2021 Quality Audit / Factory Inspection / Relevant Verification Records

Audit/Inspection/ Verification Date	Audit/Inspection/ Verification Department	Audit/Inspection/Verification Process, Key Observation Items	Audit/Inspection/ Verification Results
2021/04/07~ 2021/04/09	TFDA	Routine GMP/GDP Inspection for active pharmaceutical ingredients (APIs) and Biological medical product (injection fluids)	Extended GMP certification
2021/09/20~ 2021/09/28	U.S. FDA	Pre-License Inspection for active pharmaceutical ingredients (APIs)	Obtained GMP certification
2021/1~ 2021/12	Internal audits	A total of 12 internal audits were carried out in 2021	Completed all

GMP/GDP Quality Training at the Production Plant

Through providing annual training courses, we instill the philosophy of quality management into the day-to-day operations of all relevant personnel. In addition to internal training, PharmaEssentia also appoints colleagues to participate in external trainings sponsored by related domestic and foreign academics/associations, and hires senior foreign consultants to visit the factory every year to update the knowledge of GMP or laws and regulations.

Statistics on Good Manufacturing Practice for Medicinal Products (GMP) Training in 2021

Training topic	Sessions	Participants	Training hours
GMP training in 2021	10	789	7,890
Regulation, manufacturing or new employee quality-related GMP training	28	503	14,084
Prevention and correction training	68	928	31,552
External training	13	14	1,092
Total	119	2,234	54,618

3-4 Excellent Manufacturing and Production

Advanced and High Standard Plant Equipment

The three main facilities of PharmaEssentia Taichung Plant: Polyethylene Glycol (PEG) production factory, Drug Substance (DS) manufacturing plant, and sterile agent filling plant. Our Taichung Plant is the first biopharmaceutical plant in Taiwan to pass the EU's EMA inspection and obtain Good Manufacturing Practice (GMP) certification. The sterile agent filling plant also obtained GMP and GDP certification from TFDA in April 2020, and passed MFDS GMP audit in January 2021 and U.S. FDA plant audit in September 2021. In addition to external inspections, PharmaEssentia's Taichung Plant also completed 12 internal audits in 2021, with investment of approximately NT$20 million toward repair and maintenance as well as acquisition of new equipment to ensure the high quality of drug manufacturing process.

The U.S. FDA conducted on-site audit at Taichung Plant in 2021

Three Main Facilities of PharmaEssentia

PEG Production Factory

Sterile Agent Filling Plant

DS Manufacturing Plant

Passed EU EMA plant inspection

(certification extended)

Passed MFDS audit

(new)

Sterile Preparation Filling Plant passed TFDA plant audit

(certification extended)

Passed the U.S. FDA onsite audit

(new)

Manufacturing Process with International Standards

Our product, Ropeginterferon alfa-2b (P1101), is manufactured in four major steps. API is manufactured first, followed by the filling and packaging process. All steps strictly comply with GMP regulations and international standards of quality management and standard operating procedures.

1 Fermentation process and cellular treatme

- Manufacture interferon

Fermentation tank

2 Extraction and purification of Pro-IFN alfa-2b (P1040)

- Remove impurities through purification process

Purification system

3 PEG chemical modification

- Chemical reaction between PEG and interferon creates the intermediate product of Ropeginterferon alfa-2b (P1101)

PEG & PEGylation system

4 Purification of Ropeginterferon alfa-2b(P1101)

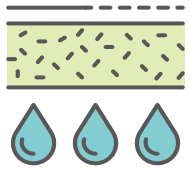
- Produce Ropeginterferon alfa-2b(P1101) API and enter into injection preparation and packaging process

Protein purification process

The Taichung plant's emergency response mechanism is implemented in accordance with the "Emergency Response Management Standards for Plant Facilities." When incidents that may cause harm to the factory due to natural disasters and equipment abnormalities occur, they can be handled correctly and effectively to ensure the normal operation of the equipment and all personnel can operate in a safe and secure working environment.

The Highest Quality Aseptic Filling and Packaging Process

After Ropeginterferon alfa-2b (P1101) goes through the aforementioned 4 steps, the filling and packaging operations are carried out based on market demand. The Company's injection filling and packaging operations can be divided into 3 stages: dispensing and sterile filtration, sterile filling, and labeling and packaging. As products that have not been fully sterilized could cause serious harm to patient health, we rigorously implement aseptic operations in our drug production processes.



1. Dispensing and aseptic filtration

The high-concentration API Ropeginterferon alfa-2b (P1101) is adjusted and diluted, and the sterile is filtered before filling

2. Aseptic filling

Filling with fully automatic prefilled syringe. Filled products are put into storage after performing 100% appearance inspections.

3. Labeling and packaging

Placing the label on the pre-filled syringe, and placing the relevant package inserts, plungers, finger flanges, and needles together into the box.

Improvement of the Next Generation Manufacturing Process

In addition to maintaining the process and product quality with high-quality equipment, professional personnel, internal and external inspections, and other mechanisms, we also continuously optimize and improve the process to reduce manufacturing process risks and improve its success rate.

Manufacturing Processes	Improvement Objectives	Results and Benefits
Fermentation	Increase yield of E. coli production.	Feeding into the fermentation tank after pre-cultivation increase the time efficiency by 23% and yield by around 5.2%.
Purification	Reduce the risk of process contamination.	Changed the process from "open operation" to "closed operation" to improve process stability and increase process success rate.

Outsourcing Manufacturing Management

PharmaEssentia's US injection filling CMO

Passed FDA inspection

Due to different market needs, on top of undertaking filling and packaging operations at our Taichung Aseptic Preparation Filling Plant, we also outsource the filling and packaging procedures to American and German CMO plants in order to supply to the local patients. To ensure that the operations performed at the outsourced production sites comply with the GMP specifications and PEC's standards, all CMO plants are verified by our suppliers. And they may only begin the outsourced filling and packaging operation after they have been determined to be qualified vendors by our QA department. Regarding CMO supplier management, in addition to the initial supplier evaluation mechanism, we also regularly monitor the service quality of such suppliers to maintain conformity to the highest quality requirements. Pyramid Laboratories Inc., a US injection filling CMO, has successfully passed the FDA inspection in early 2021 with no critical or major deficiency.