Federal Agency for Medicines and Health Products

Report No: ***BE/NC/2017/085***

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: ***INNER MONGOLIA CHANGSHENG PHARMACEUTICAL CO. LTD***
Site address: ***Industry zone, Tuoketuo, Hohhot, Inner Mongolia, 10206, China***

From the knowledge gained during inspection of this manufacturer, the latest of which was conducted on ***2017-10-20*** , 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 (see below)(en)

Manufacture of active substance. Names of substances subject to non-compliant :
AMOXICILLINE TRIHYDRATÉE(fr) / AMOXICILLINETRIHYDRAAT(nl) / AMOXICILLINA TRIID RATO(it) / AMOXICILLIN TRIHYDRATE(en)

3. NON-COMPLIANT MANUFACTURING OPERATIONS - ACTIVE SUBSTANCES	
Active Substance : AMOXICILLIN TRIHYDRATE	
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 : cristallisation 3.1.4 Other : Enzymatic synthesis
3.5	**General Finishing Steps**
	3.5.1 Physical processing steps : centrifuge / drying 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:
Nature of non-compliance: One critical and eight major deficiencies were found. The critical deficiency is related to the QA system implemented on site which was found to be weak and not capable of putting in place proper design, planning, implementation, maintenance and continuous improvement of a system that allows the consistent delivery of products with appropriate quality attributes. Therefore a risk to the safety of patients could not be excluded. This was evidenced by the high number of major deficiencies observed in the following areas: Deviation, Management, Storage, Materials Management, Quality Control, Validation, Qualification, Complaint Management, and Documentation.
Action taken/proposed by the NCA
Requested Variation of the marketing authorisation(s)

It is recommended to assess the opportunity of requesting variation to the marketing authorisation in order to delete or substitute this manufacturer of the active substance. (for information, no EU GMP certificated has ever granted. This was the first Inspection to the manufacture carried out by an EU Regulatory Authority).

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 NCA's 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
Due to the nature of the non-compliance prohibition of supply is recommended, unless there are no alternative suppliers and there is a risk of shortage.

Suspension or voiding of CEP (action to be taken by EDQM)
The CEPs suspension recommended by the inspection team was officially endorsed by the Ad Hoc Committee on the 13th November 2017.

Additional comments
This inspection was performed in the framework of EDQM's inspection scheme and related to the manufacture of Amoxicillin trihydrate in the context of dossier CEP 2007-315.

2018-01-15

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

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