World Health Organization

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WHO Prequalification Team - Inspection services

WHO PUBLIC INSPECTION REPORT (WHOPIR)

In vitro Diagnostic product

Inspected site/s	
Name of Organization	DiaSorin Italy S.p.A. UK Branch
Address/es of inspected manufacturing site/s	Central Road, Dartford, Kent DA1 5LR, UK
Inspection details	
Start of inspection	14/05/2024
Inspection duration (in inspector days)	6
Type of inspection	Re-inspection
Introduction	
Brief description of manufacturing activities conducted at the site/s inspected	Manufacturing, warehousing, and distribution of in vitro diagnostic tests.
General information about the organization	DiaSorin Italy S.p.A. UK Branch is the manufacturing site for the products in scope. The applicant is DiaSorin Italy S.p.A., located in Saluggia, Italy. The company specializes in diagnostics and healthcare.
Brief report of inspection activities undertaken – Scope and limitations	
Areas inspected	As detailed below, the areas inspected were sampled from the areas of activities performed on site that were relevant to the products in scope. The sampling was performed using a risk-based approach considering, for example, the impact of the area inspected on the product, as well as past inspection findings.
Products in scope	• Murex HBsAg Version 3 with Murex HBsAg Confirmatory Version 3 (PQDx 0121-043-00) • Murex HIV Ag/Ab Combination (PQDx 0144-043-00)
Criteria	• All applicable clauses of ISO 13485:2016 • WHO PQ requirements • Organization's own requirements
Objective(s)	Verify continued compliance to the inspection criteria.
Limitations	None.
Out of scope	Any processes or activities not related to the products in scope were considered out of scope of this inspection.

Abbreviations	Meaning
CAPA	Corrective and Preventive Action
CoA	Certificate of analysis
IQ	Installation qualification
IVD	In vitro device
MR	Management review
MRM	Management review meeting
MSDS	Material safety data sheet
NC	Non-conformity
PPE	Personal protective equipment
OOS	Out-of-specifications test result
OQ	Operational qualification
PM	Preventive maintenance
PMS	Post Market Surveillance
PQ	Performance qualification
PW	Purified water
QA	Quality assurance
QC	Quality control
QMS	Quality management system
QRM	Quality risk management
RA	Risk assessment
RCA	Root cause analysis
SOP	Standard operating procedure

Summary of the findings and comments (where applicable)

4. Quality management system

4.2 Documentation requirements

4.2.2. Quality manual

The organization`s Quality Manual adequately addressed and reflected the intended practices of the laboratory, with clear commitment from top management for the continual improvement and support of the QMS. It contained a description of the interaction between the processes of the QMS, defined the structure of the documentation system and listed/excluded non-applicable clauses of ISO13485:2016 with appropriate justification. The procedures were referenced in the quality manual.

4.2.4/5. Control of documents and records

There were documented procedures for document and record control that had been implemented to manage QMS documentation, including procedures, work instruction, records, CAPAs including quality incidents and NCs and other documents. Document control practices were compliant with the procedures, and the records reviewed provided evidence of conformity to the requirements. Generally, records and documents were readily available. The nonconformities identified during the inspection were addressed through a CAPA plan.

5. Management responsibility

5.1. Management commitment

Top management provided evidence of its commitment to the development and implementation of the quality management system and maintenance of its effectiveness by communicating to the organization the importance of meeting customer as well as applicable regulatory requirements; establishing the quality policy; ensuring that quality objectives were established; conducting management reviews; and ensuring the availability of resources.

5.3. Quality policy

Top management had an established Quality Policy. The inspectors verified that the organization had established processes that mostly met the requirements of ISO 13485:2016 (the standard) and other applicable regulations (notwithstanding the nonconformities identified during this inspection).

5.5. Responsibility, authority and communication

5.5.1. Responsibility and authority

Responsibilities and authorities were defined, documented, and communicated within the organization. The interrelation of all personnel who managed, performed, and verified work affecting quality were documented. The nonconformities identified during the inspection were addressed through a CAPA plan.

5.5.2. Management representative

The QA Director was the management representative. Their responsibility and authority included ensuring that processes needed for the quality management system are documented; reporting to top management on the effectiveness of the quality management system and any need for improvement; and ensuring the promotion of awareness of applicable regulatory requirements and quality management system requirements throughout the organization.

5.6. Management review

5.6.1. General

The organization had an established process for quarterly management reviews that met the requirements of the standard. Records from management reviews were maintained. The review included assessing opportunities for improvement and the need for changes to the quality management system, including the quality policy and quality objectives.

5.6.2. Review input

The input to management review included feedback; complaint handling; reporting to regulatory authorities; audits; monitoring and measurement of processes; monitoring and measurement of product; corrective action; preventive action; follow-up actions from previous management reviews; changes that could affect the quality management system; recommendations for improvement; and applicable new or revised regulatory requirements.

5.6.3. Review output

The output to management review were documented and included decisions and actions related to improvement needed to maintain the suitability, adequacy, and effectiveness of the quality management system and its processes; improvement of product related to customer requirements; changes needed to respond to applicable new or revised regulatory requirements; and resource needs.

6. Resource management

6.1. Provision of resources

The facility was well resourced, with trained personnel and adequate facilities for the function and activities that were performed. This ensured the QMS was implemented, and its effectiveness maintained, and that applicable regulatory and customer requirements were met.

6.2. Human resources

The facility was staffed with personnel who had the necessary education, training, technical knowledge, and experiences for their assigned functions. Staff questioned were open and forthcoming with information.

The organization had an established and well documented training procedure. Training files for staff were maintained and available for review during the inspection.

6.3. Infrastructure

The facility was well maintained with a logical workflow, and segregated activities in rooms of appropriate size and design to suit their respective functions and operations. This prevented product mix-up and ensured orderly handling of product.

The facility was well maintained, clean and orderly and clearly sign posted. Pest control management procedure was implemented.

The organization had documented requirements for the maintenance activities that applied to equipment used in production, to the control of the work environment, and to monitoring and measurement.

The nonconformities identified during the inspection were addressed through a CAPA plan.

6.4. Work environment and contamination control

6.4.1. Work environment

All production rooms were controlled and monitored for temperature and relative humidity (where relevant) with recordings available. Staff were observed to be wearing appropriate PPE, with access to appropriate coats, shoes, masks, and hair nets that were provided by the organization. There were pictorials when entering an area on the gowning requirements.

6.4.2. Contamination control

Procedures for the cleaning of the facility and infrastructure were available to prevent contamination of the work environment, personnel, and/or product. Cleaning validations for selected equipment and infrastructure were reviewed. The nonconformities identified during the inspection were addressed through a CAPA plan.

7. Product realization

7.1. Planning of product realization

The organization’s approach to the planning of production and service provision was documented in the QMS, with procedures for document management, risk management, product production, material verification, process validation, monitoring, inspection, and test activities. The nonconformities identified during the inspection were addressed through a CAPA plan.

7.3. Design and development

7.3.3. Design and development inputs

Inputs relating to product requirements were determined and records maintained. The nonconformities identified during the inspection were addressed through a CAPA plan.

7.3.9. Control of design and development changes

The organization had an established and documented procedure for the control of design and development that incorporated a description and rationale for the change; an impact assessment; proposed action plans; and review and approval of those plans.

7.4. Purchasing

7.4.1. Purchasing process

The organization had an established and well documented process for the purchasing of materials and services, that included a traceable inventory, release, and verification of critical incoming material. Supplier management and qualification procedures were implemented with criteria for selection, evaluation, approval, and re-evaluation of suppliers.

7.4.2. Purchasing information

The organization had signed quality agreements with relevant suppliers of materials and services stipulating that the supplier must notify the organization of changes in the purchased product prior to implementation of any changes that affect the ability of the purchased product to meet specified purchase requirements.

7.4.3. Verification of purchased product

The organization had implemented processes for the verification of purchased products to ensure that they met specified purchasing requirements. Records of these activities were maintained.

7.5. Production and service provision

7.5.1. Control of production and service provision

Production and service provision was carried out, monitored, and controlled to ensure that product conformed to specifications. The organization had a documented process for the control of production that included, but was not limited to, qualification of infrastructure and monitoring and measuring equipment. Batch manufacturing records were available, and identified the amount manufactured and amount approved for distribution. Records were verified and approved. The nonconformities identified during the inspection were addressed through a CAPA plan.

7.5.6. Validation of processes for production and service provision

The organization had validated processes for production and service provision that followed procedures that included the equipment qualification and qualification of personnel; the use of specific methods, procedures, and acceptance criteria; the criteria for revalidation; and the approval of changes to the processes. The nonconformities identified during the inspection were addressed through a CAPA plan.

7.5.8. Identification

There was a documented procedure for product identification that was suitable throughout product realization. There was clear segregation of released and nonconforming products within the facility.

7.5.11. Preservation of product

Each year, the organization was verifying the product stability claims by placing one lot of finished devices in real time stability. Results of these studies were maintained, and a sample reviewed. Retained samples were kept in their final packaging under controlled and monitored temperature.

7.6. Control of monitoring and measuring equipment

The organization had implemented procedures for the control of monitoring and measuring equipment. Measuring equipment was calibrated and/or verified at specified intervals, or prior to use, against measurement standards; had identification indicating its calibration status; and was safeguarded from adjustments that would invalidate the measurement result. Calibration records were available, and a sample was reviewed.

8. Measurement, analysis and improvement

8.2. Monitoring and measurement

8.2.1. Feedback

The organization had procedures in place to gather and monitor information relating to whether the organization has met customer requirements. Data were gathered from production as well as post-production activities and served as input into risk management for monitoring and maintaining the product requirements as well as the product realization or improvement processes.

8.2.2. Complaint handling

The organization had implemented a procedure for the timely handling of customer complaints. The procedures included requirements and responsibilities for evaluating information to determine if the feedback constitutes a complaint; investigating complaints; determining the need to report the information to the appropriate regulatory authorities; handling of complaint-related product; and determining the need to initiate corrections or corrective actions. Corrections and corrective actions were documented. Complaint handling records were maintained.

8.2.4. Internal audits

The organization had implemented an internal audit program and was conducting internal audits at planned intervals (yearly). The audit program was planned, taking into consideration the status and importance of the processes and area to be audited, as well as the results of previous audits. The audit criteria, scope, interval, and methods were defined and recorded. Auditors were selected to ensure objectivity and impartiality of the audit process. Auditors did not audit their own work. A sample of auditors' training records were reviewed and found appropriate. All nonconformities identified were captured and followed using the organization`s CAPA process. The nonconformities identified during the inspection were addressed through a CAPA plan.

8.2.5. Monitoring and measurement of processes

Trending and regular review of monitoring and measurement of processes was verified at the time of inspection. Detailed reports were available for the management review meetings and other relevant meetings. The nonconformities identified during the inspection were addressed through a CAPA plan.

8.2.6. Monitoring and measurement of product

The organization had implemented procedures to monitor and measure the characteristics of the product to verify that product requirements had been met. This was carried out at applicable stages of the product realization process. Evidence of conformity to the acceptance criteria was maintained. The identity of the person authorizing release of product and the test equipment used to perform measurement activities were recorded. Product release did not proceed until the planned and documented arrangements had been satisfactorily completed.

8.3. Control of nonconforming product

8.3.1. General

The organization had a process in place for the segregation of nonconforming product that met the requirement of the standard. There was clear labelling and traceability of nonconforming product throughout the various stages of production, and post-delivery.

8.5. Improvement

8.5.2. Corrective action

The organization had procedures in place to take action to eliminate the cause of nonconformities to prevent recurrence. Any necessary corrective actions were to be taken without undue delay. The procedures defined the requirements for reviewing nonconformities (including complaints); determining the causes of nonconformities; evaluating the need for corrective action; planning and documenting action needed and implementing such action, including, as appropriate, updating documentation; verifying that the corrective action does not adversely affect the ability to meet applicable regulatory requirements or the safety and performance of the medical device; and reviewing the effectiveness of corrective action taken.
Records of investigation and actions taken were maintained.

8.5.3. Preventive action

The organization had procedures in placed to determine action to eliminate the causes of potential nonconformities to prevent their occurrence. These procedures described the requirements for determining potential nonconformities and their causes; evaluating the need for action to prevent occurrence of nonconformities; planning and documenting action needed and implementing such action, including, as appropriate, updating documentation; verifying that the action does not adversely affect the ability to meet applicable regulatory requirements or the safety and performance of the medical device; and reviewing the effectiveness of the preventive action taken, as appropriate.
Records of investigation and actions taken were maintained.

Conclusion – Inspection outcome

Based on the areas inspected, the people met, and the documents reviewed, and considering the findings of the inspection, including the observations listed in the Inspection Report the company, ***DiaSorin Italy S.p.A. UK Branch*** located at ***Central Road, Dartford, Kent DA1 5LR, UK*** was considered to be operating at an acceptable level of compliance with ISO 13485:2016 and WHO *Information for Manufacturers on Pre-qualification Inspection Procedures for the Sites of Manufacture of Diagnostics* (PQDx_014).

All the non-compliances observed during the inspection that were listed in the full report were addressed by the organization to a satisfactory level prior to the publication of the WHOPIR.

This WHOPIR will remain valid for 3 years, provided the outcome of any WHO pre-qualification inspection or other audit from regulatory authorities that WHO relies on conducted during this period provides evidence of current compliance with the audit criteria.

List of WHO Guidelines referenced in the inspection report

1. WHO Information for Manufacturers on Prequalification Inspection Procedures for the Sites of Manufacture of Diagnostics (PQDx_014). (https://www.who.int/diagnostics_laboratory/evaluations/en/)

2. ISO 13485:2016 Medical devices - Quality management systems - Requirements for regulatory purposes

3. WHO Post-market surveillance of in vitro diagnostics 2020 (ISBN 978 92 4 001532 6)

4. Medical devices - Application of risk management to medical devices - ISO14971:2019

5. GHTF/SG3/N19:2012 “Quality management system – Medical devices - Nonconformity Grading System for Regulatory Purposes and Information Exchange”

6. GHTF/SG4/(99)28 'Guidelines for Regulatory Auditing of Quality Systems of Medical Device Manufacturers - Part 1: General Requirements

7. GHTF/SG4/N30R20:2006 'Guidelines for Regulatory Auditing of Quality Systems of Medical Device Manufacturers - Part 2: Regulatory Auditing Strategy

8. GHTF/SG4(pd1)/N33R16:2007 'Guidelines for Regulatory Auditing of Quality Systems of Medical Device Manufacturers - Part 3: Regulatory Audit Reports ISO 13485:2016, Commitments to WHO PQ.