Swissmedic Swiss Agency for Therapeutic Products

Report No: ***CH25-0004***

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***.Issued following an inspection in accordance with

The competent authority of Switzerland confirms the following:
The manufacturer: ***Hebei Shengxue Dacheng Pharmaceutical Co. Ltd.***
Site address: ***No 57 Zhangju Road, Luancheng, Shijiazhuang, Hebei, 051430, China***
OMS Organisation Id. / OMS Location Id.: ***ORG-100016575*** / ***LOC-100069397***

Other
(Veterinary) According to Swiss regulations in force: Therapeutic products act, TPA, SR 812.21 and Medicinal products licensing ordinance, MPLO, RS 812.212.1.

From the knowledge gained during inspection of this manufacturer, the latest of which was conducted on ***2025-12-02***, 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

Veterinary 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;

1.4	**Other products or manufacturing activity**
	1.4.1 Manufacture of
	1.4.1.3 Other: active substance and active substance intermediates(en)

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

3. NON-COMPLIANT MANUFACTURING OPERATIONS - ACTIVE SUBSTANCES

Active Substance:DIHYDROSTREPTOMYCIN SULFATE

3.1	**Manufacture of Active Substance by Chemical Synthesis**
	3.1.1 Manufacture of active substance intermediates
3.3	**Manufacturing of Active Substance using Biological Processes**
	3.3.1 Fermentation 3.3.2 Cell Culture: Bacterial 3.3.3 Isolation / Purification
3.4	**Manufacture of sterile Active Substance**
	3.4.1 Aseptically prepared
3.5	**General Finishing Steps**
	3.5.1 Physical processing steps: Filtration, Spray-drying 3.5.2 Primary Packaging (enclosing / sealing the active substance within a packaging material which is in direct contact with the substance)
3.6	**Quality Control Testing**
	3.6.1 Physical / Chemical testing 3.6.3 Microbiological testing including sterility testing

4. Non-Compliant Other Activities - Active Substances:
CEP 2018-146, Dihydrostreptomycin sulfate for veterinary use, Sterile; EDQM-Inspection Programme.

Part 3

1.Nature of non-compliance:

During the joint Swissmedic / EDQM inspection at manufacturing site (LOC ID LOC-100069397) 4 critical, 12 major and 23 other deficiencies were identified. The critical deficiencies and 9 of the major deficiencies are related to an insufficient implementation of annex 1 requirements, thus constituting a potential risk of producing non-sterile products which could be harmful to patient/treated animals. The company failed to establish an adequate Quality Risk Management to ensure product sterility. Several deficiencies were found for the execution of aseptic process simulation as well as for the sterilization of the spray dryer and filling system. Furthermore, the company was not able to establish an appropriate endotoxin control strategy which could also potentially impact non-sterile APIs. The firm's approach to environmental monitoring, aseptic behaviour in clean rooms, container closure integrity, cleaning, gowning and protection of sterile garment is contributing to an overall risk to the quality of the product and the sterility cannot be guaranteed. The design and maintenance of the clean rooms and equipments in grade A, B and C is insufficient to maintain an adequate environment for the manufacture and aseptic filling of sterile APIs. Additionally, the company failed to establish an appropriate change control management, adequate cleaning and process validation, as well as an overall insufficient preventive maintenance strategy. During the inspection it was found that the level of GMP compliance is insufficient, specifically for Annex 1 requirements it can be stated that knowledge at the site is limited.

Action taken/proposed by the NCA

Requested Variationof 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
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 sterile APIs is recommended, unless there are no alternative suppliers and there is a risk of shortage.

Suspension or voiding of CEP (action to be taken by EDQM)
Suspension of sterile CEPs is recommended. EDQM suspended on 12/01/2026 the following sterile CEPs: CEP 2018-146, Dihydrostreptomycin sulfate for veterinary use, Sterile and CEP 2019-246, Colistimethate sodium, Sterile

Additional comments
The GMP non-compliance applies to all sterile APIs and intermediates manufactured at site. However, since the deficiency classified as “critical” (Inadequate Endotoxin Control Strategy) and multiple deficiencies classified as “major” related to the quality assurance system of the site (process validation, cleaning validation and resulting risks to cross-contamination, change control management, preventive maintenance), it is considered by Swissmedic that all active substances manufactured on site using this quality system are potentially affected. This manufacturing site (LOC-ID LOC-100069397) is implied in the manufacturing of the following sterile APIs: CEP 2019-246, Colistimethate sodium, Sterile; Polymyxin B sulfate; Streptomycin sulfate sterile Swissmedic proposes to withdraw / modify the AEMPS Certificate ES/099HV/25 issued for the manufacturing site located at No. 50 Shengxhue Road (LOC-ID: LOC-100025368) which mentions in the footer this site LOC-ID LOC-100069397

2026-01-30

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

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