Government of Upper Bavaria - Central Authority for Supervision of Medicinal Products in Bavaria (GMP/GCP)

Report No: ***DE/NCR/MP/2/2017***

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 Germany confirms the following:
The manufacturer: ***Dr. Reddy`s Laboratories Ltd. - FTO 2***
Site address: ***Survey No. 42, 45 & 46, Qutubullapur Mandal, Ranga Reddy District, Bachupally Village, Telangana, 500 090, India***

From the knowledge gained during inspection of this manufacturer, the latest of which was conducted on ***2017-08-01*** , 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**
	1.2.1 Non-sterile products (processing operations for the following dosage forms) 1.2.1.1 Capsules, hard shell 1.2.1.13 Tablets 1.2.1.17 Other: Coated tablets & granules (pellets)(en)
1.5	**Packaging**
	1.5.1 Primary Packing 1.5.1.1 Capsules, hard shell 1.5.1.2 Capsules, soft shell 1.5.1.13 Tablets 1.5.1.17 Other non-sterile medicinal products: Coated tablets & granules (pellets)(en)
	1.5.2 Secondary packing
1.6	**Quality control testing**
	1.6.2 Microbiological: non-sterility *1.6.3 Chemical/Physical*

Clarifying remarks (for public users)

No manufacture of APIs or other dosage-forms than mentioned under 1.2 & 1.5 at inspected site (Dr. Reddy`s Laboratories Ltd. - FTO 2)

Part 3

1. Nature of non-compliance:

Critical deficiencies: 1. Essential elements of Pharmaceutical Quality System - PQS are not effective. (details see major deficiencies) a) OOS-results are systematically invalidated in hundreds of cases without traceable and scientific based root-cause-analysis due to “staff-errors”. b) Deviation- and OOS-management, but also protocol-, review- and reporting-systems are designed and executed in a way to systematically not document and report “discrepancies, non-conformancies, incidents, unusual events, …”. c) Cleaning of rooms and also direct-product-contact equipment were verifiable not or not successful performed, but documented as dully done in batch manufacturing/packing record - BMR/BPR. Conclusion: By this, completeness and integrity of BMR, BPR and BTR cannot be assured. In consequence, BMR, BPR and BTR and related reviews (e.g. batch record review) do not enable an objective and solely quality oriented batch-release decision for release-officer and EU-QP at importers site. From this, it is additionally to be concluded, that root-cause analysis for production-based OOS-result or investigation of market-complaints (“quality defects/defective product report”) by review of BMR/BPR cannot be performed objective and successful, because the records do not document “negative-events” and therefore continuous occur “clean”. Major deficiencies: (only examples are given for sub-items related to 5 major deficiencies) 1. Deviation-management and QP-batch-certification (7 sub-items) 1.1 Threshold for “incident-logging” unacceptable high. 1.2 Impact of “equipment-break-down” on batch-quality not evaluated in BMR/BPR 1.3 “Incidents” not contemporary evaluated 1.4 Release of batch without MA-compliance because of not proper “incident” handling (batches will be recalled from MA-holder) 2. Design, condition and maintenance of rooms and equipment. (8 sub-items) Sub-items linked to 2.1 Balance-calibration and integrity of conc. documentation 2.2 Surfaces of manufacturing rooms 2.3 HVAC-filter cleaning and maintenance 2.4 Unsuitable doors 2.5 Unsuitable dispensing-equipment 3. Cleaning of rooms and equipment. (9 sub-items) 3.1 Dirty rooms and equipment 3.2 Integrity of cleaning-documentation 3.3 Cleaning-status labeling 3.4 Status-label “clean” of uncleaned equipment 3.5 Dedicated-equipment labeling 4. Validation of manufacturing process. (4 sub-items) 4.1 Unintended approval of MBR from failed process-validation 4.2 Not proper follow-up of failed process-validation 4.3 Batches from this process supplied to client (batches will be recalled from MA-holder) 5. Investigation and handling of OOS-results. (9 sub-items) Non EU-GMP compliant handling of OOS-results (systematic invalidation) 5.1 Stability program testing 5.2 Raw-material, bulk- and finished product testing 5.3 Purified water testing

Action taken/proposed by the NCA

Recall of batches already released
Separate Rapid Alert issued on 04.08.2017 (only concerning products on german market)

Prohibition of supply
No supply to EU untill successful re-inspection

Others
Withdrawal of current valid GMP certificate (No.: UK GMP 8512/360569-0007): Decision and withdrawal of current EU-GMP certificate is to be taken in area of accountability of issuing authority (MHRA, UK).

Additional comments
A GMP certificate / withdrawal of this STATEMENT OF NON-COMPLIANCE WITH GMP) will not be issued / done without successful re-inspection.

Teleconference Date		**Teleconference Time (CET)**		**Dial in no.**	no teleconference

2017-08-08

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

---

Confidential
Government of Upper Bavaria - Central Authority for Supervision of Medicinal Products in Bavaria (GMP/GCP)
Tel: ***Confidential***
Fax: ***Confidential***