Federal Agency For Medicines And Health Products

Report No: ***BE/NC/2024/02***

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: ***Yung Shin Pharm. Ind. Co. Ltd.***
Site address: ***27 Kung Chiu Road, Tachia, 43769, Taiwan***
OMS Organisation Id. / OMS Location Id.: ***ORG-100024900*** / ***LOC-100034090***

Other
(Human) Directive (EU) 2017/1572

From the knowledge gained during inspection of this manufacturer, the latest of which was conducted on ***2024-05-31***, it is considered that **it does not comply with the Good Manufacturing Practice** requirements referred to in

•

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.

---

[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;	
1.1	**Sterile products**
	1.1.1 Aseptically prepared (processing operations for the following dosage forms) 1.1.1.2 Lyophilisates
1.5	**Packaging**
	1.5.2 Secondary packaging
1.6	**Quality control testing**
	1.6.1 Microbiological: sterility *1.6.2 Microbiological: non-sterility* *1.6.3 Chemical/Physical* *1.6.4 Biological*

Clarifying remarks (for public users)

This non conformity concerns the manufacture of amphotericine B powder for dispersion only. During the inspection of YSP, there were 2 major concerns: 1. the sterility of the drug cannot be guaranteed, and 2. the risks of cross-contamination are insufficiently known and managed.

Part 3

1.Nature of non-compliance:
During the inspection of Yung Shin Pharmaceutical Industry Co. Ltd., there were 2 major concerns: 1. the sterility of the drug cannot be guaranteed, and 2. the risks of cross-contamination are insufficiently known and managed. The following issues were identified: - In relation to the aseptic process: The firm accumulates several deficiencies related to the aseptic processing, for instance it does not correctly address the filling line set up assembly (lack of aseptic connectors and aseptic sampling port), nor the particular configuration of the booth housing the filling tank (first air concept not taken into account). In addition, the aseptic process simulation needs to be improved as well as the sterilization of : materials, filling lines and equipments. None of these elements are assessed in the CCS (Contamination Control Strategy). - In relation to cross-contamination: It was found that the plant also manufactures other drugs including corticoids. However, the ADE values of the APIs are not known, a risk analysis of the cross-contamination risks and a cross-contamination prevention strategy based on it are missing.
Action taken/proposed by the NCA **Others** Amphotericin B manufactured at Yung Shin Pharmaceutical Industry Co. Ltd.is currently not imported to the EU market and the site does not hold a MIA nor a GMP certificate. No action is required.

2025-01-13

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

---

Confidential
Federal Agency For Medicines And Health Products
Tel:***Confidential***
Fax:***Confidential***