檔　　號：
保存年限：

衛生福利部食品藥物管理署　函

地址：11561 臺北市南港區昆陽街161-2號
聯絡人：蘇子婷
聯絡電話：0227877148
傳真：0227877178
電子信箱：daisyhaha@fda.gov.tw

受文者：中華民國西藥代理商業同業公會

發文日期：中華民國105年7月19日
發文字號：FDA風字第1051103881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(A21020000I105110388100-1.pdf)

主旨：歐洲理事會European Directorate for the Quality of Medicines & HealthCare（EDQM）通報中國原料藥廠「Hebei Dongfeng Pharmaceutical Co., Ltd」（廠址：Ming jiao Road Western Yongnian County, China-057 150 Handan City, Hebei Province）嚴重違反GMP乙案，詳如說明段，請轉知所屬會員知照。－

說明：

一、EDQM併同羅馬尼亞衛生主管機關National Agency for Medicines and Medical Devices（NAMMD）查核旨揭原料藥廠，判定嚴重違反GMP，並於103年8月12日正式發布「DECISION TO SUSPEND A CERTIFICATE OF SUITABILITY」，凍結（SUSPEND）「DOXYCYCLINE HYCLATE」及「DOXYCYCLINE MONOHYDRATE」共2個原料藥品項之CERTIFICATE OF SUITABILITY（CEP）品質證明文件2年，待再次通過查廠後始得恢復。因前述處置將屆滿2年，EDQM已於105年6月28日發布旨揭工廠「WITHDRAWAL OF CERTIFICATES OF SUITABILITY」，吊銷（WITHDRAW）上述2個品項之CEP證明文件

。

二、羅馬尼亞NAMMD亦於103年8月25日發布「STATEMENT OF NON-COMPLIANCE WITH GMP」，受影響之原料藥品項包括「DOXYCYCLINE HYCLATE」、「DOXYCYCLINE MONOHYDRATE」等共7項。（詳如附件）

三、承上，且羅馬尼亞NAMMD已啟動相關後續處置，包括：

(一)使用旨揭藥廠之原料藥者，應考慮變更原料來源（Variation of the marketing authorisations）。

(二)旨揭藥廠原料藥應暫停出貨。

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：電2015-02-19 交13:08:37章

National Agency for Medicines and Medical Devices

Report No: *NCF/010/RO*

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 Romania confirms the following:
The manufacturer: ***HEBEI DONGFENG PHARMACEUTICAL Co., Ltd***
Site address: ***Mingjiao Road Western Yongnian County, Handan, 057 150, China***

From the knowledge gained during inspection of this manufacturer, the latest of which was conducted on ***2014-07-07*** , 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;	
1.2	**Non-sterile products**
	1.2.1 Non-sterile products (processing operations for the following dosage forms) 1.2.1.17 Other: Active substances(en)

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

3. NON-COMPLIANT MANUFACTURING OPERATIONS - ACTIVE SUBSTANCES	
Active Substance : DOXYCYCLINE HYCLATE	
3.1	**Manufacture of Active Substance by Chemical Synthesis**
	3.1.1 Manufacture of active substance intermediates 3.1.2 Manufacture of crude active substance 3.1.3 Salt formation / Purification steps :
3.5	**General Finishing Steps**
	3.5.1 Physical processing steps : 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)
3.6	**Quality Control Testing**
	3.6.1 Physical / Chemical testing
Active Substance : DOXYCYCLINE MONOHYDRATE	
3.1	**Manufacture of Active Substance by Chemical Synthesis**
	3.1.1 Manufacture of active substance intermediates 3.1.2 Manufacture of crude active substance 3.1.3 Salt formation / Purification steps :
3.5	**General Finishing Steps**
	3.5.1 Physical processing steps : 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)
3.6	**Quality Control Testing**
	3.6.1 Physical / Chemical testing

4. Non-Compliant Other Activities - Active Substances :
Other activities on-site: APIs: Metacycline hydrochloride, Azithromycin, Roxithromycin, Clarithromycin, Calcium acetate. Many oral solid preparations (tablets, granules, capsule).

Part 3

1. Nature of non-compliance:
26 deficiencies were found during inspection; out of these 6 was rated as Major related to: 1) weak and not fully implemented Quality Assurance system; 2) documentation management; 3) material management and qualification of the approved supplier; 4) risk of contamination in the production area; 5) risk of contamination and cross-contamination of testing samples; 6) data recording and integrity in the QC laboratory
Action taken/proposed by the NCA **Requested Variation of the marketing authorisation(s)** - **Prohibition of supply** - **Suspension or voiding of CEP (action to be taken by EDQM)** -
Additional comments Known customers Doxycycline hyclate: Sintofarm, Industria, P.S.P. ,Chemifarma, Zetercoop Italy; Ofichem, ORFFA, ALC Netherlands; Divasa Spain; Wins Czech Republik, Remedica Cyprus, Farmabase Brasil, Many others in rest of the world Doxycycline monohydrate: only local market Finished dosage forms: only local market

2014-08-25

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

---

Confidential
National Agency for Medicines and Medical Devices
Tel: *Confidential*
Fax: *Confidential*