World Health Organization

20, AVENUE APPIA – CH-1211 GENEVA 27 – SWITZERLAND – TEL CENTRAL +41 22 791 2111 – FAX CENTRAL +41 22 791 3111 – WWW.WHO.INT

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 no 88/89, Phase II C, Verna Industrial Estate, Verna, GOA, India 403722
Inspection details	
Dates of inspection	23-25 January 2019
Type of inspection	Reinspection
Introduction	
Brief description of manufacturing activities	Orchid Biomedical Systems – A division of Tulip Diagnostics (P) Ltd. is responsible for the control of the design, Development, Manufacture and Distribution of IVD Medical Devices based on Lateral Flow Immunochromatography Technology used in the Diagnosis of Infectious Diseases and Hormones.
General information about the manufacturer	The company was first established in 1988. There are currently 9 independent manufacturing sites.
History	WHO have inspected this site 5 times: • October 2010 • November 2011 • March 2014 • February 2017 • January 2019
Brief report of inspection activities undertaken – Scope and limitations	
Areas inspected	• Design and Development • Quality management system • Management responsibility • Purchasing • Production and Service Controls • Preservation (storage / delivery) • Monitoring and Measurement (in process and final) • Adverse Events and Advisory Notices Reporting • WHO pre-qualification-specific requirements
Scope	PQDx 0321-024-00 – Paracheck Pf – Rapid Test for P. Falciparum Malaria Device (Ver. 3)
Criteria	ISO 13485:2016 and WHO prequalification requirements outlined in the following documents: WHO Information for Manufacturers on the Inspection of Manufacturing Site(s) (Assessment of the Quality Management

	System) WHO document PQDx_014 WHO Post-market surveillance of in vitro diagnostics 2015 (ISBN 978 92 4 150921 3) GHTF/SG3/N19:2012 Quality management system – Medical devices - Nonconformity Grading System for Regulatory Purposes and Information Exchange GHTF/SG4/(99)28 Guidelines for Regulatory Auditing of Quality Systems of Medical Device Manufacturers – Part 1: General Requirements GHTF/SG4/N30R20:2006 Guidelines for Regulatory Auditing of Quality Management Systems of Medical Device Manufacturers – Part 2: Regulatory Auditing Strategy GHTF/SG4/N33R 16:2007 Guidelines for Regulatory Auditing of Quality Management Systems of Medical Device Manufacturers - Part 3: Regulatory Audit Reports
Objective(s)	To ensure that the requirements to ISO 13485:2016 and WHO requirements were being adequately met.
Limitations	None
Out of scope	According to the Orchid quality manual there were no exclusions from the standard (ISO 13485) and the following clauses were non-applicable: 7.5.3, 7.5.4, 7.5.5, 7.5.7 and 7.5.9.2.
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 (where applicable)

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

Orchid Biomedical Systems quality management system had been documented and implemented to meet the requirements of ISO 13485:2016. The quality management system appeared capable of routinely producing in vitro diagnostic devices that meet most customer and regulatory requirements for the 88 countries where its devices were sold or were intended to be sold.

The corporate QMS Manager is responsible for the entire Quality Management System activities of all the units.

4.2 Documentation requirements

4.2.1. General

4.2. Documentation requirements

4.2.2. Quality manual

The manufacturer's Quality Manual detailed the interaction between the processes of the QMS including non-applicable clauses of ISO 13485:2016 with appropriate justification.

4.2.3. Medical device file

The manufacturer had an established and well-maintained Medical device file that demonstrated conformity to the requirements of the standard, including labelling requirements that was verified.

4.2.4. Control of documents

The documented procedures for the control of documents met the requirements of the standard. Document retention was confirmed and found adequate. The QMS was paper-based and procedures were readily available in a timely manner.

4.2.5. Control of records

The documented procedures for the control of records met the requirements of the standard. Record retention was confirmed and found adequate and was confirmed as being at least equivalent to the lifetime of the device and had been documented to be 5 years. All reviewed records were legible, readily identifiable and retrievable, with any changes to a record identifiable.

5. Management responsibility

5.1. Management commitment

It was evident during the inspection that top management was committed to the development and implementation of the QMS.

5.2. Customer focus

The manufacturer had established and documented processes that were designed to meet the requirements of the standard and regulations.

5.3. Quality policy

Top management had established a Quality Policy that included a commitment to comply with regulatory requirements and to maintain the effectiveness of the QMS. The quality policy was displayed throughout the facility. The quality policy was applicable to the purpose of the organisation and related to the quality objectives.

5.4. Planning

5.4.1. Quality objectives

Quality objectives were established, measurable and had defined targets and were consistent with the quality policy.

5.4.2. Quality management system planning

The manufacturer had a documented organisational structure with the positions of quality manager, production manager and some other cross functional positions being filled by individuals who serviced more than one site.

5.5. Responsibility, authority and communication

5.5.1. Responsibility and authority

Within Orchid Biomedical Systems there were defined designated responsibilities and authorities for staff undertaking or verifying work affecting quality. Reporting lines for quality and production were independent of the other. All requirements of the standards were met.

5.6. Management review

5.6.1. General

Orchid Biomedical Systems had a documented management review procedure that adequately documented the requirements of the standard. Meetings were held every 4 months with attendance sheet and agenda available. The records of management review held on 27/03/2018, 10/08/2018 and 27/12/2018 demonstrated compliance with these requirements. The manufacturer monitored and measured the ability of the quality management system processes to meet planned results, including a review of the Quality Policy and Quality Objectives.

6. Resource management

6.2. Human resources

The manufacturer had determined and provided the resources needed to implement the quality management system, to maintain its effectiveness, and to meet regulatory and custo mer requirements.

6.3. Infrastructure

The manufacturing environments were adequately planned for the current volume of production.

6.4. Work environment and contamination control

6.4.1. Work environment

The premises were maintained satisfactorily and were clean and tidy. All areas were temperature monitored and where required monitored for humidity. A backup generator was available during power outages. Staff were provided with clean personal protective equipment including hair nets and shoes for the production and QC areas. Closed shoes were provided for the warehouse areas.

There were adequate instructions with pictures to guide personnel in gowning requirements.

7. Product realization

7.1. Planning of product realization

The manufacturer had a process in place for product realization that was in line with the requirements of the standard. The procedures and work instructions that were reviewed indicated that they included all relevant production processes. The requirements for risk management were documented in relevant procedures.

7.3. Design and development

7.3.1. General

At the time of inspection and upon review of the submitted documents the manufacture met the requirements according to the standard for design and development of the product that was verified at the site.

7.4. Purchasing

7.4.1. Purchasing process

The manufacturer had a well-defined and documented process for the purchasing of material. Orchid Biomedical Systems purchasing department used quality agreements with approved suppliers that specify the responsibilities of the suppliers. The criteria for selection, approval evaluation and re-evaluation of suppliers followed the requirements of the standard.

7.4.3. Verification of purchased product

The incoming goods testing was performed according to the documented procedure and were found to be incompliance with the requirements of the standard.

7.5. Production and service provision

7.5.1. Control of production and service provision

At the time of inspection, a number of manufacturing activities were observed including but not limited to production of critical reagents, buffer filling, strip cutting, cassette assembly and quality control testing and sampling.

7.5.8. Identification

The manufacture had documented procedures to identify product status throughout product realization. These included procedures to adequately identify products that had passed the required inspections and QC.

7.5.9. Traceability

The deficiencies related to provisions for ensuring traceability that were initially identified during the onsite inspection had been satisfactorily addressed and brought to compliance as part of the manufacturer's corrective/preventive action plan.

7.5.11. Preservation of product

The manufacturer had well defined and documented procedures for the preservation of product that met the requirements of the standard.

7.6. Control of monitoring and measuring equipment

The manufacturer had an adequate procedure and corresponding records for tracking and implementing equipment maintenance. A maintenance schedule for preventive maintenance was available and found adequate.

8. Measurement, analysis and improvement

8.2. Monitoring and measurement

8.2.1. Feedback

Customer feedback from domestic and export customers was requested annually by the Tulip Diagnostic Sales and Marketing department located at the Tulip corporate office in Bambolim. Legitimate domestic or export feedback that Tulip/ Orchid Biomedical Systems consider to be a complaint of a nonconforming product or process was recorded at the Head Office, Technical Services Department by Customer Support staff members in a paper-based log book. The process was in accordance with the requirements of the standard.

8.2.2. Complaint handling

At the time of inspection, the complaint handling procedures appeared to be adequately documented and implemented. However further improvement was required on the effectiveness of the domestic and export complaint handling process.

8.2.3. Reporting to regulatory authorities

A procedure was in place for the reporting to regulatory authorities including WHO. The documentation review supported the requirements of the standard.

8.2.4. Internal audits

The manufacturer had a mature internal audit program that encompassed all Tulip related companies. There were documented procedures and requirements, schedules and training records for all staff involved in internal audits.

8.2.6. Monitoring and measurement of product

The manufacturer had established QC processes to monitor and measure the characteristics of the product to verify that product requirements had been met. A process covered all aspects of manufacturing from incoming goods, various stages of in process production and final release. Evidence of conformity to the acceptance criteria was maintained and the identity of the authorizing person was recorded.

8.3. Control of nonconforming product

8.3.1. General

There was a documented process in place for managing nonconformities and corrective actions. All nonconformities were investigated according to the written procedure, root cause analysis was conducted, and findings were reported through the management review meetings to top management. The requirements of the standard were adequately met.

8.4. Analysis of data

There was a process in place for the analysis of data that satisfied the requirements of the standard. Data was sourced for a number of areas related to the QMS including but not limited to post market surveillance, customer feedback and complaints and nonconformities.

8.5. Improvement

8.5.2. Corrective action

The manufacturer had in place a process for corrective action that adequately satisfied the requirements of the standard.

8.5.3. Preventive action

The manufacturer had in place a process for corrective action that adequately satisfied the requirements of the standard.

9. WHO pre-qualification-specific requirements

The manufacturer had adequately satisfied the WHO prequalification requirements.

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***, Orchid Biomedical Systems – A division of Tulip Diagnostics (P) Ltd.*** located at *Plot no 88/89, Phase II C, Verna Industrial Estate, Verna, GOA, India 403722* 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).

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. ISO 9001:2015 Quality management systems – Requirements

4. WHO Post-market surveillance of in vitro diagnostics 2015 (ISBN 978 92 4 150921 3)

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

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

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

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

9. 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.