

**WHO Prequalification Team - Inspection services
WHO PUBLIC INSPECTION REPORT (WHOPIR)**

Inspected site	
Manufacturer	Chembio Diagnostics Malaysia Sdn. Bhd.
Address of inspected manufacturing site	N-TATT Building 2nd floor, No. 2-1 Jalan TP5, Taman Perindustrian, UEP, 47600, Subang Jaya, Selangor, Malaysia
Inspection details	
Dates of inspection	29-31 July 2019
Type of inspection	Initial inspection (addition of a new manufacturing site)
Introduction	
Brief description of manufacturing activities	Chembio Diagnostics Malaysia Sdn. Bhd. assembles, packs, labels, stores and delivers rapid diagnostic tests manufactured from uncut cards produced by Chembio Diagnostics Systems, Inc. (Medford, NY, USA).
General information about the manufacturer	Chembio Diagnostics Malaysia Sdn. Bhd. was formerly RVR Diagnostics. Chembio Diagnostics Systems, Inc. acquired it on January 10, 2017 with the view to serve as a manufacturing and distribution facility into European, African and Asian markets.
History	Being recently acquired, Chembio Diagnostics Malaysia Sdn. Bhd. had never been inspected by WHO prequalification services. Chembio Diagnostics Malaysia Sdn. Bhd. received ISO 13485:2016 certification in December 2016 with validity until January 2021.
Brief report of inspection activities undertaken – Scope and limitations	
Areas inspected	Quality management system Management responsibility Resource management Product realization Measurement, analysis and improvement WHO pre-qualification-specific requirements
Scope	HIV 1/2 STAT PAK [®] Assay, PQDx 0007-006-00
Criteria	ISO 13485:2016 and WHO Prequalification specific requirements
Objective(s)	Assess if the new manufacturing site met the audit criteria
Limitations	None
Out of scope	Exclusions and non-applications from ISO 13485:2016: • 7.3 Design and Development • 7.5.3 Installation activities • 7.5.4 Servicing activities • 7.5.5 Particular requirements for sterile medical devices • 8.2.3 Reporting to regulatory authorities • 7.5.9.2/8.2.4.2 Requirements for implantable and active medical devices

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

4.2. Documentation requirements

4.2.2. Quality manual

The manufacturer's Quality Manual applied to the intended practices of Chembio Diagnostics Malaysia Sdn. Bhd. It contained a description of the interaction between the processes of the Quality Management System (QMS), defined the structure of the QMS, how it was reflected in the documentation system, and listed non-applicable clauses of ISO13485:2016 ("the standard") with appropriate justification.

4.2.3. Medical device file

The manufacturer established and maintained documents demonstrating conformity to the requirement of the standard. These included descriptions of the labelling requirements. Labelling of the finished product was verified. The required information (e.g. the content, number of tests, preservation temperature, product codes, batch number and expiry dates) was clearly visible and would not smudge.

4.2.4. Control of documents

The documented procedures for control of documents met the requirements of the standard. Document control practices were based on a mature system from Chembio Diagnostics Systems, Inc. Document retention was confirmed as 7 years, i.e. longer than the lifetime of the product.

4.2.5. Control of records

The documented procedures for control of records met the requirements of the standard and were based on a mature system from Chembio Diagnostics Systems, Inc. Records were legible, readily identifiable and retrievable and any changes to a record remained identifiable. Records retention was confirmed as 7 years, i.e. longer than the lifetime of the product. The records reviewed were legible, readily identifiable and easily retrieved.

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 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

Senior 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 quality policy was applicable to the purpose of the organization and related to 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 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

5.5.1. Responsibility and authority

The Management Review Board identified the Director, Regulatory Affairs, Research and Development with the ultimate responsibility for Quality Assurance and Regulatory Affairs. Accountability in line with the standard was indicated, and the reporting-line was to the VP of QA/QC of regulatory affairs of the company.

5.6. Management review

5.6.1. General

Management Reviews were to take place twice a year according to a defined process. The most recent one took place on 26 July 2019. Management Review Reports prepared by the manufacturer were submitted to Chembio Diagnostics Systems, Inc.

6. Resource management

6.2. Human resources

The manufacturer had documented the processes for establishing competence, providing training, and ensuring awareness of personnel. Organization charts were available reflecting an adequate structure. Over the last couple of years preceding the inspection, the manufacturer had been building up the resources needed to implement the QMS, to maintain its effectiveness, and to meet regulatory and customer requirements (with 33 employees at the time of this audit).

6.3. Infrastructure

The manufacturing environments were adequately planned for the current volume of production. However, the manufacturer indicated that there were plans for significantly larger volumes, being manufactured at the facility in the near future and the inspected facilities did not appear necessarily suitable for significantly larger volumes of manufacturing.

6.4. Work environment and contamination control

6.4.1. Work environment

The premises were maintained satisfactorily and had an appearance of being clean and tidy. Production was carried out in rooms with environments adequately controlled for the type of products manufactured. There were adequate instructions with pictures to guide personnel in gowning requirements.

7. Product realization

7.1. Planning of product realization

The manufacturer's approach to planning of product realization was documented in the QMS, with procedures for document management, risk management, production, material verification, process validation, monitoring, inspection and test activities, as well as the device batch record. The requirements for risk management were documented in relevant procedures.

7.4. Purchasing

7.4.1. Purchasing process

The manufacturer used defined and documented requirements for purchasing controls and supplier management. Criteria for selection, approval evaluation and re-evaluation of suppliers, were determined by Chembio Diagnostics Systems, Inc. with input from Chembio Diagnostics Malaysia Sdn. Bhd. following the requirements of the standard. The list of approved suppliers of critical materials was maintained.

7.4.3. Verification of purchased product

Inwards goods testing was performed in accordance with documented specifications. Incoming QC standard operating procedures and specifications for foil, reagent bottles etc., were reviewed and found in compliance with the standard.

7.5. Production and service provision

7.5.1. Control of production and service provision

Except for the card cutting operation, all other manufacturing activities were observed, including buffer filling, cassette assembly, packaging, final kitting, QC and product release. Deficiencies initially identified during the inspection were satisfactorily addressed and brought to compliance as part of the manufacturer's corrective/preventative action plan.

7.5.8. Identification

The manufacturer 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

7.5.9.1. General

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/preventative action plan. There was good traceability of the samples used in QC, their quantity, the identity of the supplier and the nature of these samples. There was good traceability of the pouched devices and filled buffer bottles for the lot of devices inspected. Similarly, the QC log book offered good traceability of the biological samples used for QC and there was perfect accountability for the number of pouched devices manufactured, discarded, used and in stock.

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 during processing, storage, handling, and distribution. Prescribed preservation conditions were based on studies investigating real-time and in-use stability, air freight, vibration and temperature stress, including temperatures outside the recommended temperature range.

7.6. Control of monitoring and measuring equipment

The manufacturer had an adequate procedure and tracking system for equipment maintenance that utilized SAGE UBS Software for inventory management. Records for Preventative Maintenance of Manufacturing Equipment, as well as the Equipment Calibration Schedule, were reviewed and found generally adequate.

8. Measurement, analysis and improvement

8.2. Monitoring and measurement

8.2.1. Feedback

The manufacturer's feedback requirements were documented and included provisions for the collection of feedback from customer and user complaints, field evaluations or clinical studies, customer surveys, trade shows and publications for its own product.

8.2.2. Complaint handling

The manufacturer's procedure for managing customer complaints was followed. The manufacturing site had not started the supply of the pre-qualified product to the market, and hence there were very limited records of customer complaints available for review.

8.2.4. Internal audits

The manufacturer implemented an internal audit program, including documented requirements that audit schedules and audits should be performed by appropriately qualified auditors independent of the areas being audited. The audits were performed at least once per year. Records of internal auditors' training were available. Records of internal audits were available and indicated that the procedures were followed, during the most recent audit, performed by an experienced external auditor in July 2018. The internal auditing program identified a reasonable number of findings that were adequately investigated and addressed. An internal audit was undertaken in July 2019.

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. 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. QC records identified the test equipment and biological samples used. The panel of samples used for QC were validated and close to the cut-off value for the RDT. The operator performing in-process QC was blinded to the infection status of the biological samples used.

8.3. Control of nonconforming product

8.3.6. General

The manufacturer documented procedures for managing nonconformities and corrective actions that satisfied the requirements of the standard. The system for the management of nonconformities included investigating nonconformities, conducting root-cause analyses, documenting investigations, as well as their potential impact on product quality. Records of processing and management of several nonconformities were reviewed, and it was found that the investigations were undertaken in compliance with the internal procedures and the requirements of the standard. Corrective Actions were instigated for nonconformities that required them and were given independent numbers. The procedure for management of Out of Specifications (OOS) results was documented and explained the investigation process and inputs to be considered and was found to be of an acceptable standard.

8.3.8. Actions in response to nonconforming product detected after delivery

Corporate procedures for Vigilance, Reportable Incidents and Advisory Notices adequately described the processes for adverse event reporting and for product recall management. The WHO requirements were included in the reportable notifications processes. Chembio Diagnostics Malaysia Sdn. Bhd. planned to undertake a mock recall exercise, including WHO reporting in September 2019.

8.3.9. Rework

There were adequate provisions for authorizing rework as well as for the management of rejected materials and products.

8.4. Analysis of data

The manufacturer had implemented a procedure for this clause of the standard. The procedure required data sourced from several areas of the QMS to be included in the analysis, such as complaints, nonconformities, deviations, audits, internal audits, CAPA, deliveries, production, validations, maintenance delivery and the data was presented during the Management Review Meetings.

9. WHO pre-qualification-specific requirements

The product to be manufactured at the new 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, *Chembio Diagnostics Malaysia Sdn. Bhd.*, located at *N-TATT Building 2nd floor, No. 2-1 Jalan TP5, Taman Perindustrian, UEP, 47600, Subang Jaya, Selangor, Malaysia* 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 as well as those reflected in the WHOPIR, 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.

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.