2024 Hands-On Training for mRNA Vaccine Manufacturing

organized by the Global Training Hub for Biomanufacturing (GTH-B) in the Republic of Korea, supported by the World Health Organization

Call for Applications

Application Deadline: August 23, 2024, 18:00 (KST)

I. Background

Low- and Middle-Income Countries (LMICs) face significant inequities in terms of access to vaccines and other biologics and are making efforts to establish biological manufacturing within their regions. Establishing such manufacturing capacity, through bilateral technology transfer or local R&D efforts, is often hindered by the lack of a trained workforce in biomanufacturing.

To address this gap and build biomanufacturing capacity in LMICs, the World Health Organization (WHO) and the Ministry of Health and Welfare (MoHW) of the Republic of Korea established the Global Training Hub for Biomanufacturing (GTH-B). The hub's mandate is to provide training in the manufacturing of high-quality vaccines and biologics in an industrial setting, aiming to resolve inequality in access to vaccines and biologics worldwide by expanding manufacturing capacity in LMICs.

There is an urgent need for developing countries to improve vaccine access by developing local biomanufacturing capabilities, which are hindered by a shortage of trained personnel. GTH-B is helping these countries by providing essential biomanufacturing training, aiming to expand the technical know-how and capability for sustainable vaccine R&D and manufacture in LMICs by facilitating vaccine manufacturing apprenticeships.

A crucial aspect of such training is the hands-on experience provided at a real biomanufacturing facility. The GTH-B will operate two batches of hands-on training utilizing public biomanufacturing facilities in the Republic of Korea. One is a 5–6-week program (including a pre-online training course) at the International Vaccine Institute (IVI) and the Korea Biopharmaceutical CMO Centre (K-Bio CMO), targeting 20 individuals and focusing on the upstream process in cell-based vaccine manufacturing. The other is a 7-week program (including a pre-online training course) at the Korean National Institute for Bioprocessing Research and Training (K-NIBRT) and the Hwasun site (K-VCAST and JBRC), targeting 20 individuals and focusing on mRNA vaccine manufacturing and regulatory affairs.

These programs not only offer practical training in biomanufacturing and analytical techniques but also prepare participants to meet industry demands. By enhancing the skills of the workforce, this initiative strengthens the healthcare infrastructure of LMICs, fostering self-reliance and contributing to a more equitable global healthcare system.

II. Training Overview

1. Training Objectives

The purpose of the Hands-on Training is to enhance the technical knowledge and capabilities of vaccine and biopharmaceutical manufacturers from LMICs in the processes of vaccine research, development, and manufacturing. The focus is on providing extensive hands-on training in industrial facilities, enabling participants to gain practical experience and a deeper understanding of the intricacies involved in vaccine production.

The training also supports participants in applying newly acquired skills to enhance vaccine production capabilities in their home institutions through strategic collaborations among local biomanufacturers, the Korean National Institute for Bioprocessing Research and Training (K-NIBRT), and the Hwasun site (K-VCAST and JBRC), thereby contributing to the ongoing enhancement of LMICs' biomanufacturing capability.

2. Training Schedule and Venues

	Didactic Training (Online)	Hands-on Training	
Period	October 14, 2024 – November 1, 2024 (3 Weeks)	November 11, 2024 – November 22, 2024 (2 Weeks)	November 25, 2024 – December 6, 2024 (2 Weeks)
Venue	Online	K-NIBRT Incheon, Republic of Korea	K-VCAST and JBRC Hwasun, Republic of Korea

- K-NIBRT: Korean National Institute for Bioprocessing Research and Training
- K-VCAST: Korean Vaccine Center for Assisting Safety and Technology
- JBRC: Jeonnam Bio Research Center (CDMO)

3. Training Method

The training program utilizes a blend of theoretical instruction through recorded online lectures and practical hands-on training, complemented by apprenticeships and mentorship programs. Key components include networking opportunities with international biomanufacturers. Direct experience at vaccine manufacturing facilities and regular evaluations ensure a comprehensive learning experience. As a follow-up of the online lectures, live online (real-time) Q&A sessions will be provided for interactions with lecturers.

III. Application Requirements and Selection Process

1. Eligibility Criteria

Applicants must meet the following qualifications to be considered eligible for the training:

- Be a citizen of, and resident in, an LMIC.
- Be employed by a company registered as a legal entity in an LMIC conducting activities in the scope of biomanufacturing.
- Hold a position in the company as a technician, engineer, scientist, or manager in biomanufacturing or a related field, with up to 6 years of experience.
- Have an educational background in life sciences.
- Have at least an intermediate level of proficiency in spoken and written English.
- Demonstrate in the application how the acquired knowledge, skills and competencies during the training will be applied after the training in the institution the participant is coming from.

2. Application Submission

All applications must be submitted online at the following link: https://ivionlinecampus.ivi.int/ by August 23, 2024, 18:00 Korea Standard Time (KST).

Applicants must provide the following information:

- Personal information including nationality, country of residence, passport number, name, date of birth, gender, contact details, and others.
- Information about the institution.
- Information about educational background.
- Information about work experience.
- Information about English proficiency.

Applicants must upload the following documents:

- A copy of their passport.
- A letter of endorsement: A letter from the Director of the applicant's institution confirming the applicant's capability to successfully undertake the training and certifying their current employment status. (A sample endorsement letter is available on the application page of the website.)

Applicants must demonstrate the following:

- A description of their current position and justification for their selection.
- A description of the relevance of the training to their professional project.
- A description of the knowledge and skills they wish to acquire during the training.
- A description of their institution's needs related to the training and the anticipated impact on their institution.
- A description of the plan to apply and share the acquired knowledge and skills after returning to their home institution upon completion of the training.

3. Selection Process

The selection process involves the following steps:

- Eligible applications will be reviewed by a selection committee composed of members recommended by the MoHW of the Republic of Korea and WHO.
- Once the selection process is completed, selected participants will be notified of the next steps and required information via email.
- Due to limited capacity, a maximum of 5 participants from each country will be selected. The decision will be made by the selection committee in collaboration with the home institution.
- Institutions involved solely in animal vaccine production must provide a letter to GTH-B stating their institutional plan to expand into human vaccine production if they wish to send participants for training.

Priority will be given to trainees with certificates from completing the following GTH-B training programs:

- Introductory Course for Biologics Development and Manufacturing
- Introductory Course for Standard Practice (GxP)

4. Equality, Diversity, and Inclusivity

The MoHW of the Republic of Korea and WHO are dedicated to promoting equality, diversity, and inclusivity in science. Women are particularly encouraged to apply, and all qualified applicants are welcomed regardless of sexual orientation, ethnicity, religious beliefs, cultural background, social status, or (dis)ability status.

IV. Financial Provisions

The course is offered free of charge to participants. Accommodation and breakfast will be provided during the course days and weekends. Lunch will be provided on weekdays only and is not included on weekends.

The cost of travel to/from Seoul, Republic of Korea will **NOT** be covered. Applicants must secure travel costs at their own expense. Selected applicants will be responsible for obtaining any necessary vaccinations and visas for travel.

V. Contact Information

For further questions related to this, please contact the course coordinator at K-NIBRT.

Name	**Position**	**Email Address**	**Phone**
Christine Kwak	Manager, International Training	hykwak@yonsei.ac.kr	+82-32-749-3283
Hyojin Lim	Manager, K-NIBRT Training	hj.lim@yonsei.ac.kr	+82-32-749-3265

An automatic email acknowledging receipt of the application will be sent from gthb.coordinator@ivi.int. This acknowledgment does not confirm that the application is eligible for review.

Appendix I. Tentative Training Agenda

1. Didactic Training (Online, 3 Weeks): 3 Modules including a 4-hour Q&A Session for Each Module

- Module 1: Biotechnology General (30 Lectures)

Module 1	Basics for Biopharmaceutical and Bioprocess
Day 1	Introduction to Biopharma Industry (1h)
	Biologics Regulation (2h) - Regulatory needs and related regulations - Definition, characteristics, and types of biopharmaceuticals - Biosafety introduction
	Cell and Enzyme (3h) - Microbial diversity - Biomolecules and nucleic acids - Function, kinetics, and immobilized system of enzyme
Day 2	Core Technologies of Therapeutics (3h) - Gene therapy/Cell therapy - Therapeutic antibody
	Production of Recombinant Proteins in Prokaryotic Hosts (3h) - Regulating transcription - Increasing protein stability and secretion - Facilitating protein purification
Day 3	Production of Recombinant Proteins in Eukaryotic Cells (3h) - Post-translational modification - Yeast expression system - Protein engineering
	Cell Growth (3h) - Quantifying cell growth, Quantification of product - Fermentation data - Continuous manufacturing
Day 4	How Vaccines Work (3h) - Principle of vaccination immunity - Classification of vaccine - Mechanism of vaccine
	Vaccine Registration and International Cooperation (3h) - Vaccine registration - International Cooperation
Day 5	GMP for Biopharmaceuticals (3h) - Introduction of GMP for biopharmaceuticals - GMP for manufacturing - GMP for quality: QA, QC

- Module 2: Bioprocess General (30 Lectures)

Module 2	Vaccine Manufacturing Process
Day 1	Bioprocessing Basics & Aseptic Processing (3h) - Aseptic process overview - FDA guide to aseptic processing - Aseptic Technique and HAI (Healthcare Associated Infections) - Preventing infections using aseptic technique - Aseptic field management
	Upstream Processing (3h) - Bioprocessing for biopharmaceutical manufacturing - Cell line generation - Upstream bioprocess

Day 2	Downstream Processing (3h) - Introduction of downstream processing - Harvest - Chromatography - Tangential flow filtration - Virus inactivation and virus clearance
	mRNA Medicines & LNP (3h) - mRNA Vaccine & carrier - mRNA-LNP formulation & production I - mRNA-LNP production II & Analysis
Day 3	Vaccine Manufacturing Process: DNA and mRNA (3h) - DNA vaccines - mRNA vaccines - Case study
	Formulation (Stability and Quality Control, Quality Issues for Advanced Products) (3h) - Backgrounds on dosage form and drug product - Formulations and stability with analytical tools - Quality of injectables – visible & subvisible particles
Day 4	Lyophilization (Freeze-drying, Unit Operation, Cycle Development, Understanding and Monitoring Process) (3h) - Process definition - Unit operations/Lyo-cycle and monitoring - Process understanding and quality
	Performance Qualification and Process Validation for Vaccine (3h) - Process qualification and process validation for vaccine - Process development for vaccine - What is QbD (Quality by Design)? - Applying quality by design to vaccines - Critical process parameters, Critical quality attributes
Day 5	Vaccine Manufacturing Process: Drug Product (DP) (Fill and Finish) (3h) - Compounding - Filling - Aseptic process simulation
	Recent Trends in Vaccine Research and Development (3h) - Vaccine paradigm shift after COVID-19 - Vaccine development: Korean perspective - Global perspectives on future vaccines

- Module 3: Introduction to Regulatory Affairs (30 Lectures)

Module 3	**Regulation of Biopharmaceuticals**
Day 1	Biopharmaceutical Regulatory Affairs (RA) in Korea (2h) - Role of Government agencies - Regulatory Affairs for Pharmaceuticals
	ICH Guidelines (4h) - Overview, Practice in Korea - Efficacy/Safety guidelines - Quality/Multidisciplinary guidelines - ICH M9: Biopharmaceutics Classification System-based biowaivers
Day 2	CMC (Chemistry, Manufacturing and Control) (4h) - Overview of drug development process - Understanding the importance of CMC - CMC readiness for IND and BLA (NDA) - Developing CMC strategy and management
	Pharmacopeial and International Collaboration (2h) - USP-NF Overview/ How to use USP-NF/ Standard setup and available resources/ Pharmacopeial and international collaboration

	- USP Biologics / mAb standards and resources / Vaccine
Day 3	Nonclinical Drug Development (4h) - New Drug Modality - Nonclinical Study - Nonclinical Pharmacology Study - Nonclinical Toxicology Study
	Accelerated Approval of COVID-19 Vaccine during the Pandemic (1h) - Clinical development of COVID-19 vaccine - Equitable access & broad distribution to the global - Korea examples
Day 4	Clinical Research Industry Trends and International Standards (4h) - Global and Korea Clinical Research Industry Trends - ICH GCP(E6) and Relevant Guidelines - Regulation & Guideline for Clinical Research in Korea - IND Submission & Approval Process in Korea
	Drug Reimbursement and Health Technology Assessment in Korea (3h) - National Health Insurance System/ Drug reimbursement in the NHIS - Health Technology Assessment in NHIS(1,2) - Post-listing policies/ Lessons from HTA in Korea
Day 5	The Korea Drug Approval-Patent Linkage System (3h) - Introduction to Korean Patent Law - The Korea Drug Approval-Patent Linkage(1,2)
	Post Marketing Surveillance of Pharmaceuticals (3h) - Pharmacovigilance and spontaneous adverse event reporting - Signal detection and case examples - Status of PV system in Asia-Pacific countries

2. Hands-on Training at K-NIBRT (2 Weeks): Basic Skill Development for mRNA Vaccine Bioprocess

- Week 1: Fermentation & Purification

Module 1	Fermentation
Day 1	Introduction to Gene Transformation (Chemical-transformation, Electro-transformation) Microbial Subculture (Liquid, Solid Media) Transformation (*E.coli* + Plasmid) Stock - Media Preparation
	Equipment Preparation (Reactor Assembly, Sensor Calibration) - Basic structure (P&ID)/Lab bioreactor operation (disassembly and assembly) - Process flow diagram (PFD)
Day 2	Microbiome Assessment - Gram staining/IMViC test Equipment Preparation - 5L lab reactor assembly, sensor calibration - 200ml seed media preparation inoculation
	Single Use Operation - Basic structure, operation practice - Welder, Sealer, SUB-Bag Leak Integrity
Day 3 – AM	Centrifuge (Lab-scale Centrifuge, Pilot-scale Centrifuge) - Cell disruption (homogenization) - Centrifuge operation (disassembly and assembly)

Module 2	**Purification**
Day 3 – PM	Tangential Flow Filtration (TFF) - Operation of Ultrafiltration/ Diafiltration
Day 4	Chromatography System - Separation technology for bioprocess - Introduction & operation of chromatography system (lab-scale)

	- Operation of the system (process-scale)
Day 5	Technical Background and Basic Protocols for plasmid DNA Purification - Plasmid isolation and purification/Quantification of plasmid DNA
	In Vitro Transcription - plasmid DNA linearization - Gel electrophoresis

- Week 2: Bioanalysis for Quality Control & Finalization (Fill & Finish)

Module 3	**Quality Control**
Day 1	Microbial Test 1 - Microbial contamination control - Microbial Enumeration test (Bioburden) - Microbial identification test
	Analytical Test 1 - UPLC, ultra-performance liquid chromatography
Day 2	Analytical Test 2 - Capillary electrophoresis
	Microbial Test 2 - Endotoxin test
Day 3 – AM	Pharmacopoeia - Introduction of Compendia Method - Gravimetric measurement/Volumetric measurement

Module 4	**Finalization**
Day 3 – PM	Aseptic Processing & Insoluble Particulate Matter - Restricted Access Barrier Systems (RABS) - insoluble particulate matter (Light obscuration)
Day 4	Formulation Process Development - Basal Buffer System - Buffer Exchange (SCC and Dialysis) - Zeta-potential of mRNA-LNP (Lipid Nano Particle)/Interaction parameter (kD value)
Day 5	mRNA-LNP Manufacturing - microfluidics mixing/Impingement Jets Mixing - Particle size and distribution using DLS
	mRNA-LNP Quality Evaluation - Encapsulation efficacy of mRNA using Ribogreen - Quantification of mRNA-LNP using NTA

3. Hands-on Training at K-VCAST (1 Week): Vaccine Safety Training

Day	**Method (Topic)**
Day 1	Introduction of K-VCAST - Introduction of K-VCAST and responsibility Site tour Overview of Vaccine Quality Control pH - Measurement the hydrogen-ion Insoluble Particulate Matter - Light obscuration method - Description and Insoluble Particles
Day 2	Introduction of MFDS - Role of MFDS Endotoxin Test - Chromogenic method
Day 3	Understanding of Pharmaceutical Affairs Law - Pharmaceutical affairs law - National validation system

	High Performance Liquid Chromatography (HPLC) - Phenoxyethanol Content test using HPLC
Day 4	Antigen Identification Test - Enzyme-linked immunosorbent method (ELISA)
Day 5	Sterility Test - Membrane filter method

4. Hands-on Training at JBRC (1 Week): mRNA Vaccine GMP Manufacturing

Module 1	**mRNA Vaccine GMP Manufacturing**
Day 1	Production& Sanitation - Introduction of GMP field tours - Introduction of Equipment of microbial fermentation lines - Room Cleaning, disinfection - Fumigation
Day 2	Utility - Introduction of Utility(AHU) - HEPA Filter Test / Practice
Day 3	Quality Environment - Introduction of Water for pharmaceutical use (PW, WFI, PS)
	Quality Environment - Introduction of Environment Monitoring
Day 4	Quality Control - Introduction to GMP warehouse - Warehousing procedures (Sampling, Attach Label, Recording)
	Quality Control - Gowning
Day 5	Quality Assurance - Introduction of GMP Documentation - Understanding of QMS (Deviation/Change/Investigation/CAPA)
	Quality Assurance - Introduction of Validation - Validation Practice

5. Site Tour (*Tentative*)

- Ministry of Food and Drug Safety (MFDS): Introduction to Korean Governance Structure for Regulatory Affairs
- Green Cross Company (GC): Introduction to mRNA Vaccine Manufacturing