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Prequalification Team Inspection services
WHO PUBLIC INSPECTION REPORT
(WHOPIR)
Vector Control Product Manufacturer

Part 1	**General information**
Manufacturers details	
Name of manufacturer	Agricultura Nacional S.A. de C.V.
Corporate address of manufacturer	Clarke International, LLC 675 Sidwell Court Saint Charles, IL 60174, USA
Inspected site	
Name & address of inspected manufacturing site(s)	Agricultura Nacional S.A. de C.V. Km 5 Carretera Las Bocas, Barrio Santiago Mihuacan Izucar de Matamoros Puebla 74400 Mexico
Unit/Block/ Workshop	Not applicable
Inspection details	
Dates of inspection	1-3August 2022
Type of inspection	Initial inspection. The criteria for the inspection were based on the ISO 9001:2015 standard.
Introduction	
Brief description of the manufacturing activities	Agricultura Nacional S.A. de C.V (ANSA) was established in 1935. The site currently manufactures herbicides, insecticides, fungicides, and nutritional products (fertilizers). The manufacture of Cielo involved mixing, filling, packaging, and labelling.
General information about the company and site	Agricultura Nacional S.A. de C.V (ANSA) was established in 1935. ANSA manufactured Cielo ULV on contract for Clarke International, LLC. The site held ISO 9001 and 14001 certificates. ISO 9001:2015 certificate MX14/9682500 Valid from 3rd May 2021 until 21st December 2023 Scope: ‘‘Manufacture and packaging of plant protection products and phytonutrients both liquid and powders in the manufacturing operations in the complex located in Izucar matamoros.’’

	The site also held an ISO 14001:2015 Certificate MX14/19682499 Valid from 3rd May 2021 until 21st December 2023. The certificates were issued by SGS.
History	This was the first WHO audit of the site
Brief report of inspection activities undertaken – Scope and limitations	
Areas inspected	**Document review including but not limited to:** • Quality Manual • Training • Risk management • Management review • Job descriptions and responsibilities of key personnel • Complaints • Non-conforming products • Product release • Batch processing records • Control of changes • Internal audits • Calibration and equipment maintenance **Physical areas:** • Raw material and finished goods • Production areas • Quality control laboratory
Exclusions and Non-applications of requirements in the QMS	The requirements of sub clause 8.5.1 (f) - the validation, and periodic revalidation, of the ability to achieve planned results of the processes for production and service provision, where the resulting output cannot be verified by subsequent monitoring or measurement and clause 8.3 - Design and development of products and services were excluded from the requirements and applications of the quality management system.
Out of scope	The manufacture of other products not submitted to PQ were not included in the scope of this inspection.
Restrictions	None
WHO products covered by the inspection	• Cielo ULV (Prallethrin, 0.75%; Imidacloprid, 3.00%) – 020-006
Abbreviations	**Meaning**
CoA	Certificate of analysis
KPI	Key Performance Indicators
PPE	Personal Protective Equipment
QMS	Quality Management System

Part 2	Brief summary of the findings and comments

1. Organizational roles, responsibilities, and authorities

The job descriptions of the QA/QC manager and instrument technician were reviewed. The control manager was responsible for the implementation of the ISO 9001 system. The instrument technician was also responsible for release of products, analysis of the QMS and reporting on the performance of the QMS to top management. An organogram was in place the Production manager (Liquids) and the QA/QC manager independently reported to the General Manager.

2. Quality policy and quality objectives

An integrated management systems policy was in place. The policy stated the following commitments among others:

- Comply with legal and other applicable requirements
- Promoting favorable organizational environment
- Promoting continuous improvement
- Prevention of cross contamination

Established objectives related to quality, safety, environment, and health were also in place. Key performance indicators had been defined for each of the objectives. The extent to which the objectives had been achieved was regularly monitored. The objectives were discussed in management review. The Integrated management system policy and objectives were displayed at various locations within the facility.

3. Management review

Management reviews were held once annually. The minutes of the management review held in 2021 were discussed. The following were discussed in the management review meeting: Complaints, quality reports, human resource, production capacity and production performance, maintenance, occupational health etc. Changes, internal audits, and performance of external providers were also discussed. This was found satisfactory.

4. Leadership

The integrated management systems policy had been signed by the Plant Manager. Top management demonstrated commitment to the quality management system by communicating the quality policy and quality objective, monitoring and measurement of the quality objectives, management reviews, internal audits among others.

5. Control of documented information

The document control procedure was reviewed. The procedure described creation, identification, review, approval, control, and distribution of documents. The procedure provided for review and approval of changes to documents. The documents were both in electronic and paper forms. A document register was in place. The document register provided information on the name of the document, type, or nature as paper or electronic, the code, retention time and year for its edition and the number of controlled copies etc. Depending on the type, documents were retained for 2 to 5 years.

6. Personnel competence and training

The procedure for training was in place. The procedure outlined skills that need to be imparted to personnel of the various departments such safety management, production, Quality Control, etc. These trainings were conducted by both internal and external experts who were duly qualified to do so. The annual training program for the different departments i.e., for health and safety, management system, maintenance, warehouse, production, quality control, planning and human resource was in place. External trainings on lean manufacturing and preparation of a Certificate of Analysis conducted by the external training centres were also reviewed. These external training centres were duly qualified by ANSA to provide the training. The competence matrix was reviewed. Training records of personnel on safety and static electricity were reviewed. The trainings were evaluated, and records maintained.

7. Risks Management

The relevant procedure for Risk Analysis and Opportunities was discussed. The procedure described the identification, evaluation and analysis of political, legal, economic social technological, environmental, geographical risks and competition. A risk register was also place. The risks were evaluated annually. A SWOT analysis had been performed to identify and analyse internal strengths and weaknesses, and external opportunities and threats to the organization. Risk evaluation criteria included probability and impact of the risk. Risk mitigation measures were clearly defined. The risk evaluation had been performed at two levels: Plant and processes. Risks related to manufacturing processes including manufacture of Cielo were reviewed and found satisfactory.

8. Control of changes

Changes were handled as per the relevant procedure. The procedure provided for impact analysis of changes on the products, processes, regulatory compliance, health, environment, and the entire QMS. A change register was in place. Changes were reviewed. Impact assessment had been performed. This was found to be satisfactory.

9. Internal Audits

The procedure for internal audits was reviewed. The procedure described the planning of audits, conducting of audits and report generation. It provided for corrective actions, preventive actions. The procedure required verification of the effectiveness of the corrective actions, preventive actions taken. The audit plan for the year 2022 was reviewed. The areas to be audited included Quality Control, Production (Liquid and Powder), Warehouse, Human resource, Safety and Environment. Personnel could only lead an audit if he or she has a minimum qualification of been certified in ISO 9001:2015, ISO 14001:2014, ISO 45001:2018, a one-year experience working with the company and experience in the conduct of at least one internal audit and good communication skills. A criterion for the qualification of an external auditor was also provided. Training records of the auditors were in place. The internal audit report was reviewed and found satisfactory.

10. Control of nonconforming products

The relevant procedure for nonconforming products was reviewed. In the event of a nonconformance the Quality Manger was notified and an investigation to determine the root cause launched. Corrections and corrective actions would then be determined and implemented. Nonconforming products were documented. The information documented included description of the nonconformance, Product name, batch number, manufacturing date, equipment number, cause of nonconformance, conclusion etc. Nonconformities were reviewed.

11. Complaints and customer satisfaction

The relevant procedure for handling complaints was also reviewed. Complaints were categorized as critical, major, or minor. A complaint register was in place. Information retained included the description of the complaint; date of complaint, name of the customer making the complaint, name of the product affected and the date on which investigation started, corrective and preventive actions taken, the response to the client etc. No complaint related to Cielo ULV had been registered at the time of the inspection.

The procedure for Client satisfaction was reviewed. Feedback from customers was collected using customer satisfaction surveys. The areas covered in the survey for customer satisfaction included: customer evaluation of sales personnel, service to clients, distribution, and quality. The quality of product was based on its effectiveness, good packaging, wholesomeness, correct labelling, lot number, manufacturing and expiry dates, evaluation of payment portal and general evaluation as per the customer own needs and expectation. A customer survey reports for 2019, 2020 and 2021 were reviewed.

12. Performance evaluation

Performance evaluation was conducted for the following parameters among others; density, pH, appearance, Active ingredient content, right first time – formulation, right first time-filling and packaging. Evaluation was performed by used of graphs. The evaluation was performed monthly. Evaluation reports for 2021 were reviewed and found satisfactory.

13. Design and development of products

Design and development were excluded from the requirements and applications of the quality management system.

14. Support

Infrastructure and work environment

The site was well maintained. The environment was generally clean. Rodent traps were in place. The protective equipment included safety boots, overalls, full mask, gloves, helmet etc. The laboratory was equipped with a fume hood and eye shower. Material safety data sheets were in place.

Monitoring and measuring resources

Equipment were uniquely identified and with calibration status indicated. A maintenance schedule was in place. Maintenance for the mixing tanks and the magnetic filters was done every 4 months. Preventive maintenance reports for the liquid filling line and filling machine were also reviewed. The calibration certificate for the thermometer was verified. Preventive maintenance and operation qualification records for HPLC were checked. Calibration records for the balance were also verified. Breakdowns were recorded and notified to the maintenance department via an internal customized software.

15. Production and service provisions

Control of Production

Cielo was produced on the liquids line that was dedicated to the manufacture of insecticides. The manufacture of Cielo ULV involved mixing of Imidacloprid with other solvents. A sample was collected to verify complete dissolution of Imidacloprid. Following the confirmation of the dissolution of imidacloprid requisite amounts of Prallethrin technical and other co-formulants are added to the mixing vessel using a pneumatic pump. A sample of the mixture was collected from the mixing tank for finished product testing. The mixture was filtered before packaging and labelling. Packaging containers were sampled and fill volume verified. The fill volume was verified every 30 minutes and records maintained. Batch manufacturing records for Cielo ULV were reviewed. Batch number of the raw materials used in production were documented in the BMR. Cleaning instructions and cleaning matrix were in place. Cleaning records were verified. Cleaning was performed whenever there was a product change.

The quality control laboratory was situated separately from the production areas. The laboratory was well equipped. The equipment in the laboratory included HPLCs, balances, densimeters, thickness gauge, viscometer etc. The laboratory was headed by the QA/QC manager. The samples were adequately labelled. The analytical method equivalence report and the analytical method validation report for determination of Imidacloprid and Prallethrin in Cielo ULV were reviewed. The analytical test reports for Cielo ULV were verified. The standard testing procedure for determination of Imidacloprid and Prallethrin in Cielo ULV by HPLC was also reviewed.

Physical, chemical, and biological treatment on waste was carried out on site. The treated waste was analysed by an external laboratory to assess the compliance to the waste with the established specifications and standard prior to release of the waste into the environment. All issues raised related to this section were addressed satisfactorily by the manufacturer.

Post-delivery activities

A sample of each batch was retained. The samples were adequately labelled. The samples were retained for a period equivalent to the shelf life of the product plus one year. A register for retention samples was in place. Stability studies were undertaken by Clarke International.

16. Preservation

Control of materials in the warehouse was managed by a customized software. The information retained included material name, batch number, quantity, date of receipt, purchase order, status of the material (undertest/quarantine, accepted and rejected), etc. Upon receipt of materials the following were verified: quantity, physical condition of the materials, batch number, Certificate of Analysis, MSDS. A checklist for receipt of materials was in place. Inventory records for Prallethrin were verified and found satisfactory. The materials in the warehouse were color coded depending on their status i.e., red – rejected, yellow – undertest/quarantine, and green- accepted. There was a segregated area for storage of rejected materials. The procedure for sampling of raw materials and packaging materials was also reviewed. Materials were sampled according to the sampling plan outlined in the procedure.

17. Control of externally provided processes, products, and services

The procedure for Purchasing was reviewed. The performance of the suppliers was evaluated based on quality, delivery time and quantity supplied. Suppliers were categorized into international and national suppliers. However, all the raw materials used for the manufacture of Cielo ULV were supplied by Clarke International. The suppliers of the raw materials were selected, approved, and evaluated by Clarke International.

Part 3	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, as well as the corrective actions taken and planned ***Agricultura Nacional S.A. de C.V.*** located at ***Km 5 Carretera Las Bocas, Barrio Santiago Mihuacan Izucar de Matamoros Puebla 74400 Mexico.*** was considered to be operating at an acceptable level of compliance with the ISO 9001: 2015 Standard.

All the non-conformances 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 that the outcome of any inspection conducted during this period is positive.

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Part 4	List of Standards and Guidelines referenced in the inspection report

1. Quality management systems – Requirements, International Standard (ICS 03.120.10), 5th edition (2015), ISO/FDIS 9001: 2015 ***Short name: ISO 9001:2015***
   https://www.iso.org

2. Quality management system – Medical devices - Nonconformity Grading System for Regulatory Purposes and Information Exchange" Final Document, Global Harmonization Task Force, November 2, 2012, GHTF/SG3/N19:2012
   https://www.imdrf.org

3. Manual on the Development and Use of FAO and WHO Specifications for Pesticides, First edition - third revision. Pesticide specifications. FAO plant production and protection paper (228), FAO/WHO Joint Meeting on Pesticide Specifications (JMPS), Rome 2016
   http://www.fao.org/agriculture/crops/thematic-sitemap/theme/pests/jmps/manual/en/