Italian Medicines Agency

Report No: ***IT/NCR/API/3/2018***

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 Italy confirms the following:
The manufacturer: ***Yibin Lihao Bio-technology Co. Ltd.***
Site address: ***Qihang Xi Road, Luolong Industrial Park, Yibin, Sichuan, 644104, China***

From the knowledge gained during inspection of this manufacturer, the latest of which was conducted on ***2018-10-31*** , 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**
	1.4.3 Other: Manufacture of Active Substances(en)

Manufacture of active substance. Names of substances subject to non-compliant :
CRUDE HEPARIN SODIUM(en)

3. NON-COMPLIANT MANUFACTURING OPERATIONS - ACTIVE SUBSTANCES	
Active Substance : CRUDE HEPARIN SODIUM	
3.2	**Extraction of Active Substance from Natural Sources**
	3.2.2 Extraction of substance from animal source
3.5	**General Finishing Steps**
	3.5.1 Physical processing steps : 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**
	3.6.4 Biological Testing

Part 3

1. Nature of non-compliance:

The inspection identified 24 GMP deficiencies, of which 7 were categorised as major. The major deficiencies were found in the following areas: 1. Risk of contamination; 2. Buildings and facilities; 3. Equipment; 4. Storage of starting material; 5. Process; 6. Materials management, traceability of starting material; 7. Recovery of solvents.

Action taken/proposed by the NCA

Requested Variation of the marketing authorisation(s)
Variations to existing MAs to remove the site are recommended

Recall of batches already released
No recalls are recommended

Prohibition of supply
Prohibition of supply of crude heparin sodium manufactured by the site is recommended

Suspension or voiding of CEP (action to be taken by EDQM)
Variation of involved CEPs is recommended

Additional comments
Joint EMA/EDQM inspection

2018-11-22

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

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