State Institute for Drug Control

Report No: ***sukls256173/2019***

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 Czechia confirms the following:
The manufacturer: ***MEHTA API Pvt. Ltd.***
Site address: ***Gut No. 546, 571, 519 & 520, Village Kumbhavali, Tarapur, District Palghar, BOISAR, MAHARASHTRA, 401506, India***

From the knowledge gained during inspection of this manufacturer, the latest of which was conducted on ***2019-09-11***, 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 and an appropriate level of GMP as referred to in Article 46(f) 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: Manufacture of APIs(en)

Manufacture of active substance. Names of substances subject to non-compliant:
ERYTHROMYCIN(en)

3. NON-COMPLIANT MANUFACTURING OPERATIONS - ACTIVE SUBSTANCES

Active Substance:ERYTHROMYCIN

3.1	**Manufacture of Active Substance by Chemical Synthesis**
	3.1.2 Manufacture of crude active substance
3.5	**General Finishing Steps**
	3.5.1 Physical processing steps: milling, sifting 3.5.2 Primary Packaging (enclosing / sealing the active substance within a packaging material which is in direct contact with the substance) 3.5.3 Secondary Packaging (placing the sealed primary package within an outer packaging material or container. This also includes any labelling of the material which could be used for identification or traceability (lot numbering) of the active substance)
3.6	**Quality Control Testing**
	3.6.1 Physical / Chemical testing

Clarifying remarks (for public users)

starting from erythromycin thiocyanate

Part 3

1.Nature of non-compliance:
The inspection was carried out in the framework of the EDQM inspection programme on 9 - 11 September 2019. Scope of the inspection was Erythromycin. In total 24 deficiencies were identified by the inspection team, eleven as major and one as regarding compliance with CEP dossier. The observation regarding CEP dossier was related to usage of regenerated solvent (dichloromethane) which is not included form the current dossier version. The major deficiencies were identified in most of the GMP areas with regards to change control, computerised systems, material management traceability, buildings and facilities, clean areas, cleaning validation, suppliers´ qualification, deviations, CAPA, purified water system, CoAs issuance and standards usage. The company had been subjected to 3 previous inspections, these inspections had defined similar issues as were observed during current inspection indicating a lack of QA oversight and inadequate approach with regard to addressing the issues identified during GMP inspection. Based on the number and severity of the major observations, the inspector team concluded that the inspected firm cannot be considered as in compliance as in compliance with EU GMP Part II and that the combination of deficiencies identified constitutes a critical risk of production products which could be harmful to the patient.
Action taken/proposed by the NCA **Requested Variationof the marketing authorisation(s)** This manufacturer should not be authorised in any new/ongoing marketing authorization or variation application. The submission of a variation application for introducing alternative manufacturers of the active ingredient is recommended. **Recall of batches already released** A recall of medicinal products should be evaluated by involved NCAs following the assessment. **Prohibition of supply** Prohibition of supply of Erythromycin 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)** Suspension or withdrawal of CEP is recommended.

2019-11-25

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

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State Institute for Drug Control
Tel:***Confidential***
Fax:***Confidential***