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

Prequalification Team Inspection Services
WHO PUBLIC INSPECTION REPORT
(WHOPIR)
Desk Assessment of In Vitro Diagnostic Product Manufacturer

Part 1	**General information**
Manufacturers information	
Name and address of manufacturer	Cepheid – Lodi 225 North Guild Lodi, CA, California 95240 United States of America
Desk assessment details	
Dates of inspection	11-13 September 2024
Type of inspection	Initial
Products covered by this desk assessment	- PQDx 10295-070-00 Xpert MTB/RIF Ultra - PQDx 12361-070-00 Xpert Xpress CoV-2 plus
List of documents submitted	BSI Audit Report Jan 2023 Cepheid-Lodi. BSI Audit Report Sept 2023 Cepheid-Lodi Contact Information for Responsible Person Attachment 1 Post Market Data Review Template Global Safety Risk Management SOP Global SOP for Nonconforming Process Global Supplier Audits Procedure final Planned Deviation Supplier Qualification and Management Procedure Adverse Event Reporting SOP Reportability Matrix Control and Reporting of Field Actions. PMQ Review of Customer Complaints SCAR Procedure TECHNICAL SUPPORT CASE MANAGEMENT Escalation Criteria and Pathway for Product Complaints DMR for Xpert MTB RIF Ultra Failure Investigation Escalation (FIE) Procedure Nonconformance eQMS Work Instruction Trend Reporting Procedure Global Inspection & Testing SOP Global Incoming Inspection SOP Global Complaint Handling Process SOP Work Instruction_Performing Statistical Trend Analysis

	SCAR EQMS Work Instructions Procedure. ePDR Work Instructions Attachment 1 - Xpert MTB-RIF Ultra Post-Commercialization Change Log INSP-IVD-2024-0062 Cepheid Lodi Desk Assessment Documentation Request Letter (003) List of Audit NCs-Lodi LODI Facilities Map B1 FL 1 & 2 LODI Facilities Map B2 FL 1 LODI Facilities Map B2 FL 2 LODI Facilities Map B3 FL 1 & 2 Lodi Operations Organogram Lodi Quality Organogram LRQA Audit Report (CTA) May 2022 Cepheid-Lodi MD 774674_Issued 2024-01-15 MDSAP 774673_Issued 2024-07-04 MTBRIF ULTRA Critical Suppliers and Parts Outsourced processes (Direct) for MTB_RIF Ultra1 Cepheid_Global_Quality_Manual Global Risk_Management Lodi Quality Management System Document Matrix Purchasing Controls Policy Global Inspection, Testing and Acceptance Policy Global Policy for the Control of Nonconforming Product Quality Management System Procedures	
Any documents missing?	None.	
General information about the company and site	There were three buildings at the Lodi site, two buildings manufactured the plastic components (225 North Guild Avenue and 850 East Thurman Road), and one building manufactured the IVD reagents (121 North Guild Avenue) for the tests used for Monitoring and Patient Management. These sites had never been inspected by WHO PQT but had been inspected and certified by MDSAP. As such, the MDSAP inspection reports were reviewed to inform the prequalification of the Lodi site.	
Part 2	**Summary of inspection evidence considered (from most recent to last)**	
bsi audit report	Dates of inspection:	12-14 September 2023
	Type of inspection:	Hybrid surveillance audit
	Products covered:	Not listed
Bsi audit report	Dates of inspection:	24-25 January 2023
	Type of inspection:	Onsite surveillance audit
	Products covered:	Not listed
LRQA audit report	Dates of inspection:	31 March to 31 May 2022
	Type of inspection:	Hybrid change-to-approval audit
	Products covered:	Not listed

Abbreviations	Meaning
CoA	Certificate of analysis
IQ	Installation qualification
IVD	In vitro device
MR	Management Review
MSDS	Material safety data sheet
NC	Non-conformities
PPE	Personal Protective Equipment
OOS	Out-of-specifications test result
OQ	Operational qualification
PM	Preventive maintenance
PQ	PQ Performance qualification
PW	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

Part 3	Brief summary of the findings and comments (where applicable)

1. Quality Manual:
The manufacturer had implemented a quality manual that included the scope of the QMS, referred to documented procedures, and included a description of the interaction between processes. Documentation structure was outlined. The manufacturer provided organograms for the operations and for the quality departments of the Fremont site. From those, it could be established that operations were independent from quality.

The nonconformity identified was successfully resolved through a CAPA process.

2. List of current quality management procedures:
The manufacturer provided a list of 137 quality systems documents relevant to the Lodi site. The list included the latest revision of each document and its effective date.

3. Standard operating procedures for:

i. Complaint handling and vigilance:
The manufacturer provided the global complaint handling procedure that established the process for Cepheid global intake, review, assessment, investigation, and closure of complaints involving products marketed by Cepheid. It applied to any Cepheid associates.
Complaints could be received via different means (including by phone, web portal, e-mail), which was considered appropriate, even for resource-constrained settings. The global procedure appeared to meet the requirements of the standard. Complaints trend reporting procedure was documented.

ii. Control of nonconforming products/goods/processes:

The manufacturer provided separate documentation for planned or unplanned NC.

- Planned NC were managed through a global policy for the control of NC product that appeared to meet the requirements of the standard. The process for the request and approval of a temporary change to a documented requirement was documented and supported by detailed instructions.
- Unplanned NC were managed through a global policy and global risk management documents. These documents appeared to meet the requirements of the standard. A global procedure for nonconforming process that outlined the three main stages of the control of nonconforming process/product: identification, evaluation, and documentation of the NC was implemented.

iii. Risk management:

The manufacturer provided SOPs and template that described the process used to ensure that risks to patients, users, customer property and the environment from the use of Cepheid medical device products were acceptable. A semi-quantitative approach was used to determine the Safety Risk Profile. This applied to devices throughout their lifecycle.

iv. Supplier evaluation and control

The manufacturer provided the global purchasing controls policy that defined the requirements to ensure that purchased materials and services conformed to specified requirements. It applied to the procurement of components, finished goods, and services that impacted product quality and to any Cepheid organization or site that procured these items. This excluded transactions between Cepheid sites that were under the same QMS. This document appeared to meet the requirements of the standard.

It was further supported by a supplier qualification and management procedure that defined the process for identifying, selecting, qualifying, and managing internal and external suppliers to ensure that all purchased product/service conformed to Cepheid's specified requirements for production applications for all Cepheid locations.

The supplier review board would classify each supplier based on the criticality of the product/service that it provided into four categories. This guided the minimum requirements for each supplier in terms of supplier survey, quality agreement, audit etc.

The supplier audits procedure was documented and included the possibility of for-cause audits, even for suppliers in the lower risk categories. This procedure detailed the classification of audit findings and the corresponding requirements for escalation based on overall audit risk rating. This could include supplier corrective action (SCAR).

v. Verification of purchased product:

This process was supported by a global policy, as well as by global inspection and testing procedures. The extent of acceptance activities for incoming purchased components was based on supplier evaluation results and risk associated with the components to the final device. Incoming inspection included a sampling plan based on statistics that was documented. The need to identify and segregate materials undergoing incoming testing was documented.

4. Audit report of the most recent full regulatory audit and all subsequent surveillance audits:
The last two MDSAP surveillance audit reports performed by bsi were provided and reviewed. The manufacturer also provided the report of an audit performed by LRQA that was also reviewed.

5. Valid quality management system certificate(s) and scope of certification:
The manufacturer provided MDSAP certificate 774673 delivered on the 30th of August 2022 by bsi. It included the Fremont warehouse with the scope of distribution of IVDs and analysers. It was valid until the 18 December 2024. The authenticity of the certificate could be verified on the bsi website. The manufacturer also provided certificate MD 774674 delivered on the 2nd of August 2022 by bsi, it included the Fremont warehouse with the scope of distribution of IVDs and analysers. It was valid until the 18 December 2024. The authenticity of the certificate could be verified on the bsi website.

6. Manufacturing flowchart including in-process control points:
The manufacturer provided the device master record for the Xpert MTB/RIF Ultra assay. It provided a general description of the manufacturing process of the finished product kit, including in-process control points.

7. List of critical raw materials (including details of the supplier of each material):
The manufacturer provided the lists of critical suppliers and parts for each of the products in scope.

Part 4	**Conclusion – Inspection outcome**

Based on the MDSAP evidence received and reviewed, it is considered that a desk assessment is acceptable in lieu of a WHO onsite inspection. The site ***Cepheid Lodi located at 225 North Guild Lodi, CA, California 95240, United States of America*** is considered to be operating at an acceptable level of compliance with ISO 13485: 2016 and WHO *Information for Manufacturers on Prequalification Inspection Procedures for the Sites of Manufacture of Diagnostics* (PQDx_014).

This WHOPIR will remain valid until the 14th of September 2026, provided that the outcome of any inspection conducted during this period is positive.

Part 5	**List of Standards and Guidelines referenced in the inspection report**

1. WHO Information for Manufacturers on Prequalification Inspection Procedures for the Sites of Manufacture of Diagnostics (PQDx_014).

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 1001531 9)

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.