

Prequalification Unit Inspection Services
WHO INSPECTION REPORT
Finished Product Manufacturer

Part 1	General information
Manufacturers details	
Name of manufacturer	PT Tunggal Idaman Abdi (TIA)
Corporate address of the manufacturer	Jl. Jend. Ahmad Yani No. 7 Jakarta 13230, Indonesia
Contact person	Ms Tri Hidayah, Head Manufacturing & Operations tri.hidayah@tia-pharma.com
Inspected site	
Name & address of inspected manufacturing site if different from that given above	PO Box 4009, Jl. Jend. Ahmad Yani no. 7 Jakarta, 13230, Indonesia
Unit/block/workshop number	Production Plant 2 (Hormone injection Line 1 and 2)
Manufacturing license number	License No. 8120114023006 GMP certificate No. PW-S.01.04.1.3.331.04.24-0041 (validity 15 April 2024 to 14 April 2029)
Dates of inspection	30 March to 3 April 2026
Type of inspection	Routine GMP inspection
Inspection record number	INSP-FPP-2018-0173
Inspector(s)	Mr. Vimal SACHDEVA, Lead inspector, WHO Ms. Anandayu Nurfachtiyani (Temporary Advisor, for WHO)
Representative from the National Regulatory Authority	Mr. Raditya Sapta, GMP inspector, Badan POM raditya.sapta@pom.go.id
Introduction	
Brief description of the manufacturing activities	PT Tunggal Idaman Abdi, hereinafter called PT TIA, is a registered pharmaceutical company established in 1970 and has its own production facilities located in Jalan Jend. Ahmad Yani No.7, Jakarta 13230, Indonesia. In January 2012, Hormone Production Plant 2, consisting of a 4 (four) floor building with a total area of 1500m ² , was constructed with the purpose of providing a new, updated facility for hormone production capacity for both Injection and Oral reproductive health products.
General information about the company and site	In front of the PT TIA building is a highway, the land property in the back, the Customs office on the left, and the school on the right. It is a combination of residential and light-industrial areas.

History	The WHO Prequalification Inspection Services conducted the on-site inspection in August 2023, May 2018, and November 2014. The Hormone Plant 2 was certified in April 2014 by the National Agency of Drug and Food Control (NADFC) in Indonesia and began operations in Jun 2014, after which it produced commercial batches.		
Brief report of inspection activities undertaken – Scope and limitations			
Areas inspected	The following areas were inspected: - Pharmaceutical quality system - Personnel and training - Premises and equipment - Materials, supplier qualification - Production and packaging operations - Water for injection - Air handling units - External warehouse (used for storing packaging and finished products)		
Restrictions	None		
Out of scope	The products and areas not submitted for WHO Prequalification were outside the scope of this inspection.		
WHO product numbers covered by the inspection	RH090 (Medroxyprogesterone injection 150mg/ml)		
Key persons met	1	Reza Abidin	Board of Directors (BOD)
	2	Tri Hidayah	Head of Manufacturing & Plant
	3	Rinaldy Rudy	Production Manager
	4	Fivin Fitrianingsih	PPIC & Warehouse Manager
	5	Riska Lestari	QA Manager
	6	Lindya	QC Manager
	7	Sarita Kristiani	Reg Affairs & PV Manager
	8	Pepen Purwana	Plant Engineering Manager
	9	Putu Gede Oka	HSE Manager
	10	Aditya Surachman	Product Development Supervisor
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
NCA	National control authority
NCL	National control laboratory
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
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1. Pharmaceutical quality system

The pharmaceutical quality system (PQS) encompasses the regulatory requirements of a sterile product manufacturer. The procedures were described in written SOPs, policies, and other technical protocols. Upon review of several documents, it was noted that adequate consideration was not given to the current WHO GMP requirements for sterile products, and adequate controls have not been fully implemented. The PQS was manually maintained, and the following elements were reviewed:

Product quality review

The PQR SOP (QAS-021-13 dated 09/06/2025) was reviewed. The PQRs were performed by calendar year, with fewer than 30 batches reviewed in the first quarter, more than 30 in the second quarter, and so on. The procedure used Minitab to analyze the data, and the acceptance criteria for CpK were described. The SOP did not provide cross-referencing with the Minitab procedure. The SOP for statistical data processing with Minitab Software (QAS-038-03 dated 12/05/2025) was reviewed, which stated that a minimum of 30 batches was required for process capability. No mention of using batches manufactured in the previous year for cumulative analysis. No system was in place to verify the data after they were transcribed into the Minitab. The manufacturer used Minitab 17 version, whereas the current version in use was 22.1. No computerized system validation was performed on Minitab, nor was a data integrity risk assessment (DIRA) performed.

The PQR for Triclofem injection for Jan-Dec 2025, dated 26/03/2026, was reviewed. A total of 281 batches were manufactured using lines 1 and 2. Line 1 has 8 nozzles, whereas Line 2 has 4 nozzles. The list of the MPA batches was tabulated; however, no analysis was conducted. Similar was the case for excipients and packaging materials. Upon review of the yield for the filling line 2, 18 batches did not meet the predetermined yield criteria out of 79 batches. No further assessment was performed, and no action was taken. Similarly, the review of extractable volume revealed that several batches were out of control; no further action was recommended. Critical process parameters were not calculated for process capability, and it was reported that “one or more parameters during production showed no trend” without performing trend analysis. Ppk values for several parameters were calculated, whereas some Ppk values for the MPA assay (bulk) were well below 1.00. No assessment was performed, and no action was taken.

Quality risk management (QRM)

The SOP for QRM (QAS-022-08, dated 05/04/2024) was reviewed, which guided the performance of risk assessments across various areas of the GMP system. The process flowchart and FMEA template were part of the procedure. The Excel spreadsheet was used to log risks initiated by the site. It was noted that 36 risks were initiated in 2024, 13 in 2025, and one in 2026. The following risks were assessed:

- The DIRA of the hormone machine injection process was performed on 28/06/2024. The DIRA included good documentation practices, access control, user levels, audit trail, audit trail review, and backup/restore/archive. The review categorized machines by severity and identified 4 holding tanks as category 1 (non-electronic system, no data storage, no printer for data generation). The DIRA was not reviewed to ensure that holding tanks comply with the DI requirement after

installation of the HMI/PLC. The DIRA used an obsolete WHO reference. Also, the DIRA did not include quality system training, personnel, internal audits, and outsourced activities.

- The nitrosamine risk evaluation of the Triclofem injection protocol (QST-RE-001 Rev. 01 (P) dated 10/10/2025) and report (QST-RE-001 Rev. 01 (R), dated 28/10/2025) were reviewed. The assessment included a review of API, excipients, water for injection, glass vials, rubber stopper, and silicone tubing. The documents from various suppliers were available, confirming the absence of nitrosamines in API, excipients, and other materials. Farmabios, spa, Italy, was the MPA manufacturer that had confirmed the absence of nitrosamine impurity formation from the synthesis route. In addition, the materials include methyl paraben, propyl paraben, sodium chloride, polysorbate 80, PEG 3350, sodium hydroxide, hydrochloric acid, water for injection, glass vials, rubber bungs, and silicon tubes. It was, however, noted that TIA did not review the information provided by different sources. Also, TIA confirmed that WFI did not contain nitrosamine impurities because it is prepared by distillation. This assumption was not supplemented with any testing of WFI. Similarly, no testing was performed on Triclofem injection to confirm the absence of nitrosamines.

Contamination control strategy (CCS)

The CCS was first prepared after the last PQ inspection in August 2023. This initial version (CCS/HP2 Rev.00, dated 29/03/2024) covered details related to products, facilities, utilities, materials, processes, and controls, among others. The revised version (CCS/HP2 Rev.01 dated 15/01/2026) contained the same information as the previous version. Revision 01 was updated after the implementation of CAPA from the last PQ inspection. The changes made to the facility, including equipment and processes, were cross-referenced to the CCS.

Change management

The change control SOP dated 24/12/2025 was reviewed, and it was noted that changes were handled manually for the production process, equipment, utilities, facilities, raw materials/packaging materials, product systems, and the computer system, etc. The introduction of a new product was also described in the change control matrix. The changes were logged in a password-protected spreadsheet, which was accessed by the Quality System Team. The updated information related to the number of changes raised, opened/closed, and major/minor was not available.

Year	Total changes (hormone)	Major	Minor	Comment
2023	129	20	106	17 opened
2024	113	3	110	21 opened
2025	63	6	57	40 opened
2026	37	3	34	27 opened

The following opened change controls from 2023 were reviewed:

- CC/23/082/2 dated 26/09/2023 related to the addition of alternative manufacturers for PEG 3350 and Propyl Paraben was reviewed. A cross-functional team assessed the change, and several items were identified (e.g., approving the vendor list, performing process validation, submitting a variation, if applicable) before implementing the proposed changes. UENO Fine Chemicals Industry Ltd, Japan, supplied Propyl Paraben. A questionnaire was sent to the manufacturer; however, no information was available on the GMP standards applied by the Propyl Paraben manufacturer. No list of materials available to confirm no risk of contamination and cross-

contamination. For PEG 3350, no risk assessment was performed to determine the GMP standards used by the excipient manufacturer. The information provided by Clariant was not assessed to determine adequate controls at the excipient manufacturer's end. The change has not been closed as process validation batches have not been completed on line 1.

- CC/23/089/2 dated 06/10/2023 related to upgrading the existing 200L DCI holding tank with HMI/PLC panel and control system features was reviewed. Several action items were identified, including procurement of the HMI/PLC control system, installation of the system, an addendum to the IQ, PQ, and revision of the procedures. The panel was purchased and qualified in February 2026, PQ was performed, and training was completed. The proposed changes had been implemented; however, the final review was pending.
- CC/23/104/2 dated 06/11/2023, a change related to the removal of the PVC curtain in filling line 1 and replacing it with a fixed barrier was discussed. The change was classified as major, and various action items were identified. After the removal and replacement work, the HVAC performance qualification was completed, and the respective SOPs were revised. Training was imparted, and the change was closed on 30/05/2024. The cross-functional team did not adequately assess the proposed change, as QC did not determine whether the environmental monitoring program needed review. Similarly, regulatory affairs did not assess whether the WHO PQ should be informed before/after the proposed change.
- CC/23/107/2 dated 10/11/2023 for modifying filling machine line 2 (FLC 3040) to be equipped with RABS and glove ports was discussed. The RA and QC manager provided no assessment. No notification was required for Badan POM and WHO PQ. The change control identified various action plans, including an addendum to the IQ and PQ, the requalification of HVAC, and many others. The change had been closed on 16/06/2025. The focus was mainly on performing media fill to demonstrate compliance.
- CC/23/125/2 dated 14/12/2023 for the change of load pattern related to housing filter assembly modification with the PUPSIT system was discussed. The changes were proposed in upstream/downstream and venting housing filters using Midicaps Sartoflour type. However, CFT did not adequately assess the impact of the proposed changes, including no notification of this major change to Badan POM, WHO PQ. No clear rationale for implementing PUPSIT in the change control form. No confirmation if the PUPSIT implemented on 30/09/2024 was justified within the CCS. Risk assessment was not performed to ensure that there were no filter integrity failures, sterilization damage, operator handling failures, PUPSIT execution failures, suspension blockage, line contamination, or a failure to meet the sterility assurance level. No IQ and OQ were performed except for the PQ.

Line clearance

The SOP for line clearance (PGD-012-05 dated 30/05/2024) was reviewed. The procedure did not provide specific details or areas to inspect during the line clearance procedure. There was no checklist or equivalent document used to record line clearance activities, especially in critical or hard-to-detect areas. The manufacturer informed that a change control dated 03/03/2026 (CC/26/030/2) was raised to review and revise the SOP for line clearance. This change was triggered by the audit of Mission Pharma, a TIA customer.

Deviation Management

The SOP for handling deviation (QAS-013-12 dated 05/04/2024) covered procedures, classification, investigation practices, trending, and the implementation and oversight of corrective and preventive

actions (CAPA). Deviations should be reported within one business day. Deviations were classified as critical, major, and minor deviations with corresponding timelines for completion of 30, 60, and 90 days, respectively. Deviation forms had included case information, impact and risk evaluation, recurrence assessment, CAPA, and batch disposition decisions. Investigation reports also incorporate root cause analysis in accordance with SOP #FAC-007, demonstrating that formal investigative tools were in place. Despite documented procedures, significant weaknesses were observed in the implementation and effectiveness of the deviation management system, especially regarding the additional classification termed “Event,” which was used to address recurring incidents still under CAPA implementation, potentially leading to under-classification of quality issues. In practice, a substantial proportion of cases were categorized as events: 154 of 243 deviations in 2025 and 239 of 322 in 2024 fell under this category.

Yearly hormone injection trending reports covering the period from 2023 to 2025 were available. It was noted that no critical deviations were reported during this period, and the total number of deviations decreased over time, from 359 in 2023 to 243 in 2025. Most deviations (approximately 50% of cases) were associated with equipment, systems, machines, and facilities, with root causes predominantly attributed to spare parts and preventive maintenance issues, followed by breakdowns and improvement-related factors. These root causes had remained consistent over multiple years. Despite the availability of trending data, the analysis did not appear to be effectively utilized for risk mitigation or continuous improvement. Recommendations generated from trending exercises were general in nature and repetitive and had been reiterated without measurable progress. A critical area of concern was the recurring issue associated with the capping machine VRK 2005B in Line 2, which accounted for approximately 25% of deviations in 2025. The same equipment had been linked to repeated problems since 2022, particularly cracked vials identified during optical inspection, resulting in out-of-limit rejection rates and reduced yield of Triclofem products. Multiple event reports confirm the persistence of this issue, with recurrence documented as many as 37 times in 2024. This Line 2 deviation LP/24/012/2 was traced back to earlier investigations initiated in 2022. Although CAPAs such as spare part replacement, mechanical adjustments, and supplier communication were implemented, these measures have not resulted in sustained resolution. The recurring nature of the same root causes demonstrates a failure of CAPA effectiveness and indicates inadequate escalation and risk control for critical equipment-related issues.

CAPA Management

According to SOP QAS-015-06 dated 19/05/2023, changes or extensions to CAPA timelines may be submitted and approved through a defined process. However, the procedure did not establish any limitation on the number or duration of CAPA extensions, nor did it require a formal impact or risk assessment to justify such extensions. This lack of control has resulted in inappropriate and unjustified delays in CAPA implementation. Several examples of these deficiencies were noted in Part 3. By classifying ongoing or repeated incidents as “Event” while CAPA was still in progress, the company failed to adequately track and monitor recurrence. This practice reduces management visibility and delays appropriate escalation, thereby allowing chronic issues to persist without effective resolution.

Release procedure

The batch disposition procedure was defined in SOP (QAS-004-12 dated 13/02/2026). Initial review conducted by production personnel (pharmacist/supervisor and production manager), followed by QC personnel, then QA batch reviewers and QA supervisors. Final disposition was made by the QA Manager. The review process was guided by Form F-QAS-A014-02, and evidence of review was

recorded within the batch documentation. Partial-release practices were also defined in the SOP. For active ingredients, conditional use is permitted once identification and initial testing meet requirements, with additional controls applied during production. For finished products, partial release is allowed under specific conditions, including identical formulation and composition, and use of different trade names, typically for export markets. Packaging under partial release requires separate batch records, and release is contingent upon complete and compliant bulk analysis results. Despite the generally structured system, a deficiency in batch disposition was identified.

Management review (MR)

The inspection included a review of the MR system and its effectiveness in overseeing the PQS. The MR meetings were held every 6 months; the latest one was conducted on 17/03/2026, covering the period January to December 2025. The meeting report included several key quality metrics, such as follow-up on recommendations from previous meetings and batch release status. It was noted that the number of batches released has remained relatively consistent since 2023, ranging between approximately 1,358 and 1,360 batches per year, with no batches rejected during the review period. A total of 401 deviation reports were recorded in 2025, consisting of 53 major, 116 minor, and 232 classified as events. However, the MR did not include an assessment of the number of open or overdue deviations, nor did it provide an analysis of recurring issues or their impact on product quality. This limits management's ability to fully understand the status and effectiveness of deviation handling within the quality system. Similarly, a significant number (425 cases, 53.55%) remained open at the time of review, and 2,078 CAPAs were overdue out of a total of 13,683. Despite this high proportion of open cases, there was no documented discussion or direction from management on prioritization, resource allocation, or risk mitigation for these pending issues.

Deficiencies are detailed in Part 3.

2. Good manufacturing practices for pharmaceutical products

TIA has a separate facility for manufacturing hormone (injectables and OSD) and non-hormone products. The scope of the PQ inspection was limited to the injectable facility for MPA injection. The MPA injection was manufactured in Lines 1 and 2, whereas Line 2 also manufactures Estradiol Cypionate injection. Currently, Line 2 is a multi-product line producing products of different therapeutic areas. The manufacturer confirmed that dedicated change parts were used for MPA and Estradiol Cypionate injections. Upon inspection of the various manufacturing areas, the GMP for sterile products had not been adequately and fully implemented.

Deficiencies are detailed in Part 3.

3. Sanitation and hygiene

The gowning and hand-washing facility was provided before entering the cleanrooms. The instructions were displayed on the walls before the entrance. Environmental sanitation practices were implemented through disinfectant rotation. Daily cleaning was performed using 70% alcohol, 70% isopropyl alcohol (IPA), and 0.26% hydrogen peroxide. Weekly disinfection included the use of 6% hydrogen peroxide, 0.8% phenol, and hypochlorous acid, applied in a rotational manner, with phenol used in weeks 1 and 3 and hypochlorous acid in weeks 2 and 4. In addition, fumigation with hydrogen peroxide was conducted

every 6 months or in response to environmental monitoring trends. Records reviewed for sterile filling areas indicated that fumigation activities were performed on 09 April 2025 and 18 October 2025, demonstrating adherence to the defined schedule.

4. Qualification and validation

The validation master plan (VMP-P02 dated 05/01/2026) provided guidance for carrying out qualification and validation activities across the site. The following qualification and validation activities were reviewed:

Process validation related to the level indicator for the holding tank

Process validation of Triclofem injection for Line 1 was validated between October 2023 and January 2024, using three batches (007K231, 008K231, and 009K231) following the introduction of new sources of PEG 3360 and Propyl Paraben. The rationale of the sampling plan was described in the process validation document. The filling time on Line 1 took around 6 hours, and samples were collected every 10 minutes from the start to the end of the filling. The samples were tested for weight per volume, specific gravity, and content uniformity, and the results were calculated. The acceptance value and PpK were found to be well within the limit, confirming that the existing manufacturing process can continue to produce the product with consistent quality even at the end of the filling operation.

Material transfer validation

The validation protocol (VP-QA-02-001 Rev 00, dated 10/10/2024) for validating materials transferred into Grades B and A and transfer media (after use/exposure) from production to the incubator was discussed. The protocol/report did not specify which transfer method/system (bag-in/bag-out, pass-through, etc.) was used to validate the transfer system. Similarly, no worst-case was defined to confirm the largest item transferred, the heaviest item, the most frequent transfer, the maximum transfer duration, the maximum exposure time, etc. The transfer validation was not simulated, considering airflow visualization, repeated transfers, integrity testing, number of runs, and environmental monitoring, etc. It was noted that method transfer was referenced with the contamination control strategy document.

Computer system validation (CSV)

The SOP for CSV QAV-028-02, dated 11/03/2026, provided a lifecycle approach that included planning, risk assessment, testing/validation, routine application, periodic review, and retirement. The SOP included information from the WHO validation guideline on the periodic review of the computerized system; however, no timeline was specified for the review. As such, Tungal conducted no periodic review, necessitating revalidation. Upon review of the list of computerized systems dated 30/05/2023, it was noted that several software and operating systems were obsolete, e.g., filling line 2 (Windows XP and Wonder well Win 7.0, Empower 3.471, Minitab 17, and many other examples). The list did not include all the software and operating systems used by different departments. The list did not provide complete information about when the system was last validated and when it is due for the next validation. For the laboratory equipment, calibration and preventive maintenance were performed annually, whereas CSV was performed in 2019. There was no system in place to revalidate the system through periodic review. There was no system of periodic review for the CSV.

Cleaning validation and occupational hazards

The SOP for cleaning validation (QAV-004-06 dated 27/02/2026) was recently revised, and cleaning verification was added after the completion of cleaning validation. Rinse and swabbing methods were used for cleaning validation, and PDE was used to calculate MACO, besides 10ppm and LD50 as the acceptance criteria. The SOP still referred to the use of LD50 and 10 ppm criteria, which are no longer acceptable. The SOP did not mention the maximum daily dose or batch size. Upon reviewing the cleaning validation, it was found that two different products containing MPA and Estradiol Cypionate (EC) injection were manufactured in Line-2. No risk assessment was performed to determine what controls were required before manufacturing EC after MPA. The reported PDE value for EC was 3ug/day. From the review of the cleaning validation in the hormone injection plan dated 05/01/2026, it was noted that the manufacturer has a dedicated filling machine with change parts, including the hoses used to transfer the solution. It was noted that the worst case was identified as MPA instead of MPA+EC, as the manufacturer believed the MPA content exceeded the EC (50mg versus 10mg). The PDE report from M/S Azierta, Spain, was reviewed, and it was noted that the PDE value of 0.02mg/day was provided for MPA. The report did not provide any OEL value for MPA, which would have assisted the manufacturer in ensuring adequate containment measures were in place. The PDE report for Estradiol Cypionate was not available from the manufacturer. No occupational hazard assessment was performed. The occupational hazard controls were also discussed, and it was noted that OEL values were not obtained from authentic sources before conducting a risk assessment.

Dry heat sterilizer (tunnel) qualification Line 2

The requalification was performed annually by the in-house team. Air velocity was measured at several sampling points in the infeed zone, heating zone, and cooling zones I and II. The airflow pattern was performed from the same four zones using a concept air tracer. The acceptance criteria stated that there should be no turbulence, and air should flow downward. Air Trace Smoke fluid was composed of less than 50% of Propane glycol-1,2-diol, less than 10% Glycerol, and more than 40% of distilled water. A HEPA filter integrity test was performed upstream and downstream using a photometer. The particle count test was performed in-house using a particle counter, and the acceptance criteria for Grade A were met at 0.5 µm and 5 µm. A conveyor speed test was performed to measure the time required for a vial to travel 10cm along the conveyor. Heat distribution and penetration were performed using Endotoxin. The three-way cycle (waves 1, 2, and 3) was challenged using three vials of Endotoxin at each location. Fumigation of the tunnel cooling zone was performed for 2 hours using H₂O₂, and the H₂O₂ residue was calculated (NMT 0.5 ppm). A 3-log reduction was obtained when tested using the gel-clot method. The heat penetrated into the empty vials during the depyrogenation cycle for all three-wave cycles, which were within the acceptance criteria (3-log reduction). The limit of ±15 °C was set for the temperature distribution, and results were reported within this limit based on the mean of the distribution. The limit of +/-15°C was not justified and was not referenced to any credible source. Also, there was no confirmation if the cold spot was above the validated minimum temperature; depyrogenation was validated at 235 °C, and endotoxin reduction was demonstrated at this temperature. The results were tabulated, but no interpretation was performed to determine hot/cold spot and their impact on day-to-day operation.

Air handling units (AHUs)

The SOP for validation & qualification (QAV-001-16, dated 10/02/2026) provided guidance on the on-site qualification and validation activities. Based on the SOP, the protocol was prepared for the execution of Performance qualification (PQ). PQ of the HVAC system in Hormone Plant 2, dated 15/01 to

23/06/2026, was discussed. The requalification was performed after modifications to the AHU to improve access to the Service area. The PQ included an integrity test of the HEPA filter, an airborne particle count, an air change test, an air flow, an air flow pattern test, a recovery test (smoke challenge), a particle count (at rest and in operation), a %RH, a T, and a DP (at rest), a microbial environment (at rest and in operation). The requalification was performed jointly by the validation, engineering, and production teams. The bi-annual PQ for HVAC Hormone Injection Plant 2 (04/01 to 12/02/2025) was reviewed, and it was noted that the PQ was performed in response to the change related to the installation of RABS with glove ports in the filling area (Line-2). The PQ included the tests for HEPA filter integrity, airflow/air change, DP, particle count, recovery test, microbial environment (air sampler, settle plate, contact/RODOC plate, %RH, T, DP, and particle count. Air velocity was measured using an anemometer, and results were reported on the test sheet. The NVPC was performed, and no particles were found in the Grades A, B, and C areas, which is not usual. The portable particle counter was used. The tests were performed by the production personnel and verified by the QA. Air visualization study through the video recording was verified. In general, the tests were meeting the acceptance criteria.

Qualification of areas

Upon reviewing the video recording of the air visualization test for filling line 1, the door was opened for manual intervention; however, there was no confirmation of the air's laminarity. The air did not fall on the object or the working area to ensure the first air concept. Also, there was no confirmation of the air ingress from the Grade B to the Grade A area.

Deficiencies are detailed in Part 3.

5. Complaints

The SOP for the product complaint (QAS-011-09) outlined a structured process for receipt, classification, investigation, and follow-up of complaints for both local and export markets. Complaints were recorded in an Excel database, and non-medical complaints would fall under QA responsibility. Investigations were conducted through a combination of document review, sample examination, and cross-functional discussions, with the final complaint report communicated back to Marketing and relevant departments for CAPA implementation. The complaint trend indicates a relatively low number of complaints in 2024 and 2025, followed by a notable increase in 2026. Within that period, only one foreign complaint related to Triclofem was reported from Hong Kong in 2024, regarding the fading of packaging materials; the other complaints that year were sticky granules at the vial neck and cracked vials. In 2025, one complaint about Triclofem was reported, again involving sticky granules at the vial neck. However, in 2026 (up to March 2026), a total of 10 complaints were recorded, of which 8 were associated with Triclofem injection products. These complaints were predominantly related to clogging during aspiration, with multiple batches involved, including 198J21, 564E21, 489H252A, 403G251A, and 100B251A. At the time of inspection, all of these cases remained under investigation. Detailed review of specific complaint investigations, such as complaint No. 001/PC/QA/24 and Complaint No. 001/PC/QA/2025, revealed deficiencies in the depth and completeness of the investigative process, as detailed in Part 3.

6. Product recalls

The product recall system was governed by SOP QAS-006-06 dated 13/02/2026. The most recent revision of the SOP introduced provisions for conducting mock recalls, with defined frequencies of every

three years for the local market and every two years for overseas markets, taking into consideration the complexity of distribution chains. It was noted that the company has not executed any actual product recalls during the period from 2024 to 2026, and no recall cases were identified for either local or exported products. The last mock recall was conducted on 24 July 2023, involving Triclofem batch 205B232A and classified as a Class II recall. The company indicated that future mock recalls have been scheduled for May 2026 (local market) and June 2026 (overseas market) in accordance with the updated procedures, which include consideration of distribution chains when determining mock recall scenarios.

Deficiencies are detailed in Part 3.

7. Contract production, analysis, and other activities

The MPA injection (RH090) was manufactured on-site without contracting out any manufacturing activities. The manufacturer used outsourced services for device calibration, instrument and equipment maintenance, testing of certain raw materials, pest control, and other utility services.

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

The self-inspection program was governed by SOP QAS-016-1 dated 26/04/2024, which defined the structure, responsibilities, and qualification requirements for internal audits. Based on the records reviewed, a total of 38 self-inspections were planned and executed within the reporting period. These inspections were distributed across different months, with five conducted in August, thirteen in September, and twenty in October 2026. Although the total number appeared high, it was clarified that these inspections were conducted at the level of individual areas or departments. Collectively, they constitute a comprehensive self-inspection of the entire facility within a one-year cycle. The SOP specified that self-inspections were to be conducted by an audit team led by a qualified lead auditor. The qualification criteria for the lead auditor include a minimum of 5 years of experience in the pharmaceutical industry, preferably at a managerial level or in at least 2 different supervisory roles, and prior involvement in audits conducted by external authorities or regulatory agencies. The list of the Lead and Members of the Self-Inspection Team for 2025 and 2026 was available.

9. Personnel

The manufacturer has a total of 352 staff members on their payroll, and their breakdown is as follows:

Department	Numbers
Production	210
Quality (QA & QC)	78
Plant Engineering	34
Product Development	3
PPIC & WH	18
RA & PV	4
HSE	3
Plant General	2

The Head of Manufacturing and Plant (HMP) reported directly to the Board of Directors. Independent and separate functions of QA, QC, and production, each reporting directly to the HMP.

10. Training

The qualification of personnel working in aseptic areas was governed by SOP Personnel Qualification in Hormone Injection (PHP-082-04 dated 10/03/2026). As a prerequisite, personnel must complete basic GMP training, including personnel hygiene, handwashing, gowning procedures for different cleanroom grades (A, B, C, and D), and aseptic processing principles. The qualification process included classroom training, training evaluation, practical assessment, and formal reporting. Personnel were first required to successfully complete gowning qualifications before being allowed to participate in media fill activities. Requalification requirements were also defined, with gowning qualification every 2 years and media-fill qualification annually. In any case, re-qualification was also repeated after an absence of more than three months from sterile area work. Prior to participation in media fill, personnel were also subject to a practical assessment. Records reviewed during the inspection indicated that gowning and media fill qualification data were generally complete and compliant with the defined requirements.

The SOP for visual inspection/optical control (PHP-704-07, dated 10/01/2024) and the SOP on the general requirements for the qualification of visual inspection/optical control (QAV-024-05, dated 18/03/2026) were reviewed. The SOP for visual inspection defined various defect types appropriately, categorized as critical, major, minor, and cosmetic. The visual inspection process was detailed, with each inspector required to examine 15 vials at a time within a clip, allocating approximately 5 seconds per stage, and a total of 11 inspection stages were performed using both white and black backgrounds, with different vial orientations, including upright, inverted, and slanted positions. Inspection of one box containing 400 vials takes approximately 25–30 minutes. Rest periods were defined, with a short break required after two hours of continuous inspection. Qualification of visual inspectors involved testing using predefined sample sets. For finished product inspection, inspectors were required to evaluate four sets of 400 vials within 30 minutes per set, with each set containing a defined proportion of conforming and defective units. For media fill inspection, each inspector was required to evaluate 415 vials per test, with multiple consecutive test rounds conducted using different sample sets. Sample sets used for qualification were verified using a probability-of-detection (PoD) approach, in which multiple qualified inspectors performed repeated assessments. A PoD threshold of 70% is used to define acceptable detection capability. While the SOP required periodic (annual) verification of sample sets, this requirement had not been implemented.

The job descriptions for the IT manager and supervisor were reviewed and found inadequate.

Deficiencies are detailed in Part 3.

11. Personal hygiene

The facility had established a defined gowning flow and hygiene procedure to control contamination risks when entering different cleanroom grades. Personnel were required to remove street shoes and change into dedicated CNC shoes and head covers upon entry into the initial change room (Grade D). In this area, personnel remove street clothing and don Grade D garments, including shoes, masks, and

gloves, with additional inner garments required for progression into higher-grade areas. The transition from Grade D to higher-classified areas follows a stepwise gowning process. For entry into Grade B, personnel removed Grade D garments and shoes, changed into sandals, and proceeded through an airlock to the next stage, where they donned Grade B garments. This included full cleanroom attire such as booties, coveralls, gloves, goggles, and associated protective clothing. A similar transition process was applied for entry into Grade C areas, with gowning requirements equivalent in principle to those for Grade B, though conducted in designated rooms corresponding to Grade C operations such as dispensing and mixing. The gowning flow appeared to be structured and segregated to minimize cross-contamination between different cleanroom grades. Hand hygiene and disinfection practices were defined at key transition points. Hand washing was performed in the Grade D area, followed by alcohol-based disinfection prior to donning higher-grade garments and before entering Grade B areas. In Grade C areas, disinfection relied on the use of disinfectants without prior handwashing in that zone. While disinfection steps were in place, the reliance on handwashing only at the Grade D stage may warrant further consideration to ensure adequate hygiene control before entry into critical areas.

12. Premises

The Production Plant 2 (Hormone Plant) is a 4-story building that comprises:

- 1st floor: Production area for injection and Packaging
- 2nd floor: Plant utility for injection
- 3rd floor: Production area for solid/tablet
- 4th floor: Plant utility for solid product/tablet

The hormone injection production activities, such as aseptic mixing, filling & sealing vials, storage of sterile active materials, filtration of sterile vehicles, storage of sterile utensils or equipment, were carried out under Grade A/B. Grade C area was provided for sterile gowning, changing, excipient dispensing, vehicle solution mixing, and sterilization tank; Grade D area was used for preparation, washing vials, laundry, capping machine (under LAF), wash bay, WIP, material and equipment storage, and in-process control.

The QC Chemical Laboratory and QC Microbiological Laboratory for testing activities were in separate buildings on the factory/plant site.

There were two WFI distiller units supplying WFI for Hormone Injection Plant 2. The first unit (capacity 450L/hour) has been installed to support the operation of the filling line (Line-2). The new/second unit of WFI Distiller and its looping installed (capacity 1,670L/hour) to support the building capacity, which includes the new filling line (Line-1).

13. Equipment

Several major changes have been implemented since the last inspection, among them the installation of RABS on Filling Line 2, a fixed barrier in the mixing area, the installation of the PUPSIT system, additional looping for the WFI system, and modifications to the HVAC ducting to improve access. PUPSIT (Pre-Use, Post-Sterilization Integrity Testing) procedure was applied for the defined cartridge filter used for sterilization by filtration of a vehicle solution containing excipients in the formulation of hormone injection products. The critical areas, which cover the turntable for empty vials and the filling &

sealing/stoppering vials area, were under cabinets equipped with HEPA filters and fixed-barrier, supported by glove-ports (open RABS) to support aseptic process technique. There were two continuous particle counters mounted in the turn-table area of empty vials and the filling station of each filling machine.

Water for injection (WFI) and pure steam

The qualification and monitoring of critical utility systems, including WFI and pure steam, were reviewed. For the WFI system, a change control (CC No. CC/25/051/2) was implemented to activate the interconnection between WFI Loop 1 and Loop 2 with the objective of ensuring sufficient WFI supply levels. Following the change, additional supply connections were established to the WFI Loop 1 storage tank, which now receives water from both the 200S-4 distiller and the Loop 1 distribution system. The qualification of the interconnected WFI system was performed through two phases, documented in the PQ WFI Phase 1 Report No. PQR-U2-04/24A and Phase 2 Report No. PQR-U2-04/24B. Sampling was conducted at 14 points of use across the system to assess physical-chemical and microbiological parameters. Phase 1 qualification was conducted from 3 January to 17 January 2026, followed by Phase 2 from 2 February to 15 February 2026. No testing was performed between these phases, as the facility was undergoing HVAC performance qualification at rest, and no manufacturing activities involving water usage were conducted during that period. It was noted that Phase 3 qualification, typically expected to demonstrate long-term system consistency, was not executed.

The most recent review of the water trend, covering the period Oct-Dec 2025, was approved on 13/02/2026. All results were reported within specified limits, with no out-of-specification (OOS) or out-of-alert-limit (OOAL) results recorded. However, some data gaps were observed during these periods, manual measurements were performed and reviewed, and no quality concerns were identified. Isolated excursions above alert or action limits were reported in 2025, including one instance in purified water (PW) TOC during the January–March period and several instances in WFI TOC during April–June. These excursions were non-consecutive and returned to normal values without trend indication. On days when sampling was not conducted, production activities were appropriately halted.

The inspection also reviewed the pure steam system used for sterilization processes. Sampling was performed at three key points, primarily at the inlet to autoclaves and sterilization tanks. Since 2024, the frequency of testing has been increased from annual to quarterly, reflecting improved monitoring practices. All testing activities are conducted internally by the facility. Records for testing conducted in March, June, September, and December 2025 were reviewed, and it was indicated that all results met the specified acceptance criteria, with no identified issues in the pure steam system. However, a documentation inconsistency was observed.

Deficiencies are detailed in Part 3.

14. Materials

Two stories shared the main warehouse used for storage of non-hormone materials were allocated in the back area of Hormone Plant-2. Due to time restrictions, this warehouse was not inspected in detail. All APIs and hormones that remained in their original packaging (unopened) were received and stored in the dedicated API Hormone Warehouse for an outer physical check and storage. The other materials (excipients) used for the hormone product were received and stored in the main warehouse before being

gradually distributed to the hormone storage area for routine operations. All finished goods in quarantine status produced at Hormone Plant-2 after packaging would be transferred to the main warehouse and placed in the approved storage area after QA release, prior to being delivered to the distributor.

A separate warehouse for packaging material storage (primary and secondary) and finished product was located in a different location from the main warehouse, located at Jl. Jend. Ahmad Yani No.2 Jakarta 13210 (about 5 km distance or around 10 minutes by car). This warehouse was inspected and found to be generally acceptable. A manual system was used to manage materials, and a Warehouse Management System was planned for future use. The warehouse employed physical separation between quarantined and released material. The yellow label indicated the quarantine status, and it will be pasted with a green release label by QA personnel once it is released.

Deficiencies are detailed in Part 3.

15. Documentation

The document control system was governed by SOP (QAS-007-11 dated 30/05/2024). The SOP outlined a centralized system for document review, approval, distribution, and archiving. Document Control Staff were responsible for reviewing documents and stamping each page of the original document to indicate its official status. The original hard-copy documents were retained in a designated document room, which was secured and access-restricted. Approved documents were made available to users through an Electronic Document Library as an “Only for Information” document. The distribution of controlled documents is managed using Form F-QAS-A004-XX, and hard copies were stamped with a blue “Controlled Document” stamp to indicate their validity. Obsolete documents were clearly marked with a red “Superseded” stamp. SOPs were subject to periodic review every two years, with a formal review process in place. Based on the outcome of the review, documents may be revised or extended, with extensions permitted for up to two years.

Batch Numbering System

The batch numbering system for the finished product (SOP FAC-003-05), dated 29/12/2022, was reviewed. The system defined a structured format. The first three digits represent the sequential manufacturing batch number applied across all products. Once the sequence reaches 999, it is reset to 001. The number would still be unique, as the month and year were indicated by a letter in the fourth digit and a number in the fifth and sixth digits. The final digit would represent the production line. During packaging, an additional alphabetical character is appended to the batch number to differentiate packaging lots, particularly when a partial release is made for different markets. For example, repackaged products are assigned sequential alphabetical identifiers (e.g., A, B) to distinguish between distribution batches.

Batch record review

A detailed review of the batch record was conducted. Master batch records were issued by QA batch staff and formally authorized using a red stamp. A representative batch, numbered 094B261 (started dispensing on 20/02/2026 and ED Feb 2031, was reviewed. The batch documentation system included separate, detailed batch records for each stage of production, including solution vehicle manufacturing, bulk preparation, filling, and capping. Manufacturing of the solution vehicle was conducted in accordance with the Batch Record No. MI SF-005-10-08, while the bulk manufacturing, filling, and

capping stages were conducted based on Batch Record No. MI-006-22-06. A revision to the batch record (effective 27/02/2026) introduced additional instructions for disassembling the PUPSIT system and mixing tank. Weighing activities were performed using an integrated weighing system (Mettler IND780), with printed records available. The records included personnel identification and date and time stamps to ensure traceability. All manufacturing steps, including sterile preparation (the use of autoclaves and ovens, assembly of the Sartopore 2 cartridge filter (0.2 µm) and its housing, and rinsing and soaking of the system using the vehicle solution), were appropriately documented and performed in accordance with established SOPs. Good documentation practices were generally followed. Corrections in records were made appropriately by crossing out entries, with accompanying signatures, dates, and justifications. Thermal printer records were photocopied to ensure long-term legibility. In-process control (IPC) testing was defined with acceptance criteria that allowed progression to subsequent steps.

The manufacturing process included the controlled addition of the vehicle and active ingredient (MPA), followed by mixing in a high-shear mixer with defined cycles and rest periods to prevent overheating. IPC testing of the bulk solution, including pH, density, and assay, was conducted every 30 minutes. The bulk hold time was defined as up to 24 hours, but filling was normally completed within 2–3 hours. Filling operations were conducted over approximately 7 hours and 40 minutes, within the duration validated by media fill studies (8 hours). Filling was appropriately terminated upon observation of air in the tubing, with residual volumes documented. Capping integrity was verified through leak testing using methylene blue, with additional verification by QC using spectrophotometric methods. Visual inspection checks were performed every 15 minutes. Yield was calculated and recorded. Batch documentation also included a checklist section capturing deviations and change controls, where applicable. At the time of inspection, the reviewed batch had not yet been released because packaging had not been completed, and it was stored in a designated work-in-progress (WIP) area within the packaging section. The most recently released batch, 085M251 (manufactured in December 2025), was produced using earlier versions of batch records. The revised instructions were implemented starting from batch 085B261.

The SOP for aseptic filling and closing a vial using a filling and sealing machine, Bosch FLC-3080 (PHP-106-06, dated 25/03/2026), was reviewed to determine whether it described the use of WFI and glove ports without gloves. The SOP stated that autoclaved articles should be transferred to the Grade A area through glove ports before mounting the gloves. Such practices are not acceptable during equipment setup for filling activities. No validated sterilization or VHP steps were performed after the transfer of the articles was completed. The manufacturer confirmed that this part has been challenged through media fill. The manufacturer should note that media fill does not confirm sterility assurance; it demonstrates process capability. The same procedure had described how to perform a leak test on all gloves using a disc leak tester every month. The procedure also stated: “Perform a visual inspection of each glove that will be installed and record it on the provided form.” No clear instructions were provided for performing the visual inspection of the gloves. During the on-site inspection, inspectors found that operators did not consistently perform visual inspection.

Upon review of the SOP for sterilization of the holding tank DCI-200 L (PHP-012-06, dated 06/02/2026), it was noted that the Engineering Manager was granted administrator privileges. No DIRA assessed.

Deficiencies are detailed in Part 3.

16. Good practices in production

The inspection team visited the filling line-I. Separate male/female changerooms were provided before entering the production areas. The gowning instructions were displayed on the walls for both staff and visitors. At the time of the visit to the production area, the filling line-I was being set up. The 200 L holding tank contained a 116 L batch of Triclofem injection. Mobile LAF was used for transferring sterilized articles to the filling line. It was informed that the suspension in the holding tank was continuously mixed. The sterilized articles were transferred through the glove ports without gloves. The RABS was opened for an extended period, and some poor aseptic behavior was observed. The particle count sampling tube was 3 meters long. The inspectors visited Line 2. While proceeding along line 2, the inspectors observed operators performing visual inspections at different stations. A total of 16 stations were provided along with a timer. A break of 10 minutes was taken every 2 hours. The eye examination was conducted annually on operators. An annual challenge test (Knapp test) was performed. Light intensity was checked once a month, and it should be between 2000 and 3750 Lux. An AQL sampling plan was used for visual inspection of vials because 100% inspection was not performed. At the time of the visit to Line 2, Batch No. 185C262, MPA injection was in progress. In general, the line operated smoothly with very few operator interventions. Gloves were mounted on the port while the machine was in operation. The filling was carried out in Grade A with a Grade B background. The in-process samples were taken every 30 minutes by the operator to verify the filled volume. The holding tank lacked a level indicator.

Aseptic process simulation (APS) or media fill

The inspection also included a detailed review of the APS program, which was governed by SOP QAV-002-09, "Performance Qualification of Media Fill," dated 30/12/2024. The facility performs media fill studies for two categories of products, single active pharmaceutical ingredient (API) products and combination products. Media fill activities were conducted for each filling line (1 and 2), considering different equipment trains for the bulk mixing process. For single API products, media fill was performed six times per year. The facility's approach did not apply bracketing principles; instead, each media fill is designed to closely mimic the actual manufacturing process for specific products, such as Triclofem (MPA 1 mL) as a single-API product and Cyclofem as a combination product. For Triclofem, media-fill activities are conducted on both Line 1 (with Equipment Trains 1 and 2) and Line 2. For Line 2, media fills were scheduled in February 2026, following the installation of bypass ducting completed on 2 February, and again in August 2026. For Line 1, media fill for Equipment Train 1 was conducted in December 2025, covering the June–December period, while for Equipment Train 2, execution was performed in February 2026, although the report was not yet available at the time of inspection.

Inspection of the specific media fill study, documented in the Periodic Performance Qualification of Media Fill for Hormone Injection Plant 2 Line 1 (VMFP-02-01-04-25 dated 4/12/2025), indicated that the simulation was designed to represent routine manufacturing conditions. In the media fill, a 60-liter batch was prepared, and approximately 40,000 vials were filled, representing around 31% of the maximum batch size. The firm considered this to be statistically representative and sufficient to cover all planned interventions. Reconciliation of media volumes was adequately documented. The filling volume was set at 0.63 mL, and operations were conducted at normal production speed. However, the media fill duration extended to approximately 8 hours, compared to the routine production duration of 5–6 hours, with activities divided into shorter operational segments. The simulation included both inherent and

corrective interventions, with defined worst-case scenarios in both mixing and filling processes. Personnel qualification was integrated into the media fill program, with documented lists of qualified personnel, including the specific lines and activities for which they are authorized. However, several deficiencies were identified in the documentation and execution of these interventions as described in Part 3.

17. Good practices in quality control

The inspectors visited the physical chemical laboratories, which were renovated since the last PQ inspection in 2023. The incoming samples were logged in the manual logbooks, and a QC number was assigned to the sample. The competency matrix was available for the analysts. The laboratory was equipped with 7 HPLC systems containing a UV-VIS detector. Empower 3.471 was used by the laboratory. In addition, the laboratory has UV-VIS, FTIR, analytical balances, a particle tester for subvisible particles, an osmolality tester, a Karl Fisher apparatus, and others. The inspectors visited the microbiology laboratory. The laboratory can be accessed via biometric access.

The manufacturer renovated the microbiology laboratory after the last PQ inspection in August 2023. After the initial gowning procedure, the first changeroom was equipped with a handwash facility and a dryer. Separate MAL/PAL were provided before entering the testing areas. A double-door autoclave was used to sterilize media, and the media were then transferred to plates for preparation under LAF. The sterility testing was carried out in an isolator with a Grade D background. Passbox was used to transfer plates and media. Before the start of the sterility testing in the isolator, the operator was required to perform a leak test, bio-decontamination using 35% H₂O₂, monitor particulate matter, and use an air sampler. For the environmental monitoring, sterile plates were placed on both sides of the sterility testing areas. 17 samples at maximum could be tested in one campaign, whereas 5-7 samples were tested at one time. The samples were placed inside the sample compartment within the sterility isolator. A biosafety cabinet (2B2 type) was used for positive controls. Endotoxin test was performed using photometric (for WFI) and gel clot for routine testing. The inspector visited the stability section, which was equipped with several stability chambers with different temperature and relative humidity conditions. The retention samples room was briefly visited, and it was noted that split air conditioners were provided to maintain the temperature below 25 °C. The retention samples were not stored in their marketed packs. Also, the room temperature was found to be 19.9 °C, which is below the MPA injection storage condition of NMT 30 °C.

Handling of Out of Specification (OOS)

The OOS system was governed by SOP QCC-001-05 on OOS in chemical analysis, dated 8/05/2024, and SOP QCM-040-05 on OOS in microbiological analysis, dated 19/05/2023. While the overall process flow described in both procedures was the same, the level of detail and the guiding questions used during investigations differed. OOS investigations were required to be completed within one month, while laboratory incidents were to be closed within 14 calendar days. In the microbiology laboratory, no formal system was in place for managing laboratory incidents. Therefore, incidents such as undefined results or errors related to failed curve parameters in endotoxin testing were recorded and handled as OOS cases. It was noted that no actual microbiological OOS results have been recorded since 2023. In the chemical laboratory, 26 of 64 OOS cases in 2025 and 6 of 14 OOS cases in 2026 were related to Triclofem products. Many of these cases were attributed to errors in sample handling and suboptimal vial cleaning practices. These data suggest that laboratory practices, particularly related to sample preparation and

handling, remain a significant source of variability and error. OOS data were trended and presented in the Management Review Report. A total of 98 OOS cases were reported across all laboratories; among them, 20 cases were attributed to sample deficiencies or defects, which means they were confirmed as OOS. It primarily involves development samples or testing on expired stability samples. Specific case reviews of OOS/C/25/010/H, involving an assay result for medroxyprogesterone acetate (MPA) in content uniformity exceeding the maximum specification (118.7% against a limit of 90–110%) and OOS/C/25/027/H involving an assay result above specification for progesterone bulk product, highlighted deficiencies in the robustness of OOS investigations and CAPA implementation as further detailed in Part 3.

Handling of Out-of-Trends (OOT)

The OOT was governed by SOP QAS-043-03 on Trend Review and OOT dated 14/07/2025. The procedure defines a relatively broad scope of OOT monitoring, including analytical results of active pharmaceutical ingredients and other critical parameters as determined by risk assessment, in-process control results for bulk products, finished product testing such as assay and content uniformity, environmental monitoring results for microbiological parameters, water monitoring results including total organic carbon (TOC), conductivity, and total plate count (TPC), temperature monitoring in warehouse areas, as well as Product Quality Review (PQR) data. A list of trend limits has been established and is subject to periodic review and update based on observed manufacturing trends or PQR outcomes, indicating that a structured trending framework has been defined. Case of OOT/QC/24/018, involving a low assay result of progesterone product in the finished product Triclofem batch #673H241, was reviewed. The case was recorded and then closed without further investigation, as this incident was only the second occurrence of a similar OOT incident, and the SOP dictates that a formal investigation be assessed or initiated after the third occurrence. A consolidated list of OOT events for products since 2023 was available during the inspection, and 16 OOT cases were identified as being associated with Triclofem products. Further review highlighted deficiencies in the application of OOT procedures as detailed in Part 3.

Miscellaneous	
<i>Samples taken</i>	<i>None</i>
<i>Assessment of the site master file</i>	<i>The site master file (PSMF-P02-10 March 2026) was provided prior to the inspection. It provided a high-level overview of the on-site manufacturing activities.</i>
<i>Annexes attached</i>	<i>None</i>

Part 3	List of deficiencies
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Unless otherwise indicated, references below are to the WHO good manufacturing practices for pharmaceutical products: main principles. *WHO Expert Committee on Specifications for Pharmaceutical Preparations. Forty-eight Report* Geneva, World Health Organization, 2014 (WHO Technical Report Series, No. 986), Annex 2 (document 1 in Part 5 below).

Deficiencies		References
1. Critical		
1.1	None	
2. Major		

2.1	Aseptic practices were found to be inadequate and could lead to contamination, cross-contamination, and compromise of sterility assurance. Examples include but are not limited to the following: <u>Improper use of glove ports/barrier systems:</u> a) Glove ports were used without gloves being mounted during equipment setup or interventions. No validated sterilization or VHP steps were performed after the transfer of the articles was completed. The manufacturer confirmed that this part has been challenged through media fill. The manufacturer should note that media fill does not confirm sterility assurance; it demonstrates process capability. b) Materials were transferred through open glove ports without maintaining a closed barrier. c) Operators accessed Grade A areas without ensuring the integrity of the barrier system. d) When sterilized material was placed in a grade A area, the cabinet was opened for a period of time without a specified time limit. There was also no restriction on the cabinet's opening and closing, yet at this point, it defeats the purpose of having a cabinet with gloves. <u>Availability of extended LAF</u> a) In Filling Line 1, not all cabinet openings were equipped with extended LAF, but all cabinet openings can be used, so there is a risk of loss of laminar protection during opening in areas without LAF. b) In Filling Line 2, the opening for rubber stopper insertion was not equipped with an extended LAF. c) Rubber stopper inserting areas were interrupted by personnel standing under the LAF for the setup to install gloves in one of the glove points. <u>Inappropriate use of WFI in Grade A:</u> WFI was used to lubricate or facilitate the movement of machine parts (e.g., pistons) inside Grade A during setup. These practices were not clearly supported by documented procedures or validation demonstrating maintenance of aseptic conditions and contamination control. For example, microbial growth risk (if stagnant), dilution risk, and loss of equipment control, etc. <u>Poor aseptic manipulation techniques:</u> a) The operator was seen leaning on the filling line. Also, the operator was observed touching the RABS panels and the HMI without re-sanitization. b) Visual checks were not performed on the black gloves before mounting them on the ports. The SOP did not provide clear step-by-step instructions on integrity verification. c) The alarm messages that appeared on the HMI screen of the filling machine were not acknowledged. During the inspection of filling line 1, an alarm was observed throughout the setup period. In the filling line 2, during the process, an alarm regarding the bowl stopper issue was detected; it was acknowledged repeatedly, but kept recurring. No	<i>WHO TRS 1044 Annex 2, 4.18, 4.20</i> <i>WHO TRS 1044 Annex 2, 7.4,</i> <i>WHO TRS 1044 Annex 2, 4.10</i> <i>WHO TRS 1044 Annex 2, 5.9</i> <i>WHO TRS 1044 Annex 2, 4.21</i> <i>WHO TRS 1044 Annex 2, 5.2</i> <i>WHO TRS 1044 Annex 2, 7.11</i> <i>WHO TRS 1044 Annex 2, 4.4; 4.15 and 4.20.ii.a</i> <i>WHO TRS 986 Annex 2, 14.28</i> <i>WHO TRS 1044 Annex 2, 7.9</i> <i>WHO TRS 1044 Annex 2, 9.34-9.35</i>
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	action was taken, and the filling line continued as usual. d) The manufacturer used one-size-fits-all gowning for all operators, increasing the risk of falling or adjusting their gowning during the operation. e) Upon reviewing the video recording of the air visualization test for filling line 1, the door was opened for manual intervention; however, there was no confirmation of the air's laminarity. The air did not fall on the object or the working area to ensure the first air concept. Also, there was no confirmation of the air ingress from the Grade B to the Grade A area. f) The empty vials rejected during the filling operation were not stored in a locked container. g) No communication device was available for the operator to communicate with external personnel. <u>Incorrect particle counter issue:</u> a) Particle counter sampling tube length used in Line 1 was found to be 3 meters long (typically no longer than 1 meter). No documented assessment was available to use a tube that long. A similar observation was made for Line 2. b) The sampling head for the particle counter in line 1 (vial turn table) was not correctly oriented c) The tube in line 2 (vial turn table) had at least 4 unjustified bends. <u>Aseptic Process Simulation</u> a) One of the worst cases in the filling process was the installation of filling parts, including 14 pairs of gloves. The protocol was not clear about what activities were performed, even though it involved many interventions in the Grade A areas. It did not include a detailed description of the timing for opening the door, which door to open, what material to insert, or how long the door should remain open. b) The power failure duration of 5 minutes was included in the worst-case intervention, which may be used to justify unnecessary risk.	
2.2	Qualification and validation activities were not adequately carried out. Examples include but are not limited to the following: a) The validation protocol for validating materials transferred into Grades B and A and transfer media (after use/exposure) from production to the incubator did not specify which transfer method/system (bag-in/bag-out, pass-through, etc.) was used to validate the transfer system. Similarly, no worst-case was defined to confirm the largest item transferred, the heaviest item, the most frequent transfer, the maximum transfer duration, the maximum exposure time, etc. The transfer validation was not simulated, considering airflow visualization, repeated transfers, integrity testing, number of runs, and environmental monitoring, etc. b) The cleaning validation procedure did not meet the current requirement using the maximum daily dose or batch size. It still referred to the use of LD50 and other obsolete criteria. Also, the	<i>WHO TRS 1044 Annex 2, 4.12.ii</i> <i>WHO TRS 1019 Annex 3, Appendix 3, 11.5 and 11.9</i> <i>Guideline on setting HBEL for use in risk identification in the manufacture of</i>

	worst-case for MACO was not calculated based on the molecule's toxicity and potency, but instead on its composition. c) The manufacturer produces products containing hazardous hormonal substances such as Estradiol Cypionate and Medroxyprogesterone acetate. Some of these products required adequate containment based on the occupational exposure band. However, appropriate controls were not implemented to ensure containment. Also, the PDE report for Estradiol Cypionate was not available. d) Computer system validation was found deficient. - Several of the software and operating systems were found to be obsolete (e.g., Minitab, Empower, Particle Monitoring System, Bosch filling machine HMI, and Windows); however, no assessment was available to confirm existing versions were able to meet the cGMP requirements. - The periodic review of the computerized system was not carried out, hence no revalidation activities were carried out. - For the laboratory equipment (Empower), calibration and preventive maintenance were performed annually, whereas CSV was performed in 2019. There was no system in place to revalidate the system through periodic review. - The list of the computerized systems used on-site was found inadequate as it did not cover the entire list of systems used on-site. Also, the list did not provide information on when the software was last validated and when it is due for the next validation. e) Qualification label on the incubator (INK-QM-013) was found to be ambiguous. The incubator was qualified in February 2026 and the qualification label indicated that it was valid until March 2027 (13 months instead of 12 months). In addition, the label allowed for further extension of qualification. Such practices are not acceptable. f) For the dry heat sterilizer (tunnel), the limit of $\pm 15^{\circ}\text{C}$ for the temperature distribution was not justified. Also, there was no confirmation that the cold spot was above the validated minimum temperature; depyrogenation was validated at 235°C, and endotoxin reduction was demonstrated at this temperature. The results were tabulated, but no interpretation was performed to identify hot/cold spots or their impact on day-to-day operations.	<i>different medicinal products in shared facilities, Point 4.</i> <i>WHO TRS 1019 Annex 3, Appendix 5, 1.4, 13.15</i> <i>WHO TRS 1019 Annex 3, Appendix 6, 11.2-11.4</i> <i>WHO TRS 1019 Annex 3, Appendix 6, 10.2</i> <i>WHO TRS 957, Annex 3</i>
2.3	The pharmaceutical quality system did not adequately encompass and address the specific requirements for sterile products, in order to minimize the risk of microbial, particulate, and endotoxin contamination. Examples include but are not limited to the following: <u>Change controls</u> Change controls were not adequately managed to ensure the exact number of changes raised, opened, and closed. The Excel spreadsheet used for logging change controls did not provide precise information on the number of changes handled.	<i>WHO TRS 986, Annex , 1.5.n</i> <i>WHO TRS 986, Annex 2, 1.5.s</i> <i>WHO TRS</i>

	b) The change related to housing filter assembly modification with the PUPSIT system was discussed. i. No clear rationale for implementing PUPSIT in the change control form. ii. Risk assessment was not performed to ensure there were no filter integrity failures, sterilization damage, operator handling, PUPSIT execution failures, suspension blockage, line contamination, or sterility assurance level. iii. The CFT did not adequately assess the impact of the proposed changes, and no notification of this major change was made to Badan POM and the WHO PQ assessment team. c) Change control related to the addition of alternative manufacturers for PEG 3350 and Propyl Paraben was opened on 06/10/2023. A questionnaire was sent to the manufacturer; however, no information was available on the GMP standards applied by the manufacturer. Also, there was no confirmation of the materials manufactured on-site, raising concerns about potential contamination and cross-contamination. The information provided by the suppliers was not assessed to determine adequate controls at the excipient manufacturer's end. The cross-functional team neither reviewed the proposed change nor provided sufficient feedback. The change has not been closed yet. d) Another change related to upgrading the existing 200L DCI holding tank with HMI/PLC panel and control system features was raised on 06/10/2023. The implementation timeline kept getting extended, and the change has not yet been closed. e) The change related to modifying the filling machine line 2 (FLC 3040) with RABS and glove ports was discussed. The RA and QC manager provided no assessment. No notification was made to Badan POM and WHO PQ. <u>Deviation management</u> a) Cases of recurrence of cracked vials due to breakdown of capping line-2 VRK-2005 B have been happening since 2022. This had been the most frequent issue since 2023, and it has led to several low-yield cases for Triclofem. However: a. Cases of recurring incidents that were still in the fulfillment stage of CAPA were recorded as events, and the number of events was not monitored properly, so the urgency and impact of the deviation might be undervalued. In the case of LP/24/012/2 regarding the cracked vials, there were 37 recurrent cases in 2024. b. Trending was conducted for deviation, but the recommendation given was a general/ performative one without a clear follow-up plan. For example, in 2023, the recommendation was to ensure spare parts were available, and this was repeated in 2024 and 2025.	<i>1044, Annex 2, 3.1</i> <i>WHO TRS 986, Annex 2, 1.10</i> <i>WHO TRS 986, Annex 2, 1.6</i> <i>WHO TRS 986, Annex 2, 17.12</i>
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- c. During the release process of Batch 041M252, the checklist on the deviation part was checked, but the form for batch disposition on the review release batch in Event form F-QAS-A031-03 of EV/25/157/2 was filled as not available (no clear batch disposition).
- d. No deviation was raised when stability chamber #1 was turned off/ disconnected on 08 January 2026 for around 40 minutes from 09:55 to 10.35. The records were unclear about the reason for the deviation. In the logbook, it was noted that the chamber temperature exceeded 32 °C, but the alarm record indicated that the chamber was turned off. The personnel said it was for maintenance and changing the cooling system.

CAPA Management

- a) There was no limitation on the CAPA extension.
- b) Submission of CAPA changes/additions, including CAPA fulfillment target, did not require any impact assessment to assess the risk of such extension.
- c) Lack of CAPA monitoring was observed on CAPA to minor Deviation No LP24/003/2.
- d) Deviation happened on 11 January 2024, CAPA to that deviation was due on 5 April 2024, but no action was taken. CAPA extension was requested on 4 March 2025, almost one year after the CAPA was due.
- e) The justification for granting the extension was not reasonable. The reason was that the personnel needed to review the 2025 batch, which cannot be done until the end of 2025, but the extension granted was only up to June 2026.

Management review (MR)

There was no discussion or direction from the Management during the MR Meeting on 17 March 2026 regarding several outstanding cases, including 425 (53,55%) open changes, 2078 (out of 13683) overdue CAPA, and pending deviations. The QC laboratory's testing performance was also not addressed properly in the MR meeting report.

Out of specifications and Out of Trends

- a) Based on the review of the OOS trends, although several similar root causes were identified, there was no recommendation issued for improvement.
- b) Regarding OOS/C/25/010/H, it was mentioned that a vial cleaning study was conducted because similar issues regarding carryover results were found, but this study was not conducted based on a systematic trend review process. The protocol and report for the study were not available during inspection (only the results of the study on 9 March 2026 were available).
- c) Regarding OOS/C/25/027/H, which was due to an error in handling samples, there was no preventive action proposed or conducted. It

	was mentioned that personnel were briefed, but it was not documented. d) Although a low assay on Propyl Paraben and an anomaly on pH stability samples were not required to be reported as OOT as per SOP, this was recorded as OOT. Interpretation of OOT and awareness of it differed among analysts, which should be improved to ensure that any necessary OOT is recorded. <u>Review of critical data analysis</u> a) The PQRs were not critically reviewed to ensure appropriate changes were made in the manufacturing processes or specifications. b) Nitrosamine risk assessment was not appropriately performed, as the information received was not reviewed, and an appropriate assessment was not performed.	
2.4	Inadequate data integrity governance and control of computerized and manual GMP records were noted. Examples include but are not limited to the following: a) During inspection of filling lines 1 and 2, the online particle counters consistently indicated zero particle counts in the Grade A and B areas. Review of the AHU qualification for Line 2 also showed no particle detections in Grade A, B, and C areas, except immediately following smoke generation. The manufacturer did not demonstrate that the particle counters used during routine manufacturing and AHU qualification were adequately calibrated, maintained, and correctly operated. In addition, the impact of sampling tube length and bending on particle detection performance had not been assessed. These observations raise concerns regarding the reliability and integrity of environmental monitoring data generated during aseptic processes. b) The microbiology laboratory had 14 incubators, all of which were standalone. No DIRA was performed to assess any gaps and implement adequate controls for data integrity. c) The time zone and system date/time settings on the computer used for recording colony counts were not locked. This same issue was also identified in many other systems, including the particle counter system and the Windows platform used for the HPLC's Empower program. d) The CFUs were counted manually by the microbiologist, whereas there was no system in place to independently verify the counts before transcribing the results into an Excel sheet. The Excel spreadsheets were not locked. e) For the HPLC System a. The account of Administrator with super role (open access to all privileges) was said to be disabled, but the user groups still had the account name listed. b. Password for IT user account was stored in standard envelopes, which can easily be opened and changed if they	<i>WHO TRS 1044 Annex 2, 5.9</i> <i>WHO TRS 1033, Annex 4, 5.1</i> <i>WHO TRS 1033, Annex 4, 4.15</i> <i>WHO TRS 1033, Annex 4, 9.6</i> <i>WHO TRS 1033, Annex 4, 11.3</i> <i>WHO TRS 1033, Annex 4, 11.9</i> <i>WHO TRS 1033, Annex 4, 8.3</i> <i>WHO TRS 1033, Annex 4, 11.6, 4.15</i> <i>WHO TRS</i>

	were torn open. c. First verification after preparation, which was conducted by a peer analyst, was not attributable based on form FQCC-A171-00. The step was also not mentioned in the SOP #QCC-109. d. The privilege to modify integration parameters was given to the Waters Engineer without documented justification or risk assessment. e. Monthly Project data was backed up to an external hard disk without an adequate risk assessment. f. There were no documented procedures or defined acceptance criteria available for data restoration activities. f) For the double-door autoclave (Getinge), no user access or password was required before running the autoclave cycle. The leak test was performed daily. g) Sufficient resources were not provided to the IT team to support all GMP-related activities. h) Upon review of the SOP for sterilization of the holding tank, it was noted that the Engineering Manager was granted administrator privileges without any documented justification. No DIRA was performed. i) The DIRA for the hormone machine injection process did not include quality system training, personnel, internal audits, and outsourced activities. The DIRA used an obsolete WHO reference. j) The administrator privileges were given to the laboratory supervisors for analytical balances. The date/time was subject to change as observed by the inspection team. k) The cabinets used for storing the QC records were not locked. l) Generic user accounts, including those for supervisors and operators, were used for the human-machine interface (HMI) of the WFI system, and shared passwords were applied, compromising individual user traceability.	<i>1033, Annex 4, 5.1</i> <i>WHO TRS 1033, Annex 4, 11.6</i> <i>WHO TRS 1033, Annex 4, 11.9</i>
2.5	Quality control laboratory systems were not adequately designed, monitored, or controlled to ensure the reliability of testing and stability data. Examples include but are not limited to the following: a) No temperature mapping was performed where incoming samples were stored in the QC laboratory. Upon examination of the thermohygrometer placed inside the sample storage room, a temperature range of 11°C to 32.7°C and a relative humidity range of 30 to 89% were noted. b) A significant backlog of routine and stability samples was noted. The 45-day timeline for completing the testing had been extended on several occasions. No documented assessment and justification available. c) Retention samples of MPA injections were not packed in their marketed packs.	<i>WHO TRS 986, Annex 2, 12.16</i> <i>WHO TRS 986, Annex 2, 17.3</i> <i>WHO TRS 986, Annex 2, 17.21</i> <i>WHO TRS 1052, Annex 4,</i>

	d) The alarm for stability chambers was only available in the working area. Hence, any alarm excursion, especially one that occurred outside working hours, might not be detected until it is due for the monthly verification. e) If a temperature excursion of the stability chamber happened for more than 24 hours, the SOP did not dictate the actions to be taken after the mean kinetic temperature (MKT) was calculated. f) The analytical balances were not operated within their calibration ranges.	5,17 WHO TRS 1052, Annex 4, 5.36
2.6	The quality risk management systems were not effectively implemented to support GMP decision-making. Examples include but are not limited to the following: a) No risk assessment was performed to determine if containment requirements were adequate for the manufacture of products containing hazardous substances, e.g., MPA and Estradiol Cypionate. b) No containment arrangements were implemented in the QC laboratory for the safe handling of products containing MPA, Estradiol Cypionate, etc. As such, no risk assessment was performed. c) No risk assessment was performed to determine the risk of antimicrobial resistance. d) For PEG 3350, no risk assessment was performed to determine the GMP standards used by the excipient manufacturer. A similar case was that of Propyl Paraben. e) Risk assessments related to nitrosamine impurities were not adequately performed. The information provided by various suppliers regarding the materials was not reviewed to ensure there was no risk of nitrosamines. In the risk assessment, the manufacturer confirmed that on-site WFI did not contain nitrosamine impurities. However, such an assessment was not supplemented with any testing of WFI. Similarly, no testing was performed on Triclofem injection to confirm the absence of nitrosamines.	WHO TRS 986 Annex 2, 1.8, 1.9 WHO TRS 981, Annex 2, points 1 and 3 WHO TRS 1060, Annex 2, 1.10 WHO TRS 957, Annex 3, 4.1-4.4
3. Other		
3.1	Microbiology laboratory a) No hand sanitizer was used before entering the microbiology laboratory. b) The pressure differential was not maintained between the first changeroom and airlock (50 Pascal against the limit of 5-35 Pascal). No alarm provision was made. c) The biological safety cabinet (BSC) used for the microbial limit test was poorly maintained, as the return filter was found damaged (fibers from the return filter were coming out). d) Empty plates were stored inside the LAF/testing area. e) No clean hold time was established for the washed plates before using them further. f) A dynamic passbox was used in a two-way manner to receive and return materials, plates, etc. However, no instructions were provided	WHO TRS 961, Annex 2, 2.3 WHO TRS 961, Annex 2, 2.2 WHO TRS 961, Annex 2, 4.1 WHO TRS 961, Annex 2,

	to ensure adequate decontamination had taken place before/after the transfer, and activities were not carried out simultaneously. g) During extended holiday periods, temperature monitoring of incubators was not performed. No alarm system was in place to notify personnel of temperature excursions in the microbiology laboratory, and the incubators were not connected to an uninterruptible power supply (UPS), increasing the risk of undetected deviations. h) A labeling system to identify culture media that had been subjected to and passed growth promotion testing (GPT) was not implemented, resulting in inadequate status identification. i) Over-gowning was performed inside a positive-pressure area with the door open, and the pressure differential between the surrounding corridor and the area could not be verified. j) The Bowie-Dick test was performed once per month, with no documented justification. k) A toilet facility was located at the entrance opposite the first change room, which is not consistent with standard GMP facility design.	2.1.4 <i>WHO TRS 961, Annex 2, 5.3</i> <i>WHO TRS 1044, Annex 2, 8.61</i>
3.2	Product quality review (PQR) a) Review of the PQR for MPA injection covering Jan-Dec 2025 (dated 26/03/2026) showed that batch data was tabulated; however, no critical analysis or trend evaluation was performed. This included, but was not limited to, excipients, packaging materials, and the filling line yield. It was noted that 18 of 79 batches did not meet the predetermined yield acceptance criteria. No further assessment was performed, and no action was taken. Similarly, review of extractable volume data identified several batches outside control limits, for which no further actions were documented. b) Critical process parameters were not calculated for process capability, and it was reported that “one or more parameters during production showed no trend” without performing trend analysis. Ppk values for several parameters were calculated, whereas some Ppk values for the MPA assay (bulk) were well below 1.00. No assessment was performed, and no action was taken. c) The PQR SOP did not require verification of data transcribed from the raw data into the Minitab. d) The acceptance criteria used for PpK calculation were found inadequate (e.g., 1.00-1.32 stated as acceptable and less than 1.00 stated as not acceptable without providing any action plan). e) The Minitab SOP was not cross-referenced with the PQR SOP.	<i>WHO TRS 986 Annex 2, 1.10</i>
3.3	Job descriptions (JDs) a) The JDs of the IT manager (Mr. Silvan) and the IT supervisor (Mr. Dwi Fitriador) were found to be generic in nature, without clearly defined responsibilities. In particular, the JDs did not specify responsibilities related to critical GMP-relevant IT activities, including user and access management, password management, data	<i>WHO TRS 986 Annex 2, 9.3</i>

	backup, archiving, and data restoration. b) The JDs did not delegate responsibilities to other IT personnel for continued operation and support in GMP activities.	
3.4	Business continuity plan The manufacturer had no approved business continuity plan.	<i>WHO TRS 1052, Annex 4, 1.2, 4.24</i>
3.5	Line clearance The SOP for line clearance was general and did not provide specific details or areas to inspect as part of the procedure. There was no checklist or equivalent document used to record line clearance activities, especially in critical or hard-to-detect areas.	<i>WHO TRS 986 Annex 2, 15.24(f)</i>
3.6	Air handling units (AHUs) a) Pressure across the pre-filter and the filter used in the AHUs was not monitored and recorded. b) No system was in place to verify the integrity of the ducts. c) Tamper-proof seals for dampers, magnehelic gauges, and others were not used across the servicing areas.	<i>WHO TRS 986, Annex 2, 4.3(a,b,c) WHO TRS 1010, Annex 9, 7.4, 6.2</i>
3.7	Water for injection (WFI) a) No system was in place for alarm management. b) There were no sampling points from the WFI storage tank (Distiller Type 850TF) to the supply point. c) Phase 3 qualification was not executed and was replaced with routine WFI monitoring performed by Quality Control. However, a discrepancy was identified in the sampling coverage: routine monitoring included only 12 points of use, whereas qualification activities covered 14 points. Specifically, two points associated with each distiller (850TF and 200S) were excluded from the routine monitoring program without justification.	<i>WHO TRS 1044, Annex 2, 6.10, 6.13</i>
3.8	Recall The latest mock recall was conducted on 24/07/2023 for the Class II recall of Triclofem batch 205B232A. For that recall, the rationale for choosing a product based on the distribution chain, or for choosing the recall category, was not available. The SOP on Recall was renewed in 2026 to have a mock recall every 2 years for the foreign market, and the next mock recall was scheduled in June 2026.	<i>WHO TRS 986, Annex 2, 6.8</i>
3.9	Complaint Handling a) Multiple complaints received regarding Triclofem Injection for the same failure mode, namely “clogging issue during aspiration”. A total of eight complaints from different sources were reported, involving multiple batches (Triclofem batch 198J21, 564E21, 489H252A, 403G251A, and 100B251A). At the time of the inspection, all related investigations were still ongoing. b) Although the SOP on complaints required investigations to assess potential links to common materials, tools, equipment, manufacturing lines, production sequences (before/ after), and personnel or methods used, these aspects were not addressed in the	<i>WHO TRS 986, Annex 2, 5.3, 5.6-5.8</i>

	investigation of complaint No.001/PC/QA/24 concerning sticky granules in the vial neck. The investigation was limited to the affected complaint batches only.	
3.10	Training and qualification of personnel - Aseptic behavior assessment had not been included as an evaluation parameter for the qualification of personnel working in aseptic areas. Although aseptic behavior during media fill activities was observed and recorded, the recordings were not subsequently used for training. - The SOP for visual inspection/optical control did not include visual aids or photographs to support visual inspectors in the identification and classification of defects. - The procedure for preparation of sample sets used in the qualification of visual inspectors for media fills was not clearly defined in the SOP. - Annual verification of visual inspection sample sets using probability-of-detection had not been performed. Although it was stated that a verification exercise was conducted in November 2025 using fewer qualified inspectors (three), this activity was not documented. A further verification was reportedly planned for Q2 2026. - Visual inspection for vials (products) was supposed to be conducted using four sets of 400 vials over a 30-minute period to simulate a two-hour routine inspection activity; however, the start and end times of the test were not recorded.	<i>WHO TRS 986, Annex 2, 10.1-10.3</i> <i>WHO TRS 1044, Annex 2, 7.3, 8.31</i>
3.11	External Warehouse Only 1 point was used for the temperature monitoring of the warehouse, with no consideration of the size of the room.	<i>WHO TRS 986, Annex 2, 12.16</i>
3.12	Pure Steam Inappropriate documentation was used for pure steam testing, as Form F-QCC-A-230-02, intended for water system monitoring, was applied. This was not in accordance with SOP PUM-053-03 (Maintenance of the Clean Steam System), which specifies the use of Form F-PUM-A138-XX for quarterly monitoring of the clean steam system.	<i>WHO TRS 986, Annex 2, 15.9</i>

Comments: NA

Part 4	Initial conclusion – Inspection outcome
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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, a decision on the compliance of **Tunggal Idaman Abdi**, located at **PO Box 4009, Jl. Jend. Ahmad Yani no. 7, Jakarta, 13230, Indonesia**, with WHO good manufacturing practices for pharmaceutical products guidelines will be made after the manufacturer's response to the observations has been assessed.

The manufacturer is expected to respond to all observations and, for each, include a description of the corrective action implemented or planned, and the date of completion or target date for completion. In

addition, for observations classified as "Major", supporting documentation should be submitted with the response as objective evidence of completion of corrective actions. The acceptability of corrective actions will be assessed by evaluating the response to each observation and will be followed up on during the next inspection.

Name(s)	Vimal Sachdeva Anandayu Nurfachtiyani
Signature(s)	Signed on behalf of the inspection team 
Date	14 April 2026

DEFINITIONS

Critical deficiency

A *critical* deficiency may be defined as an observation that has produced, or may result in a significant risk of producing, a product that is harmful to the user.

Major deficiency

A *major* deficiency may be defined as a non-critical observation that:

- has produced or may produce a product that does not comply with its marketing authorization and/or prequalification application (including variations);
- indicates a major deviation from the GMP guide;
- indicates a failure to carry out satisfactory procedures for release of batches;
- indicates a failure of the person responsible for quality assurance/quality control to fulfil his or her duties;
- consists of several other deficiencies, none of which on its own may be major, but which together may represent a major deficiency and should be explained and reported as such.

Other deficiency

A deficiency may be classified as *other* if it cannot be classified as either critical or major but indicates a departure from GMP. A deficiency may be *other*, either because it is judged to be minor or because there is insufficient information to classify it as major or critical.

Classification of a deficiency is based on the assessed risk level and may vary depending on the nature of the products manufactured, e.g., in some circumstances, an example of another deficiency may be categorized as major.

Part 5	List of GMP Guidelines referenced in the inspection report
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1. WHO good manufacturing practices for pharmaceutical products: main principles. WHO Expert Committee on Specifications for Pharmaceutical Preparations. Forty-eight Report Geneva, World Health Organization, 2014 (WHO Technical Report Series, No. 986), Annex 2. **Short name: WHO TRS No. 986, Annex 2**
<https://www.who.int/publications/m/item/trs986-annex2>

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**
<https://www.who.int/publications/m/item/annex-2-trs-957>
3. 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://www.who.int/publications/m/item/trs-1025-annex-4>
4. Good manufacturing practices: guidelines on validation. WHO Expert Committee on Specifications for Pharmaceutical Preparations. Fifty-Third Report. Geneva, World Health Organization, 2019 (WHO Technical Report Series, No. 1019), Annex 3. **Short name: WHO TRS 1019, Annex 3**
<https://www.who.int/publications/m/item/trs1019-annex3>
5. General guidelines for the establishment, maintenance, and distribution of chemical reference substances. WHO Expert Committee on Specifications for Pharmaceutical Preparations. Forty-First Report Geneva, World Health Organization 2007 (WHO Technical Report Series, No.943) Annex 3. **Short name: WHO TRS No. 943, Annex 3**
http://whqlibdoc.who.int/trs/WHO_TRS_943_eng.pdf?ua=1
6. WHO Good Practices for Pharmaceutical Quality Control Laboratories. WHO Expert Committee on Specifications for Pharmaceutical Preparations. Forty-fourth Report. Geneva, World Health Organization, 2010 (WHO Technical Report Series, No. 957, Annex 1. **Short name: WHO TRS No. 957, Annex 1**
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7. 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://www.who.int/publications/m/item/trs957-annex3>
8. WHO good manufacturing practices for sterile pharmaceutical products. WHO Expert Committee on Specifications for Pharmaceutical Preparations. Fifty-Sixth Report Geneva, World Health Organization, 2022 (WHO Technical Report Series, No. 1044), Annex 2. **Short name: WHO TRS No. 1044, Annex 2**
[TRS 1044 - 56th report of the WHO Expert Committee on Specifications for Pharmaceutical Preparations](https://www.who.int/publications/m/item/trs1044-annex2)
9. WHO guidelines on transfer of technology in pharmaceutical manufacturing. WHO Expert Committee on Specifications for Pharmaceutical Preparations. Fifty-Sixth Report Geneva, World Health Organization, 2022 (WHO Technical Report Series, No. 1044), Annex 4. **Short name: WHO TRS No. 1044, Annex 4**
[TRS 1044 - 56th report of the WHO Expert Committee on Specifications for Pharmaceutical Preparations](https://www.who.int/publications/m/item/trs1044-annex4)
10. Model guidance for the storage and transport of time-and temperature-sensitive 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 9. **Short name: WHO TRS No. 961, Annex 9**
https://cdn.who.int/media/docs/default-source/medicines/norms-and-standards/guidelines/distribution/trs961-annex9-modelguidanceforstoragetransport.pdf?sfvrsn=b80e925f_5
11. WHO good practices for pharmaceutical microbiology laboratories. WHO Expert Committee on Specifications for Pharmaceutical Preparations. Forty-Fifth Report Geneva, World Health Organization, 2011 (WHO Technical Report Series, No. 961), Annex 2. **Short name: WHO TRS No. 961, Annex 2**
http://whqlibdoc.who.int/trs/WHO_TRS_961_eng.pdf?ua=1
12. WHO guidelines for drafting a site master file. WHO Expert Committee on Specifications for Pharmaceutical Preparations. Forty-Fifth Report Geneva, World Health Organization, 2011 (WHO Technical Report Series, No. 961), Annex 14. **Short name: WHO TRS No. 961, Annex 14**
http://whqlibdoc.who.int/trs/WHO_TRS_961_eng.pdf?ua=1

13. WHO guidelines on quality risk management. WHO Expert Committee on Specifications for Pharmaceutical Preparations. Forty-Seventh Report Geneva, World Health Organization, 2013 (WHO Technical Report Series, No. 981), Annex 2. **Short name: WHO TRS No. 981, Annex 2**
<https://www.who.int/docs/default-source/medicines/norms-and-standards/guidelines/production/trs981-annex2-who-quality-risk-management.pdf>
14. WHO guidelines on variation to a prequalified product. WHO Expert Committee on Specifications for Pharmaceutical Preparations. Forty-Seventh Report Geneva, World Health Organization, 2013 (WHO Technical Report Series, No. 981), Annex 3. **Short name: WHO TRS No. 981, Annex 3**
https://cdn.who.int/media/docs/default-source/medicines/norms-and-standards/guidelines/prequalification/trs981-annex3-who-variations-prequalified-product.pdf?sfvrsn=809e81b_2
15. WHO General guidance on hold-time studies. WHO Expert Committee on Specifications for Pharmaceutical Preparations. Forty-Ninth Report Geneva, World Health Organization, 2015 (WHO Technical Report Series, No. 992), Annex 4. **Short name: WHO TRS No. 992, Annex 4**
https://cdn.who.int/media/docs/default-source/medicines/norms-and-standards/guidelines/distribution/trs992-annex4.pdf?sfvrsn=2a1980f0_2
16. WHO Technical supplements to Model Guidance for storage and transport of time – and temperature – sensitive pharmaceutical products. WHO Expert Committee on Specifications for Pharmaceutical Preparations. Forty-Ninth Report Geneva, World Health Organization, 2015 (WHO Technical Report Series, No. 992), Annex 5. **Short name: WHO TRS No. 992, Annex 5**
https://cdn.who.int/media/docs/default-source/medicines/norms-and-standards/guidelines/distribution/trs992-annex5.pdf?sfvrsn=99aedfbc_2
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