IPQC (In Process Quality Control) is the controlling procedures involved in manufacturing of dosage forms starting from raw material purchase to dispach in final packaging.

It prevent errors during processing.

Human errors during process can be minimizing.

In process quality control (IPQC) is a planned system, To identify the materials, equipment, processes , and operators;
To enforce the flow of manufacturing and packaging operations according to the established rules and practices;
To minimize human error or to detect the error if and when it does occur;
And to pinpoint the responsibility to the personnel involved in each unit operation of the entire process .

In process Quality Control In general, In process control procedures are usually rapid and simple tests or inspection that are performed when the manufacturing of the product batch is in process.

The in-process control procedures and testes should be O penly discussed, E xperimentally justified, W ritten in detail, P roperly explained, A nd in particular, Rigidly enforced once they are established.

Objective/Importance of IPQC:

The primary objective of an IPQC system is, to monitor all the features of a product that may affect its quality and to prevent errors during processing. To large extent, IPQC is concerned with providing accurate, specific, and definite description of procedures to be employed from the receipt of raw materials to the release of finished dosage forms.

To detect variations from the tolerance limits of the product so that prompt and corrective actions can be taken.

To detect any abnormality immediately and at the same time indicate the kind of action needed. Thus, The In process checking during manufacturing plays an important role in the auditing of the quality of the product at various stages of production

USFDA c-GMP guidelines (For sampling and testing of in process materials and drug products):

To assure batch uniformity and integrity of drug products, written procedures shall be established and followed that describe the in-process controls, and tests, or examinations to be conducted on appropriate samples of in-process materials of each batch.

Why Such control procedure shall be established? To monitor the output and to validate the performance of those manufacturing processes that may be responsible for causing variability in the characteristics of in-process material and the drug product.

SPECIFICATION: Valid in-process specification for such characteristics shall be consistent with drug product final specifications. They should be derived from previous acceptable process average and process variability estimates where possible and determined by the application of suitable statistical procedures where appropriate. Examination and testing samples shall assure that the drug product and in-process material conforms to specification

IPQC TESTING: In-process materials shall be tested for identity, strength, quality, and purity as appropriate And approved or rejected by the quality control unit, during the production process e.g., At commencement or completion of significant phases or after storage for long periods.

REJECTED MATERIAL: Rejected in-process materials shall be identified and controlled under a quarantine system designed to prevent their use in manufacturing or processing operations for which they are unsuitable .

IPQC FOR PARENTERAL PRODUCTS:

Parenteral refers injectable route of administration. It derived from Greek words Para and enteron. So it is a route of administration other than the oral route.

Parenteral preparations must be sterile -free of microorganisms. To ensure sterility, parenterals are prepared using -aseptic techniques -special clothing (gowns, masks, hair net, gloves) -laminar flow hoods placed in special rooms

The in-process controls depend on the complexity of the product.

The production line for parenteral manufacturing consists of the following steps:

Material, equipment and area

Filling

Sterilization

Leak testing

Checking

MATERIAL, EQUIPMENT AND AREA

- Checking of materials for name, lot no., vendor, weighing components
- Addition should be marked in record
- Checks for potency, date of assay
- Equipment labeled with name of product, lot number
- Proper cleaning from its last usage
- Cleaning with signature of the responsible person
- Temperature 72 ± 5 °F
- Humidity 40% R.H.
- Room outlet for air, absolute filter 0.3 μ
- Gauge across the filters
- 18-20 air changes/hr
- Total fresh air
- Cleaning and disinfections before each filling operation
- Blood-agar plate exposure and air sampling by millipore filter technique
- Machine lubricants used are checked for sterility
- Checking of bulk solution before filling for drug content
- pH, color, clarity of solution.

FILLING

- Bacterial filters are bubble tested before and after use and if possible reserved for each product
- Measurement of current volume or weight from each filling head periodically
- Identification of line and equipment
- Evaluation of containers by clarity test
- Filling hood disinfections and tagged for the product
- Aseptic filling monitoring by exposure of blood agar plates
- Filling and filling station for air velocity
- Vials and ampoules, control and lot no.
- Vials washing, check for cleanliness of water, air, steam and washer
- Rubber stopper and cap washing and steam sterilization

•Bubble test or bubble point test:

Pressure at which continuous stream of bubble is seen downstream of wetted filter under gas pressure. At first gas dissolve in water. At some point pressure becomes great enough to expel water establishing path for bulk flow of air. Stream of bubbles seen.

Spordex test:

Spordex strips are biological indicator strips (filter paper strip) for determining the effectiveness of steam, ethylene oxide and dry heat sterilization.

STERILIZATION

Steam:

1. Record with time, date, product batch and chamber number
2. Temperature recording with date including time and temperature of the product
3. Weekly intervals spordex strip exposure for validation
4. At longer intervals bottles with thermocouples for uniformity of heat

Filteration:

1. Type and porosity of filters
2. Integrity results before and after
3. Sterilization records
4. If filter changes, should be recorded

1) **LEAK TEST:** for presence of pores or tiny cracks which will cause microbial contamination of product. Tip seals more likely incompletely seal than pull seal.
-Ampoules completely submerged in colored dye solution (0.5-1% methylene blue) in vacuum chamber. Negative pressure applied. Atm pressure causes dye to penetrate if leak is there. (Capillaries of about 15 μm in diameter or smaller may or may not detected by these methods)

- detection during autoclaving cycle. Both can be done at once.

2) **SPARK TEST:** apply tester probe to the outside bottle moving from liquid layer into air space. A blue spark discharge occurs if vacuum is good otherwise purple spark occurs if no vacuum.

Other tests like weight change, pressure vacuum changes, gaseous detection, burst test can be done.

3) CLARITY TEST: by dark area to light area
LVP: 50 particles of 10 μm & larger
5 particles of 25 μm & larger/ml
Instrument: light scattering, light absorbance, electrical resistance

HEPA FILTER: DOP test

Dioctylpthalate test: DOP in form of smoke or dispersed particles. DOP is condensed into mist of 0.3, 0.5, 1 micron size particles. Passed through HEPA filter and check concentration at inlet and outlet stream. Passed or filtered smoke particles measured and efficiency calculated.

CHECKING

Each filled vial and ampoules subjected to inspection for particles, volume, cap or seal condition

IPQC FOR TABLETS

1. Environmental control
2. Materials
3. Mixing/massing
4. Granulation
5. Drying
6. Compression

ENVIRONMENTAL CONTROL

1. Filter condition and changes, humidity, temperature monitoring

2. Water: release sticker at point of use for chemical and microbial purity

MATERIALS

1. Checking for name, lot no., weight, particle size, bulk density, colour and water content
2. Balances and scales, granulation and multimill with screen.

MIXING/MASSING

1. Checking for proper equipment and addition of ingredients, mixing time and sampling from top, middle and bottom
2. Checking of binder temperature rate and addition time
3. Massing time and load reading
4. Wet milling, speed, screen, equipment checking

GRANULATION

1. Amount of lubricants
2. Density
3. Hardness and dryness of granules

DRYING

1. Cleaning condition of an equipment and filter bag
2. Separate bag for each product
3. Loading uniformity, air temperature, volume and outlet temperature, time of drying
4. Moisture control and determination
5. Proper sifting and control of oversize granules
6. Fine collection and lubricants
7. Proper mixing for specified period

COMPRESSION

1. Proper labeling on drums and clean conditions
2. Proper identification of compression machine to the product, strength, lot no. and item number
3. Checking of tables diameter, thickness, weight, hardness, D.T. and friability, weight variation, color, odour, surface, flow of granules and speed of the machine
4. Weight control by frequent checking on balance or automated devices from all sides of the machine
5. Checking for defected like capping, lamination, cross contamination, color and odour
6. Color comparison or measuring devices
7. For compression coated tablets breaking to see inner tablet (core)

Capping is the partial or complete separation of the top or bottom crowns of a tablet from the main body of the tablet. Lamination is separation of a tablet into two or more distinct layers. Both of these problems usually result from air entrapment during processing.

Picking is removal of a tablet's surface material by a punch. Sticking is adhesion of tablet material to a die wall. These two problems result from excessive moisture or substances.

Mottling is an unequal color distribution on a tablet, with light or dark areas standing on otherwise uniform surface. This results from use of a drug with a color different from that of the tablet excipients or from a drug with colored degradation products with low melting temperatures in the formulation .

Hardness (crushing strength) test It is the load required to crush the tablet when placed on its edge.

Why do we measure hardness? To determine the need for pressure adjustments on the tablet machine. Hardness can affect the disintegration. So if the tablet is too hard, it may not disintegrate in the required period of time. And if the tablet is too soft, it will not withstand the handling during subsequent processing such as coating or packaging .

Factors Affecting the Hardness: Compression of the tablet and compressive force. Amount of binder. (More binder à more hardness) Method of granulation in preparing the tablet (wet method gives more hardness than direct method).

Friability test: It is the tendency of tablets to powder, chip, or fragment and this can affect the elegance appearance, consumer acceptance of the tablet, and also add to tablet's weight variation or content uniformity problems. Friability is a property that is related to the hardness of the tablet.

An instrument called friabilator is used to evaluate the ability of the tablet to withstand abrasion in packaging, handling, and shipping.

Procedure: Weigh 20 tab altogether = W1 2. Put these tablets in the friabilator and adjust the instrument at 100 rpm (i.e. = 25 rpm for 4 min) 3. Weigh the 20 tablets (only the intact ones) = W2 4. Friability (% loss) = It must be less than or equal to1% but if more we do not reject the tablets as this test is non-official. Perform this test using 20 tablets that were used first in the weight variation test

IPQC FOR CAPSULES

Steps Of Capsule Manufacturing:

1. Mfg of Gelatin Shell.
2. Drying of shells in controlled humidity.
3. Mfg of granules.
4. Filling of Shells.
5. Packaging & Labeling.

•IPQC Checks During Gelatin Shell Manufacturing:

- % purity of gelatin
- Viscosity of gelatin solution 25-45 millipoise
- Bloom strength of gelatin solution 150-250 gm
- Iron content NMT 15 ppm
- Film Thickness
- Color, surface, appearance of empty shells
- Temperature of hot air, for drying of shells
- Length of Capsule & Body of the shell
- Moisture content 12-15%

• Sorting of defective shells:

After the capsules have been inspected either electronically or manually, they are sampled by the QA inspector & checked for the defects and then sorted out.

• Printing inspection on shell

Inspection of defects like:-

- Hardening of shells
- Softening of shells
- Swelling of shells
- Cracking of shells
- Discoloration of shells
- Misprinting of logo on shells

IPQC Checks During Filling Of Empty Capsule Shells:

During filling process equipment should be labeled with :-product name, Batch No, Time of starting, Sign

During Filling: flow property of granules or powders

Weight Variation :

For hard gel caps -

Limit NMT 2 caps should deviate from avg wt.

AVG WT	%DEVIATION
<300mg	10%
>300mg or more	7.5%

For soft gel caps:

Wg 10 caps

Remove inner content by cutting with scissor/blade

Wash with solvent & evaporate solvent at room temperature for 30 min

Wg the empty shells & calculate % deviation

•SORTING DEFECTS:

•Electronic automated or manual inspection is made to sort out & reject the defected caps.

•Overprinting

PRINTING & LABELING:

Inspection of overprinting, logo, labeling are checked with the standard shade cards.

Defective ones are sorted out & rejected.

•IPQC FOR POWDERS

•Types Of Powders:
•Effervescent powders
•Dusting powders
•Insufflations (Inhalers)
•Dentifrice
•Oral powders

IPQC Checks During Powder Manufacturing:
Particle size & shape
Texture
Powder flow
Fluffiness
Density
Foreign Impurities
Moisture
Packaging
sealing, printing

•Effervescent Powders:
sample powder in 250ml of water produces effervescence & dissolves in 12sec.
•Dusting Powder:
color, texture, density, particle size, flow, fluffiness, spread ability
•Insufflations:
flow, particle size, density
•Dentifrice:
abrasion, texture, particle size, color

There are generally two types of packing:- 1.Strip sealing 2.Blister packing - 'Blister packs' are a common form of packaging used for a wide variety of products. They are safe and easy to use and they allow the consumer to seethe contents without opening the pack.
IPQC CHECKS ON PACKING LINE: Strips- number of strips, Appearance of strips, Text of strips & leak test.
Inspection of overprinting, logo, labeling are checked with the standard shade cards. Defective ones are sorted out & rejected.
Packaging - sealing, printing

IPQC FOR SOLUTIONS, EMULSIONS, SUSPENSIONS AND TOPICAL APPLICATIONS (LIQUID ORALS)

1. Weight and volume measurement
2. Potency assay
3. Ointment sampling from different corners for uniformity
4. Suspension uniformity at the time of packing
5. Specific gravity for solutions, suspensions and emulsions
6. Viscosity for fluids, ointments, creams and jellies
7. Sedimentation volume by centrifugations rapid method for suspensions
8. pH, particle size

The operations must adhere rigidity to the established standards or specification as determined through systemic inspection, sampling and testing should constantly strive for improving the levels of the current standards or specifications

The facilities, personnel, funds and environment necessary to perform their responsibilities effectively should be adequately provided.