French National Agency for Medicines and Health Products Safety

Report No: ***14MPP092***

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
Art. 80(7) of Directive 2001/82/EC as amended

The competent authority of France confirms the following:
The manufacturer: ***North China Pharmaceutical Group Semisyntech Co., Ltd***
Site address: ***No. 8 Xingye Street,, Shijiazhuang Economic & Technological Development Zone, Shijiazhuang, Hebei, 052165, China***

From the knowledge gained during inspection of this manufacturer, the latest of which was conducted on ***2014-11-27*** , 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 Article 51 of Directive 2001/82/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**
	1.4.2 Sterilisation of active substance/ excipients/ finished product 1.4.2.1 Filtration Special Requirements 1 B-lactam Antibiotics

Manufacture of active substance. Names of substances subject to non-compliant :
BENZYLPENICILIN BENZATHINE, 1% LECITHINE, 0.2% POLYSORBATE 80, 9.2% SODIUM CIT RATE (STERILE)(en)
BENZYLPENICILLIN PROCAINE (STERILE)(en)
BENZYLPENICILLIN PROCAINE +1% LECITHIN (STERILE)(en)

Part 3

1. Nature of non-compliance:
Overall, 17 deficiencies were observed during the inspection, including 2 Critical and 4 Major deficiencies: [Critical 1] Manipulation and falsification of GMP documents (rewriting of records with change of content, an inconsistency of signatures and date in many records, etc.) were observed in different department; [Critical 2] Lack of data integrity in the QC laboratory (No access control, inadequate traceability and archiving practices, no audit trail, no restriction on the deleting of data, etc.) and falsification of the analytical results for residual solvents; [Major 1] Risk of contamination in grade B area; [Major 2] The change control related to (i)- the change of the identification number of some manufacturing equipment and (ii)- the merger project of NCPC semisynthec and Hebei Huari was found deficient; [Major 3] Lack of documentation management, control, and retention of superseded or obsolete version; [Major 4] The company personnel was not adequately trained in GMPs as evidenced by the critical and major deficiencies identified during this inspection.

Action taken/proposed by the NCA

Requested Variation of the marketing authorisation(s)
Variations of Marketing Authorisation(s) to remove the site as relevant.

Recall of batches already released
Consideration of a recall of product should be given due to the lack of data integrity in the QC laboratory, falsification of the analytical results and manipulation of GMP documents. Using QRM principles, National supply situations and clinical requirements should be taken into account when making this decision.

Prohibition of supply
Consideration of a supply prohibition should be given due to the lack of data integrity in the QC laboratory, falsification of the analytical results and manipulation of GMP documents. Using QRM principles, National supply situations and clinical requirements should be taken into account when making this decision.

Suspension or voiding of CEP (action to be taken by EDQM)
Suspension of CEP 2004-001 (Benzylpennicillin Procaine, Sterile) and CEP 2004-017 (Benzylpennicillin Procaine +1%lecithin (Sterile).

Additional comments
Withdrawal of current valid EU GMP certificates issued by NCAs of Germany (# 8.87.40.13.05-02GMP) & Spain (# ES/048H/13).

2015-01-22

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

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