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An Analysis of Heparin, Accountability and Pre-emption: Where Are We Now? Part II
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 Second in a two-part series, ([first part](#))

U.S. drug facilities receive FDA visits every two years; however, domestic medical device manufacturers are not inspected in accordance with this statutory mandate. FDA officials estimated that the agency has inspected high risk device establishments every three years or five years (for medium risk devices).¹ There is no comparable requirement to inspect foreign establishments, and agency officials estimate that these establishments have been inspected every six years (for high risk devices) or 27 years (for medium risk devices).²

The fact that China is a key source of APIs in our drug supply is critical. There were less than 20 visits per year to China for 714 finished plants.³ These numbers suggest that it would take over 30 years to inspect the Chinese manufacturers at the current rate of FDA inspection.








The growth overseas is an additional key point. In 2007, FDA Generic drug approval applications consisted of 459 in India and 497 in China versus 151 in the U.S. However, the FDA Inspection services budget requests for 2009 is as follows: \$5M for criminal investigation and \$0 for increased plant inspection.⁴ FDA needs \$250 million per year to inspect every foreign drug manufacturer every other year – the current 2008 budget is \$9 million. This does not take into account device manufacturers.

FDA Initiatives

FDA has taken steps to help it select establishments for inspection by obtaining information on foreign establishments from regulatory bodies in other countries. For example, according to FDA, the agency is enhancing an arrangement to exchange information with the Swiss drug regulatory agency. FDA officials have highlighted such arrangements as a means of improving the agency's oversight of drugs manufactured in foreign countries. For example, they told us that in selecting establishments for GMP surveillance inspections, they sometimes use the results of an establishment inspection conducted by a foreign government to determine whether to inspect an establishment. FDA received drug inspection information from foreign regulatory bodies six times in 2007.

Electronic Registration - FDA plans to implement electronic registration for foreign establishments.⁵

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Implementing such a process may reduce inaccuracies in FDA's database of registered establishments. However, this will not prevent foreign establishments that do not manufacture drugs for the U.S. market from erroneously registering with FDA. For example, in some foreign markets, foreign drug manufacturers may register with FDA because registration may appear to convey an "approval" or endorsement by the agency. To reduce duplication in FDA's import database, FDA supported a proposal to create a unique government-wide identifier for all establishments whose products are imported into the United States.

FDA has proposed, but not yet implemented, the Foreign Vendor Registration Verification Program, which could help improve the accuracy of information FDA maintains on registered establishments.⁶ Through this program, FDA plans to contract with an external organization to conduct onsite verification of the registration data and product listing information of foreign establishments shipping drugs and other FDA-regulated products to the United States. As of April 2008, FDA had solicited proposals for this contract but was still developing the specifics of the program. For example, the agency had not yet established the criteria it would use to determine which establishments would be visited for verification purposes or determined how many establishments it would verify annually.

The Shared Establishment Data Service (SEDS) would provide a unique establishment identifier and a centralized service to provide commercially verified information about establishments.⁷ The standard identifier would be submitted as part of import entry data where required by FDA or other government agencies. SEDS could thus eliminate the problem of having multiple identifiers associated with an individual establishment. However, the implementation of SEDS is dependent on action from multiple federal agencies, including the integration of the concept into a CBP import and export system currently under development and scheduled for implementation in 2010.

The agency's Mission Accomplishments and Regulatory Compliance Services (MARCS) is intended to help FDA electronically integrate data from multiple systems.⁸ It is specifically designed to give individual users a more complete picture of establishments. FDA officials estimate that MARCS, which is being implemented in stages, could be fully implemented by 2011 or 2012. However, FDA officials told us that implementation has been slow because the agency has been forced to shift resources away from MARCS and toward the maintenance of current systems that are still heavily used, such as FACTS and OASIS.

Riegel⁹

The recent decision by the U.S. Supreme Court in *Riegel v. Medtronic, Inc.*,¹⁰ has rather dramatically supplanted the FDA's core mission with respect to medical devices and, in effect, given large corporate manufacturers of medical devices immunity from state and common law products-liability claims stemming from "defects" in the devices they produce.

In *Riegel*, the court held that so long as a new medical device receives pre-market approval from the FDA, the medical device manufacturer will be shielded from all state and/or common law claims for damages in the event the product is later found to be defective.¹¹

The court found that if the medical device was classified by the FDA as a Class III device and received "pre-market approval," all state or common law "requirements that are different from or in addition to" the FDA's pre-market requirements would be preempted by the 1970 Medical Device Amendments to the Federal Food, Drug and Cosmetic Act.

In light of the heparin debacle and the GAO reports it is interesting to note that the Supreme Court recognized the "rigorous" process that Class II devices undergo.

The decision now makes regulatory compliance an affirmative defense for Class III medical devices that receive pre-market approval from the FDA, except in the rare circumstance where a device maker knowingly commits fraud on the FDA. Potential plaintiffs faced with such design defects would be required to prove that the device manufacturer failed to comply with FDA regulations, or that doctors or other medical personnel misused the device, placing an even greater strain on the medical profession.

Black Hole

On its face this does not seem too egregious until one discovers the black hole that many medical device makers may now jump through to avoid the pre-market process.

This hole with respect to Class III devices allows a device maker to qualify for preemption, and be immune from suit, without ever passing the FDA's pre-market approval process so long as (1) the device was in use prior to the 1976 Medical Device Amendments¹² to the FDCA and is therefore "grandfathered-in"; or (2) if the new device is found by the FDA to be "substantially equivalent" to another device that is exempt from pre-market approval, then no pre-market approval of the device is required.

FDA's Position on Preemption

FDA's pro-preemption position gives consumers the worst of both worlds. On one hand, despite FDA's claims otherwise, FDA cannot single-handedly accomplish the task of assuring the safety of the 11,000 drugs and thousands of medical devices on the market. Thus, consumers cannot depend on FDA regulation alone to protect them from unsafe or defective drugs and medical devices. That is why, until recently, FDA recognized the importance of the legal system as an essential complement to its work.

FDA has had to strain to suggest that its approval of a device is a warrant for its safety. In fact, pre-market approval is a one-time licensing decision based on whether the device's sponsor has shown a "reasonable assurance" of safety, a standard far less rigorous than for drugs, which must be shown to be safe and effective for their intended use. FDA's track record demonstrates the agency's inability to single-handedly protect the American people against defective and dangerous medical devices. Pre-market approval is an important process intended to put an end to the marketing of devices without meaningful testing and with no assurance of safety. But the PMA process, by itself, cannot replace the continuous and comprehensive safety incentives, information disclosure, and victim compensation that state liability law has traditionally provided.

Wyeth¹³

The lower courts are deeply divided on drug preemption, although the majority of courts have rejected FDA's pro-preemption position. The question of whether federal law displaces all product liability claims brought against all manufacturers of Rx drugs will be considered by the Supreme Court in October in Wyeth v. Levine.¹⁴

FDA has long taken the view that state liability litigation for pharmaceuticals is an important, independent discipline on the market. FDA's preemption argument presupposes that the agency has the resources to perform the monumental task of ensuring that the labeling of drugs on the market reflects current safety information. It does not.

According to the November 2007 report of a blue-ribbon panel appointed by the FDA Commissioner, "[t]he scientific demands on the Agency far exceed its capacity to respond. This imbalance is imposing a significant risk to the integrity of the . . . regulatory system, and hence the safety of the public." The Institute of Medicine reported in 2006 that FDA "lacks the resources needed to accomplish its large and complex mission today, let alone to position itself for an increasingly challenging future."¹⁵

FDA regulates products that amount to one-quarter of consumer spending in the US, but it has only 9,000 employees nationwide. According to the most recent statistics, FDA's Office of New Drugs, which reviews new drug applications, employs over 1,000 physicians and scientists to review the approximately 100 new drug applications each year and to supervise post-marketing studies.

In contrast, FDA's Office of Drug Safety, the unit charged with monitoring adverse events associated with the 3,000 prescription drugs (and 11,000 drugs altogether) on the market, has about 100 professional employees.

State liability litigation helps uncover and assess risks that are not apparent to the agency during a drug's approval process, and this "feedback loop" enables FDA to be more effective. Therefore, many are looking to Congress to ensure that state liability law is not pre-empted.

The FDA Globalization Act of 2008¹⁶ is a start but will require significant modifications because the agency does not have the resources to accommodate the provisions of the Act as it is currently drafted. The Heparin incident highlights this fact. The recent Medtronic¹⁷ case is further problematic because it answers that FDA review alone is sufficient to protect the safety and efficacy of devices. It is not. We will need to wait for the Wyeth¹⁸ case to be heard and watch the development of the Globalization Act of 2008 to answer the question, "where are we now?"

¹Draft Discussion of the 'Food and Drug Administration Globalization Act of 2008', H.R. 110th Cong. (2008).

²See Drug Safety: Preliminary Findings Suggest FDA Initiatives Have Potential, but Do Not Fully Address Weaknesses in Its Foreign Drug Inspection Program, Before the H. Subcomm. On Oversight and Investigations, H.Comm. On Energy and Commerce, 110th Cong. (2008) (statement of Marcia Crosse, Dir. of Health Care GAO); FDA Faces Challenges in Conducting Inspections of Foreign Manufacturing Establishments, Before the H. Subcomm. On Health, H.Comm. On Energy and Commerce, 110th Cong. (2008) (statement of Marcia Crosse, Dir. of Health Care); Challenges for FDA in Conducting Manufacturer Inspections, Before the H. Subcomm. On Oversight and Investigations, H. Comm. On Energy and Commerce, 110th Cong. (2008), (statement of Marcia Crosse, Dir. Health Care).

³ Drug Safety: Preliminary Findings Suggest FDA Initiatives Have Potential, but Do Not Fully Address Weaknesses in Its Foreign Drug Inspection Program, Before the H. Subcomm. On Oversight and

Investigations, H.Comm. On Energy and Commerce, 110th Cong., 18 (2008) (statement of Marcia Crosse, Dir. of Health Care GAO)

⁴; Riegel v. Medtronic, Inc., 128 S. Ct. 999 (2008).

⁵; Id. at 1011.

⁶; See Wyeth v Levine, 128 S. Ct. 1118 (2008) (granting petition for writ of certiorari).

⁷; Takashi Kei Kishimoto et al., Contaminated Heparin Associated with Adverse Clinical Events and Activation of the Contact System, New Eng. J. Med. (April 23, 2008). Available at <http://content.nejm.org/cgi/content/short/358/23/2457>.

⁸; The Heparin Disaster: Chinese Counterfeits and American Failures, Before the H. Subcomm. On Oversight and Investigations, H. Comm. On Energy and Commerce, 110th Cong. (2008) (staff testimony).

⁹; Draft Discussion of the 'Food and Drug Administration Globalization Act of 2008', H.R. 110th Cong. §§ 101, 201 (2008).

¹⁰; The Heparin Disaster: Chinese Counterfeits and American Failures, Before the H. Subcomm. On Oversight and Investigations, H. Comm. On Energy and Commerce, 110th Cong. (2008) (staff testimony).

¹¹; See Drug Safety: Preliminary Findings Suggest FDA Initiatives Have Potential, but Do Not Fully Address Weaknesses in Its Foreign Drug Inspection Program, Before the H. Subcomm. On Oversight and Investigations, H.Comm. On Energy and Commerce, 110th Cong. (2008) (statement of Marcia Crosse, Dir. of Health Care GAO); FDA Faces Challenges in Conducting Inspections of Foreign Manufacturing Establishments, Before the H. Subcomm. On Health, H.Comm. On Energy and Commerce, 110th Cong. (2008).

¹²; See Draft Discussion of the 'Food and Drug Administration Globalization Act of 2008' Legislation: Drug Safety, Before the H. Subcomm. On Oversight and Investigations, H. Comm. On Energy and Commerce, 110th Cong. (2008) (statement of Dr. Janet Woodcock, Dir. Center for Drug Evaluation and Research, FDA) available at <http://www.fda.gov/ola/2008/heparin042908.html>.

¹³; Draft Discussion of the 'Food and Drug Administration Globalization Act of 2008', H.R. 110th Cong. § 111 (2008).

¹⁴; Id. at § 112.

¹⁵; 21 U.S.C. § 381.

¹⁶; FDA, Import Alert 66-40 (March 10, 1998) available at http://www.fda.gov/ora/fiars/ora_import_ia6640.html.

¹⁷; Draft Discussion of the 'Food and Drug Administration Globalization Act of 2008', H.R. 110th Cong. § 202 (2008).

¹⁸; See GAO, Food and Drug Administration: Improvements Needed in the Foreign Drug Inspection Program, GAO/HEHS-98-21 (March 17, 1998); Drug Safety: Preliminary Findings Suggest FDA Initiatives Have Potential, but Do Not Fully Address Weaknesses in Its Foreign Drug Inspection Program, Before the H. Subcomm. On Oversight and Investigations, H.Comm. On Energy and Commerce, 110th Cong. (2008) (statement of Marcia Crosse, Dir. of Health Care GAO).

¹⁹; Drug Safety: Preliminary Findings Suggest FDA Initiatives Have Potential, but Do Not Fully Address Weaknesses in Its Foreign Drug Inspection Program, Before the H. Subcomm. On Oversight and Investigations, H.Comm. On Energy and Commerce, 110th Cong. 2-3 (2008) (statement of Marcia Crosse, Dir. of Health Care GAO).

²⁰; Id. at 8.

²¹; Id.

²²; Id.

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