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DEVELOPMENT OF INTEGRATED INDUSTRIAL PROCESS LAYOUT DESIGN FOR THE PRODUCTION AND QUALITY CONTROL FACILITY OF VARIOUS PHARMACEUTICAL FORMULATIONS

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ABSTRACT

Objectives: To develop an integrated industrial production and quality control layout which facilitates the pharmaceutical industries for manufacturing, controlling quality of various types of pharmaceutical formulations in a single production unit.

Methods: For designing the integrated process layout for the production and quality control, different operations and their sequences involved in the manufacturing and official tests to be met by various formulations had been considered respectively for achieving an efficient and effective movement of material and people.

Results: An ideal integrated industrial process layout for the production and quality control of various pharmaceutical formulations had been developed.

Conclusions: In the current marketing trend it is necessary for the manufacturer to shift from single line production layout to multi-product production (integrated) layout to maintain several types of formulations (product mix) to make his presence and sustaining in the market with involvement of economics.

INTRODUCTION: According to the American Pharmaceutical association, pharmacy is the profession responsible for the appropriate use of medications, devices and services to achieve optimal therapeutic outcomes. Pharmacy is the art and science of preparing and dispensing the medications in the provision of drug-related information to the public. Various popular branches of pharmacy includes Pharmacology, Pharmaceutics, Biopharmaceutics and pharmacokinetics, Medicinal chemistry, Clinical pharmacy, Pharmacognosy, Pharmaceutical analysis and Industrial pharmacy [1]. By definition industrial pharmacy is a discipline which includes manufacturing, development, marketing and distribution of drug products including quality assurance of these activities and having contact areas with engineering and economics. All basic research in industrial pharmacy is closely applicable to the benefit of industry mainly focused on solving current general problems in pharmaceutical industry, such as miniaturization of manufacturing processes. The research can be either laborative work or case-studies [2].

Main purpose of process layout is to communicate information in a simple and explicit way and to minimize the space required for production, keeping in view of schedule M of cGMP. Layout planning of industrial plant is a continuous process as there are

always chances of making improvements over the existing arrangement.

A good layout results in comforts, convenience, safety, efficiency, compactness and profits. Integrated process layout is a coordinated effort to achieve the object to integrate machines, materials and personnel for economic production. The designing of integrated process layout may depends upon type of process and product control, space available and space required, operational convenience and accessibility, economic distribution of utilities and services, type of building, health and safety. It also depends on waste disposal and possible future expansion. Process flow involves the study of movement of materials and people in a schematic way through a production facility or process [3].

Quality control is defined as the application of universal regulatory process to problems of product quality. QC unit means any person or organizational element designated by the firm to be responsible for the duties relating to controlling quality and has responsibility to approve or reject all components, drug products, containers, closures, in process materials, packing materials, labeling and drug products. Hence, QC unit shall be responsible for approving or rejecting

- Drug products manufactured, processed, packed and held under contract by another company.
- All procedures or specifications impacting on the identity, strength, quality and purity of the drug product [4].

Each pharmaceutical formulation should face production and quality control phases in order to enter into the market. Improper material, process or procedure handling during production process ultimately affect its quality, which is most important parameter regulating its entry into the market. Now days, pharma industries are maintaining separate production units/ layouts for different types of formulations (tablets, syrups, injections etc.) in order to avoid mishandling of material and equipment during process.

There is no manufacturer tried single integrated production layout for the manufacturing of various types of pharmaceutical formulations. So, in this research paper we had tried to give an ideal integrated industrial process layout and quality control design for the production and quality control facility for various types of pharmaceutical formulations from direct knowledge of the project and partly from information supplied by the sales and marketing departments of the company requiring the new facility. This integrated layout was designed to meet the immediate and future requirements of the marketing protocol/strategy of a company and which is supposed to be having the following advantages:

- Minimum movement of materials
- Reduces material handling cost, helps in decreasing the cost of product
- Minimized chances of contamination with care
- Reduces the process inventory, space for processing
- Improves the supervision and control
- Helps in visualizing various possibilities of alteration and improvement
- Manufacture will be able to maintain several formulations (Product mix) of a drug in the market based on demand.

METHODS:

Development of Integrated Process Layout for the Production of Various Types of Pharmaceutical Formulations: For development of process flow diagrams, initially identified the operations and their sequences. So, the methodology used for development of integrated industrial process layout involves the following steps:-

a. Selection of formulations for which integrated layout to be developed
b. Study of basic operations and their sequences involved in the manufacturing process of all formulations considered above in a schematic way

c. Identification & Separation of operations/steps into common and different on the basis of process

a. **Selection of formulations for which integrated layout to be developed:** In this step, a list of formulations ranging from various conventional dosage forms like tablets, injections, etc., cosmoceutical formulations like lipsticks, face powders, etc., and some novel dosage forms like microspheres, liposomes, etc., had been selected for which an integrated process layout to be developed. The list of formulations considered for which integrated process layout design for their production was given in **Table 1**.

TABLE 1: LIST OF FORMULATIONS SELECTED FOR THE DEVELOPMENT OF INTEGRATED PROCESS LAYOUT DESIGN FOR PRODUCTION

S. No.	Name of the formulation
1	Compounding powders
2	Granules
3	Suppositories
4	Emulsions
5	Suspensions
6	Tablets
7	Capsules
8	Elixirs
9	Nasal drops
10	Ear drops
11	Throat paints
12	Mouth washes
13	Lotions
14	Liniments
15	Inhalations
16	Aerosols
17	Ointments
18	Creams
19	Syrups
20	Mixtures
21	Colloidions
22	Douches
23	Gargles
24	Linctuses
25	Micro spheres
26	Nanoparticles
27	Resealed erythrocytes
28	Liposomes
29	Face powders
30	Bleach powders
31	Cream eye shadow
32	Liquid mascara
33	Nail enamels
34	Nail lacquers
35	Lipsticks
36	Shampoos

b. **Study of steps involved in the manufacturing process of considered formulations in schematic way:** For development of integrated process flow layout, we had tried to give a simple and schematic way of manufacturing process involving sequence of steps to avoid confusion irrespective of different information sources. The schematic representation of the manufacturing process for various formulations considered in table 1 was given as follows:

1) Compound powders [6]:

Weigh required amount of powders and diluent (lactose)
↓
Mix all the ingredients in ascending order of their weights
↓
Mix thoroughly to form a homogenous powder
↓
Weigh and wrap in papers

2) Granular powders [6]:

Add Medicament, sweetening, flavoring and coloring agents
↓
Mix in a mortar
↓
Add a granulating agent (water, mucilage, gelatin etc)
↓
Press the coherent mass through sieve.
↓
Dry at warm place for 2-3 hrs (or) in oven at temp 60c
↓
Pack them in dry, well closed container

3) Suppositories [5, 6]:

Take mould, clean, lubricate and drain the excess lubricant
↓

Place the calculated quantity of powdered coca butter (acc to displacement value) in a disk.

↓

Place it in water bath and when 2/3rd base melts remove it from bath and stir

↓

Place powdered medicament on a warmed ointment slab.

↓

Place half of the melted base over it & rub it to prevent formation of lumps

↓

Mix to form uniform mass & warm for few seconds with stirring until it pourable

↓

Transfer it into cavities till overflow

↓

Keep in cool place, scratch the excess with knife

↓

Open the mould and remove suppositories

4) Emulsions [6, 7]:

Measure the required quantity of oil, water, gum

↓

Powder the gum acacia in a mortar

↓

Add water and triturate it with gum to form mucilage

↓

Add the required quantity of oil in small portions with rapid trituration to form primary emulsion

↓

Add remaining water to produce required volume; stir thoroughly to form uniform emulsion

↓

Transfer the emulsion in to a suitable container, label and dispense

5) Suspensions [5, 7]:

Finely powder any ingredients which are not fine powders

↓

Mix the insoluble powders in a mortar

↓

Add the ingredient which is smallest in bulk first and dilute it with others in increasing order

↓

Add enough vehicles to produce smooth paste

↓

Dilute with vehicle until pourable

↓

Makeup the volume with the vehicle and shake thoroughly

↓

Transfer the suspension in to a suitable container, label and dispense.

6) Tablets [5, 7]:

Weigh the sufficient amount of medicament, diluent, glidant, binder, disintegrant, etc.

↓

Preparation of granules for compression by wet/ dry method of granulation

↓

Compression of granules into tablets & Coating of tablets (if necessary)

↓

Packing of tablets

7) Capsules [6, 7]:

Take the hard gelatin capsule shell

↓

Fill the capsule with powder medicament/ granules with the disintegrant, diluents, etc., using capsule filling machine

↓

Sealing

↓

Polishing

8) Elixirs [5, 6]:

Weighing the ingredients (drug and other adjutants)

↓

Mixing the drug with solvents like water, alcohol, syrup, glycerin and sorbitol

↓

To the above drug solution add the adjutants (flavors, colors, preservatives etc.,)

↓

Mix thoroughly and make up to the required volume using suitable solvent

↓

Packing and labeling

9) Nasal drops [6, 8]:

Weigh the required amount of drug and other salts, agents.
↓
Dissolve the above in warm water & then cool
↓
Filter if necessary
↓
Make up the volume through filter
↓
Packing and labeling

10) Ear-drops [5, 6]:

Weigh the required amount of drug and other agents
↓
Mixing with suitable amount of solvent (water, glycerin)
↓
Make up to the required volume & Packing and label

11) Throat paints [6]:

Weighing the required amount of drug and other adjutants
↓
Mixing drug in vehicle (water, glycerin) to dissolve
↓
Add other ingredients (colors, flavors)
↓
Then add glycerin to make up to required volume
↓
Packing and labeling

12) Mouth washes [6, 8]:

Weighing the required amounts of drug and other like NaCl, etc.,
↓
Mixing it in flavored water
↓
Add colors and sweeteners.
↓
Mix thoroughly and make up to the required volume
↓
Packing and labeling

13) Lotions [6, 8]:

Weigh the required amounts of drug and other adjutants required
↓
Mix the drug and others (dispersing agents, stabilizers) dissolve with water or alcohol & add flavoring agents
↓
Make up the required volume using water or alcohol
↓
Packing and labeling

14) Liniments [6, 8]:

Weigh the ingredients
↓
Triturate or mix with oils or alcohol and add emulsifying agents
↓
Mix uniformly and make up to the required volume
↓
Packing and labeling

15) Inhalations [8]:

Weigh the ingredients required and powder them in glass mortar & add oil and stir
↓
Add magnesium carbonate (light) and dispersing oil in small quantities
↓
Mix well and add vehicle gradually till make up to volume
↓
Transfer it to tarred container & Label

16) Aerosols [5, 7]:

Prepare the product concentrate (active ingredients + solvents + anti-oxidants, etc.,)
↓
Fill the product concentrate into the container by using concentrate filler
↓
Place the valve by using valve placer and then vacuum crimping
↓
Fill the pressure into the container by pressure filling equipment using propellants
↓
Perform the leak test and then label

17) Ointments [6, 8]:

- **Trituration method**:

Finely powder the solid medicaments in mortar
↓
Triturate the solid medicament with suitable ointment base
↓
Incorporate any liquid ingredient (if there) & pack in container, label.

- **Fusion method**:

Melt the required ingredients
↓
Incorporate the medicament & make a homogenous mass
↓
Pack in suitable container & label

- **Emulsification method**:

Sufficient amounts of fats, oils and waxes are melted (oil phase) at 70^{o}C along with preservative
↓
Aqueous ingredients also melted at same temperature (aqueous phase) along with preservative
↓
Add aqueous solution to the melted oil phase with continuous stirring
↓
Allow to cool the product & pack in suitable container, label.

18) Creams [6]:

Melt the oil phase ingredients in china dish at 70◦c along with preservative
↓
Melt the aqueous phase ingredients in another china dish at 70◦c along with preservative
↓
Add the aqueous phase to the oil phase with continuous stirring
↓
Cool & add perfume while packing in suitable container and label

19) Syrups [5]:

Add the sucrose to purified water
↓
Heat to dissolve sucrose, with occasional stirring
↓
Cool the solution
↓
Add more of purified water to make the required weight
↓
Transfer into bottle, label and dispense

20) Mixtures [6, 8]:

- **Containing diffusible solvent**:

Finely powder the drug in a mortar
↓
Measure 3/4th of vehicle, add & make a smooth cream
↓
Add the remaining portion of vehicle & add any other liquid ingredient
↓
Add more vehicles to produce required volume
↓
Transfer in to a suitable container, label and dispense.

- **Containing in diffusible solids**:

Finely powder indiffusible solid in a mortar & add any soluble drug and mix it
↓
Measure 3/4th of vehicle &make a smooth paste
↓
Add any other liquid ingredient
↓
Transfer the mixture, measure & Add more vehicle to produce required volume
↓
Transfer in to suitable container, label and dispense.

- **Containing precipitate forming liquids:**

Finely powder the indiffusible & diffusible solid and mix them with tragacanth
↓
Add 3/4th of vehicle and make a smooth paste
↓
Measure the precipitate forming liquid in a dry measure & assess at center of cream with stirring
↓
Add more vehicles to produce required volume

↓

Transfer to the container label and dispense

21) Collodions [6]:

Measure the ingredients & all are mixed by shaking in a closed container

↓

Allow to stand for few days

↓

Impurities are settle and removed by filtration, decanting the supernatant liquid

↓

Transfer in to container, cork, label and dispense

22) Douches [6]:

Transfer the drug to a glass mortar

↓

Grind the crystals with water add more water and regrind

↓

Allow undissolved crystals to settle and pour the supernatant liquid

↓

Repeat the same procedure until all the solid has dissolved

↓

Filter through a clean sintered glass filter & make up the volume

↓

Transfer in to container, label and dispense

23) Gargles [6, 8]:

Dissolve the potassium chlorate in about 150ml of warm water

↓

Cool before adding liquefied phenol

↓

Add the drug solution, filter if necessary

↓

Transfer to suitable container, label and dispense

24) Linctuses [6]:

Weigh the codeine phosphate and dissolve it in water & heat gently if required

↓

Add benzoic acid solution compound tartrazine solution and chloroform spirit

↓

Add the lemon syrup and adjust the volume by adding more of syrup

↓

Transfer in to container, label and dispense

25) Microspheres [9]:

Aqueous solution or suspention of polymer,
↓ Stirring, sonification
Dispersion in organic phase (oil/chloroform)
↓ Cross linking

↓	↓
Heat denaturation	chemical cross linking
↓	↓
Microspheres in organic phase	Microspheres in oil phase
↓	↓

↓ Centrifugation, washing, separetion
Microspheres

26) Nanoparticles [9]:

Derivatized polysaccharide
↓aq. Buffer, stirring, 50°C, 12hr
Swollen polysaccharides
↓ Probe sonification at 25°C, 10 min
Hydrogel Nanoparticles

27) Resealed erythrocytes [10]:

- Method 1:

Take RBC & placed in hypotonic media (Swell, rupture)

↓

Formation of pores

↓

Add drug solution up to 25%

↓

Adjust to the tonicity to isotonic & allow to reseal

- Method 2: **Dialysis**

Red blood cells

↓

Place in dialysis tubes and immerse in hypotonic solution

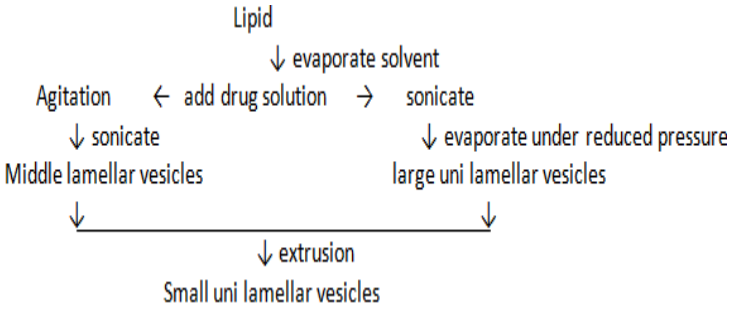
↓

Formation of pores (retention of cell components)

↓

Fill the drug solution & allow to reseal

28) Liposomes [10]:



29) Face powders [11]:

All powder ingredients passed through a coarse screen (40 mesh) (except colors)

↓

Mix for 1-3 hrs in a blender

↓

Add pigments & again mix. Pulverization done with hammer mill or Pebble mill or any other

↓

Perfume is blended by adsorbing it on absorbents like $CaCO_3$, $MgCO_3$.

↓

Binders are added and mix (if to be manufactured in cake form)

↓

Compression & pack in container, label

30) Bleach powders [11]:

Mix all the ingredients except oxidizing agents

↓

Add oxidizing agent and blend.

↓

Add anhydrous MgO (light), Mg silicate to correct the specific volume

↓

Pack in suitable container and label

31) Cream eye shadow [11]:

Mix the pigments & blend with petroleum jelly in roller mill

↓

Other fatty materials are melted in a pan and blended

↓

Pigment mass is transferred in to the fatty materials

↓

Pass through roller mill to ensure distribution of colors

↓

Fill in to containers while hot and label

32) Liquid mascara [11]:

Dissolve resin in alcohol with stirring.

↓

Carbon black + castor oil (pourable paste)

↓

The above two are mixed well.

↓

Above product filled into container, label

33) Nail enamels [11]:

Grinding of pigments

↓

Manufacture of nail lacquers.

↓

Mixing of pigments with nail lacquer

34) Liquid/cream shampoos [11]:

Aikanolamide dissolved in about half of the total amount of the detergent with heating

↓

Remaining detergent solution is added slowly

↓

Perfume is dissolved in cold concentrated detergent

↓

Color and preservatives dissolved separately in water and both are mixed

↓

Remaining water add to make up the volume & fill in container, label

35) Nail lacquers/paints/varnishes [12]:

Add 75% of the solvent and whole off the diluent in a mixer, mix well with agitation
↓
Add nitrocellulose while agitating
↓
Add resin and plasticizer and remaining of the solvent
↓
Stir still it dissolves & check the viscosity
↓
Clarify by filtration & add color
↓
Pack in suitable container and label

36) Lipsticks [12]:

Color grinding
↓
Mixing
↓
Moulding
↓
Flaming
↓
Packaging

c) Identification & separation of steps into primary and secondary on the basis of process: By carefully observing the sequence of steps involved in the manufacturing method/process of various pharmaceuticals given above, the steps were separated into common (primary) and different steps (secondary) based on the type of operation involved and were given in **Table 2**.

TABLE 2: SEPARATION OF STEPS INVOLVED IN THE PROCESS OF MANUFACTURING OF VARIOUS PHARMACEUTICALS IN TO COMMON (PRIMARY) AND DIFFERENT (SECONDARY) STEPS

Common steps	Different steps for each formulation in extension to common steps

- **Weighing/ measuring**
- **Size reduction/sonication**
- Mixing
- Sealing
- Packing
- Labeling
- Storage

- **Granular powders:**
Sieving
Drying
- **Cachets**
Filling
Moistening the edges
- **Suppositories**
lubrication
filling in moulds
scratching
- **Compound powders**
Homogenization
Wrapping in papers
- **Capsules**
Filling
Cleaning
- **Emulsions**
Trituration
- **Suspensions**
Trituration
- **Syrups**
Heating
- **Colloids**
Filtration
- **Douches**
Trituration
Filtration
- **Gargles**
Filtration
Cooling
- **Linctuses**
Heating

- **Lotions**
Trituration
- **Liniments**
Trituration
- **Pastes**
Trituration
- **Ointments**
Trituration
Tube filling
- **Creams**
Trituration
Tube filling
- **Aerosols**
Pressure filling
Vacuum crimping
Filling
Checking for leak test
- **Tablets**

1. Uncoated Tablets
Sieving
Drying
Punching
Dedusting
Cartooning

2. Coated Tablets
Coating
Drying
Polishing
- **Parenterals**
Filtration
Sterilization
Buffering
Checking for leak test

- **Liposomes**
Homogenization
Solvent extraction
Solvent evaporation
Drying
Centrifugation
- **Microspheres**
Dispersion
Centrifugation
Washing
Drying
- **Face powders**
Sieving
Blending
Milling
Compression
- **Bleach powders**
Blending
- **Cream eye shadow**
Blending
Heating
- **Nail lacquers**
Filtration
- **Lipsticks**
Grinding
Moulding
Heating
Packing
- **Shampoos**
Heating
- **Nasal drops**
Cooling
Filtration

This separation gives an idea of movement of material, people during the manufacturing through the production unit for various pharmaceuticals and helps in designing the integrated process layout.

Development of Integrated Quality Control Layout for checking and assuring the quality of various Pharmaceutical Formulations Manufactured: In order to design an integrated quality control layout for checking the quality of various types of pharmaceuticals produced by integrated production unit, the method adapted had the following steps:

a) List of formulations selected for the development of integrated Q.C layout

b) For each of formulation, the Q.C tests were taken from IP and BP

a. **List of formulations selected for the development of integrated QC layout:** Before going to design an integrated quality control layout, we had to choose or select list of formulations for which an integrated layout to be developed. The list of formulations selected for the design of integrated quality control layout was given in **Table 3**.

b. **Q.C tests for each formulation selected in (a) were taken from official pharmacopoeias like IP and BP:** To design an integrated quality control layout, we had tabulated the quality control tests recommended in the official Indian pharmacopoeia and British pharmacopoeia for each formulation considered above and was given in **Table 4**.

TABLE 3: LIST OF FORMULATIONS SELECTED FOR THE DESIGN OF INTEGRATED QUALITY CONTROL LAYOUT

S. No	Formulation

1.	Tablets
2.	Capsules
3.	Injections
4.	I.V. Infusions
5.	Aerosols
6.	Syrups
7.	Suspensions
8.	Emulsions
9.	Solutions
10.	Mixtures
11.	Linctuses
12.	Drops
13.	Elixirs
14.	Eye drops
15.	Eye ointment
16	Ear drops
17	Effervescent granules

18	Powders for oral solutions
19	Powders for injection/infusions
20	Powders for inhalations
21	Suppositories/pessaries
22	Rectal capsules
23	Granules
24	Nasal preparations
25	Ointments
26	Creams
27	Gels
28	Pastes
29	Poultices
30	Lotions

TABLE 4 (1): QUALITY CONTROL TESTS SHOULD BE MET BY VARIOUS FORMULATIONS ACCORDING TO OFFICIAL INDIAN AND BRITISH PHARMACOPOEIAS

S. No	Formulation	Indian Pharmacopoeia [13, 14]	British Pharmacopoeia [15]
1.	Tablets	Uniformity of container contents, Uniformity of weight, Uniformity of content, Content of active ingredients, Disintegration, Uniformity of dispersion for Dispersible tablets.	Uniformity of dosage units, Uniformity of mass, Uniformity of content, Dissolution, Disintegration, Uniformity of dispersion for Dispersible tablets.
2.	Injections	Uniformity of content, Pyrogen test, Sterility test, Particulate matter, Extractable volume.	Uniformity of dosage units, Uniformity of content, Pyrogen test, Sterility test, Particulate contamination.
3.	Pessaries/suppositories	Uniformity of container contents, Uniformity of weight, Uniformity of content, Disintegration.	Uniformity of dosage units, Uniformity of mass, Uniformity of content, Dissolution, Disintegration.
4.	Capsules	Uniformity of weight, Uniformity of content, Content of active ingredients, Disintegration.	Uniformity of dosage units, Uniformity of mass, Uniformity of content, Dissolution, Disintegration, Content of active ingredients.
5.	Aerosols	Content of active ingredients, Pressure test, Leak test, Particle size, No. of deliveries per container.	No. of deliveries per inhaler, Fine particle dose, Uniformity of delivered dose.
6.	Ointments	Uniformity of weight, Sterility.	Sterility.
7.	Creams	Uniformity of weight, Sterility.	Sterility.
8.	Gels	Uniformity of weight, Sterility.	Sterility.
9.	Pastes	Uniformity of weight, Sterility.	Sterility.
10.	Poultices	Uniformity of weight, Sterility.	Sterility.
11.	Eye drops	Uniformity of volume, Sterility, Particle size.	Sterility, Deliverable volume, Particle size.
12.	Eye ointment	Uniformity of weight, Sterility, Particle size.	Sterility, Deliverable mass, Particle size.
13.	I.V. Infusions	Pyrogen test, Sterility test, Particulate matter.	Pyrogen test, Sterility test, Particulate contamination.
14.	Nasal drops, sprays, powder	Uniformity of weight, Uniformity of content.	Uniformity of dosage units, Uniformity of mass, Sterility, Uniformity of content.
15.	Oral powders for solution, syrup, drops, suspension, etc.	Uniformity of weight, Uniformity of content.	Uniformity of dosage units, Uniformity of mass, Uniformity of content, Uniformity of mass of deliver doses from multi dose container.

Table 4 (2):

S. No	Formulation	Indian Pharmacopoeia [13, 14]	British Pharmacopoeia [15]
16.	Powders for injections/infusions	Uniformity of content, Sterility test, Particulate matter, Uniformity of weight, Clarity of solution.	Uniformity of dosage units, Uniformity of content, Uniformity of mass, Sterility test, Bacterial endotoxin, Particulate contamination.
17. 18. 19. 20. 21. 22. 23. 24.	Oral liquids: Syrups, Suspensions, Emulsions, Drops, Solutions, Mixtures, Linctuses, Elixirs.	Uniformity of weight or volume, Uniformity of content.	Uniformity of dosage units, Uniformity of mass, Uniformity of content, Uniformity of mass of deliver doses from multi dose container, Dose and uniformity of dose of oral drops.

25.	Ear drops or preparations	Uniformity of volume, Sterility, Particle size.	Uniformity of dosage units, Uniformity of content, Uniformity of mass, Sterility.
26.	Granules		Uniformity of dosage units, Uniformity of mass, Uniformity of content, Dissolution (for coated granules), Uniformity of delivered dose.
27.	Effervescent granules		Disintegration.
28.	Rectal capsules	Uniformity of container contents, Uniformity of weight, Uniformity of content, Disintegration.	Uniformity of dosage units, Uniformity of mass, Uniformity of content, Dissolution, Disintegration.
29.	Powders for inhalations	Uniformity of delivered dose, No. of deliveries per container, Uniformity of content, Microbial contamination.	Uniformity of dosage units, Uniformity of mass, Uniformity of content
30.	Lotions		Uniformity of mass, Uniformity of content.

RESULTS AND DISCUSSION: In order to make easy for a pharmaceutical industry, to establish a production unit for the manufacturing of various pharmaceutical formulations, we had tried to give an ideal integrated industrial process layout design, integrated quality control layout design for the production and quality control facility for various pharmaceutical formulations (product mix). The resultant integrated process layout design which was meeting the requirements for the production of formulations considered was shown in **Fig. 1**.

The above integrated layout was developed based on the sequence of steps involved in the production of various formulations. This ideal design shows the effective material movement through the production unit starting from receiving raw material, its storage in primary quarantine area, where approval of raw material allow the movement of raw material to dispensing area. From dispensing area the material will move based on the formulation to be manufactured, whether sterilized or non-sterilized. After that formulation moves to packing unit and to integrated quality control unit where its quality approval will allow its entry into final storage and distribution into market.

To check and assure the quality of final formulation from an integrated production unit, there is a need to develop an integrated quality control unit to regulate the entry of finished products into market. The resultant integrated quality control layout design meeting the requirements of entire method B was shown in **Fig. 2**.

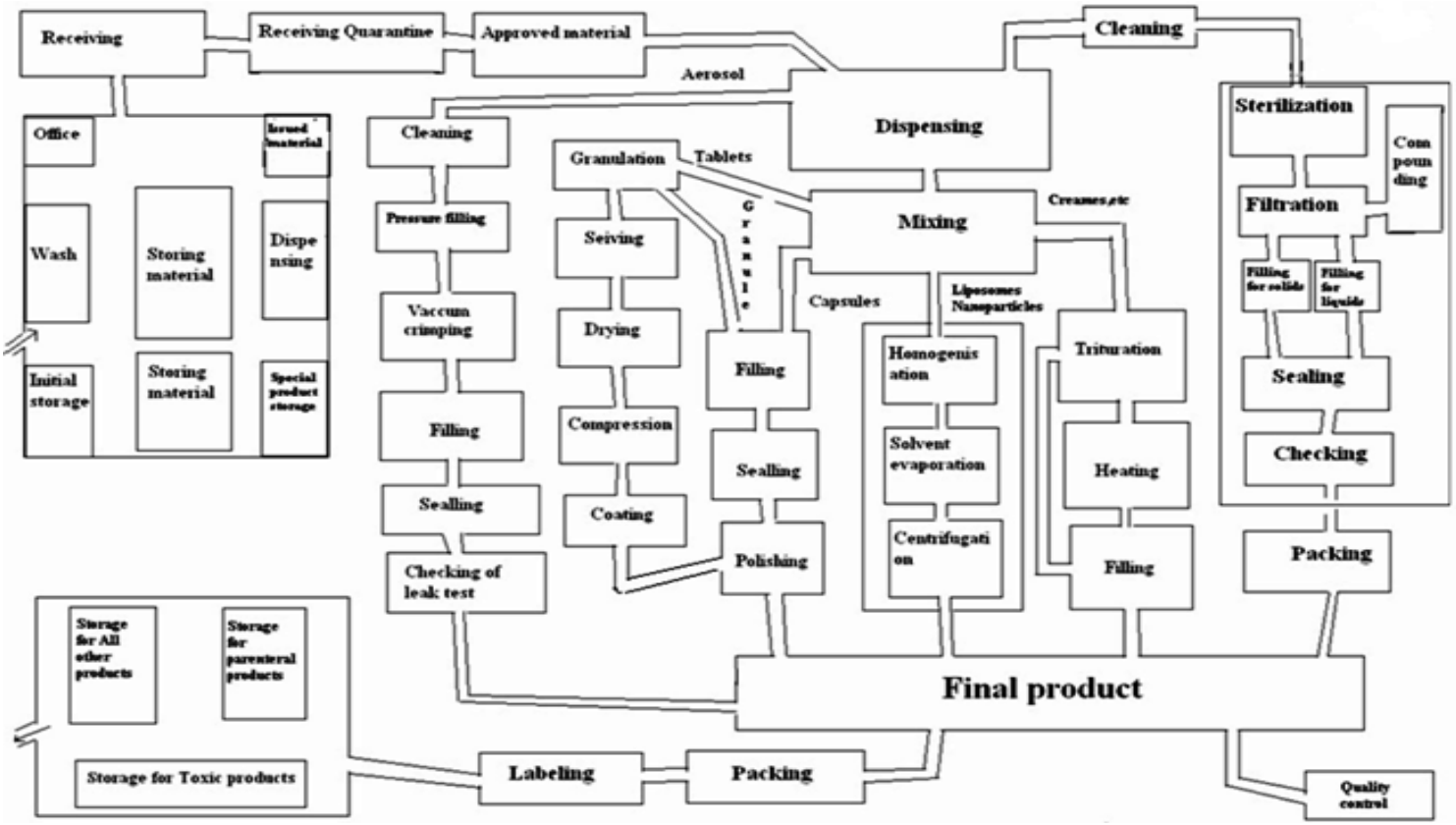


FIG. 1: THE INTEGRATED PRODUCTION PROCESS LAYOUT DESIGN SHOWING THE EFFECTIVE MOVEMENT OF PERSONNEL AND MATERIAL THROUGH THE SINGLE PRODUCTION UNIT FOR MANUFACTURING OF VARIOUS TYPES OF FORMULATIONS

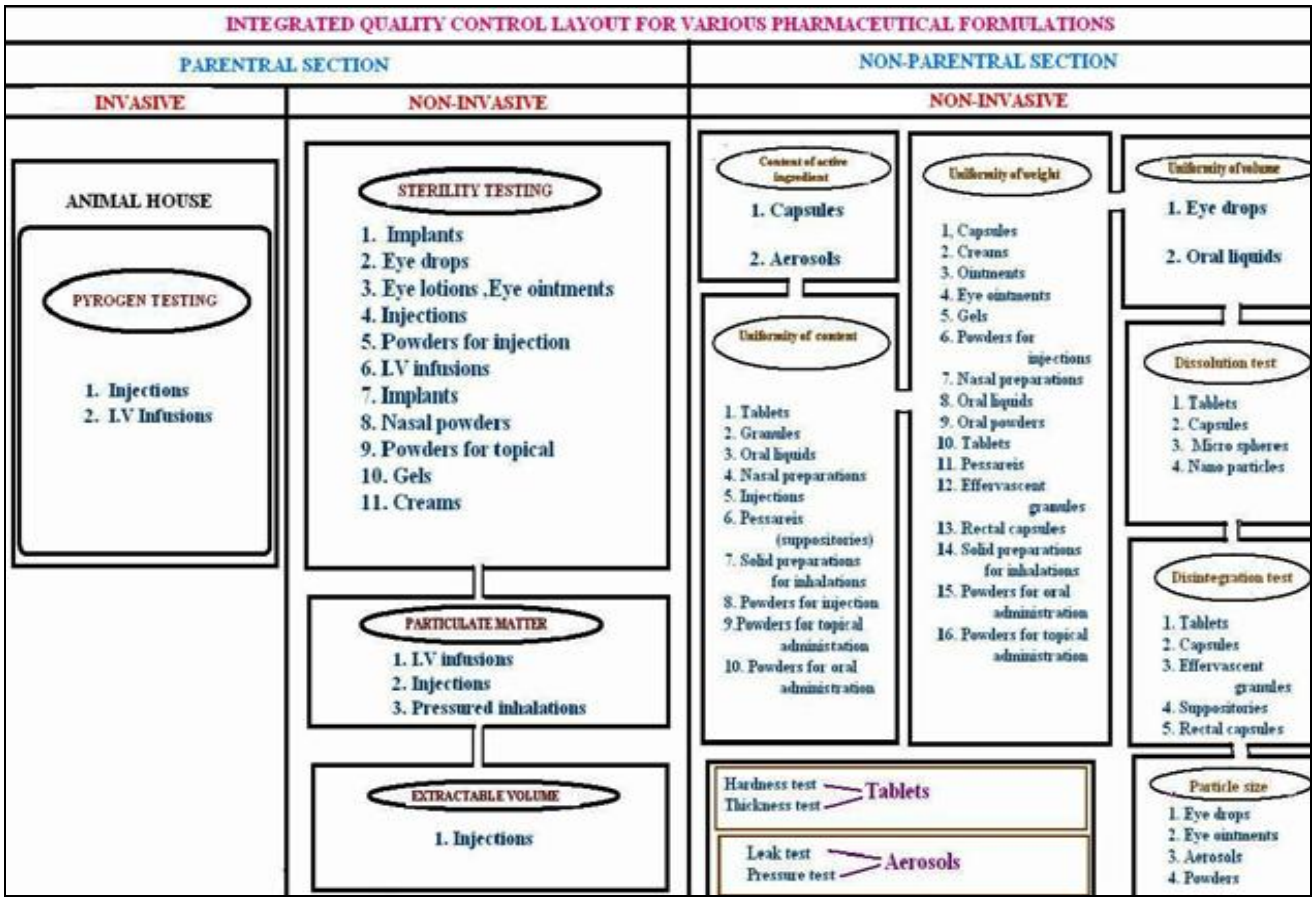


FIG. 2: THE INTEGRATED QUALITY CONTROL LAYOUT DESIGN REPRESENTING THE FACILITY FOR CHECKING THE QUALITY OF VARIOUS FORMULATIONS MANUFACTURED THROUGH THE INTEGRATED PRODUCTION UNIT

Both these integrated production process layout design and integrated quality control design ultimately helps the manufacturer to release different types of formulations of one active ingredient or more active ingredients into market at a time, can sustain in the market for longer period in the competitive world.

CONCLUSION: The current trend of pharmaceutical marketing has changed. Marketing doesn't limit to any small area. For rapid development in the information age, the globe becomes single market with ever increase grade in export and import of pharmaceuticals. So, finally we conclude that the adoption of cGMP & ICH guide lines for manufacturing and universal standards for marketing and sale of products with involvement of economics, it is necessary for the manufacturer to shift from a single line production layout to multi-product production (integrated) layout to sustain in the market for longer period in the market and there was a need to execute and validate the proposed layouts for use.

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