World Health Organization

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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 – Fremont 904 Caribbean Drive Sunnyvale, CA, California 94089 United States of America
Desk assessment details	
Dates of inspection	10 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	Re_ [EXT] Clarification of Scope for Cepheid Fremont Desk Assessment BSI Audit Report Jan 2023 Cepheid-Sunnyvale BSI Audit Report Sept 2023 Cepheid-Sunnyvale Cepheid EBLC Fremont (EMS Data Last 2 Months Aisle 32 Upper and Lower Rack Levels) Cepheid EBLC Fremont (EMS Data Last 2 months Cold Room 07) Cepheid EBLC Fremont (EMS Data Last 2 months INC Room 21) Contact Information for Responsible Person. Attachment 1 Post Market Data Review Template Rev. Y Global Safety Risk Management SOP Rev. Y Global SOP for Nonconforming Process Global Supplier Audits Procedure final Planned Deviation_Rev Y Supplier Qualification and Management Procedure (9) SCAR Procedure Nonconformance eQMS Work Instruction Global Inspection & Testing SOP (2) (1) Global Incoming Inspection SOP Rev A (1) EBLC Fremont Facility Qualification Report for Warehouse EBLC Fremont Facility Qualification Report for INC (Room 21) EBLC Fremont Facility Qualification Report for Cold Room 07 SCAR EQMS Work Instructions Procedure_Rev_A ePDR Work Instructions Rev B (2) EBLC Fremont Operations Organogram EBLC Fremont Quality Organogram Fremont EBLC Facilities Map FL 1 & 2 List of Audit NCs-Sunnyvale (Fremont)

	LRQA Audit Report Aug-Nov 2021 Sunnyvale MD 774674_Issued 2024-01-15 MDSAP 774673_Issued 2024-07-04 No changes to product and processes related to Cepheid Sunnyvale Cepheid_Global_Quality_Manual Cepheid_Sunnyvale_Document_Matrix Global Risk_Management Purchasing Controls Policy Global Inspection, Testing and Acceptance Policy Global Policy for the Control of Nonconforming Product Quality System Documents - Sunnyvale
Any documents missing?	None.
General information about the company and site	The Cepheid Fremont site was added by Cepheid AB as a warehousing site for the products in the prequalification portfolio. This site had never been inspected by WHO PQT but has been inspected and certified by MDSAP. As such, the MDSAP inspection reports were reviewed to inform the prequalification of the Fremont site. The assessment focused on the purchasing and warehousing activities, and the associated risks.

Part 2	**Summary of inspection evidence considered (from most recent to last)**	
bsi audit report	Dates of inspection:	26-29 September 2023
	Type of inspection:	Hybrid Surveillance Audit
	Products covered:	Not listed
bsi audit report	Dates of inspection:	17-20 January 2023
	Type of inspection:	On-site Surveillance 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

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 143 quality systems documents relevant to the Sunnyvale campus which included the Fremont warehouse. The list included the latest revision of each document and its effective date.

3. Standard operating procedures for:

i. Control of nonconforming goods/processes:
The manufacturer provided separate documentation for planned or unplanned nonconformities (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. The manufacturer had implemented 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.

ii. Risk management:
The manufacturer provided SOPs and templates describing 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.

The nonconformity identified was successfully resolved through a CAPA process.

iii. Supplier evaluation and control:
The manufacturer provided a 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 impact 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.

The policy 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 4 categories. This guided the minimum requirements for each supplier in terms of supplier survey, quality agreement, audit.

A procedure for supplier audits was documented. It 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). The SCAR process and its documentation were documented.

iv. 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. 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 audit reports performed by bsi were provided and reviewed. The manufacturer also provided the report of an audit performed by LRQA in August-November 2021. Given this report was 3 years old, it was not considered as part of this desk assessment.

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. Environmental controls:

The inspection team assessed the environmental control of the incoming area, the warehouse, and the cold room.

The manufacturer indicated that no production or storage occurred in the incoming area and that temperature mapping was not required. This area had been qualified and its temperature was within 18-25 °C during a 72-hour temperature monitoring. This was verified on temperature data recorded over the summer months of 2024 that indicated that temperature remained within the 18-25 °C range.

The qualification report of the warehouse was provided. It included a temperature uniformity study that indicated that the temperature recorded remained within the 2-28°C specified range. This was verified on temperature data recorded over the summer months of 2024 that indicated that temperature remained within the 2-28°C range.

The qualification report of the cold room was provided. It included a temperature uniformity study that indicated that the temperature recorded remained between ~3.8 to ~6.6°C (acceptance range 2-8°C). This was verified on temperature data recorded from 4 July 2024 to 4 September 2024 was provided. It indicated that the temperature recorded over the summer months of 2024 that indicated that temperature remained within the 2-8°C range.

The nonconformities identified were successfully resolved through a CAPA process.

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 Fremont located at 904 Caribbean Drive, Sunnyvale, CA, California 94089, 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 29th 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.