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	Shanghai Kehua Bioengineering Co. Ltd.
Address of inspected manufacturing site	1189 North Qinzhou Road, Shanghai, 200233, Shanghai, People's Republic of China
Inspection details	
Dates of inspection	24-26 July 2024
Type of inspection	Routine inspection
Introduction	
Brief description of manufacturing activities	Shanghai Kehua Bioengineering Co. Ltd. is responsible for the control of the design and development and manufacturer of in vitro medical devices and associated reagents, as well as the production process, packing, labelling, storage, and delivery of these items.
General information about the manufacturer	Shanghai Kehua Bioengineering Co. Ltd. was established in 1989. The company specializes in developing and manufacturing in vitro diagnostic devices and associated reagents.
History	The site was previous inspected by WHO (March 2016 and June 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 Measurement, analysis, and improvement Adverse Events and Advisory Notices Reporting WHO pre-qualification-specific requirements
Scope	PQDx 0267-037-00 - Diagnostic Kit for HIV (1+2) Antibody (Colloidal Gold) V2
Criteria	ISO 13485:2016 and WHO Prequalification specific requirements
Objective(s)	To assess the manufacturers compliant with the inspection criteria
Limitations	None
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

The organization and management structure of the facility was documented and defined within the organisational chart. Roles and responsibilities were available with the overall reporting structure available, with clear delineation for release of product. The nonconformities identified were addressed through a CAPA plan.

4.2 Documentation requirements

4.2.1 General

There was an established quality policy and quality objectives available. Procedures and records were available as per the requirements of the standard. The nonconformities identified were addressed through a CAPA plan.

4.2.2. Quality manual

The organization's Quality Manual was updated regularly and continued to reflect the intended practices of the manufacturer. The quality manual described the interaction between the processes of the Quality Management System (QMS), it defined the structure of the documentation system and listed/excluded non-applicable clauses of ISO13485:2016 with appropriate justifications.

4.2.3. Medical device file

The organization had established and maintained documents demonstrating conformity to the requirements of the standard. These included descriptions of the labelling requirements.

4.2.4. Control of documents

The procedures for document control were available that met the requirements of the standard. The nonconformities identified were addressed through a CAPA plan.

4.2.5. Control of records

The procedures for document control of records were available that met the requirements of the standard. All records reviewed were legible and readily identifiable. Record retention was confirmed as being longer than the lifetime of the device. The nonconformities identified were addressed through a CAPA plan.

5. Management responsibility

5.1. Management commitment

There was sufficient evidence to support claims that Top management were committed to the development and implementation of the quality management system and maintenance of its effectiveness by communicating to the organization the importance of meeting customer, as well as applicable regulatory requirements. There was an established quality policy with measurable quality objectives, and with evidence of regular management review meetings.

5.3. Quality policy

The quality policy was applicable to the purpose of the organization with clear commitment from top management in ensuring effectiveness was maintained with regular review of the quality objectives and continued review for suitability.

5.4. Planning

5.4.1. Quality objectives

Quality objectives were available and included those needed to meet applicable regulatory requirements and requirements for product. Quality objectives were measurable and consistent with the quality policy.

5.4.2 Quality management system planning

There was evidence that the planning of the QMS was carried out to meet the requirements of the standard as well as the quality objectives.

5.5. Responsibility, authority, and communication

5.5.1. Responsibility and authority

Responsibilities and authorities were defined, documented, and communicated within the organization. The interrelation of all personnel who managed, performed, and verified the work affecting quality were documented and ensured the independence and authority necessary to perform these tasks.

5.5.2. Management representative

The appointed management representative had clear roles and responsibilities defined within the quality manual and corresponding job description including reporting to top management on the effectiveness of the quality management system and any need for improvement and ensuring the promotion of awareness of applicable regulatory requirements and quality management system requirements throughout the organization.

5.5.3. Internal communication

There was sufficient evidence to ensure that communication processes were well established and available.

5.6. Management review

5.6.1. General

The organization had an established process for regular management reviews that met the requirements of the standard. Records from management reviews were maintained. The review included assessing opportunities for improvement and the need for changes to the quality management system, including the quality policy and quality objectives.

5.6.2. Review input

The input to management review included feedback, complaint handling, reporting to regulatory authorities, audits, monitoring and measurement of processes and product, corrective and preventive action, follow-up actions from previous management reviews, changes that could affect the quality management system, recommendations for improvement and applicable new or revised regulatory requirements.

5.6.3. Review output

The output to management review were documented and included decisions and actions related to improvement needed to maintain the suitability, adequacy, and effectiveness of the quality management system and its processes. This included improvement of product related to customer requirements, changes needed to respond to applicable new or revised regulatory requirements and resource needs.

6. Resource management

6.1. Provision of resources

The facility was well resourced, with trained personnel and adequate facilities for the function and activities that were performed. This largely ensured the QMS was implemented, and its effectiveness maintained, and that applicable regulatory and customer requirements were met.

6.2. Human resources

The facility was staffed with personnel who had the necessary education, training, technical knowledge, and experiences for their assigned functions. Staff questioned were open and forthcoming with information. The organization had an established and well documented training procedure, including refresher training for staff. Training files for staff were maintained and available for review during the inspection. The nonconformities identified were addressed through a CAPA plan.

6.3. Infrastructure

The infrastructure was well maintained, with the appearance of being clean and tidy. The organization had documented requirements for the maintenance activities that applied to equipment used in production, to the control of the work environment, and to monitoring and measuring equipment. The nonconformities identified were addressed through a CAPA plan.

6.4. Work environment and contamination control

6.4.1. Work environment

Production was planned and carried out in rooms with controlled environment, with daily recordings available. Staff were observed to be wearing appropriate and suitable for use PPE. There were pictorials available when entering an area on the gowning requirements. A mirror was available to ensure appropriate PPE was properly downed. The nonconformities identified were addressed through a CAPA plan.

6.4.2. Contamination control

There were procedures for the cleaning of the facility and infrastructure were available to prevent contamination of the work environment, personnel, or product. Cleaning validations for selected equipment and processes were available and verified. The nonconformities identified were addressed through a CAPA plan.

7. Product realization

7.1. Planning of product realization

The organization's approach to the planning of production and service provision was adequately documented in the QMS and met the requirements of the standard. There was evidence of procedures for document management, risk management, product production, material verification, process validation, monitoring, inspection, and test activities. The nonconformities identified were addressed through a CAPA plan.

7.2. Customer-related processes

7.2.1. Determination of requirements related to product

The organization had documented customer requirements that included applicable regulatory requirements that were related to the product.

7.3. Design and development

7.3.1. General

The organization had an established process for design and development.

7.3.3. Design and development inputs

The design and development procedure adequately identified the requirements for design inputs.

7.3.4. Design and development outputs

The design and development procedure adequately identified the requirements for design outputs.

7.3.6. Design and development verification

Through the documented procedures there was evidence that the design and development outputs met the design and development input requirements. Adequate sampling size was determined using statistical techniques.

7.3.9. Control of design and development changes

The organization had an established and well documented procedure for the control of design and development changes that incorporated a determination of any necessary regulatory affairs actions as well as WHO requirements for reporting such changes.

7.4. Purchasing

7.4.1. Purchasing process

The organization had an established and documented process for the purchasing of materials and services, that included verification of critical incoming material. Supplier management and qualification procedures were available and implemented. Criteria for selection, evaluation, approval, and re-evaluation of suppliers were available.

7.4.2. Purchasing information

Supplier management and qualification procedures were available and implemented with supplier agreements for critical suppliers. Criteria for selection, evaluation, approval, and re-evaluation of suppliers was available.

7.4.3. Verification of purchased product

The organization had implemented processes for the verification of purchased products to ensure that they met specified purchasing requirements. The extent of verification activities was proportionate to the risks associated with the purchased product. Records of these activities were maintained. The nonconformities identified were addressed through a CAPA plan.

7.5. Production and service provision

7.5.1. Control of production and service provision

Production and service provision was planned, carried out, monitored, and controlled to ensure that product conformed to documented specifications. The organization had a documented process for the control of production that included, but was not limited to, qualification of infrastructure and monitoring and measuring equipment. Batch manufacturing records were available and identified the amount manufactured and amount approved for distribution. The nonconformities identified were addressed through a CAPA plan.

7.5.6. Validation of processes for production and service provision

The organization had validated processes for production and service provision that followed procedures that included equipment and personnel qualification, the use of specific methods, procedures, and acceptance criteria, the criteria for revalidation and the approval of changes to the processes.

7.5.8. Identification

There was a documented procedure for product identification and segregation for the life cycle of the product including released and nonconforming products within the facility.

7.5.9. Traceability

7.5.9.1. General

The organization had procedures available that supported full traceability of components, materials, work environments used that were in accordance with applicable regulatory requirements. The nonconformities identified were addressed through a CAPA plan.

7.5.11. Preservation of product

There were adequate and suitable processes available to ensure the preservation of product to requirements during processing, storage, handling, and distribution. The nonconformities identified were addressed through a CAPA plan.

7.6. Control of monitoring and measuring equipment

The organization had implemented procedures for the control of monitoring and measuring equipment. Measuring equipment was calibrated, and/or verified, at specified intervals, or prior to use, there was adequate identification indicating its calibration status and was safeguarded from adjustments that would invalidate the measurement result.

The organization had procedures in place to assess and record the validity of the previous measuring results when the equipment was found out of tolerance. These included taking appropriate actions regarding the equipment and any product affected. The nonconformities identified were addressed through a CAPA plan.

8. Measurement, analysis, and improvement

8.2. Monitoring and measurement

8.2.1. Feedback

The organization had procedures in place to gather and monitor information relating to whether the organization has met customer requirements. Data were gathered from production as well as post-production activities and served as input into the risk management for monitoring and maintaining the product requirements as well as the product realization or improvement processes. The nonconformities identified were addressed through a CAPA plan.

8.2.2. Complaint handling

The organization had implemented a procedure for the timely handling of customer complaints. The procedures included requirements and responsibilities for investigating complaints, determining the need to report the information to the appropriate regulatory authorities, including WHO, handling of complaint-related products and determining the need to initiate corrections or corrective actions. Corrections and corrective actions were documented. Complaint handling records were maintained.

8.2.3. Reporting to regulatory authorities

There was a procedure available for reporting and providing the necessary notifications to the appropriate regulatory authorities.

8.2.4. Internal audits

The organization had implemented an internal audit program and included conducting internal audits at planned intervals. The audit program was planned, taking into consideration the status and importance of the processes and area to be audited, as well as the results of previous audits. The audit criteria, scope, interval, and methods were defined and recorded. Auditors were selected to ensure objectivity and impartiality of the audit process. Auditors did not audit their own work.

8.2.5. Monitoring and measurement of processes

The organization had implemented procedures to monitor and measure the characteristics of the QMS processes. Achievement of planned results were available and when not met, corrections and corrective actions were taken. The nonconformities identified were addressed through a CAPA plan.

8.3. Control of nonconforming product

8.3.1. General

The organization had a process in place for the segregation of nonconforming product.

8.3.2. Actions in response to nonconforming product detected before delivery

The organization had procedures available for taking action to eliminate nonconforming property before delivery.

8.3.3. Actions in response to nonconforming product detected after delivery

The organization had implemented a procedure to deal with nonconforming product detected after delivery by taking appropriate action to the effects, or potential effects, of the nonconformity. A procedure for issuing advisory notices was in place.

8.3.4. Rework

The organization had a procedure available for rework of a product with the necessary measures of ensuring that the reworked product met the applicable acceptance criteria and other regulatory requirements.

8.4. Analysis of data

The organization had a procedure available to determine, collect and analyse appropriate data to demonstrate the suitability, adequacy, and effectiveness of the QMS. This was verified throughout the WHO inspection.

8.5. Improvement

8.5.1 General

There was sufficient evidence available to ensure that the manufacturer could identify and implement any changes necessary to maintain the continued suitability, adequacy, and effectiveness of the QMS, incorporating medical device safety and performance through the use of the quality policy, quality objectives, audit results, post-market surveillance, analysis of data, corrective and preventive actions, and through the management review.

8.5.2. Corrective action

The organization had procedures in place to take action to eliminate the cause of nonconformities to prevent recurrence. The procedures defined the requirements for reviewing nonconformities (including complaints), determining the causes of nonconformities, evaluating the need for corrective action, planning and documenting actions needed and implementing such actions, including, as appropriate, updating documentation and reviewing the effectiveness of corrective actions taken. Records of investigation and actions taken were maintained.

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, ***Shanghai Kehua Bioengineering Co. Ltd.*** located at ***1189 North Qinzhou Road, Shanghai, 200233, Shanghai, People's Republic of China*** 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. Inspection Services – In Vitro Diagnostics and Male Circumcision Devices (https://extranet.who.int/prequal/inspection-services/vitro-diagnostics-and-male-circumcision-devices)
2. Information for Manufacturers on Pre-qualification Inspection Procedures for the Sites of Manufacture of Diagnostics (PQDx_014).
3. ISO 13485:2016 Medical devices - Quality management systems - Requirements for regulatory purposes
4. ISO 9001:2015 Quality management systems – Requirements
5. WHO Post-market surveillance of in vitro diagnostics 2020 (ISBN 978 92 4 001532 6)
6. Medical devices - Application of risk management to medical devices - ISO14971:2019
7. GHTF/SG3/N19:2012 "Quality management system – Medical devices - Nonconformity Grading System for Regulatory Purposes and Information Exchange"
8. GHTF/SG4/(99)28 Guidelines for Regulatory Auditing of Quality Systems of Medical Device Manufacturers - Part 1: General Requirements
9. GHTF/SG4/N30R20:2006 Guidelines for Regulatory Auditing of Quality Systems of Medical Device Manufacturers - Part 2: Regulatory Auditing Strategy
10. 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.