HELIS Academy GMP Course: Level I

Duration

5 days

Profession

Operational starters

Short description

The production of medicines is a profession with its own challenges. Medicines must meet high standards before they can be administered to patients. This means, among other things, that medicines are manufactured in a very clean environment where strict quality controls are in place. The guidelines for the production of medicines have been laid down by the EU as Good Manufacturing Practice (GMP).

This course covers the essential aspects of (bio)pharmaceutical manufacturing. Through lectures, practical lessons, workshops and guided tours, you will get a complete picture of, and good insight into all things related to GMP. Biotech Training Facility has a fully equipped pharmaceutical plant, which means that you will be able to instantly apply the acquired knowledge, in a realistic working environment.

When you are interested in a job that involves production or packaging this course provides a good basis for a job in the biotech or pharmaceutical industry.

Objectives

Through lectures, practical lessons, workshops and guided tours you will get a complete picture of and a good insight into the topics below:

Introduction to GMP

You will first become acquainted with the principles of Good Manufacturing Practice (GMP). This knowledge will be immediately put into practice in order to gain a good insight into the role and importance of GMP.

Contamination control

A GMP production takes place in a controlled environment aimed at preventing contamination of the product. Production personnel work in cleanrooms and wear protective clothing. There are many kinds of measures with regard to the design of production areas, the use of materials and staff behavior.

Manufacturing

You will learn about and experience the different phases in biopharmaceutical production, including fermentation, chromatography and aseptic techniques. Again, the training starts with a theoretical part and continues with practical assignments to gain experience in a real-life production environment.

Target Group

This GMP-course is suitable for anyone who wants to know more about the pharmaceutical production industry and wants to work in a production environment.

The course is divided into 2 different levels of knowledge and experience in order to ensure that the content is optimally suited to the target group.

The Level I GMP course is aimed at starters in the Health & Life Science industry. You have no background in Life Sciences? So far, you have only worked in other sectors? Is the world of medicine completely new to you? Then this course is the most suited for you. In this course you will be introduced to the industry and production of medicines. The course is a first step in preparing you for a job in production, packaging or quality control of medicines.

Program

Day 1 - Introduction in GMP

- Introduction in GMP and data integrity
- Production process at a glance (pharma and biotech)
- Building a structure based on a work instruction
- Finding errors in a document

Day 2 - Cleanroom behavior and cleaning

- Pharmaceutical microbiology
- Infrastructure
- Tour of the cleanrooms and utilities
- Personnel
- VR gowning
- Contamination control
- Cleaning

Day 3 - Fermentation and purification

- Upstream and downstream processing – an overview
- Fermentation process
- Purification process

Day 4 - Final product manufacturing

- TSB media filling by doing a hand fill and by working with a filling line
- Visual inspection

Day 5 - Raw materials, labeling and packaging

- Working according to a batch record and SOPs
- cleanESCAPEroom
- Company visit

Early 2021, the program was adjusted to limit the number of contact moments. The theoretical part was offered as E-learning, followed by a live online Q&A session with our GMP trainer. Additionally a live Fermentation Webinar was offered and and a full day of practice at the facility.

Adjusted program May 2021

E-learning

Duration (Hr)	Title	Content
1,50	**Introduction GMP and data integrity**	GMP law and guidelines
		History of GMP
		Data recording rules
		ALCOA
1,00	**Production process at a glance Pharma/Biotech** *Theory parallel demo of small scale manufacturing steps*	Bulk Drug Substance manufacturing
		Drug Product Manufacturing
		Batch records
		Testing / Quality control
		Labeling and packaging
1,00	**Find the errors in a document** *Workshop*	Find the mistakes in a document
0,50	**Infrastructure** *Theory and videofragments*	Aim of cleanrooms
		Different classifications
		What is LAF?
		Airlocks
		Utilities, water and steam
0,50	**Personnel** *Theory and videofragments*	Microorganisms and humans
		Gowning
		Hygiene: what are the people in the video doing wrong?
		Behaviour: what are the people in the video doing wrong?
		Rules for working in the cleanroom
0,25	**Contamination control: cleaning** *video*	Cleaning and disinfection how to do it Cleaning equipment Cleaning the LAF hood
1,00	**Upstream and Downstream Processing in a nutshell** *Theory*	Overview
		Upstream processing: from cell bank to large culture
		Primary recovery: Centrifugation and filtration
		Chromatography
		UF/DF (TFF)
		Virus reduction

Webinar (live demo)

10:00 - 11:30	**Fermentation process (1)** *Theory + demo*	Aseptic handling
		Inocculation
		IPC's
11:30 - 13:30	**Q&A Session**	Live session with opportunity to seek clarification and to discuss the topics as studied in the e-learning program

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Practical day at Biotech Training Facility

Time	Titel	Content
08:45 - 08:55	**Welcome with coffee and tea**	
08:55 - 09:00	**Introduction and Corona safety regulations**	Welcome to BTF
		Health and Safety BTF
		Expectations
09:00 - 10:00	**Tour**	Tour cleanrooms
	Practice	
10:00 - 10:15	***Coffee/Tea break***	
10:15-11:30	**Aseptic Handling**	Practice aseptic techniques in a LAF hood
	Practice	
11:30-12:30	**Working according to a batch record and SOP's plus discuss conclusions afterwards** *Practice*	Parcours salt solution: following a batch record (making a salt solution) and filling in a batch record. Do's and don'ts.
12:30-13:00	***Lunch***	
13:00-15:00	**Water fill filling line**	Gowning
	Practice	Line clearance, Start EM: Active air sampling, setle
		Water Filling
		Routine interventions: such as topping up stoppers,
		Non-routine interventions: pick vials at the caroussel and
		End of fill and end EM
		Document all activities in a batch record
15:00-15:15	***Coffee/Tea break***	
15:15-16:45	**DSP**	Welding and aseptic connections
	Practice	Clarification
		TFF (UFDF)
16:45-17:00	**Close out**	

Trainers

Internal trainers Biotech Training Facility

Semih Ekimler
Nancy de Jong

External trainers

Jolanda Muurman

HELIS Academy GMP Course: Level II

Duration

10 days

Profession

Academic starters (BSc, MSc, PHD)

Short description

The production of medicines is a profession with its own challenges. Medicines must meet high standards before they can be administered to patients. This means, among other things, that medicines are manufactured in a very clean environment where strict quality controls are in place. The guidelines for the production of medicines have been laid down by the EU as Good Manufacturing Practice (GMP).

This course covers the essential aspects of (bio)pharmaceutical manufacturing. Through lectures, practical lessons, workshops and guided tours, you will get a complete picture of, and good insight into all things related to GMP. Biotech Training Facility has a fully equipped pharmaceutical plant, which means that you will be able to instantly apply the acquired knowledge, in a realistic working environment.

Whether you are interested in a job that involves the development of analytical methods, production, quality control, quality assurance or process development, this course provides a good basis for a job in the biotech or pharmaceutical industry.

Objectives

Through lectures, practical lessons, workshops and guided tours you will get a complete picture of and a good insight into the topics below.

Introduction to GMP

You will first become acquainted with the principles of Good Manufacturing Practice (GMP). This knowledge will be immediately put into practice in order to gain a good insight into the role and importance of GMP. (Please note, this module on the first day of the course will be given via eLearning, so not in our facility in Leiden).
Development process in biotech and the pharmaceutical industry: The different stages of the medicine development process are covered, for instance, the pre-clinical phase, which focuses on dangerous side effects (toxicity), and the various clinical phases in which the drug is tested on humans. The commercial production phase will also be discussed.

Quality Assurance

Quality must be monitored at every stage of the production process. Processes and equipment must be validated to ensure that everything is working as expected. All procedures and actions are documented. In the case of a deviation, the effects on the quality of the finished product must be examined. At the end of a production, all information is assessed. These tasks are the responsibility of the quality assurance department.

Contamination control

A GMP production takes place in a controlled environment aimed at preventing contamination of the product. Production personnel work in cleanrooms and wear protective clothing. There are many kinds of measures with regard to the design of production areas, the use of materials and staff behavior.

Manufacturing

You will learn about and experience the different phases in biopharmaceutical production, including fermentation, chromatography and aseptic techniques. Again, the training starts with a theoretical part and continues with practical assignments to gain experience in a real-life production environment.

Quality control

During and after the production of a medicine, quality controls are performed by taking samples and analyzing them using different analytical methods. It is examined whether the product meets all standards and whether there are no contaminants. The products and raw materials, among other things, are analyzed in this way. Samples are also taken from places in the production areas and from the hands of employees in order to detect the presence of microorganisms that could threaten the quality of the product.

Target group

This GMP-course is suitable for anyone who wants to know more about the pharmaceutical production industry and wants to work in a development department, production environment or in quality control.

The course is divided into 2 different levels of knowledge and experience in order to ensure that the content is optimally suited to the target group.

The Level II GMP course is aimed at graduates (BSc, MSc, PhD and postdoc), who have studied a subject or discipline in Life Sciences, but have no experience in the GMP production industry. With this course you will gain insight and experience in the pharmaceutical manufacturing industry. You could then qualify for jobs in production, quality control (QC), analytical method development, formulation development or quality assurance (QA).

Program

In the June 2021 version of the training, Module 1 was offered as E-learning. All other modules were offered at the facility.

Module 1 - Introduction and GMP

Time (Hr)	Title	Content
09:45-10:30	**1.1 Introduction GMP** *Theory*	GMP law and guidelines
		History of GMP
		GMP framework for the biopharmaceutical industry
		Quality systems
10:30-10:45	***Break***	
10:45-11:30	**1.2 Intro data integrity** *Theory*	GxP introduction
		ALCOA
		GDP
		Data recording rules
11:30-12:45	**1.3 Introduction GMP** *Workshop*	Some exercises
12:45-13:30	***Lunch***	
13:30-14:30	**1.4 Product development in Pharma/Biote** *Theory*	Product life cycle from research to development
		Quality throughout the product life cycle
		New developments such as personalized medicines
14:30-14:45	***Break***	
14:45-15:30	**Writing a QTPP** *Workshop*	Product against Alzheimer (see 1.3)

Module 2 - Quality Management Systems & Documentation

Time (Hr)	Title	Content
9:30 - 10:30	**2.1 Quality systems** *Theory*	ICH10 QMS
		Responsibilities
		Quality Manual
		Site Master File
		Overview main quality systems
10:30 - 10:45	***Break***	
10:45 - 11:45	**2.2 Quality Risk Management** *Theory*	ICH9
		How to make use of ICH Q9 in the different phases of the product life cycle?
		How to report risk assessments?
		FMEA
		Examples
11:45-12:45	**Quality Risk Management** *Workshop*	FMEA dissolve product, aseptic fill and labeling
12:45 - 13:30	***Lunch***	
13:30-14:30	**2.3 Good Documentation Practices** *Theory*	SOPs
		MBR
		Certificate of compliance
		Certificate of analysis
14:30-14:45	***Break***	
14:45-16:00	**Writing documents** *Workshop*	Writing an MBR
		Writing and following an SOP - work instruction welder

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Module 3 - Contamination control: Infrastructure - Personnel - Cleaning

Time (Hr)	Title	Content
9:30 - 10:15	**3.1 Pharmaceutical microbiology** *Theory*	incubate some micro-biological samples
		Bacteria
		Endotoxins
		Yeast
		Fungi
		Viruses
		Growth of mico-organisms
		Cleaning and disinfection
		Micro-organisms and pharmaceuticals
		Introduction in endotoxins
10:15 - 11:15	**3.2 Cleanrooms and utilities** *Theory*	Aim of cleanrooms
		Different classifications
		What is LAF?
		Airlocks
		Environmental Monitoring
		Utilities: water/steam
11:15 - 11:30	***Break***	
11:30-12:00	**3.3 Personnel** *Theory & practice*	Hygiene
		Behaviour
		Rules for working in the cleanroom
		Gowning: do it yourself (3 persons in classroom)
12:00-12:30	***Lunch***	
12:30-13:30	**Contamination control: Personnel** *Practice*	VR Video in classroom with questions Interactive gowning course
13:30-14:00	**3.4 Cleaning and disinfection** *Theory*	Cleaning and disinfection area's and equipment
		Cleaning and disinfection LAF hood
		Clean in Place (CIP)
		Product Change Over and Line clearance
14:00-14:15	***Break***	
14:15-16:00	**Contamination control** *Practice* *Group will be divided in 2*	Gowning in Pyjamas and class C/D gowns (Tyvek)
		Visit facility
		Building a set-up of a 1L bottle with tubing and air filter

Module 4 - Fermentation and aseptic techniques

Time (Hr)	Title	Content
9:30 - 10:30	**4.1 Aseptic handling*** *Theory*	Working in a class A LAF hood with a B background
		Welding and aseptic connections
		Cleanroom vs isolator
		Do's and don'ts aseptic handling
		Aseptic handling
10:30-10:45	***Break***	
10:45-12:15	**Aseptic techniques*** *Practice*	Practice aseptic techniques in a LAF hood
12:15-13:00	***Lunch***	
13:00-14:15	**4.2 Fermentation process*** *Theory*	Regulatory background
		Cell lines
		Cell and seed lot management
		Culturing
		Production from cell bank to large culture
		Primary recovery: Centrifugation and filtration
14:15-14:30	***Break***	
14:30-16:00	**Fermentation process*** *Practice - demo*	Bioreactor
		IPC's

* Group will be split in 2, i.e. 'Aseptic Techniques - practice' and Fermentation process - theory' is given in parallel

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Module 5 - Quality Management System: deviations and Change control

Time (Hr)	Title	Content
9:30 - 10:15	**5.1 Deviations** *Theory*	Introduction
		Root cause analysis
		Impact assessment
		Deviations procedure
		CAPA
10:15-10:30	***Break***	
10:30-11:30	**Deviations** *Workshop*	Case study, ie:
		- EM excursion in grade A
		- leakage in fermentation bag
11:30-12:15	**5.2 Change Control** *Theory*	What is change control?
		When do we follow the change control procedure?
		Why is change control relevant?
		Design a change control system?
		What are key aspects of change control?
12:15-13:00	***Lunch***	
13:00 - 14:30	**5.3 Cell therapy**	Cell therapy: an introduction

Module 6 - Raw materials and labeling and packaging

Time (Hr)	Title	Content
9:30 - 11:00 11:15 - 12:45	**6.1 Material flow** *Theory: groep 1* *Theory: groep 2*	The pharmaceutical chain
		Incoming goods and raw materials
		Incoming goods and GMP
		Risks in raw material management
		Incoming Goods Status
		Incoming Goods Flow
		Sampling and testing
		Qualification of suppliers
		Use of Goods in Production
11:00 - 11:15	***Break***	
11:15 - 12:45 9:30 - 11:00	**Materials** *Practice: groep 1* *Practice: groep 2*	parcours salt solution
12:45 - 13:30	***Lunch***	
13:30 - 14:30	**6.2 Packaging and distribution** *Theory*	Labeling & Packaging
		Packaging Process
		Specialty - Packaging of IMP
		GDP
		Transport and risks
		Transport validation
14:30-14:45	***Break***	
14:45-16:00	**6.3 Packaging materials** *workshop*	Case 1: Change a packaging article for a commercial product
		Case 2: Design a clinical trial label

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Module 7 - Validation

Time (Hr)	Title	Content
09:00-10:00	**7.1 Facility and equipment validation** *Theory*	V-model
		URS
		Risk analysis (FMEA and ISPE)
		IQ
		OQ
		PQ
		Traceability matrix
		Management of equipment
		Writing a protocol
10:00-10:15	***Break***	
10:15-11:30	**7.2 Process validation** *Theory*	Definitions and regulations
		Process validation: the principle
		General approach
		Different types of proces validation
		Specific validation for biotech production processes
		Clearance validations
		Cleaning validations
11:30-12:30	***Lunch***	
12:30 - 14:00	**Consultancy**	What is it like to work as a consultant in the Biotech
14:00 - 14:30	**Online presentatie LUMC**	What is it like to work at a 'bereidingsapotheek' of LUMC
14:30 - 15:00	**Company presentation Janssen**	What is it like to work at Janssen and what are the joboppurtunities

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Module 8 - Quality control

Time (Hr)	Title	Content
9:30 - 10:15	**8.1 Typical biotech test methods** *Theory*	ie: Host cell DNA Content Bioburden Viral safety testing SDS Page ELISA Total protein TCID50 Mycoplasma HCP
10:15 - 11:00	**8.2 Analytical methods** *Theory*	Development Validation Basics in tech transfer
11:00 - 11:15	***Break***	
11:15-12:00	**Validation** *Workshop*	Case study validation
12:00-12:45	***Lunch***	
12:45 - 13:30	**8.3 Additional testing for parenteral Drug** *Theory*	ie: Sterility Endotoxins UDU Potency Purity Impurities pH Osmolality
13:30-14:00	**8.4 Out Of Specifications** *Theory*	Documentation: Specifications valid vs invalid rsults OOS procedure
14:00-14:45	**8.5 Stability studies** *Theory*	Stability program for cold and Room Temperature products Shelf life setting
14:45-15:00	***Break***	
15:00-16:30	**Basic techniques** *Practice*	Pipetting practice

Module 9 - Downstream processing (DSP)

Time (Hr)	Title	Content
9:30 - 10:15	**9.1 Production process/impurity profile**	Production-the basics
		USP and DSP
	Theory	Basic process impurities
10:15 - 11:00	**9.2 DSP techniques**	Clarification / Centrifugation
	Theory	Chromatography
		UF/DF
		Virus Inactivation
		Miscellaneous
11:00 - 11:15	***Break***	
11:15 - 11:45	**9.3 Viral safety**	Risk Assessment
	Theory	Types of viruses
		Viral inactivation
		Viral removal
		Viral clearance studies/validation
11:45-12:30	**9.4 Critical aspects in production**	Development of IMP
	Theory	Regulations and Development Products
		Bill of testing
		Batch production records
12:30-13:15	***Lunch***	
	DSP	welding
13:15 - 14:15	*Practice: groep 1*	
14:30 - 15:30	*Practice: groep 2*	
14:15-14:30	***Break***	
14:30 - 15:30	**DSP**	Clarification
		Other parts'parcours
	Practice	TFF (UFDF)

Module 10 - Aseptic production practice

Time (Hr)	Title	Content
09:30 - 10:30	**Gowning**	Gowning A/B
Group 1 + 2	*Practice*	
10:30 - 11:30	**visual inspection and sterilisation demo**	Visual inspection
Group 1	*Practice*	Sterilisation demonstration
10:30 - 11:30	**Water fill on an automatic filling line**	filling water
Group 2	*Practice*	Routine interventions: refill stoppers and caps
		Non-routine interventions: caroussel vials, filling needle
		Close fill, end EM, line clearance
11:30 - 11:45	***Break***	
11:45-13:00	**Escape room**	Try to solve the mystery
Group 2	*Practice*	
11:45 - 13:00	**Water fill on an automatic filling line**	filling water
Group 1	*Practice*	Routine interventions: refill stoppers and caps
		Non-routine interventions: caroussel vials, filling needle
		Close fill, end EM, line clearance
13:00 - 13:45	***Lunch***	
13:45 - 15:00	**Escape room**	Try to solve the mystery
Group 1	*Practice*	
13:45 - 15:00	**visual inspection and sterilisation demo**	Visual inspection
Group 2	*Practice*	Sterilisation demonstration
15:00 - 15:15	***Close out***	

Trainers

Internal trainers Biotech Training Facility

Mohamed Akoudad
Semih Ekimler
Nancy de Jong
Ingrid van Klooster
Ronald Kompier

External trainers

Wilma Meijs
Jolanda Muurman
Frank Bakx (Gilson)

Guest speakers and company presentations

Dirk Jan Drooge (Halix)
Kirsten Schimmel (LUMC)