



## PIC QUESTION OF THE WEEK: 4/19/10

Q: What is the significance of the recent FDA announcement regarding decreased heparin potency?

A: During the period from 2007 through mid-2008, the FDA received hundreds of reports of adverse effects and multiple fatalities associated with the use of heparin. After an extensive investigation, it was discovered that a major foreign supplier of bulk heparin was distributing a product contaminated with excessive amounts of over-sulfated chondroitin sulfate (PIC Question of the Week - June 17<sup>th</sup>, 2008). This resulted in a revised United States Pharmacopeia (USP) monograph that provided a new reference standard and more stringent assay methods capable of detecting minute amounts of impurities. Recent studies indicate that *new heparin* also has an approximate 10% decrease in anticoagulant activity compared to previous formulations. The USP has stated that this decrease in activity will equalize the difference in potency that has existed for years between heparin products available in the United States and those produced in foreign countries. An April 7<sup>th</sup>, 2010 FDA announcement stated that the 10% decrease in potency is likely to have little clinical significance largely due to the highly variable inter- and intra-patient response seen with heparin dosing. Studies requested by the FDA demonstrated large individual variation in activated partial thromboplastin time (aPTT) and relatively unpredictable responses to a specific dose of heparin. Consequently, in a clinical setting, the aforementioned 10% decrease in potency may not be reflected in the results of an aPTT or an activated clotting time (ACT). The FDA recommends that practitioners continue to use clinical judgment and close monitoring of patients receiving *new heparin*. The FDA does, however, identify three clinical scenarios in which dosage adjustment and intense monitoring may be beneficial due to the need for more intense anticoagulation. These include extracorporeal membrane oxygenation in pediatric patients; cardiopulmonary bypass; and treatment or prevention of life threatening thrombosis. The production of *new heparin* began in October, 2009 and there will be supplies of both *new* and *old* formulations for an indefinite period. In order to differentiate these products, manufacturers are placing distinguishing marks (see below) on the actual product label.

- *New* heparin from APP and B.Braun will be marked with an “N” after the expiration date
- *New* Hospira heparin will have lot numbers that begin with “82” or higher
- *New* Baxter heparin will have an “N” that will appear before the lot number.

Healthcare professionals should be aware of the new USP assay requirements and labeling of heparin products.

### References:

- Food and Drug Administration. FDA Drug Safety Communication. Update: follow up to the public health alert about changes to the heparin sodium USP monograph. <http://www.fda.gov/Drugs/DrugSafety/PostmarketDrugSafetyInformationforPatientsandProviders/ucm207506.htm>. Accessed April 12, 2010
- United States Pharmacopeia. Revision Bulletin. Heparin. <http://www.usp.org/USPNF/notices/heparinRB20090828.html>. Accessed April 13, 2010.

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**The PIC Question of the Week is a publication of the Pharmaceutical Information Center, Mylan School of Pharmacy, Duquesne University, Pittsburgh, PA 15282 (412.396.4600).**