World Health Organization

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WHO Prequalification Team - Inspection Services

WHO PUBLIC INSPECTION REPORT (WHOPIR)

In-vitro Diagnostic product

Inspected site	
Name of Manufacturer	Orchid Biomedical Systems – A Division of Tulip Diagnostics (P) Ltd
Address of inspected manufacturing site	Plot nos 88/89, Phase II C, Verna Industrial Estate, Verna, Goa, 403722, India
Inspection details	
Dates of inspection	25-26 April 2024
Type of inspection	Re-inspection
Introduction	
Brief description of manufacturing activities	Orchid Biomedical Systems – A Division of Tulip Diagnostics (P) Ltd is responsible for the control of the design and development of rapid diagnostic tests, as well as the production process, packing, labelling, storage, and delivery.
General information about the manufacturer	Orchid Biomedical Systems is a subsidiary belonging to the Division of Tulip Diagnostics (P) Ltd group, along with Zephyr Biomedicals. Both sites are governed by the same high-level QMS.
History	Orchid Biomedical Systems were previously inspected by WHO prequalification inspection services in January 2023.
Brief report of inspection activities undertaken – Scope and limitations	
Areas inspected	Design and Development Quality management system Management responsibility Purchasing Production and Service Controls Measurement, analysis, and improvement Adverse Events and Advisory Notices Reporting WHO pre-qualification-specific requirements
Scope	Paracheck Pf - Rapid Test for P. Falciparum Malaria Device (Ver. 3) – PQDx 0321-024-00 Lariacheck Pf (under assessment at the time of inspection) – PQDx 0694-024-00
Criteria	ISO 13485:2016 and WHO Prequalification specific requirements
Objective(s)	To assess the manufacturers compliant with the inspection criteria
Limitations	None

Abbreviations	Meaning
CoA	Certificate of analysis
IQ	Installation qualification
IVD	In vitro device
MR	Management review
MSDS	Material safety data sheet
NC	Non-conformity
PPE	Personal protective equipment
OOS	Out-of-specifications test result
OQ	Operational qualification
PM	Preventive maintenance
PQ	Performance qualification
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
SOP	Standard operating procedure

Summary of the findings and comments

The inspection findings are listed below, following the numbering of the clauses of the ISO 13485:2016 standard for easy reference.

4. Quality management system

4.1 General requirements

The organization and management structure of the facility was documented and defined within the organisational chart. Roles and responsibilities were available with the overall reporting structure available with clear delineation for release of product.

4.2 Documentation requirements

4.2.1 General

There was an established quality policy and quality objectives available. Procedures and records were available as per the requirements of the standard.

4.2.2. Quality manual

The manufacturer's Quality Manual was updated regularly and continued to reflect the intended practices of the manufacturer. The quality manual described the interaction between the processes of the Quality Management System (QMS); it defined the structure of the documentation system and listed/excluded non-applicable clauses of ISO 13485:2016 with appropriate justification.

4.2.3. Medical device file

The manufacturer had established and maintained documents demonstrating conformity to the requirements of the standard. These included descriptions of the labelling requirements.

4.2.4. Control of documents

The procedures for document control were available and met the requirements of the standard. There had been no significant changes to the document management system since the last WHO inspection. The nonconformities identified were addressed through a CAPA plan.

4.2.5. Control of records

The procedures for document control of records were available and met the requirements of the standard. All records reviewed were legible and readily identifiable. Record retention was confirmed as being longer than the lifetime of the device.

5. Management responsibility

5.1. Management commitment

There was sufficient evidence to support the claim that top management demonstrated a strong commitment to the development, implementation, and ongoing effectiveness of the quality management system by clearly communicating to the organization the importance of meeting both customer and applicable regulatory requirements. There was an established quality policy with measurable quality objectives, and with evidence of regular management review meetings.

5.3. Quality policy

The quality policy was aligned with the purpose of the organization demonstrating clear commitment from top management to maintain effectiveness through regular review of the quality objectives and continued review for suitability.

5.4. Planning

5.4.1. Quality objectives

Quality objectives were available and included those needed to meet applicable regulatory requirements and product's specifications. Quality objectives were measurable and consistent with the quality policy.

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 the work affecting quality were documented and ensured the independence and authority necessary to perform these tasks.

5.5.2. Management representative

The appointed management representative had clear roles and responsibilities defined within the quality manual and corresponding job description including 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.

5.5.3. Internal communication

There was sufficient evidence to ensure that communication processes were well established and available.

5.6. Management review

5.6.1. General

The organization had an established process for regular 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 and product, corrective and 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. This also included 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 largely 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, including refresher training for staff. Training files for staff were maintained and available for review during the inspection. The nonconformities identified were addressed through a CAPA plan.

6.3. Infrastructure

The infrastructure was well maintained, with the appearance of being clean and tidy. 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 measuring equipment.

6.4. Work environment and contamination control

6.4.1. Work environment

Production was planned and carried out in rooms with controlled environments, with daily recordings available. Staff were observed to be wearing appropriate and suitable-for-use PPE. There were pictorials on gowning requirements upon entering work environments. A mirror was available to ensure that appropriate PPE was properly donned.

6.4.2. Contamination control

There were procedures for the cleaning of the facility available to prevent contamination of the work environment, personnel, or product. Cleaning validations of selected equipment and processes were available.

7. Product realization

7.1. Planning of product realization

The organization's approach to the planning of production and service provision was adequately documented in the QMS manual and met the requirements of the standard. The organization had established procedures for document management, risk management, production, material verification, process validation, monitoring, inspection, and test activities.

7.2. Customer-related processes

7.2.1. Determination of requirements related to product

The organization had documented customer requirements that included applicable regulatory requirements related to the product.

7.3. Design and development

7.3.1. General

The organization had an established process for design and development. The nonconformities identified were addressed through a CAPA plan.

7.3.3. Design and development inputs

The design and development procedure adequately identified the requirements for design inputs.

7.3.4. Design and development outputs

The design and development procedure adequately identified the requirements for design outputs.

7.3.6. Design and development verification

Through the documented procedures there was evidence that the design and development outputs met the design and development input requirements. Adequate sampling size was determined using statistical techniques. The nonconformities identified were addressed through a CAPA plan.

7.3.9. Control of design and development changes

The organization had an established and well documented procedure for the control of design and development changes that incorporated a determination of any necessary regulatory submissions as well as WHO requirements for reporting such changes.

7.4. Purchasing

7.4.1. Purchasing process

The organization had an established and documented process for the purchasing of materials and services, that included verification of critical incoming material. Supplier management and qualification procedures were available and implemented. Criteria for selection, evaluation, approval, and re-evaluation of suppliers were available. The nonconformities identified were addressed through a CAPA plan.

7.4.2. Purchasing information

Supplier management and qualification procedures were available and implemented with agreements in place for critical suppliers. Criteria for selection, evaluation, approval, and re-evaluation of suppliers had been revised, and clarity relating to the requirements and the process was ensured. The nonconformities identified were addressed through a CAPA plan.

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. The extent of verification activities was proportionate to the risks associated with the purchased product. Records of such activities were maintained. The nonconformities identified were addressed through a CAPA plan.

7.5. Production and service provision

7.5.1. Control of production and service provision

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

7.5.6. Validation of processes for production and service provision

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

7.5.8. Identification

There was a documented procedure for product identification and segregation throughout the life cycle of the product, including released and nonconforming products within the facility.

7.5.9. Traceability

7.5.9.1. General

The organization had procedures available that supported full traceability of components, materials, and work environments used. These procedures were in accordance with applicable regulatory requirements.

7.5.11. Preservation of product

There were adequate and suitable processes available to ensure the preservation of products during processing, storage, handling, and distribution. The nonconformities identified were addressed through a CAPA plan.

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. There was adequate identification of equipment indicating its calibration status. The equipment was safeguarded. from adjustments that would invalidate the measurement result. The nonconformities identified were addressed through a CAPA plan.

The organization had procedures in place to assess and record the validity of the previous measuring results when the equipment was found out of tolerance. These included taking appropriate actions regarding the equipment and any product affected.

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 the risk management for monitoring and maintaining the product requirements as well as the product realization or improvement processes. The nonconformities identified were addressed through a CAPA plan.

8.2.2. Complaint handling

The organization had implemented a procedure for the timely handling of customer complaints. The procedure included requirements and responsibilities for investigating complaints, determining the need to report the information to the appropriate regulatory authorities, including WHO, handling of complaint-related products and determining the need to initiate corrections or corrective actions. Corrections and corrective actions were documented. Complaint handling records were maintained. The nonconformities identified were addressed through a CAPA plan.

8.2.3. Reporting to regulatory authorities

There was a procedure available for reporting and providing the necessary notifications to the appropriate regulatory authorities, including WHO, when needed. The nonconformities identified were addressed through a CAPA plan.

8.2.4. Internal audits

The organization had implemented an internal audit program and included conducting internal audits at planned intervals. 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.

8.2.5. Monitoring and measurement of processes

The organization had implemented procedures to monitor and measure the characteristics of the QMS processes. Achievement of planned results were available and when not met, corrections and corrective actions were taken.

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 the product and the test equipment used to perform measurement activities were recorded.

8.3. Control of nonconforming product

8.3.1. General

The organization had a process in place for the segregation of nonconforming products.

8.3.2. Actions in response to nonconforming product detected before delivery

The organization had procedures available for taking action to eliminate nonconforming property before delivery.

8.3.3. Actions in response to nonconforming product detected after delivery

The organization had implemented a procedure to deal with nonconforming product detected after delivery by taking appropriate action to the effects, or potential effects, of the nonconformity. Procedure for issuing advisory notices were in place. The nonconformities identified were addressed through a CAPA plan.

8.3.4. Rework

The organization had a procedure available for rework of a product with the necessary measures of ensuring that the reworked product met the applicable acceptance criteria and other regulatory requirements.

8.4. Analysis of data

The organization had a procedure available to determine, collect and analyse appropriate data to demonstrate the suitability, adequacy, and effectiveness of the QMS. This was verified throughout the WHO inspection. The nonconformities identified were addressed through a CAPA plan.

8.5. Improvement

8.5.2. Corrective action

The organization had procedures in place to take action to eliminate the causes of nonconformities to prevent recurrence. The procedures defined the requirements for reviewing nonconformities (including complaints), determining the causes of nonconformities, evaluating the need for corrective actions, planning and documenting actions needed and implementing such actions, including, as appropriate, updating documentation and reviewing the effectiveness of corrective actions taken.

8.5.3 Preventive action

The organization had a procedure available to determine the action required to eliminate the causes of potential nonconformities in order to prevent their occurrence.

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, ***Orchid Biomedical Systems – A Division of Tulip Diagnostics (P) Ltd*** located at ***Plot nos 88/89, Phase II C, Verna Industrial Estate, Verna, Goa, 403722, India*** 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 nonconformities identified during the inspection that were captured in the inspection report were addressed through a CAPA plan prior to publication of this 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, standards and other regulatory documents referenced in the inspection report

1. Inspection Services – In Vitro Diagnostics and Male Circumcision Devices (https://extranet.who.int/prequal/inspection-services/vitro-diagnostics-and-male-circumcision-devices)
2. Information for Manufacturers on Pre-qualification Inspection Procedures for the Sites of Manufacture of Diagnostics (PQDx_014).
3. ISO 13485:2016 Medical devices - Quality management systems - Requirements for regulatory purposes
4. ISO 9001:2015 Quality management systems – Requirements
5. WHO Post-market surveillance of in vitro diagnostics 2020 (ISBN 978 92 4 001532 6)
6. Medical devices - Application of risk management to medical devices - ISO14971:2019
7. GHTF/SG3/N19:2012 “Quality management system – Medical devices - Nonconformity Grading System for Regulatory Purposes and Information Exchange”
8. GHTF/SG4/(99)28 'Guidelines for Regulatory Auditing of Quality Systems of Medical Device Manufacturers - Part 1: General Requirements
9. GHTF/SG4/N30R20:2006 'Guidelines for Regulatory Auditing of Quality Systems of Medical Device Manufacturers - Part 2: Regulatory Auditing Strategy
10. 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.