

Italian Medicines Agency

Report No: *IT/ GMP/NCR/INT/1-2014*

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: ***SRI KRISHNA Pharmaceuticals Ltd.***

Site address: ***Unit II - A-35, IDA, Nacharam, Hyderabad, Andhra Pradesh, 500 076, India***

From the knowledge gained during inspection of this manufacturer, the latest of which was conducted on ***2014-12-04***, it is considered that ***it does not comply with the Good Manufacturing Practice*** requirements referred to in

- The principles and guidelines of Good Manufacturing Practice laid down in Directive 2003/94/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

Human Medicinal Products

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
	<i>1.2.1 Non-sterile products (processing operations for the following dosage forms)</i> 1.2.1.8 Other solid dosage forms: granules in bulk(en)
1.6	Quality control testing
	<i>1.6.2 Microbiological: non-sterility</i> <i>1.6.3 Chemical/Physical</i>

Part 3

1. Nature of non-compliance:

During the inspection 10 Major deviations from EU GMP have been found. In particular, main concerns were: 1. Drug products failing to meet established quality control criteria are not rejected. In particular: a) analysts routinely use the PC administrator privileges to set the controlling time and date settings back to over-write previously collected failing and/or undesirable sample results. This practice is performed until passing and/or desirable results are achieved; b) Analysts routinely perform "trial" injections of sample aliquots prior to performing the official/reported analysis. There are no documented sample preparation details for these trial analyses. The results of these trial injections are not reported, and were found to differ significantly from the subsequent reported results; c) Analysts routinely perform "trial" injections of sample aliquots prior to performing the official/reported analysis. The resulting raw data chromatogram files were often found to have been deleted and unavailable for review; d) Analysts delete undesirable and/or failing results (entire sample sequences) and retest samples until desirable results are achieved. 2. Established laboratory control mechanisms are not followed. Electronic records are used, but they do not meet systems validation requirements to ensure that they are trustworthy, reliable and generally equivalent to paper records; 3. Missing or poor quality agreement; 4. Written production and process control procedures are not documented at the time of performance. Specifically, Too Numerous to Count (TNTC) torn and discarded controlled manufacturing batch records for a variety of different products issued by the Quality Unit were found during a walk-through inspection of the facility. Five batch records were compared with the archived manufacturing one and it was ascertained that no records had been made for duplicate issuance of these five batches chosen for review, as required per SOP QA/SOP/DOC/001. Notably, after subsequent investigation it was found that the Master Batch Record (version 0) had been back-dated by the most responsible persons within your firm's Quality and Manufacturing departments, which was confirmed by these persons during our inspection.

Action taken/proposed by the NCA

Requested Variation of the marketing authorisation(s)

In case of non-critical products Marketing Authorization Holders should be required to remove the site from applicable Authorization by variation.

Prohibition of supply

Due to the nature of non-compliances prohibition of supply is recommended

Additional comments

The current GMP certificates N° IT/E/GMP/8/2013 issued on 19 March 2013 and IT/E/GMP/15/2013 issued on 6 November 2013 are invalid. It is proposed to withdraw also the GMP Certificate DE_BW_01_GMP_2014_0105 issued by Baden – Württemberg (Germany) on 04 August 2014. Based of the information gained during the inspection, at the moment there is no reason of concern regarding the quality of the batches of finished products for the following reasons: - only intermediates granules to be further processed by other manufacturing plants of finished products are manufactured in the inspected units; - the finished product is further tested by the batch release site before the release on the market. If no full testing (including impurities) of the finished product has been performed before the release, National Competent Authorities should consider immediate recall of the already released batches and prohibition of supply of further batches using Sri Krishna sourced granules. As an alternative National Competent Authorities should consider to request Marketing Authorisation Holders to conduct a risk assessment in order to evaluate the risk to product quality and patients from the issues identified.

2014-12-23

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

Confidential
Italian Medicines Agency
Tel: *Confidential*
Fax: *Confidential*