Swissmedic, Swiss Agency for Therapeutic Products

Report No: ***CH20-0177***

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

Part 1

Issued under the provisions of the Mutual Recognition Agreement between the European Union and ***Switzerland***

The competent authority of Switzerland confirms the following:
The manufacturer: ***DISHMAN CARBOGEN AMCIS LIMITED***
Site address: ***Survey No. 47 & 48, Paiki Sub Plot No. 1, Taluka Sanand, District Ahmedabad, Village Lodariyal, Gujarat, 382 220, India***
DUNS Number: ***91-562-8142***

From the knowledge gained during inspection of this manufacturer, the latest of which was conducted on ***2020-02-28*** , it is considered that **it does not comply with the Good Manufacturing Practice** requirements referred to in

The Good Manufacturing Practice requirements referred to in the Agreement of Mutual Recognition between the European Union and ***Switzerland***

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**
	1.4.3 Other: Manufacture of Active Substances(en)

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

Part 3

1. Nature of non-compliance:
During the joint Swissmedic / EDQM inspection 1 critical, 7 major and 11 other deficiencies were identified. The critical deficiency is related to an insufficient QA oversight leading to a situation that constitutes a potential risk of producing products which could be harmful to the patient. The firm's approach on materials management, including the labelling, traceability, storage conditions, dispensing, cleaning, pest control of raw materials, intermediates, solvents and recovered solvents was considered as not in compliance with EU GMP. The company failed in multipurpose facility/ies to mitigate the risks of cross-contamination and was not aware of the necessary measures to be taken before introducing a new chemical entity in the sampling, dispensing and synthesis area. A lack of effective maintenance and/or cleaning resulting in rust and dirt in hardly cleanable premises in the distillation plant, manufacturing Unit 3A and 3B and in the drum and storage area were obvious. The recovery of solvents in the distillation plant was not properly managed and documented. Shortcomings were observed with regard to the process validation activities related to Dihydrotachysterol. No cleaning validation was performed in the multipurpose intermediate manufacturing Unit 3C despite highly active material (Progesteron) was handled. The identified critical and major deviations pose a risk for all manufactured intermediates and APIs in the multipurpose plant except for manufacturing Unit 9 (see section 3 Additional Comments).

Action taken/proposed by the NCA

Suspension of the marketing authorisation(s)
This manufacturer should not be authorised in any new/ongoing marketing authorization or variation application. The submission of a variation application for introducing alternative manufacturers of the active ingredient is recommended.

Recall of batches already released
(Separate Rapid Alert to follow) The decision to be made by NCA, following an assessment between the NCA and MAH, whether to recall a batch of a particular product or not should be based on a risk assessment and on the criticality of the product.

Prohibition of supply
After issuance of the non-compliance report and as long as it remains active, prohibition of supply of APIs (except APIs manufactured in Unit 9 – see below) is recommended, unless there are no alternative suppliers and there is a risk of shortage. Several critical products will be concerned. Therefore, while qualifying alternative APIs suppliers for critical products, the MAH(s) are requested to perform risk assessments in order to establish measures – agreed by their NCA - to mitigate risks associated with the GMP deficiencies observed (e.g. full specification testing etc.).

Suspension or voiding of CEP (action to be taken by EDQM)
Suspension or withdrawal of CEPs is recommended.

Additional comments
Withdrawal of the GMP certificate # 16MPP065HPT01, issued by the French authority, is recommended. The GMP non-compliance applies to all APIs, but it is not possible to express an opinion on the applicability of the deficiencies observed with regard to the product(s) manufactured in Unit 9. This unit, dedicated to the manufacture of highly potent APIs, was segregated from other manufacturing units/areas with for instance dedicated storage and quality control facilities, and was not subject of the inspection. It is not possible to express an opinion on the applicability of the deficiencies observed with regard to products manufactured in Unit 10. This unit produces medicinal products, which are subject to different GMP requirements than those applied for APIs, thus the facility was out of the scope of the present inspection. Dishman Pharmaceuticals & Chemicals Limited and Carbogen Amcis (India) Limited were subject to a merger. The new name is Dishman Carbogen Amcis Limited and Survey No. 48 was added to the address.

2020-04-20

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

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Confidential
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