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Prequalification Unit Inspection Services
WHO PUBLIC INSPECTION REPORT
(WHOPIR)
Finished Pharmaceutical Product Manufacturer

Part 1	**General information**
Manufacturers details	
Name of manufacturer	**The Government Pharmaceutical Organization (GPO)**
Corporate address of manufacturer	The Government Pharmaceutical Organization (GPO) 75/1, Rama VI Road, Ratchathewi, Bangkok. 10400, Thailand
Inspected site	
Name & address of inspected manufacturing site if different from that given above	Rangsit Pharmaceutical Production Plant 1 138 Moo 4, Rangsit-Nakhonnayok Road, Bueng Sanan, Thanyaburi, Pathumthani, 12110, Thailand D-U-N-S No. (Data Universal Numbering System): # 661741929 Global Positioning System (GPS) details: Latitude 14.05773 Longitude 100.83699
Unit / block / workshop number	Production Module 1 (Production Section 1)
Inspection details	
Dates of inspection	12-16 August 2024
Type of inspection	Routine GMP inspection
Introduction	
Brief description of the manufacturing activities	The area of the Pathumthani site is 174,000 sq.meters (108.75 rai), situated 70 kilometers away from Bangkok. It is located on Rangsit – Nakhonnayok Road; towards the North of the site is Maha Vajiralongkorn Cancer Hospital, and towards the West is a residential area. Rangsit Pharmaceutical Production Plant 1 facility includes warehouses for raw materials, packaging materials, and finished goods, a production section (Modules 1,2,3,4,5), and a pilot plant for manufacturing and packaging. The GPO main office is responsible for the manufacturing, processing, packaging, testing, storage, and shipping of the products. Rangsit Pharmaceutical Production Plant 1 (RPP) has been manufacturing Oral Solid Dosage Formulations (Tablets and Hard Gelatin Capsules) since 2015.
General information about the company and site	The Government Pharmaceutical Organization (GPO)'s second factory is located at 138 Moo 4, Rangsit—Nakhonnayok Road, Thanyaburi District, Pathumthani 12110 Thailand. The GPO is a state enterprise under the Ministry of Public Health of Thailand. It was officially established in 1966 and has its corporate main office in Bangkok.
History	This was the third WHO PQ inspection

Brief report of inspection activities undertaken – Scope and limitations	
Areas inspected	Pharmaceutical quality system Qualification and validation Materials and equipment Document control system Self-inspection and supplier qualification Production and packaging operations Quality control laboratory Warehouse Air handling units Purified water system
Restrictions	None
Out of scope	The inspection scope was limited to Efavirenz 600mg tablets. Other products manufactured at the GPO site were not included in this inspection.
WHO products covered by the inspection	Efavirenz 600mg tablets
Abbreviations	**Meaning**
AHU	Air handling unit
ALCOA	Attributable, legible, contemporaneous, original and accurate
API	Active pharmaceutical ingredient
APR	Annual product review
APS	Aseptic process simulation
BMR	Batch manufacturing record
BPR	Batch production record
CC	Change control
CFU	Colony-forming unit
CIP	Cleaning in place
CoA	Certificate of analysis
CpK	Process capability
DQ	Design qualification
EDI	Electronic deionization
EM	Environmental monitoring
FMEA	Failure modes and effects analysis
FPP	Finished pharmaceutical product
FTA	Fault tree analysis
GMP	Good manufacturing practices
GPT	Growth promotion test
HEPA	High efficiency particulate air
HPLC	High performance liquid chromatography (or high performance liquid chromatography equipment)
HVAC	Heating, ventilation and air conditioning
IQ	Installation qualification
LAF	Laminar air flow
LIMS	Laboratory information management system
MB	Microbiology

MBL	Microbiology laboratory
MF	Master formulae
MFT	Media fill Test
MR	Management review
NC	Non conformity
NRA	National regulatory agency
OQ	Operational qualification
PHA	Process hazard analysis
PLC	Programmable logic controller
PM	Preventive maintenance
PQ	Performance qualification
PQR	Product quality review
PQS	Pharmaceutical quality system
PW	Purified water
QA	Quality assurance
QC	Quality control
QCL	Quality control laboratory
QMS	Quality management system
QRM	Quality risk management
RA	Risk assessment
RCA	Root cause analysis
RO	Reverse osmosis
SIP	Sterilization in place
SMF	Site master file
SOP	Standard operating procedure
URS	User requirements specifications
UV	Ultraviolet-visible spectrophotometer
WFI	Water for injection

Part 2	**Summary of the findings and comments**

1. Pharmaceutical quality system

The GPO was responsible for ensuring the quality of the finished pharmaceutical products (FPPs) manufactured on-site. The Deputy Managing Director (DMD) was responsible for ensuring an effective Pharmaceutical Quality System (PQS) by participating in various quality management review meetings and providing required support and resources. The quality assurance and production plant 1 separately reported to the DMD. The QA manager was responsible for quality functions, including quality control, validation, and compliance.

The manufacturing site uses the following computerized systems:

Name of the software	Function
Electronic quality management system (eQMS)	Document control, Quality events, Training records
Laboratory information management system (LIMS)	Quality control, Lab testing
Manufacturing Execution System (MES)	Electronic batch record, Material management
Chromeleon 7.3.1	Chromatographic Data System (CDS)
Building automation system (BAS)	HVAC
Supervisory Control and Data Acquisition (SCADA)	Purified water system

Annual product quality review (APQR)
The SOP for the annual product review was discussed. The SOP provided a revision history of the changes made to the SOP. The review period followed a rolling review process, where all products were regularly assessed. Products were scheduled for review based on the fiscal year, which runs from October to September. The APQR plan 2024 was prepared in Oct 2023, listing 46 products. Efavirenz 600 mg was manufactured in Module 1, where other products containing drug substances (Lopinavir, Ritonavir, TDF, Emtricitabine, Lamivudine, Dolutegravir, Favipiravir, Amlodipine, Sildenafil, Metformin, and Sertraline) were also manufactured. The APQR plan for 2023 was reviewed, and it was noted that all identified products were reviewed as per the plan. A three-month timeline was set for completing the APQR. Twelve (12) topics were identified as part of the APQR review and in line with WHO requirements. A minimum of 30 batches were required for CpK and PpK analysis. If less than 30 batches were manufactured, batches from a previous year would be considered when calculating process capability.

Change control management:
The SOP "Change control system" described the change control process. The concerned change controls were reviewed and verified. The change control processes were carried out in compliance with the SOP.

Quality risk management (QRM)
The SOP for QRM and data integrity risk assessment was discussed. The SOP was recently revised, and a risk assessment related to data integrity was added. The SOP was prepared based on the ICH Q9, PIC/S, and WHO guidelines.

The Quality management review (QMR) process was discussed. The QMR was composed of 2 levels, wherein the first level was reviewed by the quality management committee every three months, whereas the second level was reviewed once per year. The QA manager chaired the first level meeting, whereas the Managing Director chaired the second level. The procedure identified input items to be discussed as part of the QMR, which included a review of the suitability of the quality objectives, quality policy, and quality manual, follow-up actions from the previous review, review of pharmaceutical registration, review of process performance and product conformity, review of the quality system, good distribution practice, resource issues, and any other business or quality planning.

The 2024 Quality Management Review plan outlined the topics for both Level 1 and Level 2 meetings. The most recent Level 2 meeting of the quarter took place in July 2024, conducted in a hybrid format with some attendees present in person and others joining online. During the meeting, the top deviations for each quarter were discussed.

Batch release

According to the SOP "Batch release," the QA Manager or designee was responsible for reviewing and evaluating the accuracy of the information in the Electronic Batch Record (EBR) from weighing to finished product and other documents and evidence related to each batch of product to ensure that data was recorded per the requirements of GMP and drug registration documents before considering releasing the finished product. The checklist for the batch release was included in the SOP.

Deviations

The SOP "Deviation Report" described the handling of deviations. An example of deviation handling was checked. It concerned the holding time from coating to packaging of four batches of Efavirenz 600 mg. The cause of the deviation was investigated, and corrective action was implemented to prevent the recurrence of the problem. In addition, there was a supplementary report for the hold time study of Efavirenz 600mg tablets, and the results showed that the hold time study was carried out for up to 30 days for core tablets and 30 days for coated tablets (60 days hold time in total). The report was found satisfactory.

Incidents

The SOP "Incident Report", described the handling of incidents. Three incidents were identified in 2021. An example of an incident was discussed. At the beginning of the printing of secondary packaging materials, 11 boxes were not printed. The root cause was found to be the initial machine setup. CAPA was introduced, and an additional inspection was performed before starting the machine.

The deficiencies raised in this section have been adequately addressed and will be verified during future PQ inspections.

2. Good manufacturing practices for pharmaceutical products

The GPO's Rangsit Pharmaceutical Production Plant 1 (RPP) is a multiproduct facility that manufactures oral solid dosage forms in Modules 1 to 5 and in the pilot-scale plant. Efavirenz, 600mg tablets, were manufactured in Module 1 for WHO and Export Markets, whereas Modules 1 and 5 were used for the domestic market.

The manufacturing facility uses vacuum transfer systems to minimize the risk of contamination and cross-contamination while manufacturing Efavirenz 600mg tablets. The management should ensure that products of different therapeutic categories are not manufactured in different modules but rather limited to certain modules to minimize the risks of contamination, cross-contamination, and mix-ups. The management should also ensure proper production planning and control to produce products on a campaign basis in certain modules.

The deficiencies raised in this section have been adequately addressed and will be verified during future PQ inspections.

3. Sanitation and hygiene

The same production clothing were used in all Class D production areas. The clothing were washed and dried in one laundry facility. The washing and drying equipment were not dedicated, but laundry from different areas was separated by time. Personnel procedures for entering Class D areas were described in “Entry and exit for production area” and “Gowning procedure for the production area.” According to the procedures, personnel working in the generated area and in direct contact with dust (granulation room or mixing room) should wear protective equipment and a hood. Furthermore, gloves were mandatory when handling the product or part of the equipment that could come in contact with the product. The production area was cleaned according to the SOP, “Cleaning operation of the production control area.”. The procedure specified the cleaning frequency (minor and major) depending on the production being conducted, as well as the cleaning tools (lint-free cloths, mops) and the cleaning agents used."

The deficiencies raised in this section have been adequately addressed and will be verified during future PQ inspections.

4. Qualification and validation

The validation master plan/VMP was discussed. It included the objective, scope, policy, approach, validation team, and various validation activities related to facility, equipment, utility, process, cleaning, analytical method, computerized systems, analyst qualification, and revalidation. The VMP was applied to the entire OSD facility spread across Modules 1 to 5 and the pilot-scale plant. Validation activities were carried out based on the impact assessment. The validation activities were planned in a phased manner wherein VMP was first prepared/approved before the protocol was prepared/approved. The data from validation activities was compiled as part of the validation report. An annual validation plan for the process, cleaning, qualification, transportation, and calibration was available for 2024. The annual validation plan for process validation production (2024) was discussed. The plan covered 12 products to be validated during 2024. Similarly, the validation plan for cleaning identified 4 products for 2024; in particular, 600mg of Efavirenz tablets were part of the plan due to the addition of a new granulation system. Validation activities scheduled for 2023 were verified, and most activities related to process and cleaning validation were performed as planned. Some of the planned activities were not performed as no batches were manufactured. Similarly, validation activities planned for 2023 for analytical methods were verified, and noted that analytical methods for Efavirenz tablets were executed in the past and not due for revalidation.

The deficiencies raised in this section have been adequately addressed and will be verified during future PQ inspections.

5. Complaints

The SOP for handling customer complaints was discussed. The marketing team received complaints logged in the customer complaint logbook by the QA team after entering a unique number from eQMS. It was noted that 6 complaints were received for Efavirenz 600mg tablets between June 2017 and July 2019. These complaints were related to half tablet in a bottle, white tablet in a bottle, side effects of Efavirenz tablets, missing tablets from the bottle, broken tablets in a bottle, and unprinted/printed box. It was confirmed by the company that all these complaints were received from the domestic market.

Most of the complaints were related to missing tablets, broken tablets, and half tablets. The company has not supplied any batch of Efavirenz 600mg tablets to the WHO market. The complaints were classified into high, medium, and low-risk complaints. The procedure included examples of high, medium, and low risk. The complaints were reviewed quarterly, and the company's review period started from their fiscal year (October). Since October 2023, three quarterly reviews have been performed. The high-risk complaints were cross-referenced to the product recall procedure.

The deficiencies raised in this section have been adequately addressed and will be verified during future PQ inspections.

6. Product recalls

The SOP for product recall and withdrawal was discussed. The recalls were classified into classes I, II, or III and required to be carried out within 24 hours, 3 days, and 5 days, respectively. The company confirmed that no product had been recalled since 2018 from RPP Plant 1. The company performed mock recalls every year for the domestic market or international market. The mock recall could reference a Recall/Mock Recall report from another site, as per the procedure, provided it was not older than one year. For mock recall, it was noted that the Thai FDA provided details of the product and the situation to mock recall the product. However, in the actual situation, the product/batch was not recalled

7. Contract production, analysis and other activities

The manufacturer did not have contract agreements for the production and quality control testing of the finished products. Only a test concerning elemental impurities was performed outside this manufacturing site:

8. Self-inspection, quality audits and suppliers' audits and approval

The SOP for supplier qualification was discussed. The process for new and existing suppliers was depicted in the flow chart. After an initial review of the vendor and manufacturer, a questionnaire was sent to obtain the required information about the material. A change control was raised, and material was sent to the lab and production departments for testing and production. An annual evaluation was performed on the suppliers based on a scoring comprised of QA, QC, logistics, purchasing deviations, non-conformance, and events. The suppliers were audited once every 3 years but not later than 4 years. An on-site audit was mandatory for a new supplier of the APIs and primary packaging materials. A separate procedure, "supplier and contractor audit," was followed for the on-site audit. The approved vendor list for Efavirenz was reviewed.

According to the SOP, "Auditor qualification," there were 88 approved auditors (external and internal). According to the procedure, an internal auditor had to have at least 3 years of experience and relevant training (for external auditors, 5 years of experience was required). Any auditor approved following the SOP held an 'Auditor Certificate' issued by the QA Manager. The 'Auditor Certificate' for the Head of Self Inspection and Vendor Audit Section was checked.

The deficiencies raised in this section have been adequately addressed and will be verified during future PQ inspections.

9. Personnel

Production and quality assurance were separated from each other. According to the organization chart, it had two separate departments: Quality Assurance Rangist Pharmaceutical Production Plant 1 and Rangsit Pharmaceutical Production Plant 1. Rangsit Pharmaceutical Production Plant 1 contained the following Divisions: Production Division, Warehouse Division, Engineering Division, and Administrative Division. The Quality Assurance Rangist Pharmaceutical Production Plant 1 contained the following Divisions: Compliance and Quality System Division 1, Compliance and Quality System Division 2, Quality Control Division 1, Quality Control Division 2, and Validation Division.

The number of personnel engaged in the Quality Assurance, Production, Quality Control, Warehouse, and engineering of Rangsit Pharmaceutical Production Plant 1 are as follows:

Department	Number
Production	328
Warehouse	65
Engineering	51
Administration	28
QA	98
QC	85
Outsourced	40 (for warehouse and QC)

10. Training

The SOP "Training Procedure" covered all manufacturing sites and introduced a requirement for initial training (e.g., SOPs, Hygiene), refresher training, and CGMP training (GMP guides). The "Annual training schedule of production section 1 for 2024", was reviewed. One example was verified: training for production employees in the scope of the SOP "Operation and Cleaning procedure of vibro sifter size was completed on 08.08.2024.

11. Personal hygiene

The gowning procedure was found adequate during the inspection. The change rooms were adequately equipped with a hand wash/drying and sanitization facility before changing street clothes to gowning.

12. Premises

The inspector visited the air handling units. The AHU was equipped with a pre-filter (G4), medium filter (F8), and terminal HEPA filter (H13 or H14). The pressure across the prefilter and medium filter was monitored once every week, while the pressure across the final HEPA filters was monitored daily. All recorded data was documented in the respective logbooks. In addition, the AHUs were connected to BAS for real-time monitoring. The pre-filter and medium filter were not cleaned but instead replaced based on the indication from BAS as "clean or dirty." The filters were replaced from the respective chambers following the procedure. The dampers were found locked. In general, the AHUs were adequately maintained. The company should ensure there was no leakage from the AHU chambers and that screws on the magnehelic gauges were adequately locked/sealed. In addition, the inspector also

visited the dust collector used for granulation and tableting areas. The dust was collected in a closed container and placed in a plastic drum before disposal.

The purified water (PW) system was also briefly visited. The company had added another loop to distribute PW to Module 5, whereas the existing system supplied PW to Modules 1, 2, 3, 4, and the warehouse. The PW's capacity was 1.2cm^3/hour. The potable water from the roof tank was tested once a month. Before distribution to user points, the PW was equipped with single-pass reverse osmosis, EDI, and UV-VIS. The capacity of the PW storage tank was 2000L. Thermal sanitization was performed once/week for 1 hour at 80±5°C.

An external company managed pest control and signed a 12-month contract on 01.08.2023. Insect lamps were installed in the storage and production areas, and mouse traps were placed outside near the building. The external company inspected the area once a month.

The deficiencies raised in this section have been adequately addressed and will be verified during future PQ inspections.

13. Equipment

The manufacturing facility, including the laboratory and utilities, was adequately equipped with the equipment and instruments. Most of the production and packaging activities were carried out using closed or semi-closed equipment, and the materials were sometimes transferred using vacuum transfer systems. More attention should be given to containing the dust generated in areas without dust collectors. Automated systems were also used in the manufacturing, laboratory, and utility areas, such as BAS, LIMS, and SCADA, respectively. The laboratory was equally equipped with sophisticated equipment and instruments. The GPO, Rama VI, carried out the calibration and preventive maintenance.

14. Materials

The packaging material warehouse and Raw Material warehouse were visited. Mapping of the storage rooms of raw materials and of packaging materials was performed on 1.12.2021. According to the "Temperature and humidity mapping protocol", temperature and humidity were checked at 56 designated points in the raw material storage room and at 32 points in the packaging material storage room. All results met the acceptance criteria. The hotspots were chosen for monitoring purposes.

The manufacturer had a designated area for dispensing raw materials for all production lines (Module 1 to Module 5 and the pilot-scale plant), which included 5 class D rooms with airlocks. Two rooms were dedicated to weighing the active substances, while the remaining three were used for weighing excipients. The Warehouse division supervised this area. The SOP "Dispensing of raw materials" described the dispensing rules. Since the balances were connected to the EBR system, the system only allows the dispensing of active substances and excipients specified in the batch records.

QC personnel performed the raw material sampling process according to the SOP "Sampling plan of raw materials" and "Sampling process of raw material" in a small sampling room, class D. This was one place for sampling raw materials (API and excipients) in this manufacturing site.

The deficiencies raised in this section have been adequately addressed and will be verified during future PQ inspections.

15. Documentation

The SOP "Document Control System" outlined the supervision of documentation. According to SOP, there were four groups of quality documents depending on the approval path (I group, e.g., SMF, Master Formula; II group, e.g., SOP, Specifications; III group Work Instruction, IV, e. g. logbooks). The document control system was managed using eQMS. However, paper-based documents, including logbooks and forms, were also used in the laboratory and other sections. All new and revised documents must push through the document process (Document route) in the eQMS or by using the "Document Action Request (DAR) form". A review of the documentation was required every 3 years.

Batch records were kept for 5 years or 1 year after expiration, whichever is longer. According to the procedure, system documents can be printed or electronically viewed. The eQMS system assigned procedure/document numbers.

The deficiencies raised in this section have been adequately addressed and will be verified during future PQ inspections.

16. Good practices in production

The inspectors reviewed the layout of the manufacturing areas and, in particular, Module 1. The entire manufacturing facility was spread over 4 floors. The 1st floor housed the warehouse, packaging materials, pilot scale, dispensing, and Module 1 and 2, whereas the 1st-floor mezzanine housed air-handling units. Similarly, the 2nd floor housed modules 3, 4, and 5, and the QC lab and the 2nd-floor mezzanine housed air handling units and a purified water system. An automated system (BAS) was used to control and monitor temperature, relative humidity, and differential pressure. Pressure cascading was provided between different areas. The differential pressure concerning the corridor was maintained. For example, the sampling area 0+/-5Pa, the core processing areas 15+/-5Pa, the common corridor 30+/-5Pa, and 45+/-5Pa were used for storage rooms for cleaned change parts. The change rooms were equipped with biometric access. The dispensed materials were staged in the area for 2-3 days. The hold time study was performed for 45 days. The gowning instructions were displayed on the wall, and visitors had to wash/dry their hands before crossing over the bench and changing to primary and secondary gowning. Visitors were required to wear a coverall suit to access core processing. The clean hold time and dirty hold time studies were performed, and the equipment was cleaned accordingly. Some equipment had clean-in-place (e.g., FBD), whereas IBCs and containers were washed using an IBC wash station. Equipment that could be disassembled or was mobile was washed in the washing room. For cleaning the equipment, portable water with detergent and Teepol Pure are used, and the final rinse with the PW. The equipment were dried using compressed dried air.

At the time of the visit to the production area, Efavirenz 600mg Batch No A675113 (lot 3) was being processed in the granulation area. The Logbook records for Granulator were checked. Some unit operations were carried out using open processes; in some cases, in-process material was transferred manually. The company needs to consider implementing an additional pressure/vacuum transfer system. Dedicated filter cartridges were used for different products, and 800 hours of drying time was established based on the supplier's recommendation. A compression machine, double rotary, 53

stations, was used for Efavirenz 600mg tablets. The machine was equipped with metal detectors and a deduster. The in-process control (IPC) lab had analytical balances, disintegration time, friability tester, moisture content, hardness, and thickness. The logbooks were maintained for these IPC tests. Two coating machines were used, equipped with a solution preparation area, and purified water. The change part storage room had biometric access and dies and punches for Efavirenz tablets, and other products were available. The primary packaging area was equipped with change rooms. The packing line was equipped with one bottle and 3 blister lines. Compressed air was used to clean the bottles before the silica gel pouch was inserted through the machine. At the time of inspection, a finished product was being packed in the bottles. The tablet counter was challenged before the start of the operation. The electronic batch record using MES was used to record various observations. The leak test on sealed bottles was performed using potable water. The labels were printed with batch details (registration number, lot number, manufacturing, and expiry date

The deficiencies raised in this section have been adequately addressed and will be verified during future PQ inspections.

17. Good practices in quality control

An inspector visited the QC lab in the afternoon of day 4. The lab was manned by 86 personnel, including the QC manager, supervisors, and analysts, located on the 3rd floor. The lab had 27 HPLCs, 2 GCs, 2 UV-VIS, 1 FTIR, analytical balances, melting point apparatus, particle size analyzer, and other equipment and instruments. The stability study chambers and retention sample room were visited. Most of the stability studies were conducted at 30℃/75%RH using the walk-in-chambers. The company confirmed that temperature mapping of the stability chambers was performed, and a hot spot was identified to monitor the temperature and relative humidity regularly. The retention samples were stored in the compactor, and the room was monitored for temperature (15-25℃).

OOS and OOT

The handling of OOS for the chemical test was discussed in the SOP. A separate procedure titled "Laboratory Investigation Report for Chemical Tests" was cross-referenced to the OOS procedure.

- 2022 (67 OOS, 99 OOT)
- 2023 (73 OOS, 106 OOT)
- 2024 (36 OOS, 87 OOT, until July)

Between January 2022 and July 2024, 9 OOS/OOT were reported for Efavirenz 600mg tablets. Most of the OOS/OOT were related to dissolution tests. The OOT was also noted to have been calculated using 3-sigma.

Working standards (WS)

GPO's other site, located on Rama VI, prepared the working standards. The WSs were stored according to the recommended conditions. Efavirenz WS was stored in the refrigerator between 2 and 8℃. The certificate of analysis confirmed the traceability to the USP reference standard used for preparing Efavirenz WS.

Stability study

The SOP regarding the stability study was reviewed. It was noted that the procedure described the purpose, scope, responsibility, and procedure for conducting stability studies. The ongoing stability study was performed half-yearly during the first year and then yearly. The samples were withdrawn within 30 days and placed in the sample receipt area before being taken up for analysis. The analysis should be completed within 30 days. 600 tablets were collected for ongoing stability study for one batch covering 6, 12, 24, 36, and 48 months. In 2024, the Efavirenz 600mg tablets process was revalidated due to the addition of new granulation equipment. Three process validation batches were placed for stability studies in 2024. So far, 1 and 3 months of accelerated stability study have been completed. After reviewing the analytical data related to the stability study of Efavirenz 600mg tablets, it was noted that the assay test showed an upward trend from 102.8% to 103.8%.

Microbiological laboratory

The Laboratory area has a designated room for preparing, sterilizing, and storing media and two clean rooms with LAF (Laminar Airflow) for conducting microbiological tests. The laboratory performed microbiological tests for PW, portable water, hot portable water, APIs, and excipients (APIs and excipients for other finished products than Efavirenz) and finished products. Environmental microbiological monitoring in Grade D (production, dispensing, and sampling rooms) was conducted periodically as per the established procedure.

Monitoring of Purified Water (PW)

Purified Water was used for the last rinsing of the production equipment and in the production process (e.g., wet granulation). Monitoring of PW from every use point was conducted. In the production area (Module 1), PW was sampled from each using points twice a month. In Module 1 there were 8 using points of PW. The microbiological tests of PW sampled from sampling point No. 26 (in the Granulation room) were checked. According to the "Analysis worksheet of microbiological testing of water membrane filtration method," a microbiological test was conducted on 05.08.2024, and all results fulfilled acceptance criteria (result in 0 CFU/1ml).

Monitoring of potable water.

Potable water was used to clean the area and equipment. The water was monitored outside the production areas (from tanks), but this was not conducted from the usage points in the production area. The following tests were performed:

- Portable water system - free chlorine test, pour plate test (1 ml).
- Hot water system - pour plate test (1 ml), turbidity, and total hardness.

There was no specification for these waters. The manufacturer conducted the tests for informational purposes only.

The deficiencies raised in this section have been adequately addressed and will be verified during future PQ inspections.

Part 3	Conclusion – Inspection outcome

Based on the areas inspected, the people met and the documents reviewed, and considering the findings of the inspection, including the observations listed in the Inspection Report, ***The Government Pharmaceutical Organization,*** located at ***Rangsit Pharmaceutical Production Plant 1, 138 Moo 4, Rangsit-Nakhonnayok Road, Bueng Sanan, Thanyaburi, Pathumthani, 12110, Thailand***was considered to be operating at an acceptable level of compliance with WHO GMP Guidelines.

All the non-compliances observed during the inspection that were listed in the full report as well as those reflected in the WHOPIR, were addressed by the manufacturer to a satisfactory level, prior to the publication of the WHOPIR.

This WHOPIR will remain valid for 3 years, provided that the outcome of any inspection conducted during this period is positive.

Part 4	List of WHO Guidelines referenced in the inspection report

1. WHO good manufacturing practices for pharmaceutical products: main principles. WHO Expert Committee on Specifications for Pharmaceutical Preparations. Forty-eighth Report Geneva, World Health Organization, 2014 (WHO Technical Report Series, No. 986), Annex 2. ***Short name: WHO TRS No. 986, Annex 2***
   https://digicollections.net/medicinedocs/documents/s21467en/s21467en.pdf

2. WHO good manufacturing practices for active pharmaceutical ingredients. WHO Expert Committee on Specifications for Pharmaceutical Preparations. Forty-fourth Report. Geneva, World Health Organization, 2010 (WHO Technical Report Series, No. 957), Annex 2. ***Short name: WHO TRS No. 957, Annex 2***
   untitled (digicollections.net)

3. WHO Good Manufacturing Practices: water for pharmaceutical use. WHO Expert Committee on Specifications for Pharmaceutical Preparations. Fifty-fifth Report. Geneva, World Health Organization, 2021 (WHO Technical Report Series, No. 1033), Annex 3.
   Short name: WHO TRS No. 1033, Annex 3
   9789240020900-eng.pdf (who.int)

4. WHO guidelines for sampling of pharmaceutical products and related materials. WHO Expert Committee on Specifications for Pharmaceutical Preparations. Thirty-ninth Report. Geneva, World Health Organization, 2005 (WHO Technical Report Series, No. 929), Annex 4.
   Short name: WHO TRS No. 929, Annex 4
   https://digicollections.net/medicinedocs/documents/s21440en/s21440en.pdf

5. Guidelines on heating, ventilation and air-conditioning systems for non-sterile pharmaceutical products. WHO Expert Committee on Specifications for Pharmaceutical Preparations. Fifty-second Report Geneva, World Health Organization, 2018 (WHO Technical Report Series, No. 1010), Annex 8. **Short name: WHO TRS No. 1010, Annex 8**
https://digicollections.net/medicinedocs/documents/s23455en/s23455en.pdf

6. Supplementary guidelines on good manufacturing practices: validation. WHO Expert Committee on Specifications for Pharmaceutical Preparations. Fortieth Report. Geneva, World Health Organization, 2006 (WHO Technical Report Series, No. 937), Annex 4.
Short name: WHO TRS No. 937, Annex 4
https://digicollections.net/medicinedocs/documents/s20108en/s20108en.pdf

WHO good practices for pharmaceutical quality control laboratories. WHO Expert Committee on Specifications for Pharmaceutical Preparations. Fifty-seventh Report. Geneva, World Health Organization, 2024 (WHO Technical Report Series, No. 1052, Annex 4.
Short name: WHO TRS No. 1052, Annex 4
https://www.who.int/publications/m/item/who-good-practices-for-pharmaceutical-quality-control-laboratories

8. WHO Good Practices for Pharmaceutical Products Containing Hazardous Substances. WHO Expert Committee on Specifications for Pharmaceutical Preparations. Forty-fourth Report. Geneva, World Health Organization, 2010 (WHO Technical Report Series, No. 957), Annex 3.
Short name: WHO TRS No. 957, Annex 3
https://digicollections.net/medicinedocs/documents/s22358en/s22358en.pdf

9. WHO good manufacturing practices for sterile pharmaceutical products. WHO Expert Committee on Specifications for Pharmaceutical Preparations. Forty-fifth Report Geneva, World Health Organization, 2011 (WHO Technical Report Series, No. 961), Annex 6.
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