Heparin Recall: Another Crisis for China & the FDA

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Heparin is an anticoagulant drug, commonly called a “blood thinner,” that has been widely used by health care providers since the 1930s to prevent blood clots from forming in high risk patients. It is often used on patients following surgery, those on dialysis, or for those who may be bedridden for a period of time. The development of blood clots can lead to serious and even deadly complications, including heart failure or pulmonary emboli. Thus, the use of heparin is an integral part of patient treatment.

Heparin is injected into the patient’s blood stream intravenously, often with a large initial dose called a “bolus.” This bolus dose, manufactured in multiple dose vials, has been linked to at least 81 deaths and hundreds of serious adverse events in the United States since late 2007. In December of 2007, the FDA posted a press release from AM2 PAT, Inc, a health care technology company, announcing a nationwide recall of one lot of pre-filled heparin lock flush solution because the syringes were contaminated with *Serratia marcescens*, which causes serious bacterial infections in patients. AM2 PAT, Inc. distributed heparin under two brand names: Sierra Pre-Filled, Inc. and B. Braun Medical, Inc. On January 18, 2007, the FDA announced a nationwide recall of all AM2 PAT and B. Braun lots and sizes of pre-filled heparin syringes. On January 25, 2008, Baxter International, Inc. recalled nine lots of its heparin injection and multi-dose vials and on February 11, 2008, Baxter announced it had temporarily stopped manufacturing the vials because its product had been linked to severe allergic reactions in patients. By the end of February, Baxter recalled all remaining lots of heparin. Half of the U.S. supply of heparin comes from Baxter.

During the flurry of recalls, the FDA conducted a frantic investigation into the source of the contamination. A link was finally established—the source of the “bad” heparin components was

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China. The concern about Chinese manufacturing of heparin spread beyond the U.S. as European authorities announced similar allergic reactions occurring linked to heparin manufactured by a German company. Companies in Japan and Germany then recalled their heparin products. But still no one was sure what was causing the contamination or how it was occurring.

On March 6, 2008, the FDA announced the raw components of heparin that had been manufactured in China “contained a possibly counterfeit ingredient that mimicked the real drug.” Most alarming, the FDA acknowledged it did not know if the introduction of this counterfeit ingredient was accidental or deliberate. On March 14, 2008, the FDA said that all heparin imports would be stopped at the U.S. border and inspected for contaminants.

On March 19, 2008, the FDA reported that the contaminant found was “likely made in China from animal cartilage, chemically altered to act like heparin, and added intentionally to batches of the drug’s active ingredient.” The implication was that the Chinese plant had intentionally used a man-made counterfeit ingredient in order to make heparin more cheaply. This ingredient was identified as over-sulfated chondroitin sulfate. Chondroitin sulfate, a naturally occurring substance, is made from animal cartilage and can be found in supplements that treat joint pain. But oversulfated chondroitin sulfate is a modified form of the mineral that mimics heparin’s active ingredient. This is why the counterfeit ingredient was not caught by routine tests.

According to Baxter, China now provides the majority of the world’s heparin supply. The raw ingredient of heparin is made from pig intestines. Four years ago, an American company, Scientific Protein Laboratories, which processes heparin ingredients and supplies them to B. Braun and Baxter, opened a plant in China, where there was a larger supply of pigs than in the U.S. and Canada. It is this plant, in Changzhou, China, that has been linked to the heparin

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9 Japsen, supra, note 7.
12 Id.
16 Goldstein, supra note 14.
18 Harris & Bogdanich, supra note 11.
containing the counterfeit ingredient.\textsuperscript{20} Chinese officials admitted that its drug agency had not inspected this plant, which is a chemical company, and had not certified it to make pharmaceutical products.\textsuperscript{21} Although the plant was supplying heparin components for years to American heparin manufacturers, the FDA did not inspect it until February 2008, after the problems began.\textsuperscript{22} Once the inspection took place, it was found that the plant was using materials from an “unacceptable vendor” and failing to “identify impurities and deficiencies”\textsuperscript{23} and that the contaminant was found in more than half the lots.\textsuperscript{24}

The FDA admitted that the failure to inspect the Chinese plant was a violation of its own policies.\textsuperscript{25} There are approximately 700 drug plants in China, and the FDA has only inspected 10-20 each year.\textsuperscript{26} In fact, if the FDA continued to inspect foreign drug plants at its current rate, it would take 13 years to inspect them all.\textsuperscript{27} The failure to inspect these types of plants in China has been called a “regulatory void” that has been difficult to fill because Chinese chemical companies do not fall under the jurisdiction of China’s drug agency.\textsuperscript{28} In early April, China reversed itself and announced it had begun more closely regulating heparin producers.\textsuperscript{29} A few weeks later, Chinese officials expressed doubt that the contaminant found in heparin manufactured in China actually caused any deaths, and insisted it be allowed to inspect the American facilities that finalized the product.\textsuperscript{30} In the meantime, the FDA is scrambling to place permanent inspectors in China, although it has yet to get permission from the Chinese government, and there is an impending nationwide shortage of heparin.\textsuperscript{31} Most recently, the FDA has expanded the warning to manufacturers and distributors of heparin-coated devices, such as heart stents and grafts\textsuperscript{32} and has announced its discovery that 12 Chinese companies have supplied contaminated heparin to 10 other countries.\textsuperscript{33}

No matter the complications facing regulators, Americans are increasingly fed up hearing that another product manufactured or produced in China contains dangerous or deadly components.

\textsuperscript{20} Id.
\textsuperscript{22} Japsen, supra note 19.
\textsuperscript{26} Bodganich and Hooker, supra, note 21.
\textsuperscript{27} Harris, supra note 1.
\textsuperscript{28} Bodganich and Hooker, supra, note 21.
\textsuperscript{30} Harris, supra note 1.
\textsuperscript{33} Harris, supra note 1.
The deaths of hundreds of pets linked to a counterfeit Chinese ingredient in pet food and the recall of millions of toys made in China containing lead paint has led to vitriolic reactions among American consumers. China boycotts and bans are routinely discussed on blogs and TV call-in shows. Of course, talk of lawsuits has begun. But who can be held liable for this latest debacle? And who should be?

Numerous plaintiffs’ firms have their heparin claims web pages up. Baxter, as the main manufacturer of the tainted heparin, will probably face a class action lawsuit not unlike that faced by Menu Foods, the manufacturer and distributor of the tainted pet food.\(^{34}\) If the Menu Foods settlement is any indication, Baxter may well be held liable for the actions of its Chinese supplier and its failure to more closely monitor its production supply chain. Furthermore, Baxter may have violated federal law prohibiting the sale of counterfeit drugs.\(^{35}\) For its part, Baxter has now conducted its own tests, and disputes the FDA’s assertion that its product is linked to the 81 deaths.\(^{36}\) An interesting question will be whether Baxter may be able to use a preemption argument similar to medical device makers who recently prevailed at the Supreme Court against patients attempting to sue them for product liability.\(^{37}\) Baxter’s drug development process was approved by the FDA; but is that enough to preempt a patient’s cause of action in this situation? An important question will be whether the FDA will hold to the position that it is the pharmaceutical companies that are responsible for monitoring the development of the raw materials that go into their drugs.\(^{38}\) The answer will probably require years of expensive litigation.

Physicians and hospitals who have been prescribing and administering heparin since the recalls first began may also have to worry about liability. The FDA, while warning health care providers of the tainted heparin, did not initially recall all Baxter heparin products for fear of a national shortage. Are health care providers liable for their decision to continue to use the Baxter products that were not initially recalled? Because they knew or should have known about the recall, could patients argue the physician’s negligence in prescribing heparin was in fact willful and wanton? These questions will probably be answered in court at the expense of health care providers and their insurers.

And what of the FDA’s own admission of failing to follow its own procedures? Can injured patients hold it accountable? Probably not. The FDA is one of many overburdened, under-funded, and liability immune government agencies that lets consumers fall through the cracks. This time, however, the result was the death of Americans. It is imperative that the FDA be better funded and managed so that inspections of production facilities outside of the U.S. can be done on a comprehensive level. The U.S. and Europe have been expanding their production of medical products globally for several years because it is cheaper to do so. Approximately 40% of drugs and 80% of their chemical ingredients are imported from countries like China and India that do not have ample inspection and safety procedures in place. According to Dr. Bryan Liang, an advisor to the Partnership for Safe Medicines, “the problem is only going to get worse as

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\(^{36}\) Harris, supra note 1.


more materials come from suspect sources.”

This is not news, however. The FDA knows it does not have the manpower or resources to inspect every overseas facility, as do Congress and the President, all of whom have been calling for more funding. Perhaps holding the FDA liable for the damages experienced by the harmed patients is the only way to prod our government into properly funding this all-important agency and keeping American consumers safe.


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