This past April has seen nothing less than a tug of war between Congress and the US Food and Drug Administration (FDA). During April and May, FDA staffers have been on Capitol Hill to offer testimony to Congress no less than 10 times. During the entire duration of 2006, the FDA only offered 12 testimonies. Congressional scrutiny of the agency has obviously increased in the past 2 years.

Although this Capitol Hill activity has involved many issues, the 2 that emerge as the most relevant—safety and funding—are related and were sparked by the problem of contaminated heparin. In fact, during April, matters related to the heparin contamination dominated the attention of Capitol Hill and the FDA.

Beginning in February 2008, Baxter Healthcare Corporation initiated a recall of all of its heparin products because of reports of serious adverse events in patients using that drug. It was found that the blood thinner heparin had been contaminated by inferior products that were used by some manufacturers, and the problem was occurring globally. As many as 81 people died after large injections of the product. Heparin was manufactured by multiple suppliers in China, and it is not known where in the supply chain the contamination may have occurred.

An arch theme is connected with this episode of a contaminated pharmaceutical product. It must be determined how the contamination occurred (and the FDA and Baxter have offered the theory that the contamination was intentional), but the bigger issue involves questions related to the safety of the current system of drug manufacturing, and what can be done in today’s real-world system to minimize the risk of drug contamination. On April 29, Dr Woodcock, Director of the Center for Drug Evaluation and Research, told the Subcommittee on Oversight and Investigations Committee on Energy and Commerce, “While the contaminant was first identified in the US, the recall of this product is international in scope. The FDA has notified key regulatory international partners, and we are working closely with our Chinese and European counterparts in the investigation.”

The events surrounding heparin have raised a host of issues for the FDA and paved the way for realizations about the very global nature of drug manufacturing.

The heparin incidence has been at least partly responsible for a number of hearings on Capitol Hill. The first focus was on why heparin was contaminated, and whether the FDA was doing its job correctly. The secondary focus became one of how to fix the FDA so that the risk from such occurrences is minimized. This led at one point to a heated exchange between Congressman John Dingell, Chair of the House Committee on Energy and Commerce, and FDA Commissioner Andrew C. von Eshenbach during a recent congressional hearing. The commissioner was repeatedly grilled over whether the agency was doing its job correctly, and, more to the point, what funding measures would be needed to ensure that the FDA is in a stronger position when it comes to the inspection of foreign manufacturers.

The fact is, the amount of resources that would be required for the FDA to inspect each and every foreign manufacturer of every component of a medication is quite high. At question—which was unanswered in these hearings and exchanges—is whether it is reasonable to expect the FDA to successfully minimize risk abroad through a program of foreign inspections, or...
whether there is a greater role for manufacturers in ensuring quality.

In the case of heparin, even if testing had been conducted at the border, it is unlikely that the contamination would have come to light.

There is a need for a deeper inspection and analysis of the heparin contamination issue to determine whether funding for a more aggressive inspection program is in fact going to solve the problem that Congress and the FDA are facing. Heparin contamination is the symptom of a larger problem facing all drug manufacturing today, and unless it is addressed with a more comprehensive approach, history may be poised to repeat itself.

References


Mr Senak is Senior Vice President at Fleishman-Hillard in Washington, DC, and writes the Eye on FDA blog, www.eyefonfda.com.

FDA’s “Complete Response” Replaces “Approval/Nonapproval” Letter

Responding to concerns from drug manufacturers, and after several years of deliberations, the US Food and Drug Administration (FDA) announced on July 9, 2008 (www.fda.gov/bbs/topics/NEWS/2008/NEW01859.html), that starting August 11, 2008, it would no longer be sending an “approvable” or a “nonapprovable” letter to drug sponsors in response to a new drug application. Instead, the FDA's new wording is a “complete response” letter that is intended to notify the drug maker that the review process has been completed but the drug is not yet ready to be approved, because of “specific deficiencies,” as described by the FDA. When possible, the FDA will also “outline recommended actions the applicant might take to get the application ready for approval.” This last comment appears to imply a change in policy in the form of a more complete explanation of the process than just mere semantics, but this remains to be seen.

The FDA noted that complete response letters are already being used for applications for biological products, and that this change in wording is intended to remove any potential for misinterpretation by different stakeholders as a complete and final rejection of the drug. The use of “approvable” or “nonapprovable” letters was often perceived to imply a “tentative” or “conditional” approval of the drug, when in effect that was not the intent of the FDA, according to John Jenkins, director of the FDA’s Office of New Drugs. Such misinterpretation carried potential clinical and financial ramifications to drug makers, patients, and investors.