Italian Medicines Agency

Report No: ***IT/NCR/API/1/2022***

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: ***Trifarma S.p.A.***
Site address: ***Via Pavese 2, Rozzano, 20089, Italy***
OMS Organisation Id. / OMS Location Id.: ***ORG-100013844*** / ***LOC-100019765***

From the knowledge gained during inspection of this manufacturer, the latest of which was conducted on ***2022-05-27***, 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**
	1.4.1 Manufacture of 1.4.1.3 Other: active substance(en)

Manufacture of active substance. Names of substances subject to non-compliant:
MILRINONE(en)
FLUPHENAZINE HYDROCHLORIDE(en)
FLUPHENAZINE DECANOATE(en)
PROCHLORPERAZINE(en)
PROCHLORPERAZINE MALEATE(en)
PROCHLORPERAZINE EDISYLATE(en)
THIORIDAZINE HYDROCHLORIDE(en)
TRIFLUOPERAZINE HYDROCHLORIDE(en)
PERPHENAZINE(en)
PERPHENAZINE DECANOATE(en)
CLINDAMYCIN PHOSPHATE(en)
4. Non-Compliant Other Activities - Active Substances:
Importation of: Clindamycin Hydrochloride (confidential)

Part 3

1.Nature of non-compliance:

13 ‘Major’ and 1 ‘Other’ deficiencies were found during the inspection. The ‘Major’ deficiencies were related to inadequate pharmaceutical quality system, building and equipment maintenance. In particular: 1) unauthorized production and equipment records have been found during the inspection; the records, found in the production facilities, were non GMP documentation reporting information about manufacturing activities and equipment use/maintenance not recorded in the GMP documentation such as Batch record nor equipment registers. 2) lack in buildings and equipment maintenance and use and cleaning operations; most of the facilities have been found dirty, not adequately designed for the intended use and with equipment not adequately cleaned nor maintained. Other relevant findings have been found in material management, utilities, documentation management. AIFA suspended the manufacturing site, as per Company’s request. Recall from the market was not put in place. Medicinal products containing the active substances manufactured by Trifarma are considered critical; shortage of the medicinal products is considered a real risk.

Action taken/proposed by the NCA

Withdrawal, of current valid GMP certificate No. IT-API/81/H/2019
Withdrawal of current valid GMP certificate n. IT-API/81/H/2019; issue date 2019.06.05

Requested Variationof the marketing authorisation(s)
Each involved NCA should evaluate, following assessment conducted in conjunction with MAHs, if a recall of medicinal product is needed.

Prohibition of supply
Evaluation should take into account if there are alternative suppliers and potential risk of shortage. Based on the evaluation of the retested results of the batches already released at the time of the AIFA inspection but not shipped yet

and information provided by the Company, considering the real risk of shortage of the critical medicinal products containing the active substances manufactured by Trifarma, AIFA will authorised the ditribution.

Others
This supplier should not be approved in any new / on going applications. Each involved NCA should evaluate if the supplier should be removed from existing MAs. On 29 September, Company submitted a request for restoring the manufacturing activities at the site. AIFA's evalution is on going.

2022-10-26

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

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Confidential
Italian Medicines Agency
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