Health And Youth Care Inspectorate

Report No: ***NL/H 25/2057693***

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 Netherlands confirms the following:
The manufacturer: ***Indeus Life Sciences Private Limited***
Site address: ***Bal Rajeshwar Road, Mulund West, Mumbai, 400080, India***
OMS Organisation Id. / OMS Location Id.: ***ORG-100021565*** / ***LOC-100030258***

From the knowledge gained during inspection of this manufacturer, the latest of which was conducted on ***2025-06-05***, 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 (EU) 2017/1572

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;	
1.2	**Non-sterile products**
	1.2.1 Non-sterile products (processing operations for the following dosage forms) 1.2.1.13 Tablets
1.6	**Quality control testing**
	1.6.3 Chemical/Physical

Part 3

1.Nature of non-compliance:

A routine GMP inspection was carried out by the Dutch Health and Youth Care Inspectorate (IGJ) from 2 to 5 June 2025. The product in scope was LOPERAMIDE/SIMETHICONE TABLETS 2mg/125mg, that were to be reintroduced to the Dutch market. The inspection resulted in 7 (seven) Major deficiencies and 10 (ten) Other deficiencies. IGJ 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 storage and retention of documents, obsolete artwork, reference samples, spare parts and other waste is inappropriate. Two rooms with severe issues were found: a 'document room' with heavy mold and humidity stains on walls, chaotic storage of documents and unidentified drums (presumably development batches); an adjacent room with scrapped GMP documents, obsolete artwork, obsolete reference samples and other debris, uncategorized and chaotically stored, with the room as well being used as dressing room for contract workers. 2. The quality system functions insufficient. Many issues were found in the management and investigation of deviations, changes and OOS. PQR and management review were incompletely executed. 3. Outsourced activities are not sufficiently defined, agreed and/or controlled. The requalification of all suppliers of the product in scope were overdue; API suppliers were not audited as of 2018; significant lapses in the requalification procedure and incomplete supplier agreements were observed. 4. The reintroduction of Loperamide/Simeticone tablets onto the Dutch market is not controlled. The applied assay limit specification was lower than the specification as laid down in the Marketing Authorization; averaging into compliance of analytical results for these tablets was allowed; agreements with the MAH were lacking. 5. Contamination control is insufficient, as was shown by many issues in cleaning, environmental monitoring and water monitoring. Examples were seen in missing cleanliness labels, improperly stored hoses, dirty cleaning clothes and gowning, incomplete cleaning procedures, missing preventive maintenance and checks on equipment; missing QRM principles and justifications in environmental monitoring, EM measurements that were not representative for daily practice, EM and HVAC procedures not being followed; infrequent water measurements and incomplete trending. 6. Validation and qualification are structurally inadequately performed, assessed and reviewed. Severe issues were found in cleaning and process validation, analytical method validation and room qualification; mostly related to missing (crucial) elements, but also not procedures not being followed, incomplete reporting and interpretation of results. 7. Lapses in Good Documentation Practices and control of documents. A wide range of issues were found; among others uncontrolled documents, incomplete and incorrect documents, and registrations. Furthermore, unexplainable data and missing data entries and signing were observed.

Action taken/proposed by the NCA

Recall of batches already released

Consideration of recall, following NCA assessment of potential quality defects vs. supply restriction. A direct product risk could not be identified, however the nature of the Major deficiencies and the cumulative risk of the deficiencies combined could lead to an inferior product. Based on the information received from the company, as of 2021 only

LOPERAMIDE/SIMETHICONE TABLETS 2mg/125mg have been manufactured for the EU; 24 batches in 2022 and 12 batches in 2024. Based on the small scale of manufacturing (max. 100.000 tablets/batch) IGJ expects that only a limited number of tablets will still be on the market. To current knowledge, marketing authorizations are applicable in The Netherlands and Poland; further distribution to other countries is unknown.

Prohibition of supply
The company should not supply to the EU market whilst the NCS in is force. A successful reinspection is recommended before market supply is resumed.

Products manufactured at site, if known	Products	Dosage Form	Reference Member State, National or EMA
Human Medicinal Products	Loperamide/Simethicone	Tablet	NL, DK, HR
	Loperamide	Orodispersible tablet	BE

2025-10-14

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

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