Skill India
कौशल भारत-कुशल भारत

सत्यमेव जयते
GOVERNMENT OF INDIA
MINISTRY OF SKILL DEVELOPMENT
& ENTREPRENEURSHIP

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National
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LSSSDC™

Participant Handbook

Sector
Life Sciences

Sub-Sector
Pharmaceutical

Occupation
Quality

Reference ID: **LFS/Q1301, Version 1.0**
NSQF Level 5

Quality Control Chemist

> Skilling is building a better India.
> If we have to move India towards development then Skill Development should be our mission.

Shri Narendra Modi
Prime Minister of India

Certificate

COMPLIANCE TO QUALIFICATION PACK – NATIONAL OCCUPATIONAL STANDARDS

is hereby issued by the

LIFE SCIENCES SECTOR SKILL DEVELOPMENT COUNCIL

for

SKILLING CONTENT : PARTICIPANT HANDBOOK

Complying to National Occupational Standards of
Job Role/ Qualification Pack: '**Quality Control Chemist-Life Sciences**'
QP No. '**LFS/ Q1301, NSQF Level 5**'

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Authorized Signatory
(Life Sciences Sector Skill Development Council)

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About this book

This Participant Handbook is designed to enable training for the Qualification Pack(QP) of Quality Control Chemist (LFS/Q1301). Each National Occupational (NOS) given below is covered across Unit/s.

1. LFS/N0301 Perform routine analysis in lab while ensuring compliance with Good Manufacturing Practices(GMP) and Good Laboratory Practices (GLP)
2. LFS/N0101 Maintain a healthy, safe and secure working environment in the life sciences facility
3. LFS/N0302 Coordinate with Supervisors and colleagues within and outside the department
4. LFS/N0103 To ensure cleanliness in the work area
5. LFS/N0314 To carry out reporting and documentation to meet quality standards
6. LFS/N0320 To carry out quality checks in the quality control process

Key Learning Objectives for the specific NOS mark the beginning of the Unit/s for that NOS. The symbols used in this book are described below.

Symbols Used

Key Learning Outcomes

The key learning outcomes are listed at the beginning of each module. These outline the focus areas that the learners will cover in every module.

Tips

Wherever possible, tips are included in every module. They provide additional insight to learners on a particular topic being discussed.

Steps

These provide step-by-step instructions for a specific process.

Notes

Notes at the end of each module is a space for learners to list down their key points related to the topic.

Summarize

These provide the summary or the takeaways of the unit.

Unit Objectives

These are listed at the beginning of each unit under every module. They highlight the focus areas that the learners will cover in every unit.

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1. Orientation

Bridge Module

Key Learning Outcomes

At the end of this module, you will be able to:

1. Identify brief outline of Life Sciences industry and its sub-sectors
2. Gain knowledge about Regulatory Authorities and Government policies, rules and regulations and their impact on manufacturing in Life Sciences industry in India and emerging markets
3. Know the standards for manufacturing in Life Sciences (cGMP and ISO)
4. Acquire knowledge about the organization structure in Life Sciences industry (Large / Medium / Small Enterprises)
5. Discuss on typical manufacturing function in a Life Sciences organization
6. Learn about the role of a Quality Control Chemist in Life Sciences industry

Unit 1.1 Life Sciences Industry and Drug Regulatory Authorities for Life Sciences Sector

Unit Objectives

At the end of this unit, you will be able to:

1. Explain the brief outline of Life Sciences industry and its sub-sectors
2. Gain knowledge about Regulatory Authorities and follow the rules and regulations as you will understand their impact on manufacturing in Life Sciences industry in India

1.1.1 Introduction of Life Sciences Sector

The Indian Life Sciences industry currently tops the chart amongst the Indian industries. There is a huge range of science based industries with capacity of expanding in drug manufacture and technology sector. With recent advances in scientific knowledge and technological breakthrough discoveries, Life Sciences industry has gained the central platform with global giants and industry experts getting involved in research and development of new products.

Life Sciences being a diverse and vibrant global industry encompasses a wide range of activities. The activities range from drug discovery, research & development and manufacture of therapeutics, medical devices, and diagnostics and platform technologies. It also includes the specialist suppliers of products and services necessary for the functioning of various organizations related to Life Sciences. The increasingly ageing global population and their demand for improved longevity offers a very strong growth potential to Life Sciences industry.

The life sciences industry in India is huge and includes pharmaceutical companies, biopharmaceutical and contract research organization (CROs) with the support of specialized suppliers and organization. The pharmaceutical industry develops, produces, and markets drugs for use as medications.

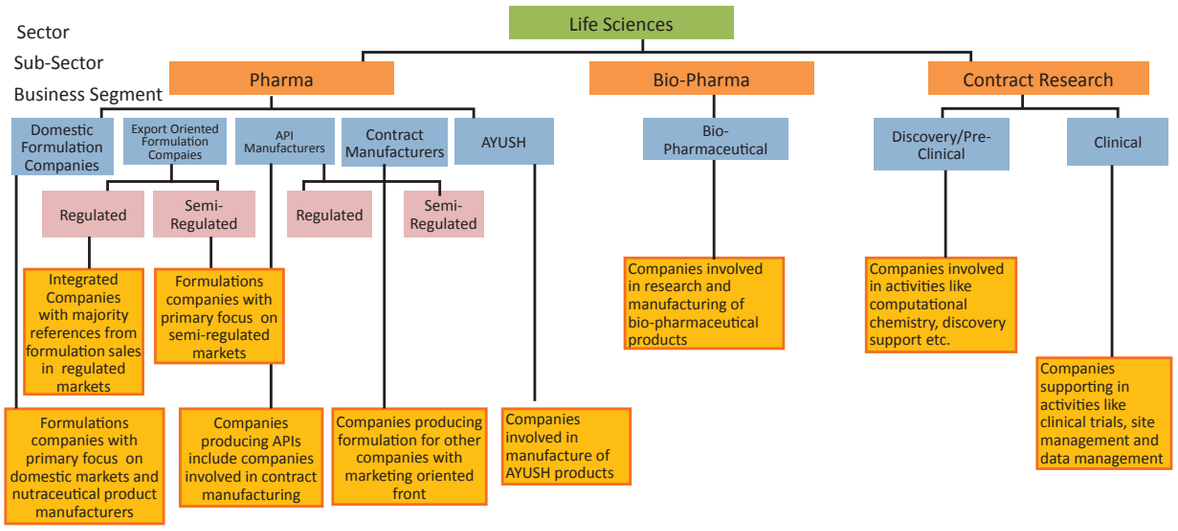

Fig 1.1.1: Life Sciences Sector

1.1.2 Sub-Sectors in Life Sciences

The Life Sciences industry in India is diverse and encompasses pharmaceutical companies, biopharmaceutical companies and contract research organisations (CROs) along with specialist suppliers and support organisations. We will now have a look at the overview of subsector in the Life Sciences Sector.

1.1.1.1 Pharmaceuticals

The pharmaceutical industry designs, develops, produces, and markets drugs for use as medications. There are many business verticals in pharmaceuticals Sub sector.

Fig 1.1.2: Medicines as Dosage Form

Domestic Formulation companies: Formulation is the process that combines different chemical substances including the active drug in order to produce a final medicinal product. Tablets, capsules, liquid form, lyophilized, etc. are a few different forms of Pharmaceutical Formulations. A large number of companies are involved in processing and supplying of different types of pharmaceutical medicines across the domestic sector. Even the nutraceutical formulation companies are part of this segment.

Fig 1.1.3: A Domestic Formulation Unit in India

Export Oriented Formulation companies: These integrated companies are engaged in exporting formulation to other parts of the globe. The global trade liberalisation and capacity building by Indian companies have enables India to export to a large number of markets and earn substantial revenue. These export oriented formulation companies target both regulated and semi-regulated markets. There has been a current benefaction in the healthcare sector in which the Indian generics have provided aide in fighting AIDS and are being recognized worldwide.

Fig 1.1.4: An export oriented Formulation Unit in India

API manufacturers: Companies producing Active Pharmaceutical Ingredients (APIs) includes companies involved in contract manufacturing. API is manufactured from raw materials through both chemical and physical means. Synthesis of any APIs might need multi-step complex chemistry utilizing a range of processing technologies. This may depend on the complexity of the molecule required. A few names to mention include Dr Reddy's, Teva Active Pharmaceutical Ingredients (TAPI), Aurobindo Pharma, Cadila Pharma.

Fig 1.1.5: API Manufacturing Unit in India

Contract manufacturing of formulations: These companies produce formulations for other companies with a marketing front-end. Contract manufacturing involves production of goods by firm, which can be The contract manufacturers render such services to various firms purely based on their own setup or by the consumers preferences, designs , formulas and specifications. Services offered by such companies include pre-formulation, formulation development, stability studies, method development, pre-clinical and Phase I clinical trial materials, late-stage clinical trial materials, formal stability, scale-up, registration batches and commercial production. Some leading names in this area include Akums, Wockhardt, Dishman Pharma etc.

Fig 1.1.6: Contract Manufacturing Formulation Plant in India

AYUSH formulation manufacturers: These companies are involved in developing, producing and supplying of different types of pharmaceutical medicines for Ayuveda, Yunani, Siddha and Homeopathy healthcare practices across the domestic and global sector.

Fig 1.1.7: Ayurveda Formulation Manufacturing Plant in India

1.1.1.2 Biopharmaceuticals

Biopharmaceutical business is engaged in discovering, developing and delivering innovative medicines to patients with serious diseases.

Fig 1.1.8: Polio Vaccine Manufacturing

Biopharmaceuticals are medical medication created victimization biotechnology.

Biologics is composed of a mixture of sugars, proteins, or Nucleic acids or is also living cells or tissues. They're isolated from Natural sources—human, animal, or organism. Some leading Companies operating during this space embrace Biocon, bodily fluid Institute of India, nostrum Biotec, Piramal care, GlaxoSmithKline etc.

1.1.1.3 Contract Research

A Contract Research Organization (CRO) role in the industry is to provide clinical trials and support to the pharmaceutical, biotechnology, and medical devices industries. These organizations are hired for specific expertise on contract basis in the form of outsourced research services.

- Discovery / Pre-clinical are those companies which are involved in activities like computational chemistry and discovery support. To name a few companies are Syngene, Jubilant Biosys, GVK Bio.
- Clinical Research companies support in activities such as clinical trials, site management, data-management. Some well-known Clinical Research Organisations in the Pharma and Biotech industry include Clingene, Quintiles, Lambda, Veeda Clinical Research, Parexcel.

1.1.3 Drug Regulatory Authorities for Life Sciences Sector

Life sciences domain cater to lives of humans, hence they come under rigorous regulatory laws. The Regulatory Affairs departments of life-science companies ensure that the company is complying with all the applicable regulations for the product discovered, produced and supplied by that company.

The regulatory bodies of India and various major countries are listed below for reference.

Country	Regulatory Agency
India	• Central Drugs Standard Control Organization
United States of America	• FDA • Center for Drug Evaluation and Research (CDER)
European Union	• European Medicines Agency
Canada	• Health Canada • Health Products and Food Branch (HPFB) • Therapeutic Products Directorate (TPD)
Australia	• Therapeutics Goods Administration(TGA)
UK	• Medicines and Healthcare products Regulatory Agency

Fig 1.1.9: Table-Various Regulatory Agencies

As a future professional of life sciences industry you are recommended to visit the websites of such foreign regulatory agencies to know more.

1.1.3.1 Central Drugs Standard Control Organization

Fig 1.1.10: FDA Bhavan, Headquarter of CDSCO

Medicines in India are regulated by Central Drugs Standard Control Organization (CDSCO), under Ministry of Health and Family Welfare, Headed by Directorate General of Health Services. CDSCO regulates the Pharmaceutical Products through DCGI - Drugs Controller General of India at Chair.

Pharmaceutical products are regulated under the Drugs & Cosmetics Act, 1940, to ensure drugs manufactured, imported, sold and distributed are safe and efficacious.

The Central Drug Standards and Control Organization (CDSCO), which is under the aegis of the Ministry of Health and Family Welfare prescribes standards and measures for:

- Ensuring the safety, efficacy and quality of drugs, cosmetics, diagnostics and devices in the country
- Regulates the market authorization of new drugs and clinical trials standards
- Supervises drug imports and approves licences to manufacture the above mentioned products

The main aspects of pharmaceutical and biopharma regulation are divided between the three ministries:

- The Ministry of Health and Family Welfare examines pharmaceutical issues within the larger context of public health
- The Ministry of Chemicals and Fertilizers focuses on industrial policy
- The Ministry of AYUSH focuses on industrial policy for AYUSH segment
- Department of Biotechnology under Ministry of Science and Technology focuses on industrial policy for Biopharma segment

However, some other ministries also play a role in the regulation process such as the Ministry of Environment and Forests, Ministry of Finance, Ministry of Commerce and Industry.

The process for drug approval entails the coordination of different departments, in addition to the DCGI, depending on whether the application in question is for a biological drug or one based on recombinant DNA technology.

- The Department of Industrial Policy and Promotion and Directorate General of Foreign Trade, both under the aegis of Ministry of Commerce and Industry, the Ministry of Chemicals and Fertilizers, Ministry of AYUSH and Department of Biotechnology govern the issues related to industrial policy such as the regulation of patents, drug exports and government support to the industry.
- The Central Drug Controller, Ministry of Health and Family Welfare, Department of Biotechnology, Ministry of Science and Technology (DST) and Department of Environment, Ministry of Environment and Forests regulate licencing and quality control issues and market authorization.
- State drug controllers have the authority to issue licences for the manufacture of approved drugs and monitor quality control, along with the Central Drug Standards Control Organization (CDSCO).

In India, drug manufacturing, quality and marketing is regulated in accordance with the Drugs and Cosmetics Act of 1940 and Rules 1945 which have witnessed several amendments over the last few decades. The Drugs Controller General of India (DCGI), who heads the Central Drugs Standards Control Organization (CDSCO), assumes responsibility for the amendments to the Acts and Rules.

Other major related Acts and Rules include:

- The Pharmacy Act of 1948
- The Drugs and Magic Remedies Act of 1954
- Drug Prices Control Order (DPCO) 1995

Some of the important schedules of the Drugs and Cosmetic Acts include:

- Schedule D: deals with exemption in drug imports
- Schedule M: deals with Good Manufacturing Practices involving premises and plants
- Schedule Y: specifies guidelines for clinical trials, import and manufacture of new drugs

Practical

Do an online search for Regulatory bodies given in fig. 1.1.9 and identify:

1. Common rules and regulations from them for Pharma and biopharma Manufacturing
2. Country Specific Common rules and regulations from them for Pharma and biopharma Manufacturing

Summarize

- The life sciences industry in India includes pharmaceutical companies, biopharmaceutical and contract research organization (CROs) with the support of specialized suppliers and organization.
- Medicines in India are regulated by Central Drugs Standard Control Organization (CDSCO), under Ministry of Health and Family Welfare
- The Central Drug Controller, Ministry of Health and Family Welfare, Department of Biotechnology, Ministry of Science and Technology (DST) and Department of Environment, Ministry of Environment and Forests regulate licencing and quality control issues and market authorization.
- State drug controllers have the authority to issue licences for the manufacture of approved drugs and monitor quality control, along with the Central Drug Standards Control Organization (CDSCO).
- Schedule D of Drug and Cosmetics Act deals with exemption in drug imports
- Schedule M of Drug and Cosmetics Act deals with Good Manufacturing Practices involving premises and plants
- Schedule Y of Drug and Cosmetics Act specifies guidelines for clinical trials, import and manufacture of new drugs

Exercise

1. How many sub sectors are included in Life Sciences Sector?

   (a) 4 (b) 6 (c) 3 (d) 4

2. What is the full name of Pharma Regulatory authority for India

   (a) Central Drug Substance Control Organization

   (b) Central Drug Standards Control Organization

   (c) Council for Drug Supplier and Cosmetic Organization

   (d) Central Drug Standards Certification Organization

3. Which Schedule of Drug and Cosmetic Act specifies the guidelines for Good Manufacturing Practices involving premises and plants for Pharma and Bio Pharma Manufacturing in India

   (a) Schedule Y

   (b) Schedule M

   (c) Schedule D

   (d) Schedule U

Unit 1.2 Standards for Manufacturing in Life Sciences

Unit Objectives

At the end of this unit, you will be able to:

1. Explain the Good Manufacturing Practices and their importance
2. Explain the Good Laboratory Practices and their importance
3. Gain knowledge about Pharmacopeia and use pharmacopeia and read monograph

1.2.1 Introduction of Life Sciences Manufacturing Standards

Drug manufacturing companies follow an international set of guidelines, 'Good Manufacturing Practices (GMP) for production of medicines and vaccines in order to ensure the manufacturing of quality products. In recent years, more than 100 countries adopt and follow GMP protocols either in the form of regulations (Japan, Korea and United States), or Directives (European Union) or Guides (United Kingdom) or Codes (Australia).

1.2.1.1 Good Manufacturing Practices

The objective of Good Manufacturing Practices is to minimize risks with reference to the manufacturing, packaging, testing, labelling, distributing and importing of drugs, cosmetics, medical devices, blood and blood products, food items etc. These protocols are largely concerned with parameters such as drug quality, safety, efficacy and potency. GMP applies to both Active Pharmaceutical Ingredients (APIs) and Finished Pharmaceutical Products (FPPs).

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 product manufacturing that cannot be eliminated through testing the final product.

The main risks are: unexpected contamination of products, causing damage to health or even death; incorrect labels on containers, which could mean that patients receive the wrong medicine; insufficient or too much active ingredient, resulting in ineffective treatment or adverse effects.

GMP covers all aspects of production; from the starting materials, premises and equipment to the training and personal hygiene of staff. Detailed, written procedures are essential for each process that could affect the quality of the finished product. There must be systems to provide documented proof that correct procedures are consistently followed at each step in the manufacturing process - every time a product is made.

In 1975, World Health Organization GMP guidelines were instituted to assist regulatory authorities in different countries to ensure consistency in quality, safety and efficacy standards while importing and exporting drugs and related products.

Many countries have formulated their own requirements for GMP based on WHO GMP. Others have harmonized their requirements, for example in the Association of South-East Asian Nations (ASEAN), in the European Union and through the Pharmaceutical Inspection Convention. India is one of the signatories to the WHO certification scheme.

In India a WHO-GMP certification, with its validity for two-years, may be granted both by CDSCO and state drug regulatory authorities (mostly called State FDAs) only after a thorough inspection of the manufacturing premises.

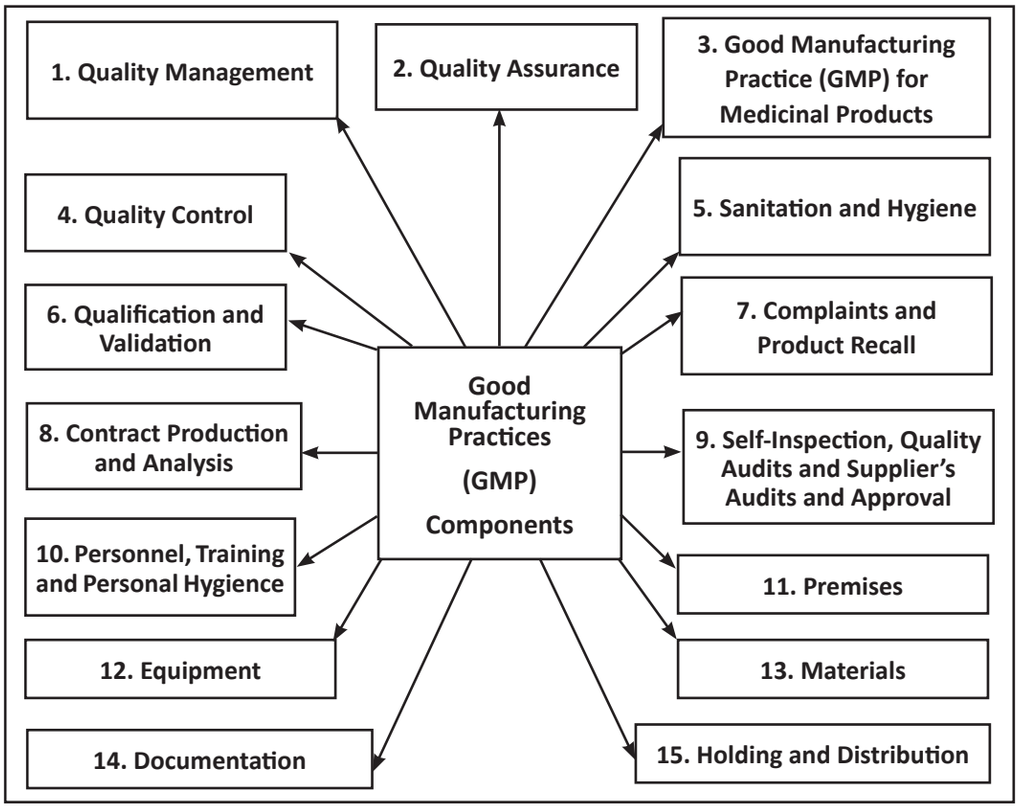

Fig 1.2.1: GMP Components

Good manufacturing practice guidelines follow a few basic principles:

- Pharmaceutical manufacturing facilities must maintain a clean and hygienic manufacturing area.
- Controlled environmental conditions in order to prevent cross contamination of food or drug product from adulterants that may render the product unsafe for human consumption.
- Manufacturing processes are clearly defined and controlled.
- All critical processes are validated to ensure consistency and compliance with specifications.
- Manufacturing processes are controlled, and any changes to the process are evaluated.
- Changes that have an impact on the quality of the drug are validated as necessary.
- Instructions and procedures are written in clear and unambiguous language. (Good Documentation Practices)
- Operators are trained to carry out and document procedures.
- Records are made, manually or by instruments, during manufacture that demonstrate that all the steps required by the defined procedures and instructions were in fact taken and that the quantity and quality of the food or drug was as expected.
- Deviations are investigated and documented.

- Records of manufacture (including distribution) that enable the complete history of a batch to be traced are retained in a comprehensible and accessible form.
- The distribution of the food or drugs minimizes any risk to their quality.
- A system is available for recalling any batch from sale or supply.
- Complaints about marketed products are examined, the causes of quality defects are investigated, and appropriate measures are taken with respect to the defective products and to prevent recurrence.

1.2.1.2 Schedule M Compliance for Indian Manufacturer

The manufacturing of medicinal products/ vaccines (drugs) in India is controlled under the Drugs and Cosmetics Rules (1945, last amended in 2005), which states that the holder of the license to manufacture drugs has to comply with the requirements of GMP as laid down in Schedule M. Schedule M is a part of the Drugs and Cosmetics Rules and embodies the Indian GMP regulations, which are based on the 1982 version of WHO GMP guidelines.

It is mandatory for Pharmaceutical units in India to follow the requirements specified under the upgraded Schedule 'M' for GMP from July 1, 2005. Schedule M classifies the various statutory requirements mandatory for drugs, medical devices and other categories of products as per the current Good Manufacturing Practices (cGMP). Schedule M protocols have been revised to harmonize it along the lines of WHO and US-FDA protocols. These revised protocols include detailed specifications on infrastructure and premises, environmental safety and health measures, production and operation controls, quality control and assurance and stability and validation studies.

Practical

Do an online search for Draft Pharma Policy of India and identify

1. Proposed changes in GMP rules

1.2.1.3 ISO Standards applicable to Life Sciences Sector

The three ISO documentary standards that is particularly relevant to the life science industry:

- ISO 17025:2005: This standard sets out general requirements for ensuring the processes for making measurements are of high quality. This leads to accurate and precise readings (Clause 4) and the general guidelines for ensuring the proper training of people taking measurements (Clause 5). This standard does not dictate acceptable tolerances, but rather helps labs create quality processes. This is done by highlighting important factors for making quality measurements, and for training people to take quality measurements.
- ISO 15189:2012: This standard translates ISO 17025:2005 into a language, which is more specific for medical testing laboratories. It helps to ensure processes for quality measurements and training in these critical applications.
- ISO 15195: This standard translates ISO 17025 into a language specific for medical reference labs. These are for labs that conduct the longer, more complex and accurate tests that are of the highest metrological order and provide traceability to the best available standards.