Date: 14 May 2009 BY E-MAIL
Ref: QOTF 09020 heparin@usp.org

The United States Pharmacopoeial Convention
12601 Twinbrook Parkway
Rockville, Maryland 20852–1790
USA

SUBJECT: USP MONOGRAPH FOR HEPARIN

Dear Madam/Sir,

The Plasma Protein Therapeutics Association (PPTA) is the trade association and standards-setting organization of the world's major producers of plasma derived and recombinant analogue therapies. PPTA members (Baxter, Biotest, CSL Behring, Grifols, Kedrion, Octapharma, Talecris) provide the majority of the world's needs for plasma protein therapies. Our member companies are committed to assuring the safety, availability and affordability of these vital life-sustaining and saving therapies.

We appreciate the joint effort of the European and US Pharmacopoeias to develop harmonized approaches pertaining to plasma protein therapies and have actively participated in the two Symposiums dedicated to this task. However, PPTA member companies were very disappointed about the proposed revision of the USP monograph for heparin, which seems to move away from a harmonized approach by not taking the previous discussions during the two Symposiums into account.

We do not see any benefit in adding several new methods for identifying the same impurities. NMR and CE (as implemented last year into both USP and EP) are sufficiently able to identify impurities of OSCS. Dermatan sulfate is a naturally occurring component of heparin products present in variable percentages. The pharmacological and safety profile of dermatan sulfate is well known and similar to heparin (see references). In our view there is neither a scientific justification for the introduction of a limit for dermatan sulfate by some of the proposed new methods nor for the requirement to perform multiple tests for the same components/impurities.

CE as well as HPLC, and anti-factor Xa to anti-factor IIa ratio, but also the hexosamine analysis are all targeting the purity of heparin with respect to OSCS and/or dermatan sulfate. We do not believe that the requirement for 4 different methods (including NMR) does add any additional information. A total of 5 methods (including CE from the EP) would be necessary to identify only two substances in order to meet both EP and USP. Tests for protein and nucleotidic impurities are already included in the EP monograph. We would like to understand why especially for the protein impurities a totally different method is used and not the same method as EP contains already. Any new test, where USP wants to include a certain parameter which is already contained in EP, should be accepted just from the other pharmacopoeia.

We would respectfully like to propose to discuss these issues at the upcoming EP USP Symposium scheduled for end of July 2009, to avoid unnecessary duplications and develop a truly harmonized approach in the interest of patients in need for these often life-saving therapies in all parts of the world.

Yours sincerely

Dr. Ilka von Hoegen
Senior Director, Quality and Safety

Cc: Dr. Jean-Marc Spieser, EDQM

References:

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