scale-up and the pilot-plant should have practical experience in pilot-plant operations. The level of education and type of education should be matched within the group because they have to understand each other perspective. The group should have personnel from different disciplines like engineering, economics, management, production, etc. The scientists with experience in pilot-plant production as well as actual production area should be preferred. The number of personnel required depends upon the number of products being supported and the level of support.

2.1.3 Space Requirements

There are four types of space requirements of a pilot-plant

i. Administrative and information processing
ii. Physical testing area
iii. Standard pilot-plant equipment floor space
iv. Storage area

Administrative and Information Processing

i. Adequate space should be there.
ii. Scientist and technicians should have adequate office and desk space.
iii. There should be proper facilities so that scientists and technicians can do proper documentation of their activities and observation.
iv. It should be near the work area but away from undue distraction.

Physical Testing Area

i. The space of physical testing area should be adequate so that analysis and physical testing of samples can be done. It helps in early detection of a production error.
ii. There should be permanent benchtop space for testing equipment (for physical testing) balances, viscometer, pH meter, etc.

Standard Pilot-Plant Equipment Floor Space

i. The equipment should be in a variety of sizes so as to enable the production of a product in a different capacity.
ii. There should be discrete pilot-plant space where the equipment need for manufacturing of all type of dosage forms/formulations can be kept.
iii. There should be space for the cleaning of equipment.
iv. The equipment should be portable so that it can be used when and wherever possible. This will also help in the storage of equipment in a small storeroom.
v. The production equipment should be of intermediate-size, as well as full-scale production sized so that the effect of scale-up of research formulations and the process can be evaluated.

Storage Area

i. There should be two separate areas—one for active ingredients and another one for excipients so as to avoid intermixing.
ii. Different areas should be provided for in-process materials, products from pilot-plant, and materials from scale-up batches.
iii. There should also be the availability of a storage area for packing material.

Fig. 7.2: The connection of regulatory affairs department with other departments in company

7.2 HISTORICAL OVERVIEW OF REGULATORY AFFAIRS

The quality assurance and regulation of medicines evolved gradually over time. Many unfortunate incidents have catalysed the development of regulations and guidelines of assuring quality, safety and efficacy of medicines. In 1947, in United States over 100 died due to sulphanilamide elixir. This event led to the introduction of Federal Food and Cosmetics Act for new drugs in 1948. In 1956, the introduction of Thalidomide (a drug prescribed to pregnant women for morning sickness) in 46 different countries resulted in an estimated 10000 babies born with phocomelia (Deformities related to limbs). This event results in reshaping of the whole regulatory system. Due to these types of incidents at different stage regulatory bodies introduce new laws and guidelines which make norms related to drug approval or site approval stricter than before. Due to more guidelines and laws, the need for regulatory affairs has been felt. It led to the emergence of regulatory affairs as a profession (Table 7.1)

Table 7.1: Chronological evolution of regulatory affairs

Sr. no.	Year	Content
1.	1540	In England the manufacturers of medicines were subjected to supervision under an act known as Apothecaries Wares Drugs and Stuffs Act.
2.	1581	The first pharmacopoeia is known as Spanish pharmacopoeia
3.	1618	The London pharmacopoeia
4.	1938	Introduction of Federal Food, Drugs and Cosmetics Act
5.	1940 and 1945	Drugs and Cosmetics Act 1940 and Rules 1945
6.	1962	Drug Amendment Act of 1962 was passed by FDA which for the first time demanded that: 1. A new drug should be proven to be effective and safe 2. All manufacturing sites are required to comply with CGMP
7.	1963	Establishment of a committee on safety of drugs

Contd.

Updating the changes: Guidelines related to the drug regulation keep on changing as per the requirements and become stricter. It is the responsibility of regulatory affairs professionals to remain updated with the changes and ensure the compliance of the company's business with these changes.

Assisting product launching: Various activities related to product launching like reviewing advertising material, presenting the product, marketing strategies for product, etc are assisted by regulatory affairs professionals so that to ensure compliance with rules and guidelines.

Reviewing of documents: There are many documents which need to be submitted with the drug approval application. The regulatory authority mentioned specific format for these documents in their regulatory guidelines. Regulatory affairs professionals review these documents to ensure that the documents are the same as expected by the regulatory authority.

Liaisoning between authorities and companies: This is the most important and critical responsibility of regulatory affairs professionals. He is the presenter of the company in front of government authority. Any loophole in the preparation of regulatory affairs professionals cost a huge to the company. Regulatory affairs professionals have to maintain the balance between expectations of government authorities and profit of the company through his strategic solutions.

Miscellaneous: It is the responsibility of regulatory affairs professionals to regulate and control any activity which directly or indirectly affects the drug development process, drug approval process, or drug monitoring process.

PRACTICE QUESTIONS

Long Answer Type Questions

1. What is regulatory affairs? Explain the evolution of regulatory affairs.
2. How does government regulatory authority regulate the pharmaceutical products in a country? Explain regulatory affairs of different countries.
3. What are the responsibilities of regulatory affairs department in a company? How regulatory affairs department of a company related with other departments of the company?

Short Answer Type Questions

1. How does regulatory affairs department of the company work as a bridge between the company and the government?
2. Why regulatory affairs department is essential for the company?
3. Explain the role of regulatory affairs department of the company.
4. Explain the responsibilities of regulatory affairs professionals.

Objective Type Questions

1. All the applications for getting a pharmaceutical product approved for entering into the market have been prepared by:

a. Regulatory affairs department
b. Manufacturing department
c. Accounts department
d. None of the above

iv. Inactive drug (pro-drug) to an active metabolite (pharmacological activation). For example, phenacetin to paracetamol.
v. Active drug to an equally active metabolite (no change in pharmacological activity). For example, digitoxin to digoxin.
vi. Active drug to an active metabolite which is having different pharmacological activity (change in pharmacological activity). For example, iproniazid to isoniazid.

Sites of Drug Metabolism

The main and major site of drug metabolism is liver. Other sites of biotransformation because a variety of metabolising enzymes are present in Liver. If metabolism occurs outside the liver or in organs other than the liver, then it is known as extra-hepatic metabolism. Secondary organs are kidney, lungs, testes, skin, intestines. Some drugs also metabolised without enzymes. It is known as non-enzymatic metabolism.

Advantages of Drug Metabolism

i. It is necessary for the termination of drug action. Therefore, decrease toxicity.
ii. It also reduced lipophilicity.
iii. It increases renal excretion.

There are two phases of drug metabolism:

Phase I: Non-synthetic/functionalization

In this phase, the metabolite may be active or inactive.

The phase I reactions are oxidation, reduction, hydrolysis, cyclization, decyclization.

Phase II: Synthetic/conjugation

In this phase, the metabolite is generally inactive.

The phase II reactions are glucuronide conjugation, acetylation, methylation, sulphate conjugation, glycine conjugation, glutathione conjugation, ribonucleotide synthesis.

Inhibition of Drug Metabolism (Fig 8.5)

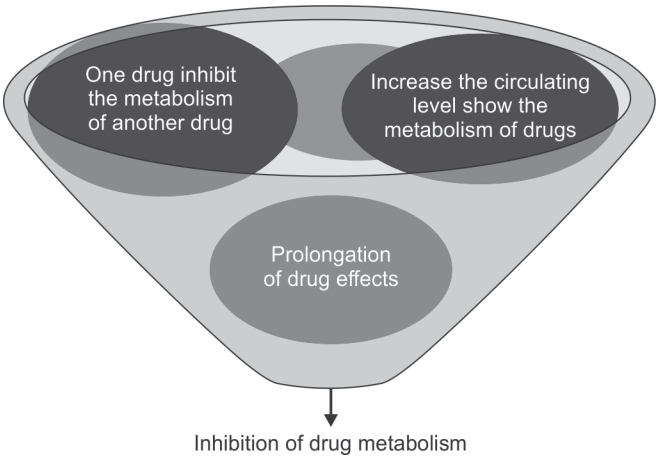

Fig. 8.5: Methods of inhibition of drug metabolism