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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	Rea S.R.L Italy
Corporate address of manufacturer	Arysta LifeScience GB Ltd (part of UPL group) Brooklands Farm, Cheltenham Road, Evesham, Worcestershire, WR11 2LS, UK
Inspected site	
Name & address of inspected manufacturing site(s)	87 – KM 20.700 - 81025 Marcianise (CE)Zona Ind. Asi Nord Aggl. S. Marco - Via L. Einaudi Italy
Unit/Block/ Workshop	Not applicable
Inspection details	
Dates of inspection	11 – 13 April 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	Rea S.R.L is a family-owned company and started the production of tablets and granules in 2005. Rea S.R.L manufactures insecticides, insect repellants and disinfectants. The activities involved in the manufacture of Diflubenzuron tablets included mixing of the different ingredients, compression, labelling, packaging. The activities involved in the manufacture of Diflubenzuron granules included mixing, preparation of the coating solution, coating, sieving, labelling, and packaging.
General information about the company and site	This was the first WHO audit. Rea S.R.L was licensed by the Ministry of Health, Directorate General of Veterinary Health and Food Office (license number 613/39877) and Ministry of Health, Department for the Evaluation of Medicines and Pharmacovigilance (license number AMM-6/2001). The site was licensed to manufacture Insecticides, insecticide repellants and disinfectants and other products intended to combat animal and plant organisms harmful to the environment. The site held an ISO 9001:2015 Certificate number 9597 issued by Certiquality S.r.l. The certificate was issued on 06/07/2005 and

	renewed on 25/6/2020. Expiry date 28/06/2023. Scope: Design, manufacturing and sale of insecticide, rodenticides, and disinfectants. The site also held an ISO 14001:2015 Certificate number 24758 issued by Certiquality S.r.l. The certificate was issued on 12/07/2017 and renewed on 25/6/2020. Expiry date 10/07/2023. Scope: Design, production through blending processes, packaging, storage and sale of insecticides, rodenticides, and disinfectants.
History	This was the first WHO audit.
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	None.
Out of scope	The manufacture of Insect repellents, disinfectants and other products not submitted for prequalification were not included in the scope of this inspection.
Restrictions	None
WHO products covered by the inspection	Diflubenzuron Tablets - 025-001 Diflubenzuron Granules – 025-003

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
An organizational chart was in place. The Production manager and the quality control manager reported independently to the Technical /Quality Assurance Director. The job descriptions of the Quality Control Technician and the Technical /Quality Assurance Director were reviewed. The Technical /Quality Assurance Director was responsible for product release and promoting the implementation of preventive and corrective actions to allow continuous improvement. Among other responsibilities the Quality Control Technician was responsible for sampling and performing quality control tests.

2. Quality policy and quality objectives
An integrated quality policy and quality objectives were in place. The quality policy included a commitment to satisfy applicable requirements. It also included a commitment to continual improvement of the quality management system. The quality policy and quality objectives were communicated to personnel through training. Quality objectives were monitored and measured. The quality objectives were discussed in management review meeting to assess the extent to which the quality objectives have been met.

3. Management review
Management review meetings were conducted once a year. Management review minutes dated 18/6/2021 were reviewed. Customer complaints and feedback, audit results, the extent to which quality objectives have been met, opportunities for improvement etc. were discussed in the management review meetings. This was found satisfactory.

4. Leadership
The Technical /Quality Assurance Director was responsible for ensuring the effective implementation of the quality management system. Top management promoted improvement through internal audits, management reviews and implementation of corrections and corrective actions. The importance of an effective quality management system was communicated to personnel through trainings.

5. Control of documented information
An established procedure for document management and control was reviewed. The procedure described the classification, management, and control of documents. The procedure adequately described the creation, version control, distribution, review and archiving of documents.

6. Personnel competence and training

The annual training plan for 2021 was reviewed. The training plan for all employees was in place. The content of training plan is tailored during the year to allow adaptation based on the needs. A training on cross contamination was provided each year to all the employees. Effectiveness of trainings was assessed. Training records for employees were maintained from the date of employment. This was found satisfactory.

7. Risks Management

The relevant procedure for management of risk was reviewed. The procedure described the methodology for risk identification, analysis, and evaluation. Risk assessment considered the severity and probability of occurrence of an event. A risk assessment index was calculated as the product of the probability of occurrence and the severity of the event. A risk register was in place. All the issues raised related to this section were addressed satisfactorily by the manufacturer.

8. Control of changes

An established procedure for change management was in place. The procedure described the management of changes related to production processes, production equipment, raw material usage and job descriptions. A change related to the change of the pistons for the tableting machine was reviewed. The impact of the change and effectiveness of the change was evaluated.

9. Internal Audits

Internal audits were conducted in accordance with the established Internal Audit Management procedure. The procedure stipulates that each of the firm internal processes should be audited at least once a year. The internal audit plans for 2021 and 2022 were reviewed and found satisfactory. The template of the internal audit report was reviewed. Corrections and corrective actions were documented in a separate document titled 'Improvement Action'.

10. Control of nonconforming products

The relevant procedure for control of non-conforming products was reviewed. The scope of the procedure covered raw material handling, equipment, services, and production processes. The procedure described the process of identification, notification and reporting of non-conforming products. In addition, a non-conformity report form was in place. The form provided information on the description of the non-conformity, for the root cause analysis, for the approval of the client and for the date of closure of the non-conformity. Reference was made to the procedure for management of corrective and preventive actions that described the process for implementing immediate, corrective, and preventive actions. Documented evidence on the investigation of the non-conformity and related corrective actions and preventive actions was maintained by the Technical/ Quality Assurance Director. UPL Ltd was responsible for recall of the Diflubenzuron tablets and granules from the market.

11. Performance evaluation

The performance and effectiveness of the quality management system was evaluated. The parameters evaluated included the quality and environmental indicators, customer satisfaction, verification of effectiveness of trainings, effectiveness of corrections and corrective actions, implementation of risk mitigation measures and opportunities. These are management review. The results of the analysis are discussed in management review.

12. Design and development of products

The design and development of the products was submitted to the World Health Organization Pesticides Evaluation Scheme (WHOPES) at the time of registration and were not available at the time of the audit. This was not inspected.

13. Support

Infrastructure and work environment

The infrastructure was generally well maintained. Personnel in production were appropriately dressed in an overcoat, gloves, shoes and masks. Safety measures and MSDS were in place.

Monitoring and measuring resources

Calibration records of the balances were in place. The maintenance records for the tableting machine, granulator, fume hood and HPLC were reviewed.

14. Production and service provisions

Control of Production

Diflubenzuron tablets and granules were manufactured in dedicated areas. The equipment used for the manufacture of the Diflubenzuron tablets and granules were also dedicated.

The manufacture of Diflubenzuron tablets included blending of the active ingredients with other raw materials, tableting, packaging, and labelling. In-process controls included average weight, friability. The tablets were packaged directly into drums or buckets. In-process test records were maintained. The humidity and temperature of the tableting area was monitored. The tableting area was fitted with a dust collection and suction system. Labels were adequately controlled. Records of issuance of labels and usage were in place.

The manufacture of Diflubenzuron granules included mixing of powdered inactive components in a mixer, preparation of the coating solution, coating, sieving, and packaging and labelling. The coating solution is prepared by mixing the active ingredient with water. The in-process controls included granulometry, size of granules, water content. The granulation area was also equipped with a dust collection and suction system.

The cleaning of the equipment used in the production areas were verified. Cleaning records were maintained. The cleaning instructions for the mixer and the granulation packaging line were reviewed.

Batch production records for Diflubenzuron tablets and Diflubenzuron granules were reviewed. The batch numbers of the raw materials used in production were recorded in the batch production records. The batch production and testing records were reviewed by the Technical /Quality Assurance Director prior to release of the product.

Laboratory test records for the determination of active ingredients in diflubenzuron tablet and granules were reviewed. The laboratory was equipped with an HPLC, friabilator, granulometer, measuring balances. The laboratory equipment was uniquely identified and calibrated. A sample log register was in place. The standard testing procedure for water content determination in diflubenzuron granules and procedure for determination of content in Diflubenzuron granules were reviewed. All the issues raised related to this section were addressed satisfactorily by the manufacturer.

Identification and traceability

Equipment were uniquely identified. There was sufficient traceability of the materials and batch numbers in the batch production records reviewed. The warehouse inventory software provided information on the names of materials in the warehouse, batch numbers, quantities of materials received, quantities of materials at hand, dates of receipt and issue etc.

15. Preservation

An inventory software was to manage inventory in the warehouse. Rodent traps were in place. Upon receipt of the raw materials the quantity, product name, batch number etc. were verified. The raw materials were supplied along with a Certificate of Analysis (CoA). All the issues raised related to this section were addressed satisfactorily by the manufacturer.

16. Post-delivery Activities

A sample of every batch was retained. The samples were retained for 3 years.

17. Control of externally provided processes, products and services

The manufacturer had an established procedure for procurement that described the selection and evaluation of suppliers. The selection and approval of the critical suppliers were managed by UPL Ltd. The raw materials used in the manufacture of Diflubenzuron tablets and granules were all received from suppliers approved by UPL Ltd.

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 ***Rea S.R.L Italy*** located at ***87 – KM 20.700 - 81025 Marcianise (CE)Zona Ind. Asi Nord Aggl. S. Marco - Via L. Einaudi Italy*** 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.

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/