French National Agency for Medicines and Health Products Safety

Report No: ***17MB002NCR***

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 France confirms the following:
The manufacturer: ***BIOCON LIMITED***
Site address: ***Biocon Special Economic Zone, Plot Nos. 2 - 4, Phase IV, Bommasandra - Jigani Link Road, Bommasandra, BANGALORE, 560 099, India***

From the knowledge gained during inspection of this manufacturer, the latest of which was conducted on ***2017-03-17*** , 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 2003/94/EC

[1] *The statement of non-compliance referred to in paragraph 111(7) of Directive 2001/83/EC and 80(7) of Directive 2001/82/EC, as amended, shall also be required for imports coming from third countries into a Member State.*

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 1.1.1.4 Small volume liquids
1.3	**Biological medicinal products (list of product types)**
	1.3.1 Biological medicinal products (list of product types) 1.3.1.5 Biotechnology products
1.5	**Packaging**
	1.5.2 Secondary packing
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*

Part 3

1. Nature of non-compliance:

The pre-approval inspection performed by ANSM on behalf of EMA from 13 to 17 March 2017 raised deficiencies concerning the biosimilar products: - Fulphila® (Pegfilgrastim), pre-filled syringe presentation: drug product manufacture (block B1) and quality control operations; - Ogivri® (Trastuzumab), vial presentation (freeze-dried product): drug product manufacture (block B1) and quality control operations; - Semglee® (Insulin glargine), cartridge presentation: secondary packaging (block B2) and drug product quality control. This NCR is limited to the drug product manufacturing activities related to these 3 products. This inspection raised 35 deficiencies, including 11 major deficiencies on the following topics: -Environmental monitoring -Training; -OOS results management ; -Cleaning validation ; -Process validation; -Vendors qualification; -Media fill test; -Cross-contamination risks; -Batch manufacturing record; -Differential pressure alarms' management in classified areas; -Access management in SAP for batch certification

Action taken/proposed by the NCA

Suspension of the marketing authorisation(s)
The EU Marketing Authorization Applications of the 3 products are under assessment and should not be approved while this NCR is in force.

Prohibition of supply
No batch of the 3 products manufactured prior to the issuance of this NCS and manufactured while this NCS is in force should be supplied to Europe.

Others

**** This NCR is limited to the drug product manufacturing activities related to Fulphila® Ogivri® and Semglee®
**** Manufacturing activities of Trastuzumab (preparation and storage of Master Cell Bank (MCB) and Working Cell Bank (WCB), manufacture and quality control operations of drug substance) and of Pegfilgrastim (quality control operations of drug substance) are not concerned by this NCR and a GMP Part II certificate ref. 17MB002HPT01 has been issued by ANSM. --- A follow-up GMP inspection is requested in order to ensure that the entire CAPA plan has been implemented and finalised by the site and that a robust quality system is in place.

2017-07-05

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

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