



BAXTER PROVIDES UPDATE ON HEPARIN INVESTIGATION

- I. **Baxter tests confirm that over-sulfated chondroitin sulfate, the contaminant found in adulterated heparin, can cause hypotensive reactions.**
- II. **Baxter tests show NO unusual adverse reactions associated with unadulterated heparin.**
- III. **Baxter updates number of fatalities potentially associated with an allergic reaction, though no fatalities have been confirmed by medical evidence to be caused by allergic reactions to Baxter heparin.**

DEERFIELD, Ill., April 21, 2008 – Baxter is providing an update on several advances related to the investigation into recent heparin adverse reactions associated with the company's U.S. vial-based heparin products, which have since been recalled.

- I. **Baxter tests confirm that over-sulfated chondroitin sulfate, the contaminant found in adulterated heparin, can cause hypotensive reactions.**

Baxter scientists have provided biological test results to the U.S. Food and Drug Administration (FDA) confirming that over-sulfated chondroitin sulfate, the contaminant found in adulterated raw heparin, can cause hypotensive reactions. They focused on hypotension (low blood pressure) because it was the most common adverse event reported to Baxter regarding heparin.

Using animal models, Baxter scientists found consistent, prolonged declines in blood pressure resulting from exposure to over-sulfated chondroitin sulfate. They found the same results from exposure to heparin contaminated with over-sulfated chondroitin sulfate. The hypotensive response was dose-dependent; increased amounts of the over-sulfated chondroitin or the contaminated heparin led to greater decreases in blood pressure.

The scientists tested heparin with contamination levels of up to 20 percent, which mirrors the levels found in the lots of heparin associated with adverse events prior to the recall of Baxter heparin. The scientists were able to repeat and confirm their findings, a standard of proof of validity in scientific research.

“These tests show that significant doses of the over-sulfated chondroitin sulfate do induce a rapid loss of blood pressure,” said Norbert Riedel, Ph.D., Baxter’s corporate vice president and chief scientific officer. “That means that the contaminant, which was introduced at the workshop or consolidator level, before it reached our API supplier and before it reached Baxter, is likely the cause of the increased adverse reactions to the heparin.”

Chondroitin sulfate is a molecule that occurs naturally and is a major component of cartilage – the tough, connective tissue that cushions the joints. Chondroitin sulfate is a common, biologically derived material that is sold in oral form as a dietary supplement. The substance found in the affected lots of heparin API is not a naturally occurring substance, but the hypersulfated version of chondroitin sulfate, which means that it has been chemically modified, resulting in a more heparin-like molecule.

But Riedel cautioned that while causation is now confirmed, other factors may also impact patients’ response to the contaminated heparin, which may explain why the adverse event rate was so low given the huge number of patients who received Baxter heparin when it was on the market.

“A reaction to contaminated heparin could also depend on the patient’s particular physiology, underlying medical conditions, such as heart disease, different medications being administered to the patient, or the dose and volume of the heparin they received,” said Riedel.

Baxter scientists are still searching to understand the mechanism of causation, to define what exactly happens in the body to cause the drop in blood pressure.

II. Baxter tests show NO unusual adverse reactions associated with unadulterated heparin.

Since the start of the investigation, Baxter has analyzed and eliminated hundreds of variables associated with the product as potential causes or variables. Baxter scientists have conducted dozens of biological and analytical tests to determine if the company’s unadulterated heparin would trigger adverse events. That animal testing has shown no unusual adverse reactions to unadulterated Baxter heparin.* These findings are consistent with those announced on April 21 by the FDA.

III. Baxter updates number of fatalities potentially associated with an allergic reaction, though no fatalities have been confirmed by medical evidence to be caused by allergic reactions to Baxter heparin.

At this point in time, neither Baxter nor the (FDA) has confirmed that reactions to Baxter's heparin have caused any fatalities.

Baxter has now determined that there are five cases (one more than Baxter was previously aware of) in which patients received Baxter heparin and suffered a reaction to heparin that may have contributed to the adverse outcome, though there is not yet enough medical data available to draw a firm conclusion that the reaction caused the death.

In each of these cases, the patient had multiple, complex medical conditions, and had either undergone, or were in the process of undergoing, invasive cardiac surgery. The company has received more than 800 heparin-related adverse reaction reports to date.

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