*Federal Agency For Medicines And Health Products*

Report No: ***BE/NC/2025/01***

# 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: ***Sm Biomed Sdn. Bhd.***
Site address: ***Lot 90, Sungai Petani Industrial Estate, Sungai Petani, 08000, Malaysia***
OMS Organisation Id. / OMS Location Id.: ***ORG-100018119*** / ***LOC-100026902***

From the knowledge gained during inspection of this manufacturer, the latest of which was conducted on ***2025-10-08***, 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
- 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: Active substance and active substance intermediate(en)* |

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

## Part 3

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

Based on the findings of the inspection, supply of falsified API to European customers was identified and were determined to be non-compliant with the EU GMP standards, and with Directive 2011/62/EU of the European Parliament and of the Council of 8 June 2011, amending Directive 2001/83/EC on the Community code relating to medicinal products for human use, as regards the prevention of the entry into the legal supply chain of falsified medicinal products, and it is proposed by consequence to issue a Statement of Non-Compliance for SM BIOMED SDN BHD. Specifically, during the inspection, 10 deficiencies against EU GMP were identified. One critical deficiency relating to supply of falsified API to European customers was identified and two major deficiencies were also observed in relation to risks of contamination and cross-contamination and process validation. In addition, 7 other deficiencies were found. (It should be noted that due to the significant amount of time spent investigating the supply of falsified API to Europe, many elements of the quality system which would normally be covered as part of a routine GMP inspection, were not reviewed on this occasion).

**Action taken/proposed by the NCA**

**Requested Variationof the marketing authorisation(s)**
Assessment of the MA to delete or substitute SM BIOMED SDN BHD should be considered. No new MAs should be approved where APIs / intermediates from this site is used as long as the non-compliance statement is active.

**Recall of batches already released**
For Clarithromycin covered by CEP 2006-240 and CEP 2022-483 The need of recall of released batches of finished products where APIs/intermediates manufactured on this site have been used should be considered unless proven risk of shortage. For Erythromycin (CEP 1999-119), Erythromycin base dihydrate (CEP 2020-007), Erythromycin Ethylsuccinate (CEP 1999-121), Erythromycin Stearate (CEP 1999-120), and for substances not covered by CEP Erythromycin Estolate and Erythromycin Lactobionate: 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. In specific cases of national legislation that require GMP certification for a specific API used in critical medicines with no alternative, each authority may decide, under their own responsibilities, to maintain locally a limited GMP certification of the company SM Biomed in order to guarantee the supply to its market. For other substances covered by CEP (Azithromycin, Betamethasone sodium phosphate, Betamethasone valerate, Deferasirox, Dexamethasone sodium phosphate), or other substances not covered by CEP (Sitagliptin Phosphate Monohydrate, Tadalafil): At that time, it is understood that no such APIs are supplied directly to EU/EEA markets. Nevertheless, if such substances have actually reached the European market through SM BioMed or other providers (manufacturers, brokers, …), similar assessment and decisions should be considered.

**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. Given the nature of non-compliances, decision to accept the supply must be based on an assessment that should include a complete retest of all imported batches of active substance.

**Suspension or voiding of CEP (action to be taken by EDQM)**
The EDQM had taken the decision to withdraw all granted CEPs and to close all CEP application currently under treatment from SM BIOMED SDN BHD. Withdrawal of the Certificate of Suitability (CEP) : Betamethasone valerate (CEP 1999-118), Clarithromycin (CEP 2006-240), Clarithromycin (Process 2) (CEP 2022-483), Dexamethasone sodium phosphate (CEP 2024-065), Erythromycin (CEP 1999-119), Erythromycin (process 2) (CEP 2020-007), Erythromycin ethylsuccinate (CEP 1999-121), Erythromycin stearate (CEP 1999-120) Certificate of Suitability (CEP) application closing : Azithromycin (CEP 2024-067), Betamethasone sodium phosphate (CEP 2024-470), Betamethasone valerate (CEP 2025-284), Deferasirox (CEP 2024-142)

***2025-12-11***

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

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