

檔 號：  
保存年限：

## 衛生福利部食品藥物管理署 函

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發文字號：FDA風字第1051103081B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(A21020000I105110308101-1.pdf)

主旨：歐洲理事會EDQM通報印度原料藥廠「J P LABORATORIES P  
RIVATE LIMITED」(廠址：Block A-76, M. I. D. C. Chemi  
cal Zone Kurkumbh, Pune District India-413801 Daun  
d, Maharashtra) 嚴重違反GMP乙案，詳如說明段，請轉  
知所屬會員知照。

說明：

- 一、歐洲理事會European Directorate for the Quality of Medicines & HealthCare (EDQM) 併同義大利衛生主管機關Italian Medicines Agency (IMA) 查核旨揭原料藥廠，判定嚴重違反GMP，並於105年4月29日正式發布「DECISION TO WITHDRAW A CERTIFICATE OF SUITABILITY」，註銷(WITHDRAW)「Isosorbide Mononitrate, diluted 80% in lactose」之品質證明(CERTIFICATE OF SUITABILITY R1-CEP 2002-104-Rev 02)。(詳如附件)
- 二、義大利IMA亦於105年4月14日發布「STATEMENT OF NON-COMPLIANCE WITH GMP」，受影響之原料藥品項包括「Isosorbide Mononitrate, diluted (80% in lactose)」等

共11項。(詳如附件)

三、承上，且義大利IMA已啟動相關後續處置，包括：評估使用受影響原料藥之製劑產品是否回收，及是否有可替代之原料來源與缺藥疑慮；鑒於該廠違反GMP，已入庫之該廠原料藥，製劑廠應重新執行完整再驗程序。

四、鑒於旨揭原料藥廠之製造品質無法符合GMP之要求，可能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輸台製劑產品是否使用旨揭原料藥廠所生產原料藥，並應依說明段三所述辦理。

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、中華民國藥品行銷暨管理協會

副本：

## 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<sup>1</sup>*

### 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: ***J P LABORATORIES PRIVATE LIMITED Block A-76***

Site address: ***M.I.D.C. Chemical Zone Kurkumbh, Pune District, Daund, Maharashtra, 413801, India***

From the knowledge gained during inspection of this manufacturer, the latest of which was conducted on ***2016-03-16***, 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 .

<sup>1</sup> *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**

<b>1 NON-COMPLIANT MANUFACTURING OPERATIONS</b>	
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;	
<b>1.4</b>	<b>Other products or manufacturing activity</b>
	1.4.1 <i>Manufacture of</i> 1.4.1.4 Other: Active substances(en)

Manufacture of active substance. Names of substances subject to non-compliant :

***ISOSORBIDE MONONITRATE, DILUTED (80% IN LACTOSE)(en)***

<b>3. NON-COMPLIANT MANUFACTURING OPERATIONS - ACTIVE SUBSTANCES</b>	
Active Substance : ISOSORBIDE MONONITRATE, DILUTED (80% IN LACTOSE)	
<b>3.1</b>	<b>Manufacture of Active Substance by Chemical Synthesis</b>
	3.1.3 Salt formation / Purification steps : Crystallisation
<b>3.5</b>	<b>General Finishing Steps</b>
	3.5.1 Physical processing steps : Drying, sifting 3.5.2 Primary Packaging (enclosing / sealing the active substance within a packaging material which is in direct contact with the substance) 3.5.3 Secondary Packaging (placing the sealed primary package within an outer packaging material or container. This also includes any labelling of the material which could be used for identification or traceability (lot numbering) of the active substance)
<b>3.6</b>	<b>Quality Control Testing</b>
	3.6.1 Physical / Chemical testing 3.6.2 Microbiological testing excluding sterility testing

**Part 3**

<b>1. Nature of non-compliance:</b>
28 deficiencies were raised by the inspectors, 9 of them classified as "Major" in the following areas: - Quality management - integrity and security of data in the quality system (1); - Personnel (2) - Building and facilities (1) - Materials management (1) - Production and In-Process control (1) - Laboratory control - integrity and security of analytical data (1); - Validation: equipment qualification (1) - Change control (1) The extent and severity of the findings, in combination with the repeated negative inspection outcome, demonstrates the inability of the company to sustain an acceptable GMP compliance level, and constitutes a critical risk for public health.
<b>Action taken/proposed by the NCA</b>
<b>Recall of batches already released</b>
Each involved NCA should evaluate, following assessment conducted in conjunction with MAHs, if a recall of medicinal product is needed. Evaluation should take into account if there are alternative suppliers and potential risk of shortage. Given the nature of non-compliance, assessment should include a complete retest of all imported batches of active substance.

**Prohibition of supply**

Prohibition of supply is recommended, unless there are not alternative suppliers and there is a risk of shortage.

**Suspension or voiding of CEP (action to be taken by EDQM)**

CEP was withdrawn.

**Others**

The observed deficiencies are considered to apply to all other active substances manufactured at the same site (Isosorbide Mononitrate Pure, Isosorbide Mononitrate Diluted 90%, Isosorbide Mononitrate Diluted 70%, Isosorbide Mononitrate Diluted 60%, Isosorbide Mononitrate Diluted 50%, Isosorbide Mononitrate Diluted 40%, Isosorbide Mononitrate Diluted 20%, Isosorbide Mononitrate Diluted 25%, Isosorbide Dinitrate Diluted 40%, Isosorbide Dinitrate Diluted 25%).

2016-04-14

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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