US Pharmacopeia announces revised heparin monographs and reference standards

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Standards updated in response to public health threat associated with blood-thinning drug's adulteration with over-sulfated chondroitin

The U.S. Pharmacopeial (USP) Convention announces that revised monographs for heparin sodium and heparin calcium in the United States Pharmacopeia (USP) are now available and official on the USP Web site. The revised monographs are accompanied by two new and two updated official USP Reference Standards. These public standards allow any party—and particularly the Food and Drug Administration (FDA) and manufacturers—to test heparin sodium and calcium drug substances to assure their quality. All drug manufacturers who market heparin in the United States are required to meet these newly revised standards. The heparin monographs were updated in the interest of public health following the deaths of more than 200 people earlier this year. These deaths are suspected to have resulted from the adulteration of the blood thinner with over-sulfated chondroitin, which is derived from the chemical chondroitin and used in dietary supplements.

The two heparin monographs are posted on the USP Web site at www.usp.org/hottopics/heparin.html?hlc. These revisions mark the end of the first stage (Stage 1) of a multi-stage process to revise the monographs. The Stage 1 revision was intended to rapidly address the immediate public health crisis associated with the drug and help ensure an unadulterated supply of heparin by taking proposed methods from the FDA and improving their robustness. The second stage of revision (Stage 2) will seek out additional methods to test for over-sulfated

chondroitin and other potential contaminants in heparin. USP co-sponsored a meeting June 19-20, 2008, in Strasbourg, France, with the European Directorate for the Quality of Medicines (the organization that elaborates the European Pharmacopoeia) and the United Kingdom's National Institute for Biological Standards and Control as part of a coordinated, worldwide effort to assure the quality and purity of heparin.

"The expedited revision of USP's heparin standards gives manufacturers, health care practitioners and patients increased confidence that this widely used drug is free of this adulterant," said Roger L. Williams, M.D., USP executive vice president and CEO. "The monograph revisions were completed quickly to alleviate a major public health concern; they were accomplished through USP's established, transparent, and scientific process. In updating the standards, USP received guidance not only from the FDA but also from the volunteer experts on USP's Heparin Advisory Panel and USP's Blood and Blood Products Expert Committee, which concluded the monograph standards, and USP's Reference Standards Committee, which endorsed the physical standards. USP thanks these colleagues and the many other national and international experts who assisted the USP Council of Experts' Expert Committees and Advisory Panel and worked with us to meet this extremely important challenge."

USP publishes official quality standards for medicines in the United States Pharmacopeia–National Formulary (USP–NF) and has worked with FDA for more than 100 years in a unique public-private partnership that helps to assure the quality of medicines in the United States. The availability of a good public monograph in the USP–NF along with allied reference materials is one of a series of safety nets that help assure that U.S. patients and practitioners have access to good quality medicines.

"While USP monographs are generally designed to test for known impurities that may result from the manufacturing process or

degradation, and not for unknown contaminants that may be added either accidentally or deliberately, we were pleased to modify our standards to help alleviate patient danger associated with the heparin product and will continue to explore methods for detecting potential contaminants," Dr. Williams noted.

Source: US Pharmacopeia