EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

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CHMP List of questions

To be addressed by the marketing authorisation holders of medicinal products for which Pharmaceutics International Inc, Maryland, USA, is included in the marketing authorisation as manufacturing site.

Referral under Article 31 of Directive 2001/83/EC

Procedure number: EMEA/H/A-31/1444

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1. Background

The manufacturing facilities of Pharmaceutics International Inc., located in Maryland, USA, were inspected last in February 2016 by the United Kingdom and the US FDA and found to be not compliant with the legal requirements and/or the principles and guidelines of GMP as provided for by Union law. Consequently, the GMP certificate was withdrawn for this manufacturer.

Following the GMP non-compliance statement, the supply of the medicines manufactured at this site is now restricted in the EU. Recall of products is recommended and further batches will no longer be supplied from this site unless they are considered to be critical to public health.

2. Questions

The marketing authorisation holders (MAHs) of medicinal products for which Pharmaceutics International Inc is included in the marketing authorisation are requested to address the following questions:

Question 1

In relation to their products manufactured at this site, the MAHs should provide in the annexed table information on type of marketing authorisation, marketing and legal status, and an overview of the approved indication(s).

Question 2

The MAHs should discuss the potential impact of the findings as outlined in the Statement of Non-Compliance with GMP of Pharmaceutics International Inc. facilities, on the benefit-risk balance of your product. As part of this discussion the MAHs should provide a detailed assessment of any safety reports or complaints that may have been collected and related to the GMP non-compliance findings identified.

Question 3

The MAHs are requested to provide details including timelines of the steps that have been taken or they intend to undertake to ensure that the manufacturing of their product will be manufactured in a GMP compliant facility again. This should include any steps that have been or that will be taken by the Qualified Person(s) at the EEA site(s) responsible for the certification of the finished product, in relation to ensuring compliance with GMP.

The action plan should take account that the restricted GMP certificate permitting release of critically medical products that has been issued is valid until June 2017.

The MAHs should specify corrective measures being already implemented by the current manufacturer for each of their concerned product.

Question 4

A list of batches currently in-date and available on the EU market should be presented and indicate to which EU national markets these batches are distributed. It should be clarified by the MAHs if after the issue of the Statement of Non-Compliance with GMP on 15 June 2016 they were instructed by any National Competent Authorities to recall their products manufactured by Pharmaceutics International Inc.

The MAHs should also indicate the number of patients currently being treated per each EU member state including forecasted demand rates and estimated stock out date, as applicable. The MAHs should

also indicate alternative treatment options per each member state in case there are no other manufacturing facilities.

Question 5

In case a shortage is foreseen, the MAHs should provide the information on the following:

- anticipated shortage dates, duration and communication action plan for each member state;
- number of patients currently being treated per EU member state;
- any on-going clinical trials that would be affected by the shortage;
- specific or vulnerable sub-populations that should be treated with the product, which should receive priority treatment.
- whether there is any patient population(s) for whom there is no other treatment option available.
- where applicable, the MAHs should indicate recommendations on how to switch treatment specifying the situation for each member state.

The MAHs should discuss the need and feasibility of stock rotation between Member States and any other measure needed.

Question 6

In cases where a product manufactured by Pharmaceutics International Inc. is not deemed to be a critical medicinal product in a Member State following consultation with the relevant Competent Authority of that country, and where a recall action is going to be carried out in line with the Statement of GMP Non-compliance, the relevant MAHs should comment on the level of the recall action within that Member State which it considers appropriate, based on patient risk considerations (i.e. recall to pharmacy/clinic level, recall to patient level, etc.).

Annex

Question 1

INN	Product name	Type of marketing authorisation	Marketing and legal status	Indications