Probably everyone, from pharmacists to pharmacy benefit management (PBM) executives to drug manufacturing honchos, is starting to feel a little nervous about the emerging witch hunt for culprits in the fiascos surrounding the second-generation (atypical) antidepressants and rofecoxib (Vioxx®, Merck). As Congress jumps into the investigation with both feet, fire-breathers on Capitol Hill are apt to uncover other instances of drugs that have been approved by the Food and Drug Administration (FDA) despite ambiguous data from clinical trials. It is against that potent political backdrop that the breathing on Capitol Hill are apt to uncover other instances of drugs that have been approved by the Food and Drug Administration (FDA) despite ambiguous data from clinical trials. It is against that potent political backdrop that the FDA will put the meat on the bones of its five-point drug safety initiative, which Acting FDA Commissioner Lester Crawford announced in November.

Four of the elements of that strategy are still speculative; they consist of steps whose ramifications are cloudy:

• a study by the Institute of Medicine
• the scheduling of workshops and advisory committee meetings to discuss complex drug safety and risk management issues (snore, snore)
• giving scientific reviewers of clinical trial data the ability to contest decisions on drug approval and labeling made by higher-ups
• appointing a director of the Office of Drug Safety, which has been without a director for a year

Only the fifth item will have immediate resonance—the publication of three guidance documents, all mandated by Congress. Draft versions were published last May, and industry comments were sought.

One of the three documents covers “premarketing risk assessment.” The guidance is supposed to come into play when a company is developing a new drug for life-threatening or debilitating diseases. (Does anyone hear a ring of depression and arthritis there?)

Says the FDA draft: these products “ . . . are often approved with relatively small safety databases and, thus, relatively greater uncertainty regarding their adverse effects.”

The other two documents relate to the post-marketing phase. One looks at pharmacovigilance and pharmaco-epidemiological assessments, and the other concerns risk-minimization tools, such as the publication of Medication Guides. These are short, simplified warning statements that are designed for consumers of especially dangerous drugs, such as antidepressants. The FDA has just ordered these for the public and plans to publish these black-and-white documents before the end of 2004.

Guidance documents do not create legal obligations for manufacturers; they are advisory. However, they carry the same weight as a “recommendation” from the Godfather.

In many instances, drug companies had been trying to convince the FDA to temper some of the aspects of the draft guidelines. But that was before antidepressants and Vioxx® hit the headlines. The agency knows that Congress is watching, so it was undoubtedly tightening all three guidance documents a few cranks before releasing their final versions.

The post-marketing risk-minimization guidance will have the biggest impact on PBMs and pharmacists. Again, before the Vioxx® recall, the FDA had intended to push drug manufacturers to produce a fairly small number of “RiskMAPs,” or plans to minimize risks. If a company decides to issue a RiskMAP, it might include some or all of these kinds of items:

• targeted education and outreach for health care practitioners or patients
• reminder systems, processes, or forms to foster reduced-risk prescribing and use
• performance-linked access systems that guide prescribing, dispensing, and use of the product to target the population and conditions of use most likely to confer benefits and to minimize particular risks

Any and all of these will add new complexities to the business of pharmacy.

The agency, in the draft guidance, talked about encouraging companies to use RiskMAPs “judiciously,” but that was then. In this new drug safety-conscious environment, the FDA will be going through clinical trial data on New Drug Applications with a fine-tooth comb. That means that instead of recommending RiskMAPs judiciously, the FDA will be pushing them like a ferris wheel operator urging riders to pull their safety bars tight against their stomachs on the way up.

Further, the agency may start ordering many more companies to do what it ordered Roche to do when that company started producing MedGuides in 2001 for isotretinoin (Accutane®), the acne medication. Not only is there a MedGuide for Accutane®; the FDA also requires physicians to put a special yellow qualification sticker on the prescription. Pharmacists are allowed to dispense a one-month supply of Accutane®, and they may fill prescriptions only within seven days from the date of qualification. Requests for refills and phoned-in prescriptions are not allowed to be honored.

With the FDA battening down the hatches, pharmacists will be spending more time at their battle stations.