NOTIFICATION TO THE CHMP/EMA SECRETARIAT OF A REFERRAL UNDER ARTICLE 31 OF DIRECTIVE 2001/83/EC
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This notification is a referral under Article 31 of Directive 2001/83/EC to the CHMP made by the European Commission:

Procedure name	Pharmaceutics International, Inc (PII)
Product Names	See Annex I

The European Medicines Agency (EMA) has been informed that on 15 June 2016, the Medicines and Healthcare Products Regulatory Agency (MHRA), the supervisory authority in the United Kingdom, issued Good Manufacturing Practice (GMP) Non-compliance Statements for the manufacturer Pharmaceutics International, Inc., located in Maryland, USA.

The MHRA inspected the above mentioned sites in June 2015 and several deficiencies were identified. A follow-up inspection was recommended to review the implementation of the agreed corrective and preventive measures.

The follow-up inspection, conducted jointly by the MHRA and the US FDA in February 2016, found that the corrective and preventive measures had not been appropriately implemented and that critical and major GMP deficiencies remained.

The following deficiencies were identified:

- Critical deficiencies relating to the failure of organisational and technical measures to minimise the risk of cross-contamination between hazardous and non-hazardous products manufactured in the same manufacturing facilities using shared equipment, as well as failures of the quality unit to ensure the effective operation of the quality system;

- Major deficiencies relating to organisational data governance failures, sterilisation and depyrogenation processes, and insufficient control of aseptic operations to provide the required level of sterility assurance.

Following the GMP non-compliance statement, the supply of the medicines is now restricted in the EU. Recall of products is recommended and future batches will no longer be supplied from this site unless they are considered to be critical to public health.
EMA is asked to assess the potential impact of the deficiencies on the quality, safety and the benefit risk balance of the medicinal products which have been authorised by the European Commission and the Member States.

In view of the elements described above and the necessity to take action at EU level, the European Commission (EC) considers that it is in the interest of the Union to refer the matter to the Committee for Human Medicinal Products (CHMP), and requests that it gives its opinion under Article 31 of Directive 2001/83/EC as to whether marketing

authorisations of the medicinal products that include the above mentioned sites should be maintained, varied, suspended, or revoked.

[redacted]

Robert Vanhoorde
Head of Unit
"Medicines: policy, authorisation and monitoring"

Date: 17 June 2016