United States Senate
Committee on Finance

Sen. Chuck Grassley · Iowa
Ranking Member

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M E M O R A N D U M

TO: Reporters and Editors
FR: Jill Kozeny, 202/224-1308
for Sen. Chuck Grassley
RE: Avandia and the FDA
DA: May 22, 2007

U.S. Sen. Chuck Grassley today made the statement below about his review of the actions of the Food and Drug Administration with Avandia, a popular diabetes drug.

Sen. Grassley's statement:

"Current and former FDA employees have confirmed for my staff investigators that when it came to concerns about congestive heart failure with Avandia, there was a clear difference of opinion between the office that approves drugs and the office that monitors the drugs once they're on the market. The office that's responsible for surveillance of drugs recommended a black-box warning, which provides the highest level, strongest warning to doctors and their patients. The FDA didn't take that advice. Instead the warning about congestive heart failure risks with this drug is currently buried on line 351 of the label.

"I've also learned that at least one of the FDA's experts on diabetes, who was described as a 'reviewer with a conscience,' was removed from involvement with Avandia. This raises questions that I intend to keep asking until there are answers."

Additional information:

Sen. Grassley has twice introduced comprehensive FDA reform legislation (S.468 in the 110th Congress and S.930 in the 109th Congress) that would give the Office of Surveillance and Epidemiology – the office that monitors drugs once they're on the market – independent authority to review FDA-approved drugs and determine the need to provide information about newly identified risks associated with these pharmaceuticals. He introduced a modified version of his legislation to strengthen the post-market review function within the FDA by giving the Office of Surveillance and Epidemiology shared authority with the Office of New Drugs on these matters when the Senate considered and approved the FDA Revitalization Act (S.1082) earlier this month. Sen. Grassley's amendment was defeated by a single vote. As a result, the

Senate version of the FDA proposal that is making its way through the legislative process gives the FDA more authority and power, but it doesn't specify that it's for the Office of Surveillance and Epidemiology. Unless the FDA Commissioner decides to change the way the FDA operates, the Office of New Drugs will continue to be the office that decides when label changes need to be made for new warnings and whether and what studies to require from drug companies after a drug is approved. Under the Senate bill, the Office of Surveillance and Epidemiology will be kept at its current status as a consultant to the Office of New Drugs. More detailed information about Sen. Grassley's amendment to S.1082 is in a May 9, 2007 news release at the bottom of this document.

Also, the statements made yesterday by Sens. Grassley and Max Baucus about The New England Journal of Medicine article on Avandia, the text of their letters to the FDA and GlaxoSmithKline, the maker of Avandia, and Sen. Grassley's May 21, 2007 floor statement about Avandia follow here.

M E M O R A N D U M

TO: Reporters and Editors
FR: Carol Guthrie, 202/224-6769
for Sen. Max Baucus
Jill Kozeny, 202/224-1308
for Sen. Chuck Grassley
RE: Avandia (rosiglitazone)
DA: Monday, May 21, 2007

Sens. Max Baucus and Chuck Grassley, Chairman and Ranking Member of the Committee on Finance, today made comments and sent letters regarding the contents of a study just released by the The New England Journal of Medicine. The study is on cardiovascular problems linked to Avandia, a pharmaceutical used for the treatment of type 2 diabetes.

Comments from each senator are below, along with the text of their letters to the Food and Drug Administration and GlaxoSmithKline, the maker of Avandia. Sens. Baucus and Grassley are asking the Food and Drug Administration to tell them about what the FDA knew about Avandia and when they learned about it. The senators are asking the drug maker to respond to allegations that company executives sought to silence independent scientist(s) about risks with this particular drug.

Sen. Baucus' comment:

"What we are learning about the handling of Avandia by both GlaxoSmithKline and the FDA is appalling and unacceptable. Both the drug company and the FDA have some major explaining to do about what they knew about Avandia, when they knew it, and why they didn't take immediate action to protect patients. The number one priority for drug manufacturers and the FDA must be patient safety. Medicare and Medicaid patients—and all Americans—must never be put at risk like this again," Baucus said.

Sen. Grassley's comment:

"We need to know if this is another Vioxx, where the FDA sat on its hands and endangered lives. The FDA has talked a good game about how it's beefed up post-market surveillance over the last two years, but a case like this undermines that claim. It'll take more than administrative reforms to fix the system within the FDA. Congress ought to take advantage of the opportunity that we have right now with the FDA funding bill to make a real difference for public safety. Study after respected study has said that the FDA office responsible for post-market review of drug safety ought to have equal footing with the FDA's drug approval office. It's hard to understand how there's any resistance to this kind of reform if you care about public safety and public access to the never ending flow of new information about pharmaceuticals. I won't stop making the case for giving the post-market review office real clout," Grassley said.

Baucus/Grassley letter to the FDA:

May 21, 2007

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 ensure that beneficiaries receive drugs that are both safe and effective.

Today, the New England Journal of Medicine published a study on adverse effects of rosiglitazone (Avandia), a pharmaceutical manufactured by GlaxoSmithKline (GSK) to treat type II diabetes. The study reported a 43% increase in the risk of myocardial infarctions/heart attacks in people taking Avandia and potentially a 64% increase in the risk of cardiovascular deaths. Since the Food and Drug Administration (FDA/Agency) approved Avandia in 1999, physicians have written tens of millions of prescriptions for the drug. This could mean tens of thousands of cardiovascular adverse events attributable to this drug.

Diabetics take Avandia to improve their overall health as well as avoid one of the major causes of death among diabetics, heart attacks. It is troubling to say the least that by taking Avandia, diabetics may be increasing their risk of the very adverse event that they hope to prevent by controlling their blood sugar. To make matters worse, American taxpayers have spent hundreds of millions of dollars on this drug through the Medicare and Medicaid programs.

In addition, the Committee has received reports that executives with GSK met with FDA officials in October 2005 and later in August 2006 after further exploring these cardiovascular

problems. We understand that during the same time period, other concerns were raised by FDA employees.

Ironically, on May 9, 2007, Dr. Steven Galson, Director of the Center for Drug Evaluation and Research, testified before Congress that FDA guidance approved in March should protect the public against problems with pharmaceuticals such as what we are now seeing with Avandia. Dr. Galson testified, "The guidance affirms the Agency's commitment to communicate important drug safety information in a timely manner including in some situations when the Agency is still evaluating whether to take any regulatory action." Dr. Galson's testimony flies in the face of FDA's leisurely reaction to GSK's briefing over a year ago on cardiovascular problems attributed to Avandia.

It appears that the new guidance on communicating drug safety information has not improved the FDA's ability to protect the American people in a timely manner. We are greatly concerned about these alleged missteps and would like to further understand why FDA has not taken any action.

In light of the serious concerns raised in this letter, we would like to have you personally brief us on Avandia. We request that Dr. Galson and the lead safety official in Office of Surveillance and Epidemiology who has been monitoring Avandia join you for the briefing.

Additionally, we would also appreciate responses to the following questions and requests for documents and records in advance of the briefing. Please respond by repeating the enumerated question, followed by the accompanying response.

1. When did you first become aware that Avandia may cause a higher incidence of myocardial infarctions, cardiovascular disease, and/or cardiovascular death?

2. How did the FDA first become aware of this problem? Describe in detail FDA's actions to address this problem.

3. Given the effects of Avandia on blood glucose levels and other cardiovascular risk factors like cholesterol levels and body weight, did the FDA consider requiring GSK to conduct a long-term randomized trial to demonstrate risks and/or benefits such as how Avandia affects heart attack risk? What were the discussions, if any, around this issue at the FDA? Did the FDA make the suggestion to GSK? If so, what was GSK's response? Please provide a complete account of the evolution of these discussions, including related communications, documents, and records.

4. Please provide a formal, detailed timeline of your agency's actions regarding Avandia beginning with the date on which FDA staff first became aware of this higher incidence of cardiovascular problems related to Avandia and/or were notified by GSK of these problems. This timeline should identify, among other things, any internal or external communications and/or meetings, including meetings with GSK. Please provide relevant documents and/or records.

5. Describe in detail actions that FDA has taken to investigate the potential for Avandia to cause cardiovascular problems since FDA was first advised or became aware of such risks.

6. Please provide all documents and/or records regarding Avandia since your agency first began examining whether patients taking the drug might be at a higher risk for myocardial infarctions, cardiovascular disease, or cardiovascular death.

7. Please identify all agency personnel (including full name, title and contact information) who have examined the issue of Avandia and myocardial infarctions, cardiovascular disease, and/or cardiovascular death. Also, explain what role they played in investigating and/or communicating that Avandia may cause these adverse reactions. In responding to this question, please include internal and external communications.

8. When did the FDA first learn of the study and/or work of Dr. Steven Nissen, one of the authors of the New England Journal of Medicine article, regarding Avandia and myocardial infarctions? Please provide all communications, documents and records, both internal and external, regarding Dr. Nissen's study and/or work on Avandia.

In cooperating with the Committee's review, no documents, records, data or information related to these matters shall be destroyed, modified, removed or otherwise made inaccessible to the Committee.

We look forward to hearing from you regarding the concerns and questions set forth in this letter by no later than June 4, 2007 in accordance with the attached definitions and general instructions.

Sincerely,

Max Baucus
Chairman

Charles E. Grassley
Ranking Member

Baucus/Grassley letter to GlaxoSmithKline:

May 21, 2007

Mr. Christopher Viehbacher
President
U.S. Pharmaceuticals
GlaxoSmithKline
5 Moore Drive
P.O. Box 13398
Research Triangle Park, NC 27709

Dear Mr. Viebacher:

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 ensure that beneficiaries receive drugs that are both safe and effective.

Today, the New England Journal of Medicine published a study on the adverse effects for rosiglitazone (Avandia), a pharmaceutical manufactured by GlaxoSmithKline (GSK) to treat type II diabetes. The study reported a 43% increase in the risk of myocardial infarctions/heart attacks in people taking Avandia and potentially a 64% increase in the risk of cardiovascular death. Since GSK began selling Avandia in 1999, physicians have written tens of millions of prescriptions for it. This could mean tens of thousands of cardiovascular adverse events attributable to Avandia.

Diabetics take Avandia to improve their overall health as well as avoid one of the major causes of death among diabetics, heart attacks. It is troubling to say the least that by taking Avandia, diabetics may be increasing their risk of the very adverse event that they hope to prevent by controlling their blood sugar. To make matters worse, American taxpayers have spent hundreds of millions of dollars on this drug through the Medicare and Medicaid programs.

One of the most immediate concerns to us are reports that GSK employees silenced one or more medical professionals who attempted to speak out about the potential for cardiovascular problems with Avandia. This allegation is very serious and warrants further investigation.

In addition, the Committee received reports that GSK executives met with FDA officials in October 2005 and later in August 2006.

In light of these allegations and concerns, we request a briefing for our Committee staff, focusing in particular on: (1) allegations that GSK executives sought to silence medical professional(s) regarding possible serious adverse events related to Avandia, and (2) the reports and any other information that GSK provided to the FDA regarding adverse events related to Avandia.

We also request that GSK provide responses to the following questions and requests for documents and records. Please respond by repeating the enumerated question, followed by the accompanying response.

1. When did GSK first become aware that Avandia may cause a higher incidence of myocardial infarctions, cardiovascular disease, and/or cardiovascular deaths? How did GSK first become aware of this problem?

2. Describe in detail what actions GSK took to address this problem. Please include copies of all responsive documents. In responding to this inquiry, please be specific as to what raised GSK's suspicion that people taking Avandia might be at a higher risk for cardiovascular problems.

3. When it was approved or soon after, there was evidence that Avandia improved the control of blood glucose but had adverse effects on other risk factors like weight and cholesterol. An important scientific question is whether Avandia thus reduces or increases the risk of heart attack in diabetics. Answering this question would require a large long-term randomized trial with heart attack as one potential outcome. Please provide all communications, documents, and records relevant to a discussion on conducting such a trial, from the time that the New Drug Application was first submitted to the FDA. Did GSK conduct such a trial? If not, why not? What were the arguments for and against conducting such a trial? What was the decision-making process regarding such a trial?

4. Please provide a detailed timeline of GSK's actions regarding Avandia beginning with the date on which your company first became aware of the potential for a higher incidence of cardiovascular problems related to the use of Avandia and the time GSK notified the FDA of such potential. This timeline should identify specifically, among other things, any internal or external communications and/or meetings, including meetings with the FDA. Please provider relevant documents and/or records.

5. Please identify all GSK personnel (including full name, title and contact information) who have examined the issue of Avandia and myocardial infarctions, cardiovascular disease, and/or cardiovascular death. Also, explain what role they played in investigating and/or communicating that Avandia may increase the risk of these adverse reactions. In responding to this question, please include internal and external communications.

6. Please provide any and all contracts or similar instruments between GSK and any outside scientists/medical professionals regarding Avandia and efforts to either directly or indirectly limit that individual's ability to discuss adverse events related to Avandia. For each contract or similar instrument, please provide all related documents, records and/or communications.

7. Please identify any and all third parties (e.g., corporations, individuals, universities, etc.) engaged by GSK to examine, review, evaluate or analyze Avandia and/or the effects of its use. Please be sure to include the nature of the work performed and provide a copy of any and all draft and final products provided to GSK.

8. When did your company first learn about the study and/or work of Dr. Steven Nissen on Avandia and cardiovascular problems? Please provide all communications, documents and records, both internal and external, regarding Dr. Nissen's study and/or work on Avandia, including any consultants who may have been hired to examine/discuss Dr. Nissen's work.

In cooperating with the Committee's review, no documents, records, data or information related to these matters shall be destroyed, modified, removed or otherwise made inaccessible to the Committee. In addition, we would appreciate your identifying a GSK representative with whom we can discuss matters relating to Avandia as soon as possible.

We look forward to hearing from you regarding the allegations, concerns and questions set forth in this letter by no later than June 11, 2007, in accordance with the attached definitions and general instructions.

Sincerely,

Max Baucus
Chairman

Charles E. Grassley
Ranking Member

Floor Statement of U.S. Senator Chuck Grassley of Iowa
Safety of Avandia
Monday, May 21, 2007

I'm here today to talk about another potential failure by the FDA that may have endangered the lives of millions of Americans. Avandia is a drug that was approved by the FDA in 1999. It is a diabetes drug and is used to lower blood sugar. This is important because lowering a diabetic's blood sugar can help prevent or at least postpone two of the biggest killers among diabetics: heart attacks and strokes.

But today, Dr. Steven Nissen, the Chairman of Cardiovascular Medicine at the Cleveland Clinic and the immediate past president of the American College of Cardiology, and his colleague Ms. Kathy Wolski reported in the New England Journal of Medicine that there is a serious problem with Avandia. Avandia, according to Dr. Nissen and Ms. Wolski is increasing the likelihood that a diabetic will have a heart attack and maybe even die. I want everyone to pay attention to the fact that the New England Journal of Medicine accepted this analysis of Avandia on a "fast track" review. The New England Journal of Medicine did that because it was requested by the authors and because in its opinion, the analysis of adverse effects related to Avandia suggests serious patient health risks.

Dr. Nissen and Ms. Wolski based their finding on an analysis of 42 clinical trials.

FDA also decided to say something to the American people today in response to Dr. Nissen's analysis. Around 1pm today, the FDA told the American people that they intend to call for an advisory board meeting to discuss Avandia and that they could not yet reach a "firm conclusion" on what to recommend to people taking Avandia. It was interesting to listen to the call because Dr. Dal Pan, who is the head of the Office of Surveillance and Epidemeology, didn't say a word, although he is in charge of post-marketing surveillance. I guess the FDA thinks that the decision to go to an advisory committee meeting takes the heat off what looks like another failed decision-making process. We'll see.

Avandia has a long history. It's been on the market for about eight years. Tens of millions of prescriptions have been written for Avandia, and Medicare and Medicaid have paid

hundreds of millions of dollars for this drug.

There have been many clinical trials involving Avandia over the years and there have been numerous post-marketing changes to Avandia's label. I also understand that FDA has known about the possibility of problems with this drug since about October 2005. That's about 19 months ago.

The article appearing today in the New England Journal of Medicine raises a lot of serious questions for me about the real story behind the safety of Avandia. When I couple that article with the FDA conference call that ducked lots of questions I become very suspicious.

Over the last three years my investigations into the FDA showed that the agency was too cozy with the drug industry and did not always put safety of the American people first. The FDA is supposed to regulate the drug industry, but in the case of Vioxx-just to name one debacle-American lives were endangered unnecessarily.

My question today is: do we have another Vioxx on our hands with Avandia? I am not sure, but I intend to find out. In fact, today Senator Baucus and I sent out several document requests including one to the FDA and one to the drug sponsor. We want to understand what did FDA know about this drug, when did it know it, and what did it do about it?

The authors of The New England Journal of Medicine article report a 43 percent increase in the risk of myocardial infarction/heart attack and potentially a 64 percent increase in the risk of cardiovascular death. I need the FDA to tell me why a diabetic would take a drug that may increase the risk of the very thing they are trying to avoid-a heart attack. I also want to know why the FDA did not require the drug sponsor to conduct long-term safety studies instead of small, short-term trials that resulted in few adverse cardiovascular events or death. I want to know what the FDA has been doing for the last 18 months. We want to know the same from the drug sponsor.

Interestingly, in an editorial that accompanied the study, two other veterans of the Vioxx controversy-Dr. Bruce Psaty of the University of Washington and Dr. Furberg of Wake Forest University-write: "…the rationale for prescribing rosiglitazone at this time is unclear." Additionally they call for the FDA to take regulatory action and note that bigger and better long-term studies of long-term treatments for conditions such as diabetes should be completed as soon as possible after a drug is approved.

Let me also say something else to all those FDA employees trying to do their job who probably know the answers to many of my questions; please feel free to call the Finance Committee if you have any information about this drug and how the FDA handled the situation. You can also call or contact us anonymously if you want. And if you want to fax information to me, here is my fax number: it's 202-228-2131. We welcome your help and insight because I know that many of you want to protect the American public first and foremost and sometimes that is not as easy as it should be at the FDA.

You will also remember that just a few weeks ago I came before the Senate several times

to talk about drug safety. I told everyone then-as we were discussing S.1082, a bill that was intended to dramatically improve post-marketing drug safety, that I was concerned that the bill would not do that. In my mind and in light of all the work I have done over the past three years on the FDA, I told everyone that the litmus test for me was whether or not the new drug safety bill would prevent another Vioxx.

My position has consistently been that S.1082 did not go far enough and would not prevent another Vioxx. That was why I proposed and insisted on a vote giving joint authority between the office that approves new drugs for the market and the office that is responsible for post-market safety. Forty-six Senators agreed, but I was one vote short and the amendment did not pass.

Drs. Psaty and Furberg also said in their editorial, "On May 10, 2007, the Senate passed the Food and Drug Administration Revitalization Act. Although the Senate bill has many strengths, including the allocation of new authority to the FDA, none of its provisions would necessarily have identified the cardiovascular risks of rofecoxib or rosiglitazone in a timely fashion."

The drug industry has brought us miracle drugs. These drugs have vastly improved the lives of millions throughout the world. At the same time, we all know that drugs have risks and benefits. Each of us tries to consider those risks and benefits when we consult with our doctors to make the best decision for ourselves or our family members as to whether or not we will take a particular drug. But we can't do what is best for ourselves or our family members if we don't know all the relevant information in a timely manner.

For Immediate Release
Wednesday, May 9, 2007

Grassley wins Senate passage of amendment to strengthen new FDA authority

WASHINGTON — Sen. Chuck Grassley today won an important victory in his crusade to improve the work of the Food and Drug Administration in monitoring the safety of FDA-approved drugs and devices.

Senators voted 64 to 30 for his amendment to increase the civil monetary penalties contained in the Food and Drug Administration Revitalization Act of 2007. The penalties would apply to companies that fail to comply with FDA directives that include label changes, post-approval studies, and communicating information about newly identified drug risks.

"The civil monetary penalties that were in the bill didn't pack enough punch to get the attention of corporations," Grassley said. "By approving my amendment today, senators recognized that it doesn't do much good to give the FDA new kinds of authority if the penalties designed to enforce that authority aren't meaningful."

Grassley's legislation increases the minimum civil monetary penalty from $10,000 to $250,000 that can be imposed on a drug maker that is knowingly out of compliance. It also says

that the amount of the penalty will double for every 30-day period of non-compliance after that and up to $2 million. Previously, the overall bill capped the penalty at $1 million.

"These penalties need to be more than just an insignificant cost of doing business in order to affect behavior," Grassley said.

Attached in pdf is the language of Grassley's amendment no. 998, which was cosponsored by Sens. Christopher Dodd of Connecticut, Olympia Snowe of Maine, and Jeff Bingaman of New Mexico.

Grassley offered a second amendment today which was narrowly defeated 47 to 46. This measure would have made the FDA office that studies drugs after they're on the market an equal partner with the FDA office that initially approves drugs for all post-approval decisions related to the safety of drugs that are on the market. Grassley said the amendment was fundamental to reforming and improving the FDA's performance and ability to monitor the safety of FDA-approved drugs and devices. Strengthening the Office of Drug Surveillance and Epidemiology has been a central focus of Grassley's effort to fix problems at the FDA.

In an article published in last week's Journal of the American Medical Association, Grassley's arguments for the two offices carrying equal weight on post-market matters were echoed by two members of the Institute of Medicine committee that evaluated FDA's drug safety system. The authors wrote, "the IOM identified the imbalance in authority between the Office of New Drugs and the Office of Surveillance and Epidemilogy (formerly the Office of Drug Safety) as a major weakness in the drug safety system. In an effort to facilitate a collaborative and constructive team approach, the IOM recommended joint authority for the Office of New Drugs and Office of Surveillance and Epidemiology in the post-approval setting."

"Defeat of this amendment is a lost opportunity when it comes to improving drug safety for American consumers," Grassley said. "The amendment responded directly to well-documented problems and expert advice on how to address those problems. Congress won't be acting responsibly if we don't continue working to strengthen post-market surveillance by the FDA."

The prestigious Institute of Medicine of the National Academies issued a report on its assessment of the nation's drug-safety system last fall. The Institute said the FDA had systemic problems and needed to exercise more vigilance over the life-cycle of drugs and provide more information to the public about drug risks. Grassley said this review validated concerns expressed by the watchdog community and added muscle to the reform effort. Last spring, the Government Accountability Office issued a separate report that said improvement was needed in the FDA's post-market decision making and oversight process.

Grassley has conducted active oversight of the FDA for the last three years and has put pressure on the drug safety agency to act with more independence and transparency in order to restore public confidence and strengthen public safety especially when it comes to drugs already on the market. Grassley has called the FDA's relationship with the drug industry "too cozy" and revealed how agency leaders have acted to suppress scientific dissent regarding agency actions

and drug-safety recommendations.

In January, Grassley and Sen. Christopher Dodd introduced for the second time two bills to revamp and prioritize the post-market surveillance process within the FDA and to greatly expand public access to information about all clinical trials through a registry and results database. Their bills are S.468, the Food and Drug Administration Safety Act of 2007, and S.467, the Fair Access to Clinical Trials Act of 2007.

The FDA Revitalization Act on the Senate floor this week is S.1082. It would reauthorize the FDA's user fee authority, which collects money from drug and device companies for review of their products. The House of Representatives is expected to consider its versions of the drug safety and user fee reauthorization bills in the coming weeks.

Floor Statement of U.S. Sen. Chuck Grassley of Iowa
on Amendment No. 1039

Mr. President, I am here today to offer Amendment No. 1039 to S. 1082, the Food and Drug Administration Revitalization Act. I ask unanimous consent that Senators Mikulski, Brown, Snowe, and Bingaman be added as cosponsors to my amendment, no. 1039. I am offering Amendment No. 1039, because S. 1082 does not sufficiently address the underlying problem that exists at the Food and Drug Administration. That problem is the lack of equality between the Office of New Drugs, which reviews drug applications and decides whether or not to approve a drug for marketing, and the Office of Surveillance and Epidemiology, the office which monitors and assesses the safety of a drug once it's on the market. The Institute of Medicine recognized this problem. The Institute of Medicine recommended joint authority between the two offices for post-approval regulatory actions related to safety. Having equality between the pre-approval and post-approval offices at the FDA is fundamental to real reform of the FDA. Concentrating on the entire life-cycle of drugs is critical. After all, the vast majority of a drug's life-cycle is spent post-approval. In essence, S. 1082 promotes the status quo when it comes to the role played by the Office of Surveillance and Epidemiology-that means the Office of Surveillance and Epidemiology will remain nothing more than a "mere" consultant to the Office of New Drugs. This is not acceptable. Amendment No. 1039 gives the Office of Surveillance and Epidemiology "sign-off" authority. They are the experts on post-marketing safety. Even the Institute of Medicine recognized that through their recommendation. Let me be clear here, this is a lesser amendment than what Senator Dodd and I originally proposed. I still believe an independent post-marketing safety center is the best solution to the problem, but, that will not happen. At least joint post-marketing decision-making between the Office of Surveillance and Epidemiology and the Office of New Drugs will allow the office with the post-marketing safety expertise to have a say in what drug safety actions will be taken by the FDA. The problem here is not only about FDA having enough tools, it's about FDA managers disregarding the concerns raised by FDA's own scientists in the Office of Surveillance and Epidemiology and not taking prompt action. This amendment makes common sense when you weigh the evidence I have presented over the last three years. Opponents to this amendment say that this amendment is unnecessary because S.1082 includes a dispute resolution process with strict deadlines. But that process is for disputes between FDA and the drug company, not internal disagreements between FDA offices. I also want to add that this amendment provides an

approach with checks and balances between the office that approves a drug for marketing and the office that watches a drug once it is on the market. I ask that each Senator ask himself or herself one question before voting on this amendment today: Since the Institute of Medicine recommends equality between the pre-approval and post-approval offices at the FDA, why not vote for this amendment and improve post-marketing safety for the American people?

Floor Statement of U.S. Sen. Chuck Grassley of Iowa
on Amendment No. 998

Mr. President, I am here today to offer Amendment No. 998 to S. 1082, the Food and Drug Administration Revitalization Act. I ask unanimous consent that Senators Dodd, Snowe, and Bingaman be added as cosponsors to my amendment, No. 998. Amendment No. 998 provides for the application of stronger civil monetary penalties for violations of approved risk evaluation and mitigation strategies. Currently, S. 1082 contains penalties but those penalties won't mean much to large global corporations. In fact, the penalties amount to nothing more than the cost of doing business. This amendment is intended to give FDA, the watch-dog, some bite along with its bark. There is opposition to having strong civil monetary penalties. But that just does not make sense to me. The reality here is this: Drug companies provide life-saving pharmaceuticals to the world. They make miracles happen. Before a drug is approved, a drug sponsor has an incentive to provide evidence of a drug's effectiveness to the FDA. Without it, they can't sell the drug to Americans. However, once a drug is already being sold in the marketplace, drug companies have almost no incentive to look for and evaluate safety issues. The bottom line is that, sometimes, market forces guide businesses in ways that may be contrary to the public interest. We have seen this happen. For FDA's new authorities to be meaningful, there must be strong civil monetary penalties. If fines are nothing more than the cost of doing business, you can't change behavior. More importantly, you can't deter bad behavior. After all, if a company does what it is supposed to do, a drug company doesn't need to fear any penalties. It's just that simple. In closing, I ask that Members of the Senate support Amendment No. 998 and add some teeth to the FDA's bite. I thank Senators Kennedy and Enzi for the tremendous efforts that went into bringing this bill to the floor. And I again thank them for incorporating a number of the provisions set forth in the two bills filed by Senator Dodd and me.