United States Senate
Committee on Finance

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Floor Statement of U.S. Senator Chuck Grassley of Iowa
Ranking Member of the Committee on Finance
FDA Legislation
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Mr. GRASSLEY. Mr. President, I'm here today to speak about S. 1082, the Food and Drug Administration Revitalization Act, and H.R. 2900, the Food and Drug Administration Amendments Act of 2007.

The Senate passed S. 1082 in May and the House passed H.R. 2900 earlier this month. As the House and Senate go into conference and work to resolve differences between these two bills, I urge my colleagues to keep in mind the public's interest. Both bills contain provisions that attempt to address some of the problems that have been plaguing the FDA over the past three years. Some of these issues are better addressed by the Senate bill and others by the House bill.

I'm going to spend the next few minutes to comment on what the bills don't do and point out some of the provisions that I believe are important to improving drug safety at the FDA that will benefit all Americans.

Two months ago, I offered Amendment No. 1039 to S. 1082, because I believed-and still believe-that S. 1082 does not address a fundamental problem at the Food and Drug Administration-the lack of equality between the pre-approval and post-approval offices of the agency, the Office of New Drugs and the Office of Surveillance and Epidemiology, respectively. The Office of New Drugs approves drugs for the market, while the Office of Surveillance and Epidemiology monitors and assesses the safety of the drugs once they are on the market. My amendment was intended to curb delays in FDA actions when it comes to safety.

The Institute of Medicine recognized the imbalance between the Office of New Drugs and the Office of Surveillance and Epidemiology and recommended joint authority between these two offices for post-approval regulatory actions related to safety. My amendment did just that.

While I believe an independent post-marketing safety center is still the best solution to the problem, joint post-marketing decision-making between the Office of Surveillance and Epidemiology and the Office of New Drugs at least would allow the office with the post-marketing safety expertise to have a say in what drug safety actions the FDA would take.

Unfortunately, this amendment lost by one vote. But the fact that it lost by such a narrow margin demonstrates that many of my Senate colleagues also recognize the seriousness of this problem and believe action by Congress is necessary.

I have seen time and time again in my investigations that serious safety problems that emerge after a drug is on the market do not necessarily get prompt attention from the Office of New Drugs, the office that approves drugs to go on the market in the first place. We saw this with Vioxx and more recently with the diabetes drug Avandia.

FDA has disregarded and downplayed important concerns and warnings from its own best scientists. We saw evidence of that in the way FDA treated Dr. Andrew Mosholder's findings on antidepressants and Dr. David Graham's findings on Vioxx. The FDA even attempted to undermine the publication of Dr. Graham's findings in the journal Lancet.

My current review of FDA's handling of Avandia has unearthed concerns similar to those we have seen in the past-a situation where FDA ignored its own post-marketing safety experts and once again left the public in the dark regarding potential, serious health risks. Not only did the FDA disregard the concerns and recommendations from the office responsible for post-marketing surveillance, but I have found that it also attempted to suppress scientific dissent.

As I've said many times before, FDA employees dedicated to post-marketing drug safety should be able to express their opinions in writing and independently without fear of retaliation, reprimand, or reprisal. But in the past two months, I've had to write to the FDA regarding the suppression of dissent from not one but two FDA officials involved in the review of Avandia. Last month, I expressed concerns about FDA's treatment of the former Deputy Director of the Division of Drug Risk Evaluation. I urged the Commissioner to take appropriate corrective actions. That deputy director had been verbally reprimanded because she signed off on a recommendation that a black box warning be placed on Avandia for congestive heart failure. This week, I wrote to the Commissioner about a senior medical officer in the Office of New Drugs who was removed from the review of potential cardiovascular safety problems associated with Avandia. This medical officer also believed that there was enough evidence to support a black box warning on Avandia regarding congestive heart failure. But I guess that FDA management just did not want to hear about drug safety problems---again.

Of the two bills up for discussion, neither the Senate nor the House version will give post-marketing surveillance the equal footing it deserves with drug approval. But I appreciate the attempt by my colleagues in the House to provide some transparency in FDA's post-marketing drug safety system. Transparency is the key to accountability. In particular, I welcome the provision in H.R. 2900 that would require FDA to report to Congress on drug safety recommendations received in consultation with, as well as the reports from, the Office of Surveillance and Epidemiology. If FDA does not act on a recommendation from the Office of Surveillance and Epidemiology or it takes a different action, the agency would be required to provide its justification to Congress.

In its report released last fall, the Institute of Medicine called for specific safety-related

performance goals in the Prescription Drug User Fee Act (PDUFA) of 2007 to restore balance between speeding access to drugs and ensuring their safety.

I've heard from FDA employees that because of the PDUFA deadlines, the staff in the Office of New Drugs is under tremendous time pressure to approve new drugs quickly, so safety concerns often needed to be "fit in" wherever they could. This reinforces a point I've frequently made in the past-the Office of New Drugs doesn't give post-marketing drug safety the attention or priority it deserves.

The House bill attempts to address this, in part, by requiring that post-marketing safety performance measures be developed that are "as measurable and rigorous as the ones already developed for premarket review."

S. 1082 requires that the Secretary assess and implement the Risk Evaluation and Management Strategies in consultation with the Office of New Drugs and the Office of Surveillance and Epidemiology. It also calls for a report to Congress on the assessment of that coordination.

The requirement that these two offices be consulted doesn't necessarily change the status quo. The Office of Surveillance and Epidemiology is still just a consultant to the Office of New Drugs, and the Office of New Drugs decides-and will continue to decide-what, if any, action will be taken to address a safety issue. But I hope that requiring that the office responsible for post-marketing surveillance be at the table would encourage FDA to better define the role of this office on drug safety matters and give this office a greater voice, albeit a limited one.

Last fall, the Government Accountability Office reported that the Office of New Drugs typically sets the agenda and chooses the presenters at FDA's scientific advisory meetings. The GAO recommended that the role of the Office of Surveillance and Epidemiology be clarified. After all, this office is the expert on post-marketing safety matters.

This week, Senator Baucus and I sent a letter to the FDA to express concerns regarding an upcoming advisory committee meeting on Avandia. As usual, the Office of New Drugs is setting the agenda here. We pointed out to the FDA that it doesn't make sense that it is the drug approval office and not the post-marketing safety office that controls the advisory committee meeting convened for the purpose of discussing post-marketing safety matters.

In addition to the provisions I've mentioned so far, both the Senate and House bills would give FDA the much needed authorities to require labeling changes and post-approval studies, however, the House bill includes additional provisions outside of the Risk Evaluation and Management Strategy process that's established under both bills.

The House bill specifically enables the Secretary to initiate action on drug labeling and post-approval studies. For example, outside of the Risk Evaluation and Management Strategy process, the Secretary may require a manufacturer to conduct post-approval research to assess or identify potential health risks.

Another provision that would improve transparency at the FDA is a provision in the Senate bill that requires FDA to post on its website, the "action package" for the approval of a new drug within 30 days of approval. That action package would contain any document generated by the FDA related to the review of the drug application, including a summary review of all conclusions and, among other things, any disagreements and how they were resolved.

Further, in light of the many allegations that FDA safety reviewers are sometimes coerced into changing their scientific findings, I believe it is critical that the following provision in S. 1082 survives the legislative conference process-the provision that states that a scientific review of a drug application must not be changed by FDA managers or the reviewer once it is final.

S. 1082 also requires FDA to seek outside expert opinions on drug safety questions at least 2 times a year from its Drug Safety and Risk Management Advisory Committee and other advisory committees. Another important provision in S. 1082 is a requirement that FDA establish and make publicly available clear, written policies on the review and clearance of scientific publications by FDA employees.

Some of the stronger provisions regarding the expansion of the clinical trial registry come from the House bill. While both bills address clinical trial registration, the House bill adopts a much broader definition of applicable clinical trials. Thus, information about many more trials would be made publicly available through the Internet under the House bill.

Clinical trial registries serve an important function-they foster transparency and accountability in health-related research and development by ensuring that the scientific and medical communities and the general public have access to basic information about clinical trials. Mandatory posting of clinical trial information would help prevent companies from withholding clinically important information about their products.

I've heard from some scientists that they can't disclose the findings of their studies because the data belongs to the manufacturer. It's up to the manufacturer to decide if and when the results would be published, and those results don't always see the light of day. But scientists need access to all of the evidence to conduct a full and independent review of a product's safety. However, we know that relevant data are not always made available for further review by independent scientists. While the House bill does not require manufacturers to share its data with other scientists, it does require the sponsor of a study to report whether or not agreements were made restricting individuals from discussing or publishing trial results.

In addition, for FDA's new authorities to be effective, there has to be strong civil monetary penalties. In May, I also offered Amendment No. 998 to S. 1082. That amendment passed. Amendment No. 998 provides for the application of stronger civil monetary penalties for violations of approved Risk Evaluation and Mitigation Strategies. While significant monetary penalties may be imposed under the House bill for continuous violations, the minimum penalty for a violation under the Senate bill would be higher because of my amendment. We need to make sure that we're giving FDA, the watch-dog, some bite to go with the bark. If monetary penalties are nothing more than the cost of doing business, you won't change behavior. More

importantly, you can't deter intentional bad behavior.

In closing, I would like to thank Senators Kennedy and Enzi and Congressmen Dingell and Barton for their tremendous efforts on these bills. We have an opportunity to reform, improve, and re-establish the FDA as the gold standard for drug safety. If Congress is going to make meaningful changes to the FDA to increase transparency and accountability, it is critical that the provisions I've discussed today make it into the bill that comes out of conference. To do less would deny the American people safer drugs when they reach into their medicine cabinets.