Landesamt für soziale Dienste Schleswig-Holstein

Report No: ***DE_SH/NCS/API/01/2016***

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 Germany confirms the following:
The manufacturer: ***Artemis Biotech (A Division of Themis Medicare Limited)***
Site address: ***Industrial Development Area, Plot No. 1 & 5 Jeedimetla, Hyderabad, 500 055, India***

From the knowledge gained during inspection of this manufacturer, the latest of which was conducted on ***2016-06-29*** , 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 .

[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

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
	1.4.1 Manufacture of
	1.4.1.4 Other: Active Substance (Simvastatin Antioxidant Butylated Hydroxy Toluene 0.01%)(en)

Manufacture of active substance. Names of substances subject to non-compliant :
SIMVASTATIN(en) / СИМВАСТАТИН(bg) / SYMWASTATYNA(pl)

Part 3

1. Nature of non-compliance:

In total 35 observations were made by the inspection team over the course of the inspection. Five of them were categorised as major deficiencies and therefore potentially leading to a risk to the human and veterinary patient when using active pharmaceutical ingredients manufactured at the inspected site. - The installation and execution of an Enterprise Resource Planning System, hosting GMP relevant data but outside of the quality management system, demonstrated a lack of QA oversight. - Repackaging operations were conducted without any documentation and QA approval. - The issuance of labels for raw materials and APIs was found inadequately controlled. - Within the instrumental laboratory the Company violated basic principles on data integrity, i.e. manual integration without justification and QA oversight. - The Company's approach on the validation of computerised systems (Shimadzu LabSolutions) was considered as not in compliance with the requirements.

Action taken/proposed by the NCA

Recall of batches already released
No immediate recall is needed. Each involved NCA should evaluate, following assessment conducted in conjunction with MAHs, if a potential recall of medicinal product is needed. The risk based evaluation should take in account if there are alternative suppliers and potential risk of shortage. 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 non-compliances, prohibition of supply is recommended.

Suspension or voiding of CEP (action to be taken by EDQM)
This inspection was carried out as part of the EDQM inspection Programm. The impact of this NCS on the CEPs is to be decided by the EDQM. The concerned CEPs are Simvastatin Butylated Hydroxy Anisole 50 - 150 ppm R1-CEP 2006-091-Rev 00; Simvastatin Butylated hydroxy anisole 0.18-0.22% R1-CEP 2007-155-Rev 01; Simvastatin Antioxidant Butylated Hydroxy Toluene 0.01% R1-CEP 2003-257-Rev 03

Others
This supplier should not be approved in any new/ongoing applications. Each involved NCA should evaluate if the supplier should be removed from existing MAs.

Additional comments
This inspection was performed in the framework of the CEP dossier for the manufacture of Simvastatin Antioxidant Butylated Hydroxy Toluene 0.01% R1-CEP 2003-257. The company also produces Fumagillin (antibiotic manufactured from fermentation) for the French market. This API was not within the scope of this inspection.

2016-08-12

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

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Confidential
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