

Presentation on
“Optimization of organic reactions
and processes”

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Optimization of Organic Reactions and Processes:

1. Introduction
2. Approaches for selection of appropriate synthetic and scale up routes
3. Choice of raw materials, reagents etc
4. Effect of process variables on yield and quality of product
5. Types Of Health Hazards In API Manufacturing
6. Work up & product isolation
7. Planning for scale up
8. Design of environment friendly processes
9. Effluent minimization and control
10. Types of health hazards in API manufacturing unit and their prevention.
11. Material Safety Data Sheet (MSDS)

Approaches for selection of appropriate synthetic and scale up routes

Route Selection

A) Expedient routes:

Characteristics of Expedient Routes

- Familiarity
- Technical Feasibility
- Availability of Suitable Equipment

B)(Cost-effective)Optimal routes

Characteristics of (Cost-effective)Optimal routes:

- Technical Feasibility
- Availability of Suitable Equipment
- Availability of Inexpensive Reagents and Starting Materials

- ❖ Convergent Synthesis
- ❖ Using Telescopic Work-up
- ❖ Minimizing Impact from Protecting Groups
- ❖ Use of Enzymatic transformations
- ❖ Minimized Number of Steps
- ❖ Avoiding Adjusting Oxidation States
- ❖ Rework for Final Product and Intermediates
- ❖ Minimized Environmental Impact

Choice of raw material

Choice of solvent

Reagent selection

Characteristics of Ideal Reagents

Specific for the desired synthetic transformation

Non toxic to operators and analysts

Poses no chemical reaction hazard to personnel

Inexpensive

Readily available

Consistent quality from batch to batch

Readily generated and used if not stable

Handled without attention to special conditions, e.g., stable to the moisture and oxygen in air

Readily transferred into reactors

Chosen to facilitate the work up and efficient isolation of pure product

Produces non toxic by products

Catalytic reagents should readily recovered and reused

Requires no specialized equipments or facilities

Has desired solubility for reaction and work up

❖ Effect of process variables on yield and quality of product

❖ Process variables

- Choice of reagents, starting materials, and solvents
- Employ inert conditions if needed
- Change starting materials and solvents
- Select reaction temperature
- Select the duration and temperature of an addition
- Select reaction pressure
- Adjust stirring

❖ Types Of Health Hazards In API Manufacturing–

Any chemical that may produce acute or chronic health effects in exposed employee

- Carcinogens
- Toxic or highly toxic agents
- Reproductive toxins
- Irritants
- Corrosives
- Sensitizers
- Chemicals which irritate or damage pulmonary tissue
- Hepatotoxins
- Nephrotoxins
- Neurotoxins
- Agents which act on the hematopoietic system
- Agents which damage the lungs, skin, eyes, or mucous membranes

❑ **Threshold Limit Values**

(TLVs) are the concentrations of airborne substances to which it is believed that people can be exposed daily without adverse health effects.

❑ **Categories of TLVs:**

TLV-Time-Weighted Average (TLV-TWA):

average exposure on the basis of 8 hours a day ,40-hour week work schedule.

TLV-Short-Term Exposure Limit(TLV-STEL):

Spot exposure for a duration of 15-minute, that cannot be repeated more than 4 times per day with atleast 60 min between exposure periods.

TLV-Ceiling limit(TLV-C):

absolute exposure limit that should not be exceeded at any time.

Green Chemistry

Green Chemistry is the utilization of a set of principles that reduces or eliminates the use or generation of hazardous substances in the design, manufacture and application of chemical products.

E = MASS OF WASTE

MASS OF PRODUCT

Green Chemistry Is About:

- Waste Minimization
- Use of Catalysts in place of Reagents
- Using Non-Toxic Reagents
- Use of Renewable Resources

❖ **The principle by US Scientist Mr. Paul Anastas are :**

- Waste Prevention
- Atom Economy or efficiency
- Use of Less Hazardous Chemicals
- Designing Safer products
- Safer Solvents and Auxiliaries
- Use of Renewable Feedstocks/raw material
- Reduce Derivatives
- use of Catalyst rather than reagent
- Design environmental degradable pdts
- Pollution Prevention using analytical method
- Use of Safer Chemistry for Accident Prevention

WORK-UP AND PRODUCT ISOLATION

❖ Work -up

Series of treatment required to purify and isolate the product of chemical reaction.

❖ The purposes of work-up

- Quenching
- Cooling
- Removal of solids and solvents
- Separation of reaction mixture
- Purification
- Safety of personnel

Aspects of Work-ups

- Quenching.
- Extraction
- Activated Carbon Treatment
- Filtration
- Concentrating Solutions and Solvent Displacement
- Deionization and Removing Metals

Tools For Purifying The Product

- Purification by Column chromatography
- Purification by Crystallization
- Purification by Reslurrying

PLANNING FOR SCALE-UP

The process of transferring the results of Rand D obtain on lab scale to production scale.

1) Anticipating Scale-up Problems

- Time is money
- safety of personal during process
- parameter like temp,pressure etc. changes during scale up
- type of reaction involved i.e exothermic/endothermic
- issue of mixing and type of agitater used for agitation

2) Scale up Considerations

Identify the Goal for Scale-up

identify quality and quantity to be provided to customer

Identify Critical Processing Steps

PH ,Temp,addition of reagent,end point of rx

Define Equipment limitation

use of multipurpose equipment

Prepare Contingency Plan for Rx

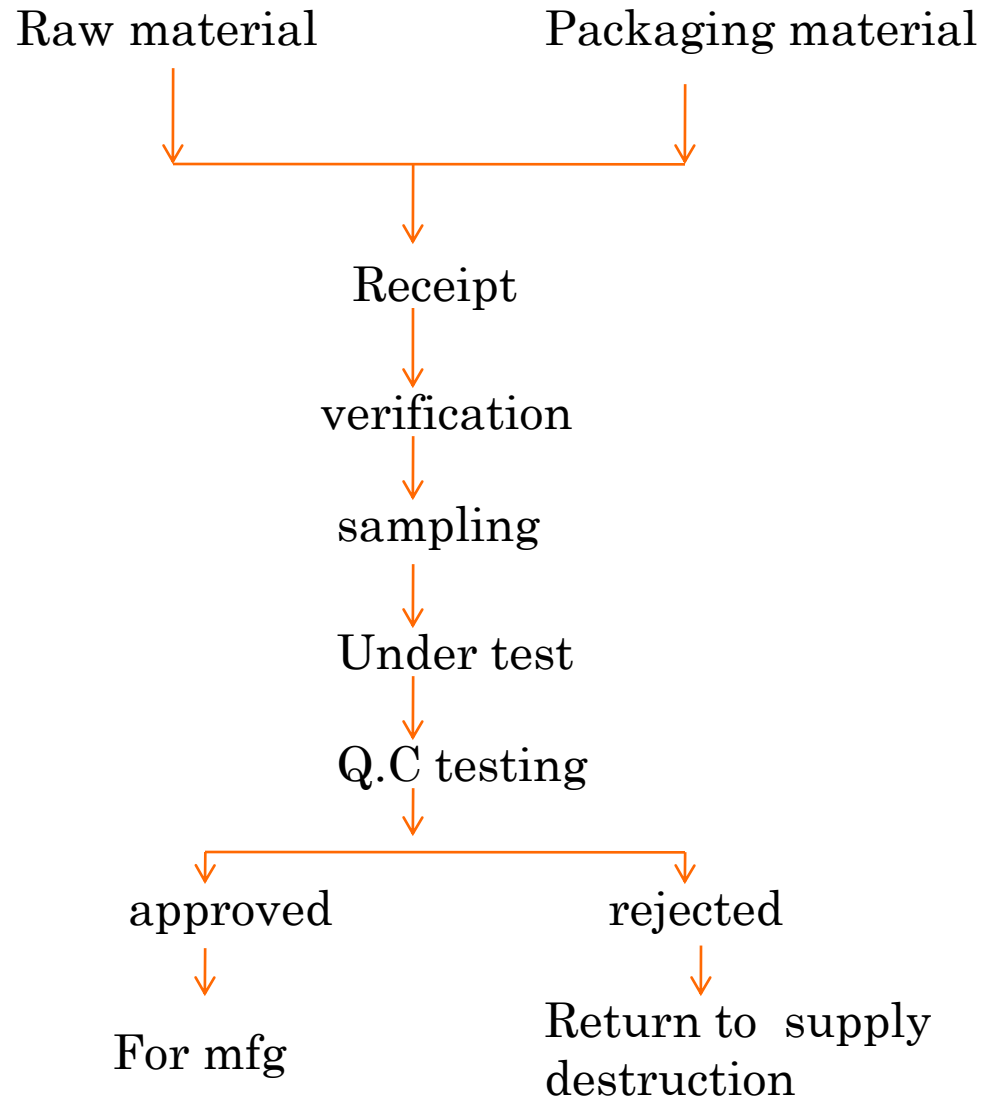
Quality control in process analysis as an aid to optimization

Used to verify that all stages of processing have been completed as expected, including

- To check completion of rx by HPLC,IR .
- Conducting reactions/extractions at the desired pH
- Complete displacement of a solvent by a higher-boiling solvent (for higher yield)
- Thorough washing of a filter cake
- Complete drying of product

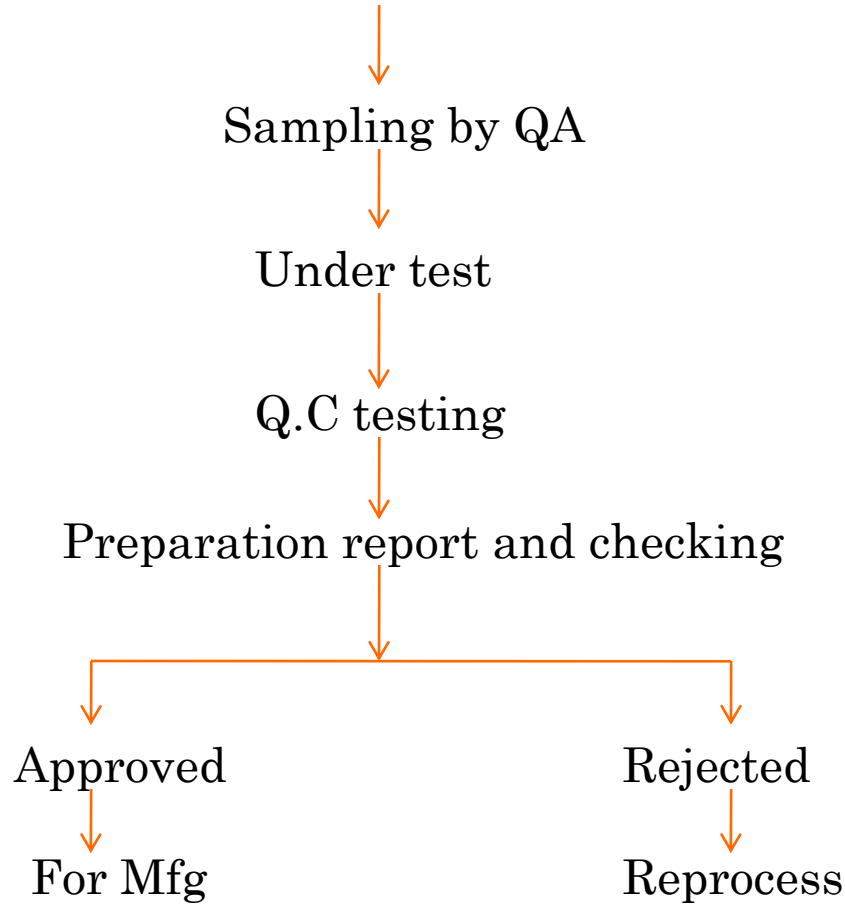
Quality control For API ,Finished Products and in process control

API inspection



❖ Finished Product Inspection

Completion of batch of finished pdt



In-Process Checks

Received inprocess requisition
along with sample



Testing as per requisition



Results conveyed to production

❖ Analytical Methods

HPLC-UV

Refractive Index

Gas Chrom.

TLC

Material Safety Data Sheets

It is a document that contains information on the potential hazards (health, fire, reactivity and environment) and how to work safely with chemical products.

- Provides basic information on a material or chemical product
- Describes the properties and potential hazards of the material
- Essential starting point for the development of a complete health and safety program for the material
- MSDSs are prepared by the manufacturer or supplier of the material

The information on MSDSs is organized into **16 sections as per ANSI (American National Standard Institute)**

1. Product and Company Identification
2. Hazards Identification
3. Composition, Information on Ingredients
4. First Aid Measures
5. Fire Fighting Measures
6. Accidental Release Measures
7. Handling And Storage
8. Exposure Controls, Personal Protection
9. Physical and Chemical Properties
10. Stability And Reactivity
11. Toxicological Information
12. Ecological Information
13. Disposal Considerations
14. Transport Information
15. Regulatory Information
16. Other Information