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SENATOR CHUCK GRASSLEY, OF IOWA - CHAIRMAN
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Introduction of and Remarks by Sen. Chuck Grassley
before the Consumer Federation of America on the FDA and Prescription Drug Safety
Thursday, March 10, 2005

Introduction by Ms. Jo Reed, AARP director of consumer issues

It gives me great pleasure to introduce our keynote speaker, the Honorable Charles (Chuck) Grassley, Chairman of the U.S. Senate Finance Committee, and member of a number of other key Senate panels, including Judiciary, Budget, and Agriculture. Usually, people put the word "powerful" before "Finance Committee," and that would be an accurate description of both the Committee and our speaker this morning. Senator Grassley, a lifelong Iowan, is known as an unpretentious pragmatist who tells it straight and gets things done. He is the only working family farmer in the U.S. Senate, and his common sense and down-to-earth manner, along with substantive knowledge and legislative skills honed over nearly half a century in elected office, make him both approachable and extremely effective. AARP is particularly appreciative of Senator Grassley's leadership on, and his support for, lower prescription drug costs through importation – and especially, his emphasis on consumer safety. Senator Grassley also played a critical leadership role in adding, for the first time, a prescription drug benefit in Medicare. Low income individuals in particular will benefit from the new drug coverage that will begin in January. We are delighted to have Senator Grassley here today and are looking forward to hearing his comments on "Medications, Safety, and the FDA." Before passing him the microphone, however, I've been asked to share with all of you a personal note from one of his friends at CFA, Bob Hunter, Director of Insurance. The note reads as follows:

Dear Chuck,
I am very sorry that I am unable to be in town for your speech on drug safety issues. But you will understand since I am in a place we both know well: Uganda. I am over here looking for ways to help the children abducted and brutalized by the so-called Lord's Resistance Army. I'll report to you on this when I return. I am proud to be your friend and that you are doing so much in Congress to better protect the public from unsafe prescription drugs. I pray that you and Barbara will continue to be blessed with the strength and good health to keep up your efforts. ... and I'm sure that's a sentiment that all of us here share.

Remarks of Sen. Chuck Grassley
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Good morning. Thank you for the invitation to be with you today and for the kind introduction. I'm lucky enough not to need any prescription drugs. But my wife of 50 years and six months has arthritis. A year ago, I wouldn't have thought twice if Barbara had taken Vioxx. Now I'd be very concerned. Taking prescription drugs used to be easy. Americans took the pill and figured, if they thought about it at all, if it's on the market, the government must have proven its safety. Vioxx and Accutane and other drugs showed us the reality is not so simple. Our confidence has been shaken. Now we have a list of complicated issues to consider.

* Did the drug company conduct enough trials to ensure the drug's safety?
* Did the Food and Drug Administration follow up with enough of its own trials?
* Did the FDA listen to any naysayers in its ranks who had scientific evidence in contradiction to the majority?
* Is the FDA too cozy with the drug companies to ensure proper oversight?
*If there were negative findings, does our doctor have the benefit of those findings?

And we have a series of sad stories on our minds. Congressman Bart Stupak of Michigan is convinced that his 17-year-old son committed suicide on Mother's Day because the boy took Accutane for acne, and had a side effect of depression. The congressman found many other parents who are sure their children suffered a similar fate. My constituent in Cedar Falls, Iowa, believes the anti-depressant her son took didn't help him. He was depressed, went to the doctor for help, got medicine, and ended his life regardless. And there are many other tragic stories. The job for Congress, the FDA, and consumer advocates is to get to the bottom of drug safety procedures and figure out, once and for all, what it'll take to make sure Americans can trust what's in our medicine cabinets.

Drug safety is the subject of major congressional oversight. The FDA is undergoing top-to-bottom scrutiny of how it does business. Until now, the FDA did its work pretty quietly. What changed things is the tenacity of a couple of whistleblowers who spoke out about scientific findings that blew away the status quo. Those whistleblowers got the attention of guys like me who believe in the constitutional responsibility of congressional oversight. And who believe that sunshine is the best disinfectant when it comes to government operations. I'll tell you the story of the two whistleblowers who have done more to shake up a complacent FDA than probably anybody in recent history. Today I'm speaking about the FDA. But I've dealt with a lot of government whistleblowers over the years, and one factor is pretty consistent. If an agency isn't doing the right thing, typically there's an effort to keep information suppressed. Early last year I heard that the FDA was muzzling one of its own scientists. In February 2004 the FDA held a meeting to decide whether there was a link between some antidepressant drugs and suicidal behavior in kids. Dr. Andrew Mosholder – the FDA's expert in this area -- concluded there was a link. However, FDA management disagreed. So, when Dr. Mosholder stuck by his findings, his supervisors canceled his presentation to an advisory committee.

The FDA argued that it should present a united front and not confuse the committee with differing agency interpretations. Instead of allowing Dr. Mosholder to present his findings publicly and subject them to committee scrutiny, the scientific process and his peers, the FDA effectively muzzled him. But despite the FDA's best efforts, Dr. Mosholder wouldn't be silenced. Ultimately, months later, Dr. Mosholder was proven right. Today there's a black box warning on Vioxx.

This incident illustrates one of my fundamental concerns about the FDA. The agency had argued that it didn't want to alarm the public unnecessarily about drug safety problems. I respectfully disagreed and said so. Patients and doctors should know exactly what the FDA and the drug companies know. Better-informed patients and doctors can make informed decisions about whether a drug is right for them. The scientific community should also be fully informed. Good scientists know that their work will be subject to peer review. The rank-and-file scientists at the FDA are no different. Unfortunately, some of the higher-ups have had the attitude, "We'll let the public know what we think they need to know. No more."

A second case was equally explosive. As it handled Dr. Mosholder, the FDA also disregarded and stonewalled concerns raised by another one of its scientists, Dr. David Graham. Dr. Graham completed a study that found an increased risk of heart attacks and strokes in patients taking Vioxx. His immediate supervisor, however, dismissed this study as "scientific rumor." The very same month that Dr. Graham warned the FDA of the cardiovascular risks of Vioxx, the FDA approved the use of Vioxx for children. The director of FDA's office of new drugs suggested that Dr. Graham water down his Vioxx conclusions. Dr. Graham replied that in good conscience he could not. When Dr. Graham was asked to present his findings at my committee's Vioxx hearing, he was also undermined. News reports that day show that Acting FDA Commissioner Dr. Lester Crawford called Dr. Graham QUOTE "a maverick who did not follow agency protocols" UNQUOTE. This statement -- made on the eve of the hearing – could logically serve no purpose other than to intimidate Dr. Graham. This statement came despite the fact Dr. Crawford had met with Dr. Graham. At that meeting Dr. Crawford acknowledged that there was a culture problem at the FDA and a problem with drug safety. Dr. Crawford even asked Dr. Graham to consider helping to improve drug safety programs. Most recently, the FDA failed to prioritize the internal review of another study by Dr. Graham. Post-Vioxx, the FDA scheduled an advisory committee meeting – held just last month – to evaluate the safety of the whole class of drugs like Vioxx.

Coincidentally, Dr. Graham was finishing a study on Medicaid patients taking these drugs. Dr. Graham's findings had not been reviewed internally or published, but they were on point. Instead of making it a priority to clear the study, Dr. Graham's supervisor told him he could <u>not</u> present his findings at the meeting. And then it he told him it was his call. But it wasn't Dr. Graham's call to make, and the FDA shouldn't have placed that burden on him. Dr. Graham did testify before the advisory committee and his science was subjected to public scrutiny from his peers. Dr. Crawford had to overrule Dr. Graham's supervisors to allow him to testify. In the end, the scientific process prevailed. But again, not before Dr. Graham's supervisors attempted to intercede.

We've learned some fundamental points from these experiences. (1) First, we're reminded again that whistleblowers are patriots. Think about the guts it takes to undermine your career, and to go against your supervisors at a huge federal agency, and in this case, the multi-billion-dollar drug companies. Whistleblowers are the rare birds who refuse to go along to get along. Their courage leads to the protection of public safety, and the public fisc. The only thing they're guilty of is "committing truth."

(2) Second, we know now that the FDA had gotten too complacent. The agency charged with protecting the public from unsafe prescription drugs was too cozy with the drug companies. The

Vioxx example showed that the FDA and Merck were too close for comfort. Testimony and documents at our Finance Committee hearing showed that the FDA allowed itself to be manipulated by Merck. What's known as the VIGOR trial found that heart attacks were five times higher for Vioxx patients than for patients on another drug. Merck completed the VIGOR trial in March 2000. But nearly two years passed before the FDA made any label change. During these 22 months, Merck aggressively marketed Vioxx to you and me and the nightly TV audience across the country. Merck and the FDA knew that consumers and doctors were largely unaware of the cardiovascular risks found in the VIGOR trial. The FDA's overriding concern should have been the health and safety of the American people. Unfortunately for some, the FDA's priorities were misplaced. I recognize that evaluating the safety of a drug involves balancing risks and benefits. Vioxx is no different. But we need to know the risks to make calculations. And with Vioxx, doctors and patients didn't have that opportunity.

Another disturbing issue came to light during the Finance Committee hearing. Merck managed to negotiate the cardiovascular risks of Vioxx right out of the "warnings" section on the drug's label. Contrary to the FDA's own scientist's recommendation, the risk information went in the less prominent "precautions" section. Several witnesses believed the FDA should have required a black box warning for Vioxx. That's the FDA's strongest label warning. A few weeks ago, as I've already mentioned, the FDA joint advisory committee did just that. It recommended black box warnings on all drugs in the same class as Vioxx.

(3) Third, we've been made to recognize the enormous implications of getting drug safety right or wrong. Reportedly 20 million Americans took Vioxx. Many of those Americans were Medicare and Medicaid beneficiaries. That's 20 million Americans who took one prescription drug out of the dozens on the market. If one drug has safety risks, millions of people may face those risks. The public safety concerns are most important. But there's an important financial concern as well. The Finance Committee has a responsibility to 80 million Americans who receive health care coverage, including prescription drugs, under the Medicare and Medicaid programs. The Medicaid program paid more than $1 billion for Vioxx before Merck withdrew it from the market. We absolutely have to make sure that every tax dollar paid for prescription drugs is spent on safe drugs. And federal healthcare beneficiaries and their doctors should know all there is to know about the safety and effectiveness of a drug.

Now that the FDA has had its shake-up, the question is what's next. We need reforms -- both administrative and legislative -- to bring greater responsiveness and transparency to the FDA. The first one of those – the FDA changing its own culture – is the really tough one, and the fundamental one. This agency needs to demonstrate that it is unequivocally committed to the scientific process – and those who speak up on its behalf -- when it comes to drug safety and that nothing gets in the way of that, whether it's pressure from profit-oriented drug makers or institutional ego that doesn't want to admit a mistake. The one and only client of the FDA must be John Q. Public. And the leadership of the FDA must make that clear with its actions to everyone inside the agency and to all of us outside the agency. Whoever becomes the new permanent commissioner of the agency has got to be up to meeting the very big challenge of transforming the FDA's culture.

On Capitol Hill, work is under way on legislative reforms. On February 28th I introduced the Fair

Access to Clinical Trials Act – the FACT Act -- with Senator Christopher Dodd. This legislation should be part of a sustained effort to restore public confidence in our nation's drug safety system. It will create a publicly accessible national data bank of clinical trial information. This national data bank will include both a clinical trial registry and a clinical trial results database. Our legislation also takes advantage of an existing website called www.clincialtrials.gov, managed by the National Institutes of Health. Right now, the audience for this website is patients and their doctors who want (1) some basic information about clinical trials related to life-threatening illnesses and (2) how to register in those trials -- so it's a registry for those who want to sign up for experimental studies on potentially life-saving treatments.

Under the FACT Act, this website will be expanded to also include a results database of all publicly and privately funded clinical trials. The results database will have a very different audience in mind. The focus here is for the scientific community, as well as the general public. The new clinicaltrials.gov go a long way toward preventing drug companies from publishing only "good" studies and hiding "bad" studies. The bill also will require the FDA to make its internal drug approval and safety reviews publicly available. Enactment of the FACT Act will be a meaningful step toward greater transparency and accountability in clinical trials and the scientific process. In addition, Senator Dodd and I are working on a bill to establish an independent office for drug safety within the FDA. The independence of the office would NOT exist solely on an organizational chart.

On drug safety, intra-agency communication is essential. However, the existing Office of New Drugs is hampered by real and perceived conflicts of interest. An independent drug safety office would more effectively regulate drugs once they're on the market. If you want accountability, it doesn't make sense to have the office that reviews the safety of drugs to be under the thumb of the office that puts the drugs on the market in the first place. The drug safety office would have an independent director and the regulatory authority to require label changes. Right now, I'm told the Office of Drug Safety has no regulatory authority. For example, the FDA cannot suspend advertising or drug sales while a drug safety issue is assessed.

Primary jurisdiction of the FDA resides in the Senate Health, Education, Labor, and Pensions Committee. I've reached out to Senator Mike Enzi, who chairs the committee. Last week his committee held two hearings on drug safety. And I was pleased that he concluded that something must be done to address drug safety.

Historically the FDA has met its charge to protect the health and safety of the American public. The FDA earned its prized reputation through decades of good work. Those who work at the agency are, by and large, committed to their mission. The FDA has approved dozens of prescription drugs that save lives and ease pain for millions of Americans. Meanwhile, the pharmaceutical industry has developed miracle drugs that heal and cure. We can't imagine life without these miracle drugs. They're here to stay. Yet the drug companies profit from their good works. Sometimes the incentive of huge profits leads to rampant fraud. According to the Department of Justice, there are currently under seal in the neighborhood of 100 whistleblower cases involving allegations against over 200 drug companies. During the past four years, the department recovered nearly 2 and a half billion dollars from whistleblower cases against drug companies. Unfortunately, it appears that some drug companies are placing greed ahead of drug safety. In this fraudulent environment, the FDA's mission

is more important than ever before. The FDA absolutely has to do a top-notch job on ensuring drug safety. When the FDA approves a drug, it should be a Good Housekeeping seal of approval. Americans should be able to bank on the benefits outweighing the risks. Consumers shouldn't have to second-guess the safety of what's in their medicine cabinets. That's true for my wife, my neighbor, a father like Congressman Bart Stupak who lost his son, and all other Americans.

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