United States Senate
Committee on Finance

Sen. Chuck Grassley · Iowa
Ranking Member

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Grassley says changes to improve FDA post-market review remain elusive

WASHINGTON -- Senator Chuck Grassley is asking Food and Drug Administration officials to explain how a new agency initiative to improve its oversight of drugs approved for the marketplace is more than cosmetic.

Grassley said he's concerned that the "Safety First" initiative launched in February may not get at the problem with post-market surveillance by the FDA. "The office in charge of approving drugs in the first place is allowed to have power over the office that specializes in what happens with drugs after they've been on the market for awhile," he said. "This structure creates a conflict where the pride that goes with having approved a drug can get in the way of an objective review of whether a drug is turning out to be as safe and effective as it ought to be, and there's no evidence that this structure has changed with the 'Safety First' initiative."

Since 2004, Grassley has conducted active oversight of the FDA's post-market surveillance of drugs, biologics, medical devices and veterinary medicines. He has repeatedly shown that serious adverse events that emerge after a drug is on the market do not necessarily get prompt attention from the Office of New Drugs. He has also revealed that safety concerns raised by the Office of Surveillance and Epidemiology were sometimes ignored by the Office of New Drugs, which is responsible for determining any regulatory actions taken to address a post-marketing drug safety issue.

Legislation introduced by Grassley in 2005 and 2007 would have set up a new and independent center within the FDA called the Center for Postmarket Evaluation and Research for Drugs and Biologics which would have been responsible for monitoring the safety of drugs and biologics once they are on the market in consultation with other existing Centers at the FDA, and would have had the authority to take corrective action if a drug or biologic presented a risk to patients. Congressional leaders did not incorporate Grassley's initiative in the broad-based, 10-year reauthorization legislation for the FDA that was enacted in 2007.

The prestigious Institute of Medicine and the independent Government Accountability Office issued separate reports in 2006 identifying major shortcomings with the FDA's post-market surveillance of drugs.

Grassley asked the FDA Commissioner for a staff-level briefing on the "Safety First" initiative in a letter sent today. The text of that letter, which spells out Grassley's concerns about the initiative, follows here.

March 13, 2008

The Honorable Andrew C. von Eschenbach, M.D.
Commissioner
U.S. Food and Drug Administration
5600 Fishers Lane
Rockville, MD 20857

Dear Commissioner von Eschenbach:

The United States Senate Committee on Finance (Committee) has jurisdiction over the Medicare and Medicaid programs and, accordingly, a responsibility to the more than 80 million Americans who receive health care coverage under those programs to oversee the proper administration of the programs, including the payment for prescription drugs regulated by the Food and Drug Administration (FDA or Agency). As Ranking Member of the Committee, I have the duty to ensure that FDA upholds its responsibility to the public's health by properly regulating the nation's drug supply and ensuring that the drugs Americans use are safe and effective.

Recently, the FDA announced its "Safety First" Initiative, an effort within the Center for Drug Evaluation and Research (CDER) to "strengthen and modernize" FDA's oversight of drugs on the market. In an email to all CDER staff, Acting Center Director Janet Woodcock outlined some of the steps that will be taken to implement this initiative, including establishing the positions of Deputy Director for Safety and Safety Regulatory Project Manager within the Office of New Drugs (OND) and laying out the respective responsibilities of OND and the Office of Surveillance and Epidemiology (OSE) in addressing drug safety issues.

Over the last four years I have investigated and questioned how the FDA handles post-market surveillance of drugs, biologics, medical devices, and veterinary medicines to assess whether or not the Agency is fulfilling its primary mission to protect public health. In particular, my investigations have shown repeatedly that serious adverse events that emerge after a drug is on the market do not necessarily get prompt attention from the Office of New Drugs (OND). Further, safety concerns raised by the Office of Surveillance and Epidemiology (OSE) were sometimes ignored by OND, which is responsible for determining what, if any, regulatory actions will be taken to address a post-marketing drug safety issue.

I have frequently pointed out that this imbalance between the office responsible for monitoring post-marketing drug safety and the office that puts drugs on the market in the first place has resulted in delayed action and even inaction on serious post-marketing safety concerns. As you are aware, the Institute of Medicine also identified this imbalance in authority between OND and OSE as a major weakness in the drug safety system

and recommended joint authority in the post-approval setting.

Congress didn't take the opportunity to address this fundamental problem, and it appears that FDA's response to the call for strengthening and better defining OSE's role may be merely cosmetic. Dr. Woodcock claims in her email to CDER staff that "OSE will be playing an expanded role in the resolution of certain drug-related safety issues and assuming lead regulatory responsibility for areas related to observational epidemiologic studies and medication error prevention." As I understand it, however, these regulatory responsibilities have always been in OSE's domain; so there's nothing new there. The memorandum of agreement to be established under the Safety First Initiative will only be making these responsibilities explicit. In addition, according to The Wall Street Journal, an FDA official stated that, "I think we really believe that…the team that has been in charge of drug development, that knows the drug best of all, really needs to be in charge."[1]

Accordingly, I request that the FDA provide a briefing for my Committee staff to discuss the Agency's Safety First Initiative. I would appreciate FDA elaborating on the details of the initiative and the timeframes for implementation. In particular, please explain FDA's decision to maintain what appears to be the status quo—OSE continuing to play the role of consultant to OND on post-marketing safety matters. In addition, I would appreciate a discussion of the specific responsibilities of the new positions to be created within OND and what their roles and responsibilities will be vis-à-vis OSE.

The Wall Street Journal also reported that the FDA is creating a new appeals process so that scientific disagreements between offices can be appealed to higher-level officials, up to the Office of the Commissioner. Please have your staff prepared to describe FDA's plans for the new appeals process and how it would improve on the current ad hoc system for resolving disputes.

I look forward to hearing more about the Safety First Initiative and request that the briefing be scheduled by no later than March 26, 2008. Thank you for your cooperation.

Sincerely,

Charles E. Grassley
United States Senator
Ranking Member of the Committee on Finance