*Austrian Federal Office For Safety In Health Care*

Report No: ***INS-484367-101052478***

# 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. 111(7) of Directive 2001/83/EC as amended

The competent authority of Austria confirms the following:
The manufacturer: ***PT Novell Pharmaceutical Laboratories***
Site address: ***Jalan Wanaherang No 35, Tlanjung Udik, Gunung Putri, 16962, Indonesia***
Additional details on units inspected: ***Sterile manufacturing areas in NBL-1 and NBL-2***
OMS Organisation Id. / OMS Location Id.: ***ORG-100004456*** / ***LOC-100002168***

Other
(Human) Directive (EU) 2017/1572:

From the knowledge gained during inspection of this manufacturer, the latest of which was conducted on ***2023-11-02***, it is considered that **it does not comply with the Good Manufacturing Practice** requirements referred to in

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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

Human 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;

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| **1.1** | **Sterile products** |
| | *1.1.2 Terminally Sterilised (processing operations for the following dosage forms)*<br>1.1.2.3 Small volume liquids |
| **1.5** | **Packaging** |
| | *1.5.2 Secondary packaging* |
| **1.6** | **Quality control testing** |
| | *1.6.1 Microbiological: sterility*<br>*1.6.3 Chemical/Physical* |

## Part 3

**1.Nature of non-compliance:**

The production of sterile products at the facilities of PT Novell Pharmaceutical Laboratories in NBL-1 and NBL-2 is considered not compliant with Annex 1 EU GMP as listed in the deficiencies raised in the inspection report as well as the gaps identified in the CCS which was submitted in the response on 08 March 2024. The following products were in scope of the inspection: Tranexamic acid 500 mg/5ml Solution for Injection (Tranexamsäure Medicamentum 25 mg/ml Injektionslösung) in NBL1 1st floor line 2, NBL2 2nd floor line 1; Esketamine 25 mg/ml Solution for Injection (Esketamin Medicamentum 25 mg/ml Injektionslösung) in NBL1, 1st floor line 3; Midazolam 1 mg/ml Solution for Injection (Midazolam Medicamentum 1 mg/ml Injektionslösung) in NBL1, 1st floor line 3; Amiodarone 50 mg/ml Solution for Injection (Amiodaron Medicamentum 50 mg/ml Injektionslösung) in NBL1, 1st floor line 3; Dexmedetomidine 100 mcg/ml concentrate for Solution for Infusion (Dexmedetomidin Medicamentum 100 mcg/ml Konzentrat zur Herstellung einer Infusionslösung) in NBL-1, 2nd floor; Vitamin B1 100 mg/2ml and 50 mg/2ml Solution for Injection (Vitamin B1 Medicamentum 100 mg/2ml bzw. 50 mg/2ml Injektionslösung) NBL1, 1st floor line 3; The implementation of suggested actions in order to solve the raised deficiencies needs to be reevaluated during an on-site inspection. A paper-based evaluation of proposed actions is considered not adequate. Furthermore, the company intends to move the production of EU products from NBL-1 to NBL-2. A marketing authorization variation for transfer of the production to NBL-2 should be submitted and accepted prior to start EU production. The approval of the variation should be submitted to the respective EU authority. Following points addressed, but not limited to these points, need to be implemented and reevaluated on-site before starting the production of sterile products: - The continuous monitoring of alarm differential pressure of clean rooms including a pressure alarm system. - Smoke studies of clean rooms and filling lines - Cleaning validation of aseptic filling lines - Integrity test validation for vials - Sterile filtration system: o allow sterilization in place o allow integrity testing after assembling as closed system o allow integrity testing pre-use post sterilisation and post use (PUPSIT) o allow filter in line testing o product specific filter validation o single use of the bioburden and sterile filter - The access of technical area of the oven and the autoclave from clean room - The manual transfer of washed equipment from CRC C to CRC A via trolley - Suitablity of epoxy coating of clean room walls and floors. - Suitability of Clean rooms for sterile production in general - Distinguishability of cleanroom garments of production and cleaning personnel - Clear pressure difference of clean rooms to adjacent area - Clear requalification requirements and implementations for clean rooms, filling lines and autoclaves For details also refer to response of the inspectors in the final report INS-484367- 101052478-19224178.

**Action taken/proposed by the NCA**

**Others**
-Restriction of current valid GMP certificate -Suspension/revocation/requested variation/ refusal to grant * of Marketing Authorisation(s)

***2024-04-26***

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

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