Health And Youth Care Inspectorate

Report No: ***NL/V 25/2056902***

STATEMENT OF NON-COMPLIANCE WITH GMP

Exchange of information between National Competent Authorities (NCAs) of the EEA following the discovery of serious GMP non-compliance at a manufacturer[1]

Part 1

Issued following an inspection in accordance with
Art. 94(2) of Regulation (EU) 2019/6 as amended

The competent authority of Netherlands confirms the following:
The manufacturer: ***Intervet Inc.***
Site address: ***P. O. Box 318, Millsboro, DE, 19966-0318, United States***
OMS Organisation Id. / OMS Location Id.: ***ORG-100012220*** / ***LOC-100021219***

From the knowledge gained during inspection of this manufacturer, the latest of which was conducted on ***2025-09-05***, it is considered that **it does not comply with the Good Manufacturing Practice** requirements referred to in

- The principles and guidelines of Good Manufacturing Practice laid down in Directive 91/412/EEC. Article 93(2) of Regulation (EU) 2019/6

Note to receiving authorities: Please contact the issuing authority within 20 working days in case there are critical(2) medicinal products potentially affected by this statement.
Manufacturing Authorisation Holders directly affected by this statement have failed to comply with their obligations under Art. 46 of Directive 2001/83/EC or Art. 93(1)(j) to (l) of Regulation (EU) 2019/6 and as a consequence the Qualified Person referred to in Art. 48 of Directive 2001/83/EC and Art. 97(1) of Regulation (EU) 2019/6 is unable to perform the batch certification referred to in Art. 51 of Directive 2001/83/EC and Art. 97 (6) and (7) of Regulation (EU) 2019/6.
In exceptional circumstances there may be no objection to the Qualified Person certifying affected batches thereby allowing their release provided all of the following conditions are fulfilled:

1. Batch certification is performed in order to maintain supply of critical medicinal products only.
2. A documented risk assessment has been performed by, or on behalf of, the Qualified Person and additional actions have been implemented by the manufacturing and/or batch release site to mitigate the risks posed by the non-compliance. Note: Repeated testing alone is not normally sufficient risk mitigation but, together with other actions, can form part of a strategy commensurate with the nature and the level of risk.
3. A thorough risk-benefit evaluation has been performed for the acceptance of risk and a report prepared that takes full account of the nature of the non-compliance with the involvement of:
   - The Manufacturing Authorisation Holder and the Qualified Person of the site responsible for batch certification.
   - The manufacturing site subject to this Statement of Non-Compliance, if different from the above.

- The relevant Marketing Authorisation Holder(s).

The report has been shared with the National Competent Authorities of the countries in which distribution of the affected batches is anticipated and that any comments from those authorities have been taken into account.

4. Written confirmation has been obtained from the National Competent Authorities in whose territories the affected batches are intended to be distributed that the product is considered critical on its territory, and that there is no objection to distribution.
5. The Supervisory Authority has been informed, if different from the above, and it has not suspended or revoked the relevant Manufacturing Authorisation.
6. The affected Marketing Authorisations have not been revoked or suspended.
7. Any further conditions imposed by the Supervisory Authority and other involved National Competent Authorities are met.

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[1] *The statement of non-compliance referred to in paragraph 111(7) of Directive 2001/83/EC and Art. 94(2) of Regulation (EU) 2019/6, as amended, is also applicable to importers.*

[2] *See Appendix 3 of the relevant procedure in the Compilation of Union Procedures.*

Part 2

Veterinary Medicinal Products

1 NON-COMPLIANT MANUFACTURING OPERATIONS

Include total and partial manufacturing (including various processes of dividing up, packaging or presentation), batch release and certification, storage and distribution of specified dosage forms unless informed to the contrary;

1.1	**Sterile products**
	1.1.1 Aseptically prepared (processing operations for the following dosage forms) 1.1.1.1 Large volume liquids 1.1.1.2 Lyophilisates 1.1.1.4 Small volume liquids
1.3	**Biological medicinal products (list of product types)**
	1.3.1 Biological medicinal products (list of product types) 1.3.1.2 Immunological products
1.6	**Quality control testing**
	1.6.1 Microbiological: sterility *1.6.2 Microbiological: non-sterility* *1.6.3 Chemical/Physical* *1.6.4 Biological*

Part 3

1.Nature of non-compliance:

A routine joint GMP inspection was carried out by the Health and Youth Care Inspectorate (IGJ, The Netherlands) and the Veterinary Medicines Directorate (VMD, United Kingdom) from 2 to 5 September 2025. Products in scope were Innovax (ILT-IBD/ILT/ND-IBD/ND-ILT), AE/Pox and DHPPi (all veterinary vaccines) and Rabies bulk antigen. The inspection resulted in 8 (eight) Major deficiencies and 10 (ten) Other deficiencies. IGJ and VMD jointly concluded that the Company is not in compliance with GMP, based on the amount and severity of the deficiencies. The Major deficiencies were the following: 1. The company had failed to – depending on the product - adequately or completely fulfil its obligation to incorporate the requirements of the revised Annex 1 of the GMP Guideline. Annex 1 was not implemented for Rabies antigen (pending transfer of production foreseen for 2027), Innovax (as not being manufactured) and for DHPPi just prior to a campaign in 2025. An initial GAP analysis could not be shown. 2. The capacity for continuous improvement is insufficient. This was evident from the recurrence of various (significant) deficiencies of the last EU GMP inspection in 2022. This includes Major observations on Environmental Monitoring and Aseptic Process Simulation, as well as Others from 2022 that were now Major deficiencies (Good Documentation Practices, Aseptic behaviour). 3. Precautions to minimize the risks on contamination were deficient. The company did not have a CCS for products Rabies and Innovax, and a CCS for DHPPi that was not a holistic overview and missing several elements. Moreover, processes for cleaning, disinfection, and clean hold time of primary packaging materials were not appropriately defined; premises failed in pressure differences, non-cascaded airlocks. 4. Aseptic behavior and (gowning) practices were deficient in many cases and corresponding procedures were not followed. Many examples were observed for e.g. (de)gowning practices, hand washing, movements in grade B cleanrooms, changing gloves, not changing wipes for disinfection – some of these examples not following the corresponding procedures. 5. Maintenance, repair and housekeeping activities across the site were deficient, as highlighted by many examples. In many cases rust, dirt and dust was observed in production facilities and gowning rooms; cleanrooms were not orderly; personal items (e.g. backpack, headphones) were found in grade D rooms; panels, walls, seals, accessories were damaged in many cases; clean status of rooms was not evidenced by the appearance of rooms. 6. The company's environmental monitoring (EM) programme was deficient. Examples relate to not measuring non-viable particles in grade A, inconsistent approach for measuring locations, missing risk assessments, not following procedures for measurements, too limited personnel monitoring, too limited room monitoring, missing limits and missing justifications for limits and selection of house isolates, missing sampling after critical interventions and missing investigations for excursions. 7. The design and operation of the aseptic process simulation program failed to provide adequate sterility assurance. Examples include the possibility for a compliant APS despite growth, process design that does not take into account filling time, campaigns, intervention frequency, consideration of all worst cases, equipment holding time; in the execution elements could not be verified (e.g. maximum amount of people in cleanrooms, attendance, correct EM monitoring and roles of involved people). 8. Good Documentation Practices were not applied in many cases. This includes uncontrolled, outdated and obsolete documents, procedures with missing/incorrect elements, insufficient controlled storage and retention of documents, documents not being reviewed in time; wrong, missing and changed data and signatures, documents that were not updated according to changes.

Action taken/proposed by the NCA

Withdrawal, of current valid GMP certificate No. NL/V 22/2043225V1

Certificate NL/V 22/2043225V1 (an extended GMP certificate after 3-year expiry of the previous certificate) is withdrawn.

Recall of batches already released

Consideration of recall, following NCA assessment of potential quality defects vs. supply restriction. A direct, critical product risk has not been identified. However, the nature and cumulative risk of the combined deficiencies could have lead to an inferior product. Authorities are recommended to assess the criticality of the products before considering recall (e.g. rabies antigen). Based on information from the company the following applies for products: - Innovax (all varieties): not manufactured in this site after September 2022. - AE/POX: currently manufactured. - DHPPi: manufactured in campaign between March-July 2025. - Rabies bulk antigen: currently manufactured.

Prohibition of supply

The company should not supply to the EU market whilst the NCS in is force with the exemption of product that is considered critical for the market. A successful reinspection is recommended before full market supply is resumed.

2026-05-19

Name and signature of the authorised person of the Competent Authority of Netherlands

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