French National Agency for Medicines and Health Products Safety

Report No: ***15MPP013***

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 France confirms the following:
The manufacturer: ***HUZHOU SUNFLOWER PHARMACEUTICAL CO., LTD.***
Site address: ***692 North Zhiyuan Road, Wukang Town, Huzhou, Zhejiang Province, 313 200, China***

From the knowledge gained during inspection of this manufacturer, the latest of which was conducted on ***2015-01-30*** , 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;	
1.2	**Non-sterile products**
	1.2.1 Non-sterile products (processing operations for the following dosage forms) 1.2.1.17 Other: active substance(en)

Manufacture of active substance. Names of substances subject to non-compliant :
POVIDONE, IODINATED(en)

3. NON-COMPLIANT MANUFACTURING OPERATIONS - ACTIVE SUBSTANCES	
Active Substance : POVIDONE, IODINATED	
3.1	**Manufacture of Active Substance by Chemical Synthesis**
	3.1.1 Manufacture of active substance intermediates 3.1.3 Salt formation / Purification steps : Complexation reaction
3.5	**General Finishing Steps**
	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

Part 3

1. Nature of non-compliance:

Overall, 27 deficiencies were observed, including 1 critical deficiency and 4 major deficiencies: [Critical 1] The controlled area and the equipment that were used for the final synthesis step in the manufacture of Povidone Iodinated, namely the complexation reaction of Iodine with Povidone K30, presented a risk to the patients due to contamination issues with particles and degradation products ; [Major 1] Materials and quality documents were found at a scrap yard outside the main building of the company as well as inside the neighbouring company's building without any written justification ; [Major 2] The purified water production and distribution systems were deficient (presence of a dead-leg, replacement of conductivity controllers without formal change control, mistakes in calibration documentation, etc.) ; [Major 3] Issuance of 2 different Certificate of Analysis in a Batch Record of Povidone K30 without an appropriate deviation management ; [Major 4] Deficient IR spectrophotometer management (no user requirements prior to acquisition of the equipment, no evidence that the instrument was suitable with its intended use, no evidence that the instrument was belonging to the inspected site).

Action taken/proposed by the NCA

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

Suspension or voiding of CEP (action to be taken by EDQM)
Withdrawal of CEP # 2009-166 (effective as of 19 March 2015 by the EDQM)

Additional comments
It has to be noted that the CEP # 2009-166 was originally suspended on 21 June 2012 by the EDQM following the refusal of a scheduled inspection.

2015-03-25

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

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