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)
DEVICE MANUFACTURER

Inspected site	
Name of Manufacturer	Plexus Manufacturing Sdn. Bhd.
Address of inspected manufacturing site	Plot 87, 88, 89 Lebuhraya Kampung Jawa, Bayan Lepas Pulau Pinang 11900 Malaysia
Inspection details	
Dates of inspection	01-02 August 2019
Type of inspection	Initial
Introduction	
Brief description of manufacturing activities	Plexus Manufacturing Sdn. Bhd. is a large contract manufacturer, with a scope of manufacturing activities that includes production, testing, labeling, shipping, and servicing of general active medical devices, devices for imaging monitoring, in vitro diagnostic medical devices, and printed circuit boards, high level assemblies, and accessories for active medical devices. The site was audited as a critical supplier to Abbott Rapid Diagnostics Jena GmbH (formally Alere Technologies GmbH Jena).
General information about the manufacturer	Founded in 1979, Plexus is now a global force of over 19,000 team members spread across more than a dozen locations worldwide. The headquarters are in Neenah, Wisconsin. At the time of inspection, the operation had 1286 staff with 300 of them working in shifts.
History	Plexus Manufacturing Sdn. Bhd. had never been inspected by WHO prior to this August 2019 inspection. This inspection was initiated after *Abbott Rapid Diagnostics Jena GmbH* indicated the transfer of the assembly of the prequalified m-PIMA Analyser (PQDx 0226-032-00) to Plexus Manufacturing Sdn. Bhd.

This inspection report is the property of the WHO
Contact: prequalinspection@who.int

Brief report of inspection activities undertaken – Scope and limitations	
Areas inspected	Quality management system Management responsibility Purchasing Design Transfer Production and Service Controls Measurement, analysis and improvement
Scope	m-PIMA Analyser PQDx 0226-032-00
Criteria	ISO 13485:2016 and WHO Prequalification specific requirements
Objective(s)	Establish whether the applicable requirements to ISO 13485:2016 and WHO were met
Limitations	None.
Out of scope	Exclusions and non-applications from ISO 13485:2016: • User training (Clauses 7.2.1 and 7.2.2) • Design and Development (Clause 7.3) • Installation (Clause 7.5.3) • Traceability for implantable medical devices (Clause 7.5.9.2) • Reporting to regulatory authorities (Clauses 5.6.2, 8.2.2, and 8.2.3) • Issuing advisory notices (Clause 8.3.3)
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

This inspection report is the property of the WHO
Contact: prequalinspection@who.int

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

4.2. Documentation requirements

4.2.2. Quality manual

The manufacturer's Quality Manual addressed and reflected the intended practices of the manufacturer. It contained a description of the interaction between the processes of the Quality Management System (QMS), defined the structure of the documentation system and detailed the manufacturer's compliance with the requirements of ISO 9001 and ISO 13485:2016. The Quality Manual listed exclusions and non-applications with acceptable justification.

4.2.4. Control of documents

There were documented procedures for document and record control which met the requirements of the standard. Largely, electronic document and records control practices were generally compliant. The procedures and the records reviewed provided evidence of conformity and completion of requirements.

4.2.5. Control of records

Generally, records were readily available. The requirements for record retention will be included in the Quality agreement with Abbott Rapid Diagnostics Jena GmbH (formally Alere Technologies GmbH Jena) and were confirmed as being at least equivalent to the lifetime of the device.

5. Management responsibility

5.1. Management commitment

There was evidence of top management's commitment to the development and implementation of the quality management system and maintenance of its effectiveness. Top management had established an adequate quality policy including a commitment to comply with regulatory requirements and to maintain the effectiveness of the quality management system.

5.3. Quality policy

The manufacturer had established an adequate quality policy, including a commitment to comply with regulatory requirements and to maintain the effectiveness of the quality management system. The quality policy was applicable to the purpose of the organization and related to quality objectives.

This inspection report is the property of the WHO
Contact: prequalinspection@who.int

5.4. Planning

5.4.1. Quality objectives

Quality objectives were established, measurable and had defined targets and were consistent with the quality policy. Staff interviewed during the inspection were informed of the manufacturer's quality priorities and were willing to share information and contribute to the inspection process. The staff interviewed were aware of the relevance and importance of their activities and how they contributed to the achievement of the quality objectives

5.4.2. Quality management system planning

The manufacturer had documented the organizational structure and defined designated responsibilities and authorities for staff undertaking or verifying work affecting quality. Reporting lines for quality and production were independent of the other.

5.5. Responsibility, authority and communication

5.5.2. Management representative

There was continuity in the role of the management representative, with the responsibilities and authorities as defined in the standard. The quality manager was the nominated management representative, and had the responsibilities and authorities as defined in the standard.

5.6. Management review

5.6.1. General

Documented requirements for management review were implemented and the review meetings were held twice a year. The manufacturer monitored and measured the ability of the quality management system processes to meet planned results, as indicated in the records of Management Review. The records of management review held on 9 May 2019 demonstrated general compliance with these requirements.

6. Resource management

6.1. Provision of resources

The manufacturer had determined and continued to provide the resources needed to implement the quality management system, to maintain its effectiveness, and to meet regulatory and customer requirements.

6.2. Human resources

The necessary competence of personnel performing work affecting product quality had been determined and satisfactorily addressed in the procedures. As part of the transfer program, Abbott Rapid Diagnostics Jena had its trainers assisting with Plexus employees' training on site.

6.4. Work environment and contamination control

6.4.1. Work environment

Manufacturing activities were spread over various factories within the same site. The premises were spacious, secure and allowed for an acceptable work flow. The premises were maintained satisfactorily and had an appearance of being clean and tidy. The manufacturer determined and maintained the work environment suitable for the type of product manufactured.

This inspection report is the property of the WHO
Contact: prequalinspection@who.int

6.4.2. Contamination control

Production was carried out in rooms with adequately controlled environments, and adequate SP protection.

7. Product realization

7.1. Planning of product realization

The manufacturer's approach to planning of product realization followed the requirements of the standard and the procedures and work instructions reviewed indicated that they included all relevant production processes. The requirements for risk management were documented in relevant procedures. The deficiencies that were initially identified during the onsite inspection had been satisfactorily addressed and brought to compliance as part of the manufacturer's corrective/preventative action plan.

7.3. Design and development

7.3.8. Design and development transfer

The manufacturer had defined and documented the design and development process in the relevant SOPs. However, the review of the design activities was limited to the design transfer activities as the product within the scope of this audit was designed at Abbott Rapid Diagnostics Jena GmbH.

7.4. Purchasing

7.4.1. Purchasing process

The manufacturer had defined and documented the requirement for purchasing controls and supplier management in relevant procedures. These appeared suitable. The manufacturer had been classified as a key supplier to Abbott Rapid Diagnostics Jena GmbH. There was sufficient evidence that the manufacturer was being qualified as a supplier of finished device instruments and controlled according to Abbott Rapid Diagnostics Jena GmbH's supplier management procedure, based on an on-site inspection of the quality management system of the manufacturer, the ongoing presence and observation of Abbott Rapid Diagnostics Jena GmbH's representative on site during the process of design transfer and a final audit by Abbott Rapid Diagnostics Jena GmbH was planned for Q4 2019.

7.4.3. Verification of purchased product

Processes for the verification of received components were adequate and records of a few receiving inspection records were reviewed. The manufacturer appeared to be closely monitoring performance of its current suppliers of electronic parts and services. Abbott Rapid Diagnostics Jena GmbH was to control all suppliers in the validation/verification stage. Inwards goods testing was performed in accordance with documented specifications. The incoming QC standard operating procedures and specifications reviewed were found in compliance with the standard.

7.5. Production and service provision

7.5.1. Control of production and service provision

Several manufacturing activities were observed, including assembly of a plunger module. Deficiencies initially identified during the inspection were satisfactorily addressed and brought to compliance as part of the manufacturer's corrective/preventative action plan.

This inspection report is the property of the WHO
Contact: prequalinspection@who.int

7.5.6. Validation of processes for production and service provision

The manufacturer had procedures and corresponding records for the validation of processes for production and service provision demonstrating the ability of these processes to achieve planned results consistently. Deficiencies initially identified during the inspection were satisfactorily addressed and brought to compliance as part of the manufacturer's corrective/preventative action plan.

7.5.9. Traceability

The manufacturer had documented provisions to ensure traceability and status identification of products at all stages of manufacturing, including during quality control testing. Deficiencies initially identified during the inspection were satisfactorily addressed and brought to compliance as part of the manufacturer's corrective/preventative action plan.

7.5.11. Preservation of product

The manufacturer had documented the procedures for preserving the conformity of the product to the requirements of the standard. There were no additional plans for product preservation studies which was considered reasonable, seeing that only the transfer of instrument was included in this change.

8. Measurement, analysis and improvement

8.2. Monitoring and measurement

8.2.1. Feedback

Post-market surveillance remained the responsibility of Abbott Rapid Diagnostics Jena GmbH. Post-market surveillance was to continue to be carried out as per Abbott Rapid Diagnostics Jena GmbH's procedures VA-0016 (complaint management and reporting), VA-0015 (ATJ vigilance reporting system) and VA-0042 (market surveillance).

8.2.2. Complaint handling

A process for managing customer complaints was in place and was considered adequate and reflected the requirements of the regulations and the standard. Customer complaints management was to continue to be managed as per Abbott Rapid Diagnostics Jena GmbH's procedures VA-0016 (complaint handling), and VA-0015 (vigilance reporting) that include both proactive and reactive activities to monitor the safety and performance of the product.

8.2.4. Internal audits

The manufacturer implemented an internal audit program including documented requirements, audit schedules and audits performed by appropriately-qualified auditors, independent of the areas being audited. The schedule took into account the status and importance of the areas to be audited. Records of internal audits were available and indicated that a relatively small number of findings was identified.

8.2.6. Monitoring and measurement of product

The manufacturer had established quality control processes to monitor and measure the characteristics of the product to verify that product requirements had been met. This was carried out for incoming goods, during product realization and before lot release. Evidence of conformity to the acceptance criteria was maintained and the identity of the person authorizing release recorded.

This inspection report is the property of the WHO
Contact: prequalinspection@who.int

8.3. Control of nonconforming product

8.3.1. General

The manufacturer implemented procedures for managing nonconformities and corrective actions that mostly satisfied the requirements of the standard. The handling of nonconformities included conducting root cause analyses, documenting investigations and assessing the effectiveness of corrective actions taken as well as their potential impact on product quality. The provisions for the control of nonconforming and rejected parts and devices were in place and were suitable.

8.4. Analysis of data

The manufacturer had implemented a procedure for data analysis. The Manufacturer's review meetings indicated that data was sourced from several areas of the quality management system to be included in the analysis of complaints, nonconformities, customer feedback, performance of suppliers, conformity of product requirements. The manufacturer also utilized the analysis of data for monitoring product and supplier's quality.

9. WHO pre-qualification-specific requirements

The products manufactured at the site had already been pre-qualified. As such, the assessment of compliance to WHO pre-qualification requirements was limited to site-specific requirements, which were met.

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, ***Plexus Manufacturing Sdn. Bhd.***, located at ***Pulau Pinang, Malaysie*** 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 manufacturer, 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.

This inspection report is the property of the WHO
Contact: prequalinspection@who.int

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 - ISO14971:2007
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.

This inspection report is the property of the WHO
Contact: prequalinspection@who.int