are still serious problems with the PATRIOT Act, but I think this conference report, as amended by Senator SUNUNU's bill, is a positive step forward. That is why I am supporting it.

I promise, as they say, eternal vigilance, watching this administration and every administration to make certain they don't go too far. If they overstep, if they step into areas of privacy and constitutional rights, I will speak out and do my best to change the PATRIOT Act and make it a better law.

I yield the floor.

The PRESIDING OFFICER (Mr. ALEXANDER). The Senator from Iowa.

REPORT ON FDA APPROVAL PROCESS FOR VNS

Mr. GRASSLEY. Mr. President, I want to address my fellow Senators, in cooperation with my friend, Senator BAUCUS from Montana, on an issue that our respective staffs have been working on together for a long time. As chairman of the Finance Committee and as ranking member, we are releasing today a report. We come to the floor with our duties in mind to our constituents, to Medicaid and Medicare beneficiaries, and to all Americans, to speak of urgent matters that should concern all of us.

For more than 2 years, I have followed, with increasing concern, the performance of the Food and Drug Administration. It seems as though every week, if not every day, some new danger or risk is brought to light about an FDA-approved drug or device. As chairman and ranking member of the committee, Senator BAUCUS and I have a responsibility to American taxpayers to ensure that Medicare and Medicaid programs pay for medical products that have been appropriately approved in accordance with all laws and regulations. Whether a product is safe, whether a product is effective is not only a major public safety concern; it also has important financial concerns.

We understand there is a human element to the Food and Drug Administration's approval process. As a society, we recognize the anguish of families who must rely on the development of innovative, experimental, new medical products and treatments that may or may not save the life of a loved one. Our Nation is lucky to have a private marketplace that is incredibly resourceful and prolific in the field of medicine. An integral role of the Food and Drug Administration is to get these potentially lifesaving products to the market without undue delay. We also have a Government-regulated system where patients have the option to receive potentially lifesaving but unproven products by participating voluntarily in clinical trials. In the end, however, our Nation's well-founded medical system, despite its weaknesses, must always rest on sound science.

The report we are releasing today focuses on the FDA's approval process for medical devices. It is indisputable that all medical devices carry risks, but Food and Drug Administration approval is still considered the gold standard for safety and effectiveness. However, our committee staff report raises legitimate questions about the FDA's decision to approve a specific medical device. Last February, a number of concerns were raised to our committee about an implantable device called the vegus nerve stimulator or VNS, as I will refer to it. This product, VNS, is manufactured by a company called Cyberonics. Senator BAUCUS and I asked our committee staff to review the concerns that were given to us and report their findings. This report has three major findings which I will summarize briefly.

First, the Food and Drug Administration approved VNS for treatment-resistant depression, a new indication for this surgically implanted device. That was based upon a senior manager overruling more than 20 Food and Drug Administration scientists, medical, and safety officers, as well as managers, who reviewed the data on VNS. The high-level official approved the device despite a resolute conclusion by many at the FDA that the device did not demonstrate a reasonable assurance of safety and effectiveness.

Second, the Food and Drug Administration has not made public the level of internal dissent involved in this device approval, despite the fact that the FDA has publicized differences of scientific opinion within the agency when it has announced other controversial regulatory decisions.

Third, the Food and Drug Administration has not ensured that the public has all the accurate, science-based information on the safety and effectiveness of the VNS for treatment-resistant depression. So health care providers, relying on the FDA's information about this device, may not be able to convey complete risk information to each patient.

In the end, this senior Food and Drug Administration official not only overruled more than 20 Food and Drug Administration employees, but he stated to our committee staff that the public would not be made aware of the scientific dissent over whether the device is reasonably safe and effective. Until today, this official's detailed conclusions remain confidential and unavailable to the public. We are releasing these confidential conclusions in the appendix to the report. Some of his own conclusions raise serious questions in our minds. For example, I quote from his override memorandum:

> I think it needs to be stated clearly and unambiguously that [certain VNS data] failed to reach, or even come close to reaching, statistical significance with respect to its primary endpoint. I think that one has to conclude that, based on [that] data, either the device has no effect, or, if it does have an effect, that in order to measure that effect a longer period of follow-up is required.

The events and circumstances surrounding the Food and Drug Administration's review and approval of VNS for treatment-resistant depression, which you will find detailed in this report we are releasing, raises critical questions about the Food and Drug Administration's so-called ''authoritative'' approval process. I am greatly concerned that the Food and Drug Administration standard for approval may not have been met here. If that is the case, it raises further difficult questions, including whether Medicare and Medicaid dollars should be used to pay for this device now.

Accordingly, we are forwarding the report to Secretary Leavitt, Administrator McClellan, and Acting Commissioner von Eschenbach for their consideration and comment. These are difficult matters that deserve their full attention.

Before I close, I commend the commitment and dedication of the more than 20 FDA scientists who tried to do the right thing in this case, as they probably do in every case, and not stray from evidence-based science. I applaud their effort on behalf of the American people.

I ask unanimous consent that the executive summary of the report be printed in the RECORD.

There being no objection, the material was ordered to be printed in the RECORD, as follows:

I. EXECUTIVE SUMMARY

The United States Senate Committee on Finance (Committee) has exclusive jurisdiction over the Medicare and Medicaid programs. Accordingly, the Committee has a responsibility to the more than 80 million Americans who receive health care coverage under Medicare and Medicaid to oversee the proper administration of these programs, including the payment for medical devices regulated by the Food and Drug Administration (FDA). Given the rising health care costs in this country, and more importantly, in the interest of public health and safety, Medicare and Medicaid dollars should be spent on drugs and devices that have been appropriately deemed safe and effective for use by the FDA, in accordance with all laws and regulations.

In February 2005, Senator Charles Grassley (R–IA) and Senator Max Baucus (D–MT), Chairman and Ranking Member of the Committee, initiated an inquiry into the FDA's handling of Cyberonics, Inc.'s (Cyberonics) pre-market approval application to add a new indication—treatment-resistant depression (TRD)-to Cyberonics's Vagus Nerve Stimulation (VNS) Therapy System, an implanted pulse generator. The Chairman and Ranking Member initiated the inquiry in response to concerns that were raised regarding Cyberonics's VNS Therapy System for TRD. On July 15, 2005, the FDA approved the device for TRD.

The investigative staff of the Committee reviewed documents and information obtained and received from the FDA and Cyberonics and found the following:

As the federal agency charged by Congress with ensuring that devices are safe and effective, the FDA approved the VNS Therapy System for TRD based upon a senior official overruling the comprehensive scientific evaluation of more than 20 FDA scientists, medical officers, and management staff who reviewed Cyberonic's application over the course of about 15 months. The official approved the device despite the conclusion of the FDA reviewers that the data provided by Cyberonics in support of its application for a

new indication did not demonstrate a reasonable assurance of safety and effectiveness sufficient for approval of the device for TRD.

The FDA's formal conclusions on safety and effectiveness do not disclose to doctors, patients or the general public the scientific dissent within the FDA regarding the effectiveness of the VNS Therapy System for TRD. The FDA has publicized differences of scientific opinion within the agency when it has announced other controversial regulatory decisions. Throughout the review of Cyberonics's application, the team of FDA scientists, medical officers, and management staff involved recommended that the device not be approved for TRD. However, at every stage of the review, the team was instructed by the FDA official, who ultimately made the decision to approve the device, to proceed with the next stage of pre-market review.

The FDA has not ensured that the public has all of the accurate, science-based information regarding the VNS Therapy System for TRD it needs. Health care providers relying on the FDA's public information on the safety and effectiveness of this device may not be able to convey complete risk information to their patients, because not all of the relevant findings and conclusions regarding the VNS Therapy System have been made available publicly.

The FDA has an important mission:

The FDA is responsible for protecting the public health by assuring the safety, efficacy, and security of human and veterinary drugs, biological products, medical devices, our nation's food supply, cosmetics, and products that emit radiation. The FDA is also responsible for advancing the public health by helping to speed innovations that make medicines and foods more effective, safer, and more affordable; and helping the public get the accurate, science-based information they need to use medicines and foods to improve their health.

As part of that mission, the FDA weighs the risks and benefits of a product, in this case a medical device, to determine if the product is reasonably safe and effective for use.

The facts and circumstances surrounding the FDA's approval process for the VNS Therapy System for TRD raise legitimate questions about the FDA's decision to approve that device for the treatment of TRD. While all implantable medical devices carry risks, it is questionable whether or not the VNS Therapy System for TRD met the agency's standard for safety and effectiveness. The FDA's approval process requires a comprehensive scientific evaluation of the product's benefits and risks, including scientifically sound data supporting an application for approval. Otherwise health care providers and insurers as well as patients may question the integrity and reliability of the FDA's assessment of the safety and effectiveness of an approved product. In the case of VNS Therapy for TRD, the FDA reviewers concluded that the data limitations in Cyberonics's application could only be addressed by conducting a new study prior to approval. However, in the present case, instead of relying on the comprehensive scientific evaluation of its scientists and medical officers, it appears that the FDA lowered its threshold for evidence of effectiveness. Contrary to the recommendations of the FDA reviewers, the FDA approved the VNS Therapy System for TRD and allowed Cyberonics to test its device post-approval.

In addition, given the significant scientific dissent within the FDA regarding the approval of the VNS Therapy System for TRD, the FDA's lack of transparency with respect to its review of the device is particularly troubling. The FDA has limited the kind and quality of information publicly available to patients and their doctors and deprived them of information that may be relevant to their own risk-benefit analysis. Patients and their doctors should have access to all relevant findings and conclusions from the comprehensive scientific evaluation of the safety and effectiveness of the VNS Therapy System for TRD to enable them to make fully informed health care decisions.