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速別：普通件
密等及解密條件或保密期限：
附件：原料藥廠違反GMP警訊乙份 (A21020000I_1141100941_doc2_Attach1.pdf)

主旨：印度原料藥廠「Maithili Life Sciences Private Limited」（廠址：Plot No 2, Apiic Industrial Estate, Gajulamandyam, Tirupati, Renigunta, Andhra Pradesh, 517520, India」經國外官方判定違反GMP乙案，詳如說明段，請轉知所屬會員知照。

說明：

一、比利時衛生主管機關FAMHP於2024年11月29日查核旨揭原料藥廠，判定違反GMP，並於2025年1月13日發布「STATEMENT OF NON-COMPLIANCE WITH GMP」。

二、鑑於上述原料藥廠未符合GMP之規定，具影響藥品製造品質之風險，請轉知所屬會員釐清相關國產及輸台製劑產品是否使用旨揭原料藥廠所生產原料藥，並應依風險管理原則執行相關後續處置。

正本：中華民國西藥商業同業公會全國聯合會、中華民國西藥代理商業同業公會、台北市西藥代理商業同業公會、中華民國開發性製藥研究協會、台灣藥品行銷暨管理協會、台灣製藥工業同業公會、中華民國學名藥協會、中華民國製藥發展協會

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Federal Agency For Medicines And Health Products

Report No: ***BE/NC/2024/01***

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 Belgium confirms the following:
The manufacturer: ***Maithili Life Sciences Private Limited***
Site address: ***Plot No 2, Apiic Industrial Estate, Gajulamandyam, Tirupati, Renigunta, Andhra Pradesh, 517520, India***
OMS Organisation Id. / OMS Location Id.: ***ORG-100042329*** / ***LOC-100069941***
DUNS Number: ***87-219-9920***

From the knowledge gained during inspection of this manufacturer, the latest of which was conducted on ***2024-11-29***, it is considered that **it does not comply with the Good Manufacturing Practice** requirements referred to in

- The principles of GMP for active substances referred to in Article 47 of Directive 2001/83/EC.

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;

1.4	Other products or manufacturing activity
	1.4.3 Other: Active substance and active substance intermediate(en)

Manufacture of active substance. Names of substances subject to non-compliant:
BIPERIDENHYDROCHLORIDE(en)
4. Non-Compliant Other Activities - Active Substances:
Manufacture of active substance intermediate : biperiden (base)

Part 3

1.Nature of non-compliance:

During the inspection, 24 deficiencies against EU GMP were identified. Of these, based on a number of major EU GMP failures that could potentially lead to contamination/cross-contamination of the final APIs produced, and as a risk for the patient's safety cannot be excluded, a general deficiency was raised as critical. The major GMP failures were observed in the areas of raw materials contamination/degradation and mix-up control, advanced intermediates contamination/cross contamination control, APIs contamination/cross contamination control, design, cleaning and maintenance of equipment, cleaning validation, change control management and quality risk management, deviation management, data integrity and quality control.

Action taken/proposed by the NCA

Requested Variationof the marketing authorisation(s)
It is recommended to assess the opportunity of requesting variation to the marketing authorisation in order to delete or substitute this manufacturer of active substances and intermediates.

Recall of batches already released
If there are alternative suppliers and there is no risk of shortage, recall of medicinal product should be evaluated by involved NCA's following assessment conducted in conjunction with MAHs. Given the nature of non-compliances, assessment should include a complete retest of all imported batches of active substance.

Prohibition of supply
Due to the nature of the non-compliance prohibition of supply is recommended, unless there are no alternative suppliers and there is a risk of shortage.

Suspension or voiding of CEP (action to be taken by EDQM)
CEP 2021-360 / Biperiden hydrochloride, CEP 2020-317 / Biperiden hydrochloride were suspended by EDQM December 25, 2024, and CEP 2022-168 / Sumatriptan succinate application was closed.

2025-01-13

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

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Federal Agency For Medicines And Health Products
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