Caution – FDA Could Be Hazardous to Your Health

by Steve Brozak

FDA is a troubled agency in need of fundamental reorganization. It has been criticized by Congressional watchdogs for years and recently, staff members sent a letter to Congress highlighting some of the problems they see within the agency. On October 14, a group of scientists and physicians in the FDA's Center for Devices and Radiological Health (CDRH) wrote to Representative John Dingell (D-MI) saying "managers at CDRH with no scientific or medical expertise in devices, or any clinical experience in the practice of medicine have ignored serious safety and effectiveness concerns of FDA experts and have ignored scientific regulatory requirements." The letter further accused FDA management of knowingly "allowing a continuation of management reprisals" against those who raised these and other concerns.

Putting aside any political analysis, when members of a Federal agency complain to Congress, it is time to take notice. FDA may have more impact on the health and well-being of adults and children in the United States than any other federal government agency, and it always operates one failure away from disaster.

As presently constituted, the FDA has too many objectives. It is an agency that needs focus. That focus could be achieved by dividing FDA's responsibilities among three Federal Departments. The consequence would be to concentrate expertise and responsibilities within individual agencies, to more sharply define budgets and more closely track expenses. In splitting up FDA, food and veterinary oversight could go to the Department of Agriculture, Cosmetics regulation could go to the Department of Commerce and the drug and medical device oversight could remain with the newly constituted Drug and Device Agency at the Department of Health and Human Services.

The author's firm provides investment analysis and commentary on biotechnology, medical device, specialty pharmaceutical and healthcare companies. The firm is often asked to comment on the challenges the U.S. pharmaceutical and medical device industries face and how FDA can help the United States maintain preeminence in those industries. This article will focus on the broader challenges of drug and medical device regulation in our current environment, leaving the legal intricacies under which FDA operates to others.

The author's overarching message is that FDA needs a significant overhaul to meet even a portion of the challenges the agency now faces. With Representative Henry Waxman (D-CA) taking over Chairmanship of the House Energy and Commerce Committee, the likelihood of a major overhaul of food and drug regulation has increased. Perhaps the agency could overcome some of the current skepticism of Congress by embracing such an overhaul.

With a proposed budget of $1.738 billion, to assure the safety of human and animal drugs, blood, human tissues and medical devices, FDA will spend about $5.80 per U.S. citizen on drug and medical device safety in 2009. If FDA does its job well, the price the U.S. consumer pays for this service is truly a bargain. If FDA fails in its mission, it is wasted money.

The agency may well be facing the most difficult time in its history. Staffing, budget and policy have languished in the past few years. Political influence has been exerted in unprecedented ways both on appointments and on policy. Total U.S. healthcare expense is more than $2 trillion and growing in a shrinking economy. Attempts to control drug costs through introduction of generics have given a boost to off-shore businesses, encouraged large pharmaceutical companies to recover their costs for new drugs more quickly and to develop follow-on improvements to extend the life of their intellectual property, while the pharmaceutical pipeline shrinks.

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Effective and timely remedial work is needed to quickly and effectively kick-start FDA and the pharmaceutical industry in a new direction. Among the challenges FDA faces are the following:

- Large-scale staff retirements with close to 30 percent of the regular staff now eligible for retirement.
- Competition for budget increases in a period of economic downturn.
- Increased need for international surveillance of raw materials, intermediate products and finished drugs.
- Increasingly sophisticated criminal conspiracies to adulterate, dilute and produce counterfeit drugs.
- New medical challenges that will require new drug approaches, such as antibiotic-resistant bacteria and the spread of newly emerging and newly spreading infectious diseases.

Today, FDA needs focus. The agency has a fragmented mission, sharing authority for oversight of food regulation with 15 other agencies, governed by a matrix of 30 laws, regulating cosmetics and tackling the complex and highly technical job of drug regulation.

Over the past several years there have been multiple, high-profile instances of oversight failures. A primary example of the need for a fresh approach to drug regulation is the way the agency is approaching the challenge of foreign-produced drugs and drug components.

FDA has announced it would open international offices in China, India, Europe and Latin America before the end of 2008 to meet the threat of tainted food and drugs from abroad. The first office opened in China in late November 2008 and FDA announced it will be staffed with eight "inspectors and senior technical experts in foods, medicines and medical devices." This staff size is absurd. Eight people will have little or no impact on a problem as large as China. It is an unworkable solution to a monumental problem.

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China is a vast geographic entity. It is the Wild Wild East. The central government has only the most rudimentary network of national oversight and inspection. The central government itself admits it has little control over what happens in some of the remote provinces.

It is true that the United States cannot just impose itself on China. A larger staff may not be possible because of diplomatic or budget constraints. It is just as true that a staff of eight cannot have significant impact on the problem. Clearly another approach is needed one that will not bankrupt the United States, offend the Chinese or allow shoddy goods to slip through to the United States.

Looking back at the history of FDA may give us some insight into steps that can be taken now to refocus the agency. The last major overhaul of FDA took place in 1938, long before much of the science that governs today's pharmaceutical and medical device industry was even envisioned. It was a time before antibiotics, before chemical or radiological therapy for cancer, before CT scans or devices to separate stem cells from fat and bone marrow, even before the role and function of stem cells was fully understood.

There are some striking similarities in the overall environment between 1938 and 2008. It was a time of nationwide economic stress, when the U.S. world economic position was under pressure and it was a time when new science and technology were promising breakthrough medical treatments. It was also a time of significant oversight failures. The tipping point was discovery that the liquid, Elixir Sulfanilamide, killed over 100 people, mostly children, because it contained a deadly solvent, diethylene glycol.

Though many of the challenges then and now are similar, some are unique. In today's regulatory environment, FDA faces six significant external challenges and at least four internal challenges that will determine the drugs and devices medical practitioners will have at their disposal. The ability to meet these challenges will, in large measure, determine the competitiveness of U.S. pharmaceutical and biotechnology companies and the health of the U.S. population.

The six external challenges are:

- Regulating drug quality and reliability in a global manufacturing environment.
- Encouraging drug companies to create a pipeline that will enable them to bring a continuing stream of new products to market.

Our pharmaceutical industry is facing significant challenges from foreign competition, the economy and government.

- Minimizing the cost and time required for managing regulation without sacrificing safety.
- Creating an environment that allows U.S. pharmaceutical and medical device companies to compete successfully in the world arena.
- Dealing with introduction of new treatment modalities such as Embryonic Stem Cells that pose unknown medical consequences and significant political ramifications.
- Holding down the cost of medical care to individuals and government agencies under Medicare and Medicaid by introducing generics and bioequivalents, but doing so without depriving the businesses that developed the originals of the profits necessary to finance the next generation of medicines.

Among the internal challenges to FDA, four need to be addressed quickly to position the agency to meet its external challenges:

- Staffing the agency with enough people with the necessary credentials and expertise to tackle the complex challenges they face in light of anticipated staff retirements in the coming years.
- Getting adequate funding to do an appropriate regulatory job without bankrupting the federal government or the pharmaceutical businesses that pay PDUFA and MDUFA fees.
- Resolving the conflicting interests and priorities of the Executive and Legislative Branches of the Federal government.
- Modifying the legal structure of the agency to enable it to efficiently and effectively do its job in a 21st century environment.

Just these 10 challenges alone should be sufficient for a thorough examination of the organization and responsibilities of FDA. There are multiple precedents for reorganizing FDA. The agency and its predecessors have been reorganized, moved, had responsibilities added and removed many times since it was formed under Abraham Lincoln in 1862.

Over 146 years, there have some 20 changes in structure, assignment, location within the Cabinet and added or diminished responsibilities, of which there were four major reorganizations mandated by Congress or Executive Order. The last major reorganization having taken place in 1938, it is not too soon to consider another reorganization to provide more focus for the agency by narrowing its mission and expanding its ability to implement new scientific advances. In addition to meeting the external and internal challenges outlined above, following are some of the important objectives that should be accomplished by reorganizing and refocusing the agency:

- Place food surveillance under the Department of Agriculture and cosmetic safety under the Department of Commerce.
- Create diverse, science-based panels drawing on widely respected members of academia, National Institutes of Health (NIH), Centers for Disease Control and Prevention (CDC), the medical community and pharmaceutical developers to review new medical technologies and advise the agency on potential risks, benefits and methods of procedure to initiate clinical studies and grant new drug authorizations.
- Expand surveillance of international sources of raw materials, interim products and finished pharmaceuticals to assure that products are not adulterated, contaminated or counterfeited. Perhaps limit critical and life-threatening materials to sources only within the United States where they can be closely monitored.
- Review the drug review process and compare it with processes from other regulatory bodies such as the European Medicines Evaluation Agency (EMEA) or Japan's PMDA to determine how the U.S. system can be modified to improve efficiency and speed deliberations while maintaining safety standards and adapting to new medical treatments.
- Create an inventory management system for high-margin drugs that prevents adulteration or forgeries.
- Do a better job building relationships with some of the critical members of Congress to learn what their concerns are and to address them.

What is laid out here is not necessarily a comprehensive proposal for adapting FDA to the current environment, but some of the factors that must be considered in any evaluation of the future role of the agency. Changes must be made and they must be made soon. They are required because our pharmaceutical industry is facing significant challenges from foreign competition, the economy and government. They are required because we have already experienced several drug oversight close calls and total loss of confidence is one disaster away.

Government must not abandon its role as watchdog for safety and efficacy of newly introduced drugs, but it must abandon its role as adversary in the development process. Last year, FDA approved 19 new medicines, the fewest in 24 years, and announced about 75 new or revised "black-box" warnings about potential side effects—twice the number in 2004. The number of approvable letters, which typically postpone FDA decisions by asking for more data, increased by 40 percent last year.[1] Those are not successful performance metrics for any organization.

In the past, some critics accused the government of being too lenient with the pharmaceutical industry. More recently, critics have accused government of being too stern or too cautious. This author believes the recent behavior by FDA has neither been a case of being too harsh nor too lenient, but rather being unpredictable. This author believes consistency of oversight rigor and standards is lacking, which is the most dangerous regulatory environment, because there is no way to test the outcome of one regulatory decision against another by the government or the companies. Companies coming before FDA cannot know what to expect, how to prepare or how best to respond. The consequence is to run up costs for navigating the approval process, force applicants to rely more on relationships than science and delay the availability of new treatments that sick people need.

Government agencies need to re-evaluate their relationship with the industries they regulate, acting more like coach than cop—holding industry up to the highest standards, punishing when necessary and praising when warranted. This relationship needs to be continually reviewed and adjusted to maintain the proper equilibrium.

1 In 2008, FDA replaced Approvable/non-Approvable Letters with Complete Response letters.