There is a hunger for reform of the US Food and Drug Administration (FDA). To a great extent, that hunger is fueled by the prevailing sentiment in today’s regulatory atmosphere—a drive to make our environment as risk free as possible when it comes to medical treatment.

The 1990s Regulatory Reform

During the 1990s, when the HIV epidemic was raging out of control, and the amount of time it took to approve a new drug was a worrisome reality to the medical community fighting the epidemic, there was a tremendous public outcry for faster access to medicines. That public outcry, in turn, led to policymaker action. The result was an FDA reform through the Prescription Drug User Fee Act and the FDA Modernization Act, which brought fast-track authorization and accelerated approval. These regulatory reforms brought new medicines faster and broadened our understanding of the use of surrogate end points. For example, anti-HIV medications had to be approved using a surrogate end point, namely, viral load in the bloodstream. The clinical benefit of lower viral load is now obvious; the drugs have saved hundreds of thousands, if not millions, of lives.

Postmarketing Reform Focus in 2008

Today's environment is much different. Since 2004, confidence in the FDA has been waning, and the gold image of the agency tarnished, as several high-profile issues washed over the agency during a time when it was mostly without steady leadership. The crisis of confidence on the part of the public has led to an outcry for safety, and policymakers are correspondingly responding as they did in the early 1990s, yet not from the benefit end of the spectrum, as was the focus then, but rather from the safety end point.

The late 2000s are a completely different environment. An indicator for the types of reforms that are going to be proposed these days are visible today in the kinds of investigations Congress is conducting into FDA practices. For example, in January 2008, Senator Sherrod Brown (D-Ohio) asked the Congressional Research Service, a research arm of the Library of Congress, to conduct an investigation of fast track at the FDA, to see whether the practice of fast track is indeed speeding up the availability of drugs.

Senator Charles Grassley (R-Iowa) is known for his dramatic antic last June, when he marched from Capitol Hill to the offices of Health and Human Services to demand answers regarding the FDA’s handling of the approval of the branded antibiotic Ketek (telithromycin). In March 2008, he has moved on to more substantive means to get the information he wants, when he issued a letter asking the Government Accountability Office to investigate the FDA approval standards and postmarketing practices.

Specifically, Senator Grassley has requested investigation into:

- The number of drugs that were approved based on surrogate end points
- The surrogate end points that the FDA uses to approve drugs
- The date of approval for each of these 3 drugs—Avandia (rosiglitazone), Avastin (bevacizumab), and Vytorin (ezetimibe/simvastatin)—and whether the FDA required the relevant companies to complete phase 4 trials on these drugs
- The date each of the phase 4 trials were started and completed or are expected to be completed
- A description of the tools the FDA has to compel companies to complete phase 4 trials
- A description of any actions the FDA has taken against companies for failing to complete phase 4 trials or failing to complete trials in a timely manner
- A description of any additional powers the FDA may need to compel companies to complete phase 4 trials, in the event the tools that the FDA has presently are insufficient.

Senator Grassley is asking questions to which he already knows the answers. The FDA has very limited authority when it comes to postmarketing phase 4 studies. A section on the FDA website lists postmar-
marketing commitments and informs about progress, but the FDA has no ability to strictly enforce phase 4 study commitments.

The investigations and research by these senators clearly point the way for future proposed reforms. These senators believe that in the interests of safety, and even of efficacy, they may have to refashion or even abolish the reforms of the 1990s that brought drugs to the market more quickly to minimize risk.

Winds of Change: FDA Surveillance

These reform proposals will be cast on fertile ground. There is a sweeping decline in regard for the FDA on the part of members of Congress. In February 2008, Congresswoman Rosa DeLaurio (D-Connecticut) referred to the management of the FDA as “Keystone cops.” Also in February, Congressman Bart Stupak (D-Michigan) called for the resignation of FDA Commissioner Andrew C. von Eschenbach. The House Committee on Energy and Commerce, Subcommittee on Oversight and Investigations is conducting 6 investigations of various aspects of FDA operations.

In addition, each of the 3 leading candidates for president—Barack Obama, Hillary Clinton, and John McCain—is a proponent of the importation of prescription drugs and the renegotiation of Medicare Part D to allow the federal government to have the power to negotiate prices. Both issues present the FDA with unique challenges.

The winds of change blow naturally during an election cycle. But of all federal agencies, perhaps one of the most sweeping sets of reforms stand to be blueprinted by the reports that will result from the many investigations currently being conducted by Congress. Those who want to know the shape of the reforms to come need look no further. It stands to reason that at a minimum there will likely be proposals to:

• Modify the use of surrogate end points in assessing drug candidates
• Modify in some way fast-track authority to ensure that more rigorous standards are applied
• Give postmarketing surveillance authority and teeth to the FDA.

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Call for Papers

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Articles should discuss key issues that can improve the quality and efficiency of our healthcare delivery system in general and of formulary and drug benefit strategies in particular. Types of articles and topics sought include:

• Clinical topics:
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  ■ Asthma/allergies
  ■ Cholesterol management
  ■ Diabetes
  ■ Depression
  ■ Hypertension
  ■ Infectious diseases
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  ■ Schizophrenia
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