World Health Organization

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

PART 1	**GENERAL INFORMATION**
MANUFACTURERS DETAILS	
Name of the manufacturer	Maphar Laboratories
Corporate address of the manufacturer	Boulevard Alkimia N°6, Quartier industriel Sidi Bernoussi Casablanca, 20250 Morocco
INSPECTED SITE	
Name and address of the inspected manufacturing site	Boulevard Alkimia N°6, Quartier industriel Sidi Bernoussi Casablanca, 20250 Morocco
Unit / block / workshop number	OSD Block
Manufacturing license number	N° 93/16 DMP/23
INSPECTION DETAILS	
Dates of inspection	11 – 14 February 2025
Type of inspection	Routine
Inspection record number	INSP-FPP-2020-0052
INTRODUCTION	
Brief description of the manufacturing Activities	A wide range of pharmaceutical manufacturing activities are undertaken at the site including production and quality control of finished pharmaceutical products including oral solid dosage forms (OSDs), semisolids and liquids.
General information about the company and site	MAPHAR is a subsidiary of the CFAO Healthcare group. Its Sidi Bernoussi site is located in the Sidi Bernoussi Industrial District, Casablanca. The total surface area of the site is 25,670 m², with a built area of 13,560 m². The workforce of the production site corresponds to 315 people The annual production is approximately 40,792 million units. The activities licensed at this site include manufacturing, importation, exportation and distribution of medicinal products for human use. In addition to the manufacturing site subject to this inspection, the company has a distribution centre located on Route de Rabat RP1 20250 , Ain Sebaa, in Casablanca.

History	The site is subject to regular WHO inspections since 2004. The last WHO inspection was conducted in November 2019. In addition, the site is inspected by the Moroccan Ministry of Health (MoH) on a regular basis.
Major changes since last WHO inspection	The following is a summary of key changes which were introduced at Maphar since the last WHO inspection. • Organizational changes including the appointment of a new Qualified Person, Quality Director, Site Head, and Quality Control Director • New HPLC equipment at the quality control laboratory. • HPLC network (SDS).
BRIEF REPORT OF INSPECTION ACTIVITIES UNDERTAKEN – SCOPE AND LIMITATIONS	
Areas inspected	Manufacturing areas including oral solid dosage forms production block and quality control premises along with their relevant utilities.
Restrictions	Not applicable
Out of scope	Products other than, and areas not relevant to, the below listed WHO prequalified products.
WHO products numbers covered by the inspection	1. MA056: Artesunate/Amodiaquine (as Hydrochloride) 25mg/67.5mg tablets. 2. MA057: Artesunate/Amodiaquine (as Hydrochloride) 50mg/135mg tablets. 3. MA058: Artesunate/Amodiaquine (as Hydrochloride) 100mg/270mg tablets.
ABBREVIATIONS	**MEANING**
AHU	Air handling unit
ALCOA	Attributable, legible, contemporaneous, original and accurate
API	Active pharmaceutical ingredient
APR	Annual product review
APS	Aseptic process simulation
BMR	Batch manufacturing record
BPR	Batch production record
CC	Change control
CFU	Colony-forming unit
CIP	Cleaning in place
CoA	Certificate of analysis
CpK	Process capability
DQ	Design qualification
EDI	Electronic deionization
EM	Environmental monitoring
FMEA	Failure modes and effects analysis
FPP	Finished pharmaceutical product
FTA	Fault tree analysis
GMP	Good manufacturing practices
GPT	Growth promotion test
HEPA	High efficiency particulate air
HPLC	High performance liquid chromatography (or high performance liquid chromatography equipment)
HVAC	Heating, ventilation and air conditioning
IQ	Installation qualification

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

PART 2	SUMMARY OF THE FINDINGS AND COMMENTS

1. Pharmaceutical quality system

Maphar Laboratories, , maintained a comprehensive Quality Management System (QMS) to ensure compliance with Good Manufacturing Practices (GMP) and regulatory requirements. The system covered all aspects of manufacturing, quality control, and distribution to guarantee the safety, efficacy, and quality of pharmaceutical products.

Maphar Quality Manual outlined the current Quality Management System (QMS) implemented since 2009, ensuring compliance with ICH Q10 and various Good Practices (GLP, GVP, GMP, GDP). It applied to all activities related to product manufacturing, distribution, and marketing. The Quality Department oversaw product quality, compliance, audits, risk management, and supplier evaluations. The Supply Chain Quality Department ensured product safety, traceability, and compliance throughout distribution. The Quality Documentation System defined hierarchical procedures for regulatory compliance. Continuous improvement was driven by quality performance indicators, risk assessments, and audits to maintain high standards in patient care.

The site management held the ultimate responsibility for the Quality Management System's effectiveness. The management participated in the QMS design, implementation, monitoring, and updates as needed. The Management ensured clear role assignment, effective communication, and understanding at all levels. It conducted reviews to verify system effectiveness and allocated necessary resources for implementation, maintenance, and continuous improvement.

The Pharmacist in Charge was responsible for the release of Maphar products and regulatory follow-up of marketing authorisation dossiers, including registration, renewal, and variations. They managed pharmacovigilance activities, ensured regulatory compliance of industrial practices, represented Maphar before authorities and professional associations, and supervised pharmaceutical acts as per Article 117 of Law 17-04.

The Quality Department managed the site's Quality System and was responsible for various tasks. It decided on the acceptance or rejection of raw materials, intermediates, and finished products while ensuring compliance with Good Manufacturing Practice guidelines. The department implemented and monitored training programs in accordance with regulatory requirements and oversaw the stability program for marketed finished products. It verified and approved changes impacting product quality and ensured that deviations, claims, and out-of-specification results were documented, investigated, and closed. The department also maintained equipment and calibration systems efficiently, followed up on corrective and preventive actions, and ensured product conformity with the registration dossier. Additionally, it prepared, organized, and followed up on regulatory inspections and interactions with health authorities. The management of claims, establishment and communication of quality indicators, definition of the self-inspection program, and oversight of the supplier and subcontractor audit program were also within its scope. Furthermore, the department was responsible for risk management.

The overall Maphar organogram was reviewed. An organogram was also available for the Quality department and included four units with 4 managers. The Manager of QA system and Quality supply chain also reported to the Director of quality operations, who was different from the Director of the Supply chain Industrial Activity.

The following job descriptions (JDs) were randomly selected and reviewed:

- Quality director
- Quality control director (in Quality team)
- QA and Quality supply chain responsible
- Product Quality Assurance
- General Manager of Pharmaceutical Affairs and Pharmacy who had a supervisory role overseeing both the technical industrial and quality operations to make sure that the process is compliant with the requirements set out in the local law. The General Manager was designated as the QP with responsibility related to the batch release delegated to Quality director, QA manager, and another QA staff following well-established procedure.
- Technical industrial director
- Supply Chain director

In terms of data integrity, an SOP for management of data integrity was in place.

Management Review

Periodic management reviews of the operation of the PQS were conducted with the involvement of senior management in accordance with SOP for Review of Quality system to identify opportunities for continual improvement of products, processes, and the system itself. Management reviews were conducted at least annually.

The last MR record was available and reviewed: At the time of MR, a presentation was consolidated and prepared by the Quality Director to be presented to the MR meeting participants. A participant list was also available to document the leadership and top management's participation. An action plan was introduced at the end of the presentation (for 2023-2024). The key performance indicators (KPIs) and the follow-up of the previous action plans were also included in the presentation.

Handling of deviations

The SOP for deviations was in place. The SOP provided for roles and responsibilities, annotations, declaration, receipt, evaluation, risk analysis, investigation, and closure of deviations. The definition of deviations was comprehensive and covered a wide range of subjects. Deviations were subject to regular review and trending on a quarterly basis. The Q4/2024 trending of the deviations was reviewed and few deviations were spot-checked.

CAPA management

Deviations, suspected product defects, and other problems were reported, investigated, and recorded. An appropriate level of root cause analysis was applied during such investigations. The most likely root cause(s) were identified, whenever possible, and appropriate corrective and/or preventive actions (CAPAs) were determined and implemented. The effectiveness of CAPAs was monitored. An electronic system was used for the management of CAPA. The related CAPA process management was outlined in a well-established SOP.

Batch release
Batch release was performed in accordance with an established SOP for FPP release. WHO products were owned by SANOFI. Consequently, the batch release of the WHO prequalified products was assigned to Produits AMM SANOFI, as per section 6.3 of the mentioned procedure as well as the quality agreement in place between SANOFI and Maphar.

SANOFI Products:
After the decision of Maphar's Quality Control Manager, the batch was transferred to the "Batch Record Verification" queue, where the review manager updated key data before forwarding it to "QA Decision". The Responsible Person/Pharmacist or Delegate verified analytical results and approved or rejected the batch. The decision was then transferred via the LIMS-SAP interface. For accepted batches, stock was transferred to the designated storage location, followed by invoicing through the appropriate system. The stock remained in "Quarantine" until the Responsible Pharmacist or a delegate of SANOFI received the analysis report and Certificate of Compliance from MAPHAR, before finalizing the release.

The batch release documentation was reviewed and the CoA of the batch release by Maphar was reviewed in the system.

Change Control
The SOP for Change control was in place. The SOP's scope was broad and covered almost all the changes. The change controls were recorded and handled in software application. Few changes were spot-checked.

Quality risk management
An SOP for quality risk management was in place. The procedure covered different stages and phases of QRM, including risk assessment, risk control and risk communication. The risk register was reviewed and few risk assessments were spot-checked.

Product quality review
The SOP for Product Quality Review was in place. The procedure provided for drafting, conclusion, and approval of the PQR within 90 calendar days from the end of the review period. For WHO prequalified products, PQR was established for the period from Jan to Dec every year and PQR was to be concluded and approved by March of the next year. The SOP also provided for the calculation of the process capability if more than 10 batches were manufactured. If an insufficient number of batches were produced during the review period (i.e., fewer than 10 batches), batches produced from earlier PQR review periods could be used. In addition, a PQR had to be conducted, even if no batches were produced during the review period.

The PQR of ASAQ 100/270 mg 6 tablets per blister as well as PQR of ASAQ 50/135 mg 6 tablets per blister were reviewed. In addition, the annual review of the purified water system and the annual review of the environmental monitoring were also reviewed.

2. Good manufacturing practices for pharmaceutical products

In general, the site maintained a GMP-compliant quality management system to ensure that pharmaceutical products were consistently manufactured and controlled in accordance with regulatory requirements and marketing authorizations. The GMP system aimed to minimize manufacturing risks and ensure product quality, safety, and efficacy. In addition, the manufacturing processes were clearly defined, validated, and systematically reviewed to confirm compliance with established specifications. Adequate resources were provided, including qualified personnel, appropriate facilities, equipment, materials, and documented procedures. Production and quality control activities were conducted according to written instructions, with records maintained to demonstrate compliance. Deviations were documented, investigated, and addressed through corrective and preventive actions (CAPA). Batch records ensured full traceability of manufacturing operations. Furthermore, the site implemented GSDP-compliant storage and distribution operations to minimize risks to product quality. A recall system was in place, and complaints and quality defects were investigated, when needed, with appropriate measures taken to prevent recurrence.

For a comprehensive understanding of these aspects, please refer to the respective sections detailing each component of the system.

3. Sanitation and hygiene

In general, a high level of sanitation and hygiene was maintained in all aspects of manufacturing, including production and control. Sanitation and hygiene practices covered personnel, premises, equipment, production materials, and containers.

The selection of the detergents took place in accordance with SOP for General procedure of cleaning and disinfection. The cleaning process was validated. The cleaning and disinfection procedure, accompanied by a comprehensive risk assessment, was implemented.

4. Qualification and validation

Validation and qualification activities were performed according to the well-established policies and documented procedures. The validation master plan was in place. The master VMP provided for the key elements of a qualification and validation programme including personnel qualification and training, equipment qualification, qualification of utilities and premises, management of deviations and non-conformities, risk management, change management, analytical method validation, process validation, cleaning validation and computerized system validation. The VMP also provided for the commitment to maintain continued validation status including aspects of ongoing qualification and validation programme through regular re-validation according to annual review.

Validation of heating, ventilation, and air-conditioning systems

The HVAC system was initially qualified and regularly requalified as per the requirements of GMP guidelines and ISO 14644 standard. The requalification reports of a number of HVAC systems were spot-checked and found acceptable.

The protocol for qualification of classified areas was reviewed. The PQ aspects included the flow rate, differential pressure, temperature, humidity, non-viable particle counts, recovery test, smoke test, and filter integrity. The last qualification of the dispensing room (including the dispensing box/booth) and the one of 2024 were spot-checked.

Validation of water systems for pharmaceutical use
The qualification of purified water was determined following the SOP for purified water, and the SOP for sampling of purified water at the site. The site had two sources of water, Prim II, and Prim III. The evidence of testing for conductivity, nitrates, oxidizable substances and microbiology and the respective logbooks were available and reviewed. The annual report of control of purified water 2024 was also reviewed.

Cleaning validation (CV)
The SOP for CV was in place. It provided for roles and responsibilities related to CV, principles and approach, analytical documentation requirements, periodic reviews, hold time studies, and revalidation. The SOP for CV provided for calculation of the acceptance criteria based on four methods including residual limits, lethal dose (LD50), 10 ppm and the PDE. The SOP provided for consideration of the most restrictive limit among the four mentioned methods. The CV of a number of key production equipment were reviewed.

Analytical procedure validation
Please refer to the respective information under the section entitled “Good practices in quality control”.

Validation of computerized systems
The SOP for validation of computerized system was in place and provided for validation activities throughout the lifecycle of the critical computerized systems used in production and control operations. In general, the computerized system used during the manufacturing processes were validated in accordance with the principles of quality risk management where the level of validation was commensurate with the identified risks, complexity and intended use.

A list of software systems (critical systems) was provided. One software (LIMS) was selected to check the respective validation. The computerized system was validated in accordance with the SOP for Validation of computerized systems.

The documentation relevant to the validation of selected computerized systems was spot-checked.

Procedures were in place for the computerized systems, which defined the use and control of the same. Similarly, appropriate segregation of roles between personnel responsible for the operational process and personnel for system administration and maintenance was well noted. An up-to-date list of the individual user rights for the software, individual computer systems and networks were maintained and subjected to change control.

Suitable security measures were in place to prevent unauthorized entry or manipulation or deletion of the computerized systems' relevant data.

Computerized systems were required to be periodically reviewed according to the respective SOP to determine whether the system remains in a validated state.

Process validation
The practice of process validation was established as per the SOP for process validation of production and packaging operations. The reports of the last PV of the ASAQ 25mg/67.5mg and ASAQ 100mg/270mg were reviewed.

5. Complaints
The SOP for complaints management was in place. The SOP provided for definitions related to complaints, classification, roles and responsibilities, receipt, logging, and handling. One designated person (Product Quality Assurance), supported by sufficient staff, was responsible for complaint handling and decision-making. Given that the person responsible for managing complaints was different from the authorized person, the latter was kept informed of all complaints, investigations, and recalls. The Complaints trend analysis, including categorization (type), classification (system-wise) and management for Q4/2024 was reviewed. The trend analysis was comprehensive and covered data back to 2019. The list of complaints reported in 2024 was reviewed and one complaint was spot-checked. The checked complaint was related to an empty box, which was raised by a wholesaler.

6. Product recalls
Since SANOFI was the marketing authorization holder of ASAQ, the responsibility for any recall of the product rested with them. This included the decision and notification to the authorities in accordance with the quality agreement. However, Maphar was assumed to actively participate in any recall activity.

A system was in place in accordance with the SOP for Management of recall. SANOFI was required to perform one exercise a year for the purpose of assessment of their recall system. In the absence of real recall, the company was required to perform a mock recall.

7. Contract production, analysis and other activities
All the testing, with the exception of magnesium stearate, was done by Maphar QCL. However, the batch release of ASAQ was done by the QP of SANOFI located in Casablanca at the EPI SANOFI office which was a separate office located within the same complex of Maphar.

Maphar was the sub-contractor for ASAQ, and was responsible for execution of the respective production and control operations including quality control tests to issue the certificate of analysis (CoA) of the product in accordance with the contract. A table of roles and responsibilities was incorporated into the contract. The contract defined the documentation required to be sent to the contract giver for the batch release. The CoA, and certificate of conformity, and on request, the complete dossier (batch manufacturing and packaging records along with analytical records) were required to be sent to the contract giver at the end of the operation of manufacturing of the batch. The job description of the Qualified Person (QP) at Sanofi was available and reviewed.

Analytical testing was subcontracted under quality agreements, and supply chain integrity was ensured through controlled sourcing, audits, and compliance monitoring. According to the list of subcontractors for analysis of ASAQ WHO product, the only subcontractor was a laboratory located in France. The

laboratory was responsible for testing of Magnesium Stearate. The contract between Maphar and the laboratory was available and reviewed. The contract acceptor was audited on in October 2024 through an outsourced audit arranged by the contract giver. Audit report was available and the CAPA was provided with corresponding deadlines. Maphar confirmed that the CAPA was satisfactorily executed.

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

The SOP for self-inspection was well-established. The SOP guided the self-inspection planning, frequency, team, inspection preparation, conduct and reporting, and documentation.

9. Personnel

The site maintained a structured organization for quality management, production, quality control, storage, and distribution. An organizational chart outlined key roles, including the Responsible Pharmacist, Deputy Pharmacists, Technical Directors, and Commercial Directors (Annex 5 of SMF).

Sufficient number of employees was engaged in pharmaceutical operations. Staffing levels ensured compliance with regulatory requirements and GMP standards.

10. Training

Personnel working in manufacturing and QC areas, including technical, maintenance, and cleaning staff, received training in accordance with a well-established procedure. Newly recruited personnel were trained on GMP principles and job-specific duties, with continuous training provided and periodically assessed. Approved training programs and records were maintained.

Visitors and untrained personnel were restricted from production and QC areas. If entry was necessary, they received prior instructions on hygiene and protective measures and were closely supervised.

11. Personal hygiene

Personnel underwent health examinations before and during employment. Training in personal hygiene was provided, and strict hygiene practices were followed, including mandatory handwashing before entering production areas.

Direct hand contact with materials and products was avoided. Personnel wore clean, appropriate protective clothing, including hair coverings, with reusable garments stored separately and sanitized as needed. SOP for gowning hygiene and behaviour was in place. Gowns were regularly sent for cleaning at a vendor who was subject to regular audits.

Smoking, eating, drinking, and personal items were prohibited in production, QC, and storage areas. Hygiene procedures and protective clothing requirements were applied to all personnel, including temporary staff, visitors, and contractors entering production areas.

12. Premises

In general, the premises were well designed and maintained, providing measures to reduce the risks of contamination and cross-contamination. Operators at the production areas, particularly those where dust is generated (e.g., compaction, sieving and compression rooms), were supported with filtered breathing air respirator for safety reasons.

The WHO prequalified products were manufactured at defined production areas namely the materials dispensing at dispensing rooms 2 and 4 (ground floor next to the central warehouse), compaction at the compaction room (ground floor next to the compression room), sieving at the sieving room (ground floor next to the materials airlock from the dispensing area/corridor), intermediate storage area (the corridor at 1st floor next to the punch and dies storage room), mixing at the blending room (1st floor), materials dispensing to the compression room by gravity from the 1st floor, compression of the bilayer tablets at the tableting/compression room (ground floor), bulk tablets storage area (the corridor on the ground floor) and primary as well as secondary packaging at line packaging line 2.

The SOP for installation, utilization and cleaning of the HVAC system was in place. The SOP provided comprehensive instructions on HVAC system, including deviations, pressure monitoring and limits for different filter types, and qualification requirements.

The temperature record of the laboratory used in Salle Chimie for the period from 31 January 2025 to date of the inspection was requested and reviewed for both temperature and humidity. Both the temperature and humidity were within the acceptable range.

The temperature mapping process for the sample storage area in the QCL was reviewed. The mapping was conducted in accordance with the SOP for storage facility mapping. Evidence of temperature mapping for both winter and summer periods, including hotspot identification and sensor placement, was assessed. The mapping frequency was established as every three years. The most recent records were documented in August 2023 for the summer season and March 2023 for the winter season.

The SOP for environmental monitoring was in place. The procedure provided for EM of all classified areas once every three months in the production and control premises. The annual review of the EM of 2024 was checked and found acceptable in general. The EM involved microbiological testing for active air monitoring, passive air monitoring and surface swabbing once every three months during operation and once every year at rest.

The logbook of the HVAC of the sieving area was spot-checked. The filters at the AHU as well as those at the terminal inlet and exhaust (return) were subject to regular (weekly) check/monitoring for pressure drop.

The SOP for nitrogen monitoring was in place. The SOP required quarterly microbiological testing of the nitrogen system, noting that nitrogen was used at the dispensing room. Nitrogen was supplied in cylinders by an approved supplier as no nitrogen generation system was available at the site. The nitrogen distribution system was qualified annually, including testing for particles, oil, and moisture content; however, no regular monitoring of the latter was in place. Similarly, compressed air was annually qualified but not regularly monitored for any of the relevant parameters, including microbiological testing.

The warehouse areas were equipped with a pest control system. One service provider was responsible for the pest control and cleaning procedures of the warehouse. The service provider took care of the management of disinfection, pest control, and insect control.

13. Equipment

The SOP for equipment calibration and qualification was in place for management of qualification activities throughout the equipment lifecycle. The requalification reports of a number of equipment as below listed were spot-checked:

- The requalification report of the blistering machine
- The requalification report of the blender
- The requalification report of the tableting machine

In general, equipment logbooks were available documenting equipment use and related activities (e.g., cleaning, daily verification).

14. Materials

The SOP governing the reception of components at the industrial site along with the corresponding list of approved suppliers, was available for review and discussion.

Wooden pallets were widely used at the warehouse for the storage of materials, including raw materials and packaging materials. The pallets were subject to check and verification upon receipt from the supplier and the same was documented within the logbook for control of delivered pallets.

Materials were received, stored and dispatched from the central warehouse which was separate from the production and control areas. The warehouse utilized an electronic system for materials segregation. Dedicated secured area with restricted access was utilized for storage of rejected, returned and recalled materials. The inventory of the latter area was reviewed and spot-checked. The warehouse was equipped with four gates for materials receipt and dispatch.

15. Documentation

Good documentation practices were maintained as part of the quality assurance system, ensuring compliance with GMP requirements. Documentation defined specifications, procedures, and controls for all materials and manufacturing processes, ensuring traceability, batch release decisions, and audit trails for investigation and validation.

Documents were designed, reviewed, approved, and distributed according to regulatory requirements. They were clear, legible, and systematically organized to prevent errors. Regular reviews and updates were conducted, with measures in place to prevent the unintended use of superseded versions.

Data entries were legible, indelible, and appropriately spaced, with any alterations signed, dated, and traceable. Records were completed in real-time and retained for at least one year after product expiry.

Electronic documentation systems had controlled access, audit trails, and data integrity safeguards, with backup storage to ensure data availability during the retention period. Backup was performed in accordance with a well-established SOP.

The SOP for document control was in place. Documents were required to be subject to regular review with the exception of "static documents" which were listed in the SOP (e.g., reports, annexes, etc.).

Analytical sheets were issued in LIMS, with specific number and pagination. The results of chromatography, weighing and other similar records were kept together with the analytical sheet when applicable.

The SOP for issue of batch records was reviewed. It outlined access rights and control measures for essential and supplementary batch record-related documentation.

16. Good practices in production

The master formula of ASAQ 100/270 mg was reviewed and confirmed to be aligned with the CPP and CQA stipulated by the PV. Some key production documentation was reviewed, including the SOP for management of the punches and dyes of the compression machine. The latter SOP provided for how to purchase, receive, use, store, and perform an annual check of the punches. The regular check of the punches was provided for before and after each use as well as on an annual basis (for dimensions). The last annual check of the punches for the compression of ASAQ 100/270 mg was spot-checked and found acceptable. The equipment used for the annual control was subject to regular calibration.

The batch manufacturing and analytical records of two batches of ASAQ 100/270mg were reviewed and found acceptable in general in terms of documenting the different related activities. An improvement of the manufacturing records was already considered by the manufacturer by adding a column for the verification by a second person of key production operations. The amended batch records were observed in use during the tour of the production areas and witnessing of the production operations of a number of batches of ASQA 100/270mg.

17. Good practices in quality control

QC laboratories were separated from production areas and designed to prevent cross-contamination and mix-ups, with adequate storage for samples, reference standards, reagents, solvents, and records. QC operations were independent of production, operating under the authority of qualified personnel with adequate resources.

Laboratory design considered the suitability of construction materials, proper ventilation, and prevention of fumes, with separate air-handling units for QC and production areas. Sensitive instruments were placed in separate rooms to protect against electrical interference, vibration, moisture, and other external factors.

The QC function ensured that all sampling activities were performed in accordance with the SOP for sampling of raw material and the SOP for FPP sampling. For materials used in the production of WHO prequalified product (ASAQ), Maphar performed identity test on each received container of all API and excipients using IR spectroscopy. Testing activities of the APIs and excipients, other than the identity test, were performed according to the requirements stipulated in the respective SOP.

QC activities included sampling, inspection, and testing of raw materials, packaging materials, intermediates, bulk, and finished products. Environmental monitoring was also conducted where needed. All tests were performed according to validated procedures, with records maintained to document compliance and any deviations investigated.

Finished products met approved specifications, ensuring correct composition, purity, labelling, and packaging. Reference standards were maintained, and stability monitoring was performed.

The SOP for handling of OOS was reviewed and discussed in relation to few OOS cases.

Retention samples of each finished product batch were stored for at least one year beyond the expiry date, in the final packaging under recommended conditions.

All retention samples were sufficient in quantity to allow at least three full re-examinations if required. Retained samples were stored appropriately for future examination in accordance with the respective instructions.

The preparation of the solution for the system suitability test (SST) was recorded in a dedicated logbook. Similarly, the usage of reference and working standard (RS/WS) was recorded for reconciliation purposes in a logbook. The RS/WS were kept in a vials for one-time use for each specific test. Information about the RS/WS receipt, expiry date, opening date, and lot no were recorded. Consequently, the date was recorded in LIMS. The usage was also recorded in the analytical sheets specific to each batch.

Few analytical records were reviewed and spot-checked.

The microbiological laboratory premises were separate from the chemical laboratory. Proper gowning was necessary prior to access to the microbiology laboratory. The microbial limit test area was separated from all other microbiological activity (such as media preparation).

The microbiology laboratory was basically used for performing microbial limit tests. Recognized reference cultures (American Type Culture Collection [ATCC]) were utilized at the laboratory. The number of microbial passages was limited to a maximum of five passages. The growth promotion test was performed for each prepared media. There were two separate autoclaves, one for the sterilization of the media and the other for decontamination purposes.

PART 3	CONCLUSION – INSPECTION OUTCOME

Based on the areas inspected, the people met and the documents reviewed, and considering the findings of the inspection, including the observations listed in the Inspection Report, a decision on the compliance of **Maphar Laboratories** located at **Boulevard Alkimia N°6, Quartier industriel, Sidi Bernoussi, Casablanca, 20250 Morocco** with WHO good manufacturing practices for pharmaceutical products guidelines will be made after the manufacturer's response to the observations has been assessed.

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

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

PART 4	LIST OF GMP GUIDELINES REFERENCED IN THE INSPECTION REPORT

1. WHO good manufacturing practices for pharmaceutical products: main principles. WHO Expert Committee on Specifications for Pharmaceutical Preparations. Forty-eighth Report Geneva, World Health Organization, 2014 (WHO Technical Report Series, No. 986), Annex 2.
   Short name: WHO TRS No. 986, Annex 2
   https://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 guidance on good practices for desk assessment of compliance with good manufacturing practices, good laboratory practices and good clinical practices for medical products regulatory decisions. WHO Expert Committee on Specifications for Pharmaceutical Preparations. Fifty-second Report. Geneva, World Health Organization, 2018 (WHO Technical Report Series, No. 1010), Annex 9.
   Short name: WHO TRS 1010, Annex 9
   https://www.who.int/publications/m/item/trs1010-annex9

4. WHO Good Manufacturing Practices: water for pharmaceutical use. WHO Expert Committee on Specifications for Pharmaceutical Preparations. Fifty-fifth Report. Geneva, World Health Organization, 2021 (WHO Technical Report Series, No. 1033), Annex 3.
   Short name: WHO TRS No. 1033, Annex 3
   https://www.who.int/publications/m/item/annex-3-trs-1033

5. 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/annex-4-trs-929

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