檔　　號：
保存年限：

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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(A21020000I105110391600-1.pdf)

主旨：歐洲理事會European Directorate for the Quality of Medicines & HealthCare（EDQM）通報印度原料藥廠「Wockhardt Limited」（廠址：Plot No. L-1, M.I.D.C. Area Chikalthana, India 431 210 Aurangabad, 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、英國衛生主管機關Medicines and Healthcare Products Regulatory Agency（MHRA）查核旨揭原料藥廠，判定嚴重違反GMP，EDQM正式發布「DECISION TO SUSPEND A CERTIFICATE OF SUITABILITY」，凍結（SUSPEND）「OXYBUTYNIN HYDROCHLORIDE」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另於105年6月28日發布旨揭工廠「WITHDRAWAL OF CERTIFICATES OF SUITABILITY」，吊銷（WITHDRAW）上述品項之CEP證明文件。

二、英國MHRA亦於104年1月16日發布「STATEMENT OF NON-COM

PLIANCE WITH GMP」（詳如附件），所有該廠製造之原料藥品項皆受影響。

三、承上，且英國MHRA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)英國MHRA未啟動回收作業，仍建議使用受影響原料藥之產品應評估是否回收。

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

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Medicines and Healthcare Products Regulatory Agency

Report No: *UK API 8913 Insp GMP 8913/18322-0006 - NCR*

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 United Kingdom confirms the following.
The manufacturer: ***WOCKHARDT LIMITED***
Site address: ***L-1, MIDC, JALGAON ROAD, CHIKALTHANA, AURANGABAD, IN-431 210, India***

From the knowledge gained during inspection of this manufacturer, the latest of which was conducted on ***2013-11-15*** , 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
- 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

Human 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 1.4.1.4 Other: Active starting materials (See part 3 for more details)(en)

4. Non-Compliant Other Activities - Active Substances :
All active substances manufactured at this facility

Part 3

1. Nature of non-compliance:
1. A critical deficiency was cited with regards to data integrity of GMP records, entries were seen to be made when personnel were not present on site, documentation was seen that was not completed contemporaneously despite appearing to be completed in this manner. 2. A second critical deficiency was cited regarding potential product contamination, this included the use of inappropriate materials close to product e.g. asbestos coated PTFE seals for centrifuge manways. 3. A major deficiency was cited with regards to equipment and facility, maintenance, design and qualification. Examples included, inappropriate pressure differentials that were not in line with the original design but had not been changed using change control, cleaning validation that was not sufficiently robust to confirm cleaning practices and maintenance issues, such as the failure to spark test glass lined reactor vessels for integrity especially following maintenance.
Action taken/proposed by the NCA **Requested Variation of the marketing authorisation(s)** Marketing Authorisation Holders should be requested to remove the site from applicable authorisations by variation **Recall of batches already released** No recall action is proposed.
Additional comments The initial statement of serious non-compliance permitted continued supply of critical APIs. Following a company decision to cease supply of API to the EU market, this statement of non-compliance was updated to cover all active substances in January 2015. Re-inspection by an EU national; competent authority will be required prior to gaining approval to supply the EU market in future.

Products manufactured at site, if known	**Products**	**Dosage Form**	**Reference Member State, National or EMA**
Human Medicinal Products	Captopril		CEP 1998-052
	Oxybutynin HCl		CEP 2003-020
	Pramipexole Dihydrochloride monohydrate		CEP 2012-149

2015-01-16

Name and signature of the authorised person of the Competent Authority of United Kingdom

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