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保存年限:

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發文字號：FDA品字第1111106799號
速別：普通件
密等及解密條件或保密期限：
附件：原料藥廠違反GMP警訊乙份 (A21020000I_1111106799_doc1_Attach1.pdf)

主旨：有關義大利原料藥廠「Bioindustria Laboratorio Italiano Medicinali S.p.A.」經國際通報違反GMP乙案，詳如說明段，請轉知所屬會員知照。

說明：

一、義大利衛生主管機關Italian Medicines Agency於2022年9月1日查核義大利原料藥廠「Bioindustria Laboratorio Italiano Medicinali S.p.A.」（廠址：Via De Ambrosis 2-6, Novi Ligure, 15067, Italy」，判定嚴重違反GMP，並於2022年10月7日發布「STATEMENT OF NON COMPLIANCE WITH GMP」（詳如附件）。

二、鑑於上述原料藥廠之製造品質恐無法符合GMP之要求，可能導致對藥品製造品質帶來影響與危害，請轉知所屬會員釐清相關國產及輸台製劑產品是否使用上述原料藥廠所生產原料藥，並應依風險管理原則辦理相關後續處置。

正本：中華民國西藥商業同業公會全國聯合會、中華民國西藥代理商業同業公會、台北市西藥代理商業同業公會、中華民國開發性製藥研究協會、台灣藥品行銷暨管理協會、台灣製藥工業同業公會、中華民國學名藥協會、中華民國製藥發展協會

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Italian Medicines Agency

Report No: ***IT/NCR/API/02/2022***

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: ***Bioindustria Laboratorio Italiano Medicinali S.p.A.***
Site address: ***Via De Ambrosis 2-6, Novi Ligure, 15067, Italy***
OMS Organisation Id. / OMS Location Id.: ***ORG-100001870*** / ***LOC-100004325***

From the knowledge gained during inspection of this manufacturer, the latest of which was conducted on ***2022-09-01***, 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 Article 47 of Directive 2001/83/EC
- 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:
HYALURONIDASE(en)

Part 3

1.Nature of non-compliance:

The Company is manufacturing only the active substance Hyaluronidase, enzyme extracted from bovine testes. Almost all the API manufactured was utilized to produce in house Injectable medicinal products according to Art. 5 (1) of Directive 2001/83/EC. No Registration File/Marketing Authorization was submitted by any MAH. Concerns raised about the following: Risks of cross contamination between pre and post viral inactivation activities due to absence of HVAC systems. Furthermore, same equipment were utilized for both manufacturing steps. Failure to manage the containment during pre- viral inactivating acitivities: some operations were not performed in closed systems. Failure to manage cleaning activities: no contact time of inactivating agent (NaOH 1M) was validated for contact parts equipment. Only one washing room was available to clean equipment used for pre and post inactivation activities, finishing steps and storage of cleaned equipment. Failure to manage bovine testes' supplier validation: supplier was never audited. No risk assessment respect to viral safety was carried out for evaluation of risks related to manufacturing of active substance Hyaluronidase. No analytical testing for determination of eventual adventitious agents were performed on industrial batches but only laboratory testing were available. Suspension of the manufacturing authorisation No. API - 151/2021, issue date 2021/09/21. No Registration File/Marketing Authorization was submitted by any MAH.

Action taken/proposed by the NCA

Withdrawal, of current valid GMP certificate No. IT-API/154/H/2018
Withdrawal of current valid GMP certificate n. IT-API154/H/2018, issue date: 2018-09-05

Recall of batches already released
No active substance Hyaluronidase batches were released on the market for manufacturing medicinal products. Active substance Hyaluronidase was utilized to produce in house Injectable medicinal products according to Art. 5 (1) of Directive 2001/83/EC.

2022-10-07

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

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