Agency for medicinal products and medical devices of the Republic of Slovenia

Report No: ***INSP 2015-002 P01***

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 Slovenia confirms the following:
The manufacturer: ***POLYDRUG LABORATORIES PVT. LTD.***
Site address: ***Plot No. 37, Anand Nagar, M.I.D.C., Ambernath (East), Maharashtra, IN - 421 506, India***

From the knowledge gained during inspection of this manufacturer, the latest of which was conducted on ***2015-03-18*** , 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.*

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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 :
CHLOROBUTANOL HEMIHYDRATE(en)

3. NON-COMPLIANT MANUFACTURING OPERATIONS - ACTIVE SUBSTANCES Active Substance : CHLOROBUTANOL HEMIHYDRATE	
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
3.5	**General Finishing Steps**
	3.5.1 Physical processing steps : milling 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

Clarifying remarks (for public users)

The statement of non-compliance is valid for all APIs. The Plant I produced Metoprolol Tartrate, Metoprolol Succinate, Chlorobutanol Hemihydrate, Chlorobutanol Anhydrous and Fluconazole. The plant II manufactured Ferrous Fumarate. The plant III produced Losartan Potassium and Carisoprodol.

Part 3

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1. Nature of non-compliance:
Overall, 17 deficiencies were found, of which 5 Major consisting in: - Customer complaints deliberately unregistered in the official logbook - Storage of quality documents in an uncontrolled location, involving staff from QC, QA, maintenance and production - Deficient management of paper documents - Deficient management of the computerised system - Failure to address risks of cross contamination for APIs sent out to micronisation subcontractor. The combination of these major deficiencies represents a critical deficiency leading to a potential risk for the patient.
Action taken/proposed by the NCA **Requested Variation of the marketing authorisation(s)** change of API supplier **Suspension or voiding of CEP (action to be taken by EDQM)** All CEPs have been suspended: CEP 2009-112 (Chlorobutanol hemihydrate), CEP 2009-152 (Metoprolol tartarate), CEP 2009-170 (Metoprolol Succinate), CEP 2010-147 (Ferrous fumarate), CEP 2010-247 (Fluconazole), CEP 2011-304 (Metoprolol tartarate), CEP 2011-312 (Metoprolol Succinate)

2015-06-12

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

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