State Institute for Drug Control

Report No: ***sukls206914/2015***

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 Czech Republic confirms the following:
The manufacturer: ***HUBEI HONGYUAN PHARMACEUTICAL CO., LTD.***
Site address: ***No. 8 Fengshan Road, Industrial and Economic Development Zone, Luotian County, Huanggang City, Hubei Province, 438 600, China***

From the knowledge gained during inspection of this manufacturer, the latest of which was conducted on ***2015-10-30*** , 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 substances(en)

Manufacture of active substance. Names of substances subject to non-compliant :
METRONIDAZOLE(en) / METRONIDAZOLUM(cs)

3. NON-COMPLIANT MANUFACTURING OPERATIONS - ACTIVE SUBSTANCES

Active Substance : METRONIDAZOLE

3.1	Manufacture of Active Substance by Chemical Synthesis
	3.1.1 Manufacture of active substance intermediates 3.1.2 Manufacture of crude active substance 3.1.3 Salt formation / Purification steps : crystallization, centrifugation
3.5	**General Finishing Steps**
	3.5.1 Physical processing steps : milling, sieving, blending 3.5.2 Primary Packaging (enclosing / sealing the active substance within a packaging material which is in direct contact with the substance) 3.5.3 Secondary Packaging (placing the sealed primary package within an outer packaging material or container. This also includes any labelling of the material which could be used for identification or traceability (lot numbering) of the active substance)
3.6	**Quality Control Testing**
	3.6.1 Physical / Chemical testing 3.6.2 Microbiological testing excluding sterility testing

Part 3

1. Nature of non-compliance:

This inspection was performed in the framework of the CEP dossier for the manufacture of Metronidazole R1-CEP 2007-309-Rev 01. The inspection identified in total 24 deficiencies to EU GMP. One of them was categorized as critical and related to the Company's Quality Assurance System for production of Metronidazole. 10 deficiencies were categorized as major and were related to: QA, Documentation, Supplier Qualification, Data Integrity, Out-of-Specification handling, Quality Control, Computerised System validation, Change Control.

Action taken/proposed by the NCA

Recall of batches already released
If there are alternative suppliers and there is no risk of shortage, recall of medicinal product should be evaluated by involved NCAs' 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.

Prohibition of supply
Prohibition of supply is recommended, unless there are not alternative suppliers and there is a risk of shortage.

Suspension or voiding of CEP (action to be taken by EDQM)
CEP suspensed.

Additional comments
This supplier should not be approved in any new/ongoing applications.

2016-01-20

Name and signature of the authorised person of the Competent Authority of Czech Republic

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State Institute for Drug Control
Tel: ***Confidential***
Fax: ***Confidential***