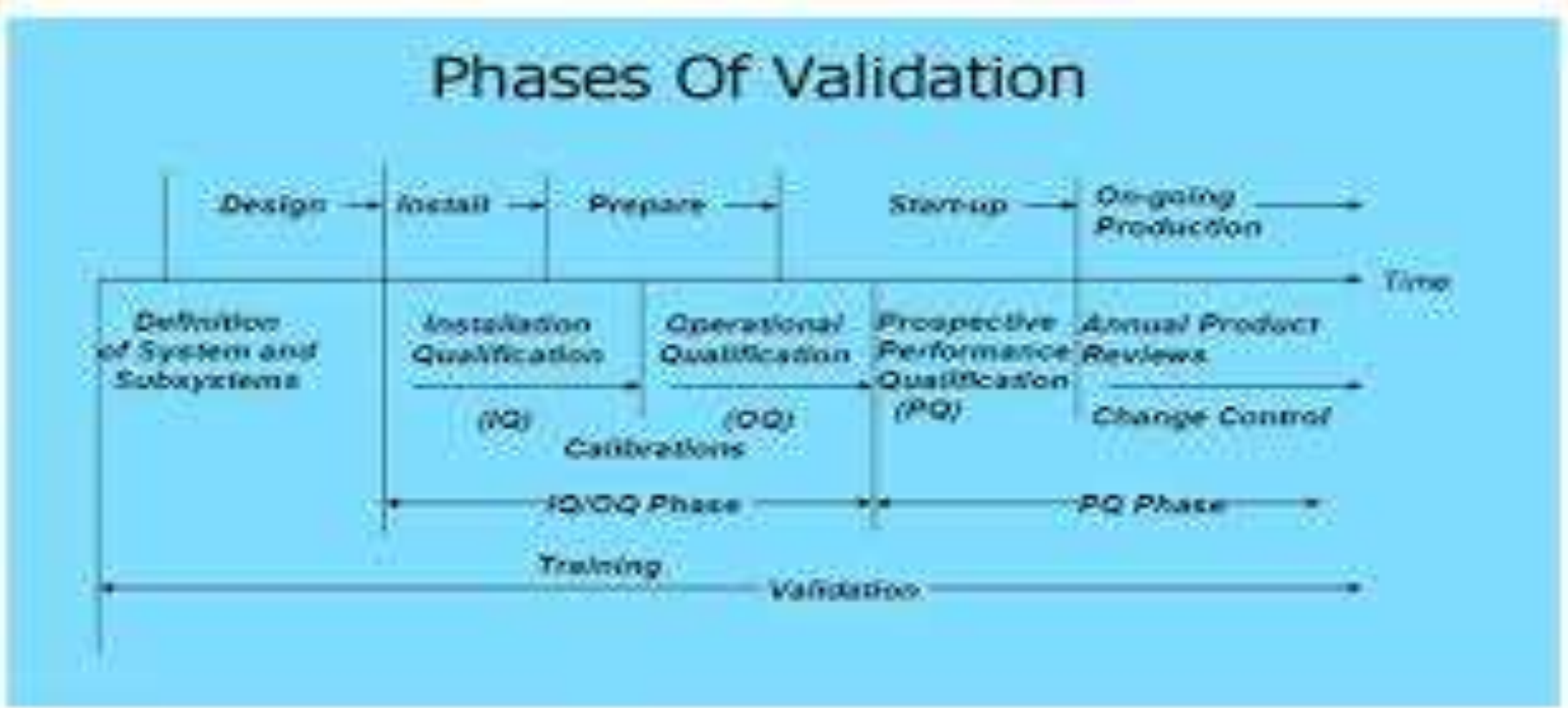
Material



Facilities & Equipment



Facilities & Equipment



Packaging & Labelling

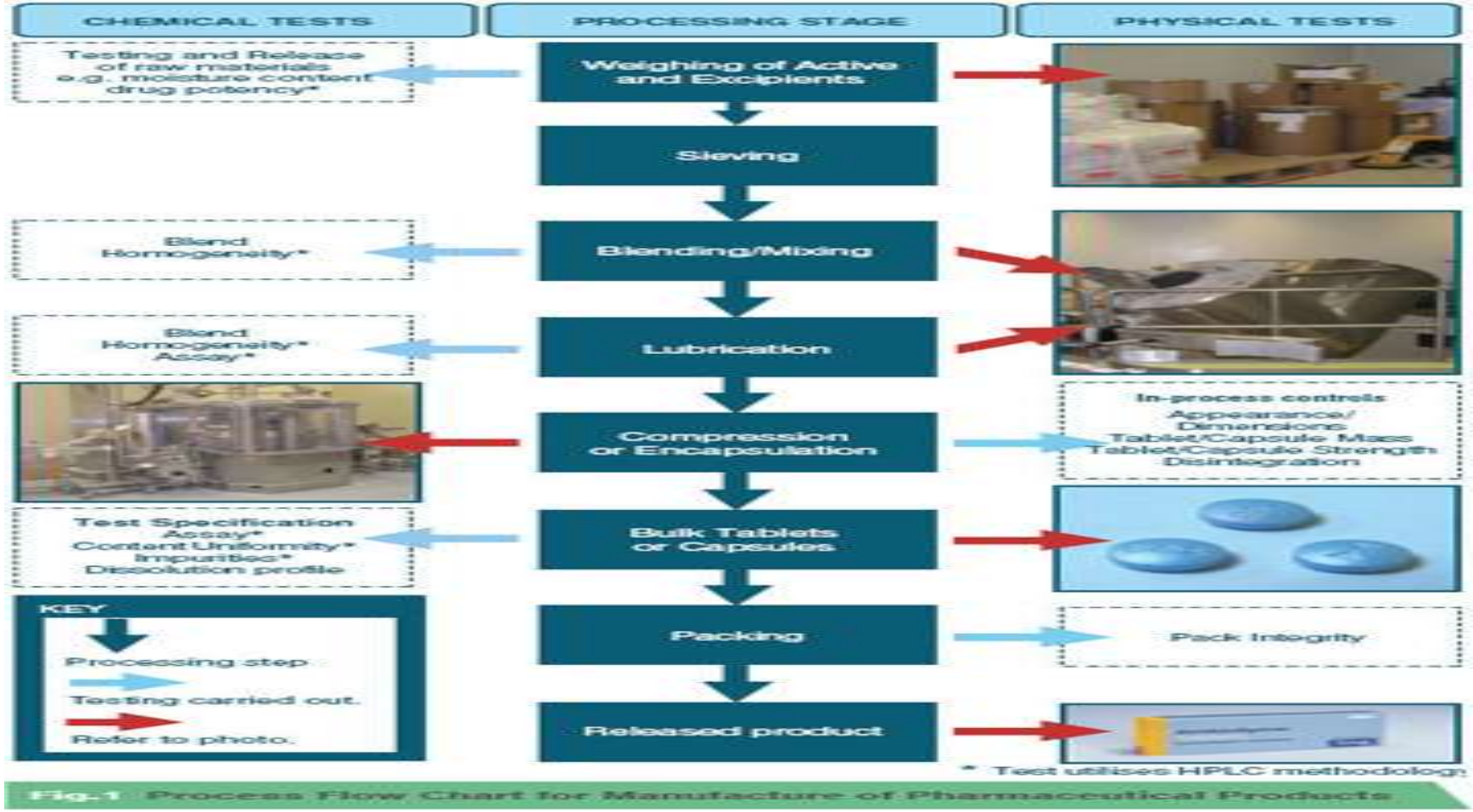


Fig.1 Process Flow Chart for Manufacture of Pharmaceutical Products

Glossary & Terminology in Pharma Companies

- API – Active Pharmaceutical Ingredient
- ANDA – Abbreviated New Drug Application
- BPR – Batch Packaging Record
- CFR – Code of Federal Regulation
- CIP – Clean In Place
- CTD – Common Technical Document
- FDA – Food and drug Administration
- cGMP - Current Good Manufacturing Practices
- GCP – Good Clinical Practices

Glossary & Terminology in Pharma Companies

- GMP – Good Manufacturing Practices
- GDP – Good Documentation Practices
- GLP – Good Laboratory Practices
- HEPA - high-efficiency particulate air
- ICH – International Conference on Harmonisation
- ISO – International Standards Organization
- IQ – Installation Qualification
- NDA – New Drug Application
- OQ – Operational Qualification

Glossary & Terminology in Pharma Companies

- PQ – Performance Qualification
- PhRMA – Pharmaceutical Research and Manufacturers of America
- QP – Qualification Protocol
- QA – Quality Assurance
- QC - Quality Control
- RA – Regulatory Affairs
- SOP – Standard Operating Procedure
- SQ – System Qualification
- TQM – Total Quality Management

Glossary & Terminology in Pharma Companies

- ULPA – Ultra Low Particulate Air
- USP – United states of Pharmacopoeia
- FAT – Factory Acceptance Test
- CAPA – Corrective and Preventive Action
- ALCOA – Attributable, Legible, Contemporaneous , Original And Accurate
- QMS – Quality Management System
- BMR – batch Manufacturing Record
- APQR/APR/PQR – Annual Product Quality Review
- WHO – World Health Organization

Definition

- Acceptance Criteria – The specification and acceptance/rejection criteria, such as acceptable quality level and unacceptable quality level , with an associated sampling plan that are necessary for making a decision to accept or reject a lot or batch of raw material , intermediate , packaging material or active pharmaceutical ingredient. This term can also be applied to validation
- Active Pharmaceutical Ingredient – Any substance that is represented for use in a drug and that , when used in manufacturing , processing or packaging of a drug , becomes an active ingredient or a finished dosage from the drug. APIs include substances manufactured by processes such as 1. chemical synthesis 2. fermentation 3. recombinant DNA or other biotechnology methods 4. isolation/ recovery from natural sources or 5. any combination of these processes

Definition

- Batch – A specific quantity of an intermediate or API intended to have uniform character and quality , within specified limits, and produced according to a single manufacturing order during the same cycle of manufacture. A batch may also mean a specific quantity of material or API processed in one process or series of processes so that it could be expected to be homogenous.
- Calibration - is a process that demonstrates a particular instrument or device produces results within specified limits, as compared to those produced by a traceable standard over an appropriate range of measurements

Definition

- Contamination - is defined as the undesired introduction of impurities of a chemical or microbiological nature, or of foreign matter, into or onto a raw material, intermediate, or API (Active Pharmaceutical Ingredient) during production, sampling, packaging or repackaging, storage or transport. Manufacturing
- Dosage Formulation – The form in which a drug is produced. Pharmaceutical companies use many methods of drug delivery , including oils, gels, creams, and sprays; capsules and tablets ; injects ; implants ; suppositories ; and liquids and syrups.

Definition

- Efficacy – Measure of the therapeutic effectiveness of a drug.
- In-process controls- Testing and activities performed during to monitor and , if necessary , adjust the process
- Installation Qualification – Establishing confidence that process equipment and ancillary systems are capable of consistently operating within established limits and tolerances
- Investigational New Drug (IND) application – The document that a sponser (usually a drug company) must submit to the FDA before beginning testing of a new drug on humans. This IND application contains the plans for the clinical studies and gives a complete picture of the drug , including its structural formula , animal test results and manufacturing information. The IND application contains information resulting from several years of research and testing.

Definition

- Lot – A batch , or a specific identified portion of a batch having uniform character and quality within specified limits, For an API produced by continuous process, it is specific identified amount produced in a unit of time or quantity in a manner that ensures its having uniform character and quality within specified limits.
- Lot number (control number, or batch number) – Any distinctive combination of letters , numbers , or symbols or any combination of them from which the complete history of the manufacture , processing , packing , holding and distribution of a batch or lot of an API or other material can be determined.

Definition

- Pilot Scale – The manufacture of an API on a reduced scale by processes representative of and simulating those to be applied on a larger commercial manufacturing scale.
- Placebo – Inactive agent without therapeutic value used in controlled studies to determine the efficacy of the potential therapeutic agent which it is being compared. The placebo is made to look exactly like the therapeutic agent.

Definition

- Process validation – Establishing documented evidence that provides a high degree of assurance that a specific process will consistently produce a product meeting its predetermined specifications and quality characteristics.
- Protocol – Written documentation establishing strict and detailed guidelines and requirements for the proper execution of an activity designed to verify the proper installation or operation of a specific component, segment or system of a new or existing facility.
- Qualification – The action of proving that any equipment or process works correctly and consistently and produces the expected results . Qualification is a part of , but not limited to , a validation process , i.e Installation Qualification (IQ), Operation Qualification (OP), and performance qualification (PQ)

Definition

- Quality Assurance (QA) – the sum total of the organized activities performed with the intent to ensure that all APIs are of the quality required for their intended use.
- Quality Control (QC) unit – Any person or organizational element designated by the firm to be responsible for the duties relating to quality control
- Raw material – Any ingredient intended for use in the production of APIs. These may include starting materials, process aids , solvents and reagents.
- Recovery – Any treatment of materials by a process intended to make them suitable for further use.

Definition

- Validation – The procedure for establishing documented evidence that a specific system or facility is constructed and operates according to a predetermined set of specifications and guidelines
- Validation Protocol – A written plan stating how validation will be conducted while identifying specific acceptance criteria. For example, the protocol for a typical manufacturing process identifies processing equipment , critical process parameters / operating ranges , product characteristics , sampling and test data to be collected , number of validation runs , and acceptable test results.

Definition

Other definitions

Airborne Particulate Count (also referred as Total Particulate Count) – Particles detected are 0.5 µm and larger. When a number of particles is specified, it is the maximum allowable number of particles per cubic meter of air (or per cubic foot of air)

Airborne Viable Particulate Count (also referred to as Total Airborne Aerobic Microbial Count) – When a number of microorganisms is specified , it is the maximum number of colony forming units (cfu) per cubic meter of air (or per cubic foot of air) that is associated with a cleanliness class of controlled environment based on the Airborne Particulate Count.

Definition

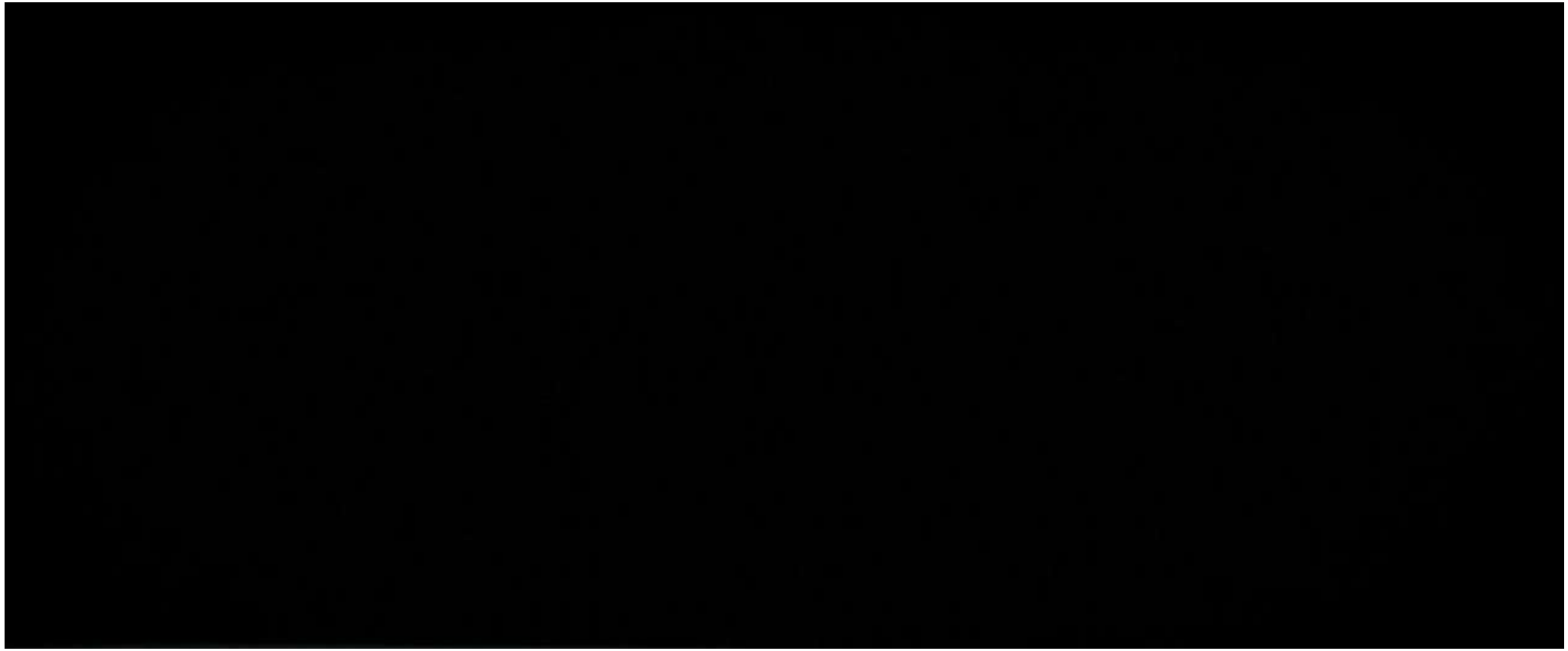
Aseptic Processing – A mode of processing pharmaceutical and medical products that involves the separate sterilization of the product and of the package (container/closures or packaging material for medical devices) and the transfer of the product into the container and its closure under microbiologic critically controlled conditions

Action levels – Microbiological levels in the controlled environment , specified in the standard operating procedures, which when exceeded should trigger an investigation and a corrective action based on the investigation.

Definition

- Alert levels – Microbial levels , specified in the SOPs , which when exceeded should result in an investigation to ensure that the process is still within control. Alert levels are specific for a given facility and are established on the basis of a baseline developed under an environmental monitoring program . These alert levels can be modified depending on the trend analysis done in the monitoring program. Alert levels are always lower than Action levels .
- Bioburden – Total number of microorganisms detected in or on an artcle.

GMP



Thank You!