EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

10 January 2017
EMA/INS/GMP/18696/2017

Dear Sir/Madam,

Subject: **Required information regarding intermediate heparin manufacturing sites used for medicinal products containing heparin or low molecular weight heparins and their derivatives**

This letter is being sent to all Marketing Authorization Holders of medicinal products containing unfractionated heparin or low molecular weight heparin, as well as their derivatives, registered in the EU.

In order to strengthen supervision of the supply chain of heparin and heparin derivate biological active substances, the CMDh in collaboration with the EEA GMP/GDP Inspectors Working Group and the EMA is collating information regarding manufacturing sites involved in intermediate heparin manufacturing sites.

In this context, you are being asked to provide the following information for the medicinal products as listed in the attached Annex I:

- A current list of all manufacturers involved in the manufacturing process of the active substance, starting from the pooled intestinal porcine mucosa (slaughterhouses/abattoirs not included), including all intermediate heparin manufacturers (such as resin bound heparin, partly purified crude heparin or heparin sodium/calcium) up to the manufacturer of the final active substance.

The list should be provided in form of "QP declaration" (EMA/196292/2014), according to the relative guide-line EMA/196292/2014 (Guidance for the template for the qualified person's declaration concerning GMP compliance of active substance manufacture - The QP declaration template).

http://www.ema.europa.eu/ema/index.jsp?curl=pages/regulation/general/general_content_000696.jsp&mid=WC0b01ac0580028bfd

Please note that intermediate manufacturers are often referred to as "raw" or "crude" heparin suppliers in the registration dossier, but since this terminology may vary in the different dossiers, you are kindly requested to provide the a.m. information regardless how they are called in each dossier, according to the guide-line EMA/CHMP/BWP/429241/2013 *"Use of starting materials and intermediates collected from different sources in the manufacturing of non-recombinant biological medicinal products"*. If information is missing from the dossier, you are requested to present appropriate variation(s) to update this part of the dossier accordingly, as soon as possible, and anyway, but no later than 6 months from the present date.

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An agency of the European Union

You are kindly requested to provide this information within 1 month of this letter being sent to you to the following e-mail address: GMPINS@ema.europa.eu

Please do not hesitate to contact me if you have any queries or comments.

Yours sincerely,

Andrei Catalin Spinei

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