

Statement of U.S. Senator Chuck Grassley of Iowa
"The Adequacy of FDA Efforts to Assure the Safety of the Drug Supply"
Subcommittee on Oversight and Investigations
House Committee on Energy and Commerce
February 13, 2007

Chairman Dingell, Chairman Stupak, Ranking Members Barton and Whitfield and distinguished colleagues, thank you for holding this important hearing on drug safety and the Food and Drug Administration. Thank you also for inviting me to speak today on this important subject.

During the last three years, I conducted extensive oversight of the Food and Drug Administration while I was Chairman of the Senate Finance Committee, which is responsible for Medicare and Medicaid. I view my role as working to ensure the safety and well-being of the more than 80 million Americans who are beneficiaries of these programs. The Medicare and Medicaid programs spend a lot of money on prescription drugs and medical devices, and that money should be spent on drugs and devices that are safe and effective.

In the course of my oversight of the federal bureaucracy, I have developed many good relationships with whistleblowers. And it was FDA whistleblowers and concerned FDA scientists who first drew my attention to problems at the Food and Drug Administration.

It started in early 2004 with an FDA psychiatrist named Dr. Andrew Mosholder, who realized through his work that there was a serious suicide risk for teenagers taking certain antidepressants. He wanted to make a presentation about his findings to an FDA advisory committee. But for some reason, FDA supervisors didn't want this information to get out. They canceled Dr. Mosholder's presentation and instructed him to write a script approved by his supervisors that he would use if anybody asked him why he was no longer presenting.

That Fall, I held a hearing on drug safety in the aftermath of Vioxx – the blockbuster pain medication – being pulled from the market by its manufacturer, rather than the Food and Drug Administration. The testimony at my hearing turned a bright spotlight on problems with the FDA's postmarket surveillance effort. The FDA works tirelessly, as it should, to approve new life-saving and life-enhancing drugs. But it could do a lot better job of keeping track of developments with these drugs after they're on the market. Reviewing what happened inside the FDA with Vioxx, and in working with a number of whistleblowers who bravely stuck their necks out and came to me after that landmark hearing, I've identified problems at the FDA that consistently fit into a few themes.

First, scientific dissent is discouraged, quashed, and sometimes muzzled inside the Food and Drug Administration. Second, the FDA's relationship with drug makers is too cozy. The FDA worries about smoothing things over with industry much more than it should with its regulatory responsibilities. Third, inside the FDA there's widespread fear of retaliation for speaking up about problems. And fourth, the public safety would be better served if the agency was more transparent and forthcoming about drug safety and drug risks.

These problems involve the culture of the Food and Drug Administration. They're not isolated but systemic. And they can be partly attributed to the organizational structure of the FDA.

My concerns are not isolated either. During the last year, they've been validated by the highly regarded Institute of Medicine, as well as the independent Government Accountability Office and respected medical journals. What's at stake is public safety and public confidence in our nation's world-renowned Food and Drug Administration.

My investigations of FDA issues have also revealed a deeply troubling disregard for Congress' responsibility to conduct oversight of the executive branch of government. The FDA and the Department of Health and Human Services have put up so much resistance to my effort to find out what happened inside the FDA with a relatively new antibiotic called Ketek that I can only wonder what there is to cover up.

Every excuse under the sun has been used to create roadblocks, even in the face of Congressional subpoenas requesting information and access to FDA employees.

In denying access to documents responsive to the subpoenas, the Department and FDA have claimed "prosecutorial deliberative process," "confidential communications," and "agency prerogative to determine who will be interviewed or testify before a jurisdictional committee." Yet, during my years in the Senate, my investigators have obtained access to every single one of these categories of so-called confidential information from HHS as well as other executive branch agencies.

Furthermore, I asked the Congressional Research Service to look into the Department's policies regarding this matter and CRS told me that there is "no legal basis" for the Department's executive branch assertions.

Nevertheless, the Department and FDA not only withheld documents that do not appear to be privileged, but they also won't say what has been withheld and why. The subpoenas compel a privilege log, but the Department and FDA will not provide one.

The Department and FDA say that they have been responsive to the Finance Committee's Ketek investigation because they made available millions of pages of documents to the Committee. But what they provided is quantity, not quality.

They delivered hundreds of pages simply marked, for example, "57 pages removed," or "43 pages removed." (see attachments 1-5) Other documents have whole pages, paragraphs or sentences redacted with no explanation for what has been withheld or redacted and why. (see attachment 6) In fact, the FDA redacted some of the same documents differently¹ and even redacted one of my own letters to them on a different matter (see attachment 7)

When I point out the absurdities in the Department's responses to my requests for documents and interviews related to Ketek, the Department argues it could not provide access to information and individuals related to open criminal investigations. But I didn't

¹ For example, FDA redacted a paragraph from one copy of an email without redacting the same paragraph in the second copy. The documents are not attached to this statement because the unredacted portions contain information related to ongoing investigations.

ask for access to open criminal investigations; I don't want to jeopardize a criminal matter. The Department and the FDA know that, yet they keep using that excuse anyway.

Even so, what I've learned about what happened with Ketek troubles me. I've learned that:

- FDA gave its advisory committee questionable data on Ketek and did not tell them about problems with that data. I sent a letter to the FDA in December regarding my findings on this matter and am awaiting a response from the agency.
- FDA approved Ketek without much safety data from the U.S.; the agency relied almost exclusively on foreign, post-marketing safety data; and
- Ketek's sponsor in all likelihood was aware of the fact that it submitted some questionable data to the FDA regarding its large safety study; the sponsor was informed of problems with one of the study sites prior to data submission to the FDA. However, according to FDA reviewers, the sponsor never raised these problems to the FDA. FDA learned about them after its own investigators inspected the site.

I plan to continue my investigation of Ketek and issue more reports. But I am heartened to hear that FDA came to a decision yesterday that mirrors the recommendations of its internal scientists as well as its advisory committees.

During the last three years, I've also tried to work in a productive way with the Commissioners and Acting Commissioners of the FDA. It will take bold leadership to get on top of the FDA's troubles and turn the agency around. So far, the lip service has been fine. The reality a lot less so.

Last month, Senator Chris Dodd and I reintroduced two reform bills that we first proposed in 2005 to get at the safety shortcomings of the FDA. Our first bill would elevate and empower the office with the FDA that is responsible for monitoring FDA-approved drugs after they're on the market. It would make the "postmarket drug safety" function independent within the FDA, instead of under the thumb of the office and center that puts the drugs on the market in the first place, the way it is today.

Chairman Dingell, the *Wall Street Journal* has reported that you're intrigued by the idea of a drug safety center within the FDA. I appreciate that view. It doesn't make any sense that the FDA officials who are supposed to monitor the safety of a drug on the market serve only as consultants to the FDA officials who approved the drug in the first place. ~~The officials who approved the drug would obviously be conflicted in making a judgment that approval is no longer appropriate or was a mistake in the first place. A separate center for drug safety within the FDA is a vital lynchpin when it comes to meaningful reform and improvement of the agency's postmarket surveillance work.~~

The second bill that Senator Dodd and I introduced would expand an existing public database by mandating the registry of all clinical trials and the results of those trials. This reform is key to establishing greater transparency regarding clinical trials, the good ones and the bad ones, and to holding drug makers and drug regulators accountable.

Both of these legislative initiatives would make drug information used by doctors and patients more complete and more accessible. American consumers should not have to second guess the safety of the pills in their medicine cabinets.

I appreciate the attention all of you are giving to this important national issue with this hearing. You will hear from some of the heroic whistleblowers who have helped my work, without whom my work wouldn't have been possible. Two of the whistleblowers have left the FDA. It's a tremendous loss for our country when an agency like the Food and Drug Administration gets so dysfunctional that specialists like these whistleblowers are forced to leave the agency to avoid retaliation. I want to work closely with you to make sure FDA whistleblowers can communicate to Congress without fear.

In addition, the existing agreement between the Inspector General for the Department of Health and Human Services and the Food and Drug Administration gives too much power to the FDA when it comes to how allegations of criminal misconduct by FDA employees are investigated. That agreement should be revisited by reform minded leaders in Congress.

I look forward to reform opportunities in the year ahead. There's no doubt that the FDA needs additional tools and resources to do its work. The FDA also needs an overhaul to make the agency more transparent, more forthcoming, and more independent-minded.

I look forward to working with this Committee and in particular with you, Chairman Dingell and Stupak and Ranking Members Barton and Whitfield, as well as my colleagues in the Senate to enact reforms at the FDA.

Thank you. I would be happy to stay and take a few questions. Unfortunately, I have several other hearings that I must attend so I can't stay long.

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KOLAN DAVIS, STAFF DIRECTOR AND CHIEF COUNSEL
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August 24, 2005

Via Electronic Transmission
Original via USPS Mail

The Honorable Lester M. Crawford, D.V.M., Ph.D.
Commissioner
U.S. Food and Drug Administration
5600 Fishers Lane
Rockville, MD 20857

Dear Commissioner Crawford:

Thank you for the Food and Drug Administration's (FDA) timely response to my letter dated June 24, 2005. I requested that the FDA address questions and provide documents related to non-arteritic anterior ischemic optic neuropathy (NAION) and the use of drugs prescribed by physicians to treat erectile dysfunction (ED), including Viagra, Cialis and Levitra.

In particular, I asked the FDA to describe, in detail, any actions that will be taken to ensure that patients are informed of NAION and its association with ED drugs. The FDA stated in a letter dated July 20, 2005, that Patient Information Sheets for each ED drug have been posted on the FDA's website that include information about possible vision loss and patients who may be at risk for NAION. That letter also stated that information was provided to over 50,000 individual subscribers by e-mail through MedWatch, the FDA's safety information and adverse event reporting program.

According to IMS Health, a company that monitors prescription drug sales across the nation, prescriptions for ED drugs in 2004 totaled more than 7,300,000 including (b)(4) prescriptions for Viagra, (b)(4) prescriptions for Cialis, and (b)(4) prescriptions for Levitra. Although there is a possibility that the 50,000 subscribers to the MedWatch e-mail list and individuals who have accessed the Patient Information Sheets may now be aware of the NAION risks associated with ED drug use, there are millions more who remain in the dark. It seems likely that many millions of men with ED drugs sitting in their medicine cabinets have not visited the FDA's website and/or seen the media reports about the risk of permanent vision loss. In addition, it is unlikely that these millions of men have followed up with the physicians who prescribed them the medication because ED drugs are typically used on an as-needed basis. Dr. Crawford, who will inform these patients and consumers of the concerns that have come to light with regard to the use of ED drugs? Has the FDA considered initiating other action(s) to inform adequately these millions of patients about NAION and its association with ED drug use? More importantly, in the future, how will the FDA attempt to inform patients who do not

require regularly scheduled physician follow-up about important safety information regarding their medications?

Finally, the FDA has still not addressed two issues that concern me. Why did it take so long for the FDA to negotiate the label changes for ED drugs and to notify the public of the NAION risk associated with ED drugs? The FDA has a duty to notify the public promptly about a serious risk associated with a drug and identified in the post-market. Permanent blindness surely is such a serious risk.

In closing, I look forward to hearing from you regarding this important matter by no later than September 14, 2005. Should you have any questions regarding this letter, please do not hesitate to contact Emilia DiSanto or Tom Novelli at (202) 224-4515. All formal correspondence should be sent electronically in PDF searchable format to thomas_novelli@finance-rep.senate.gov or via facsimile to (202) 228-2131. All originally material should be sent via USPS mail.

Sincerely,



Charles E. Grassley
Chairman

Memorandum of Understanding
Between the Food and Drug Administration
and
Office of Inspector General
Department of Health and Human Services

PURPOSE:

Recognizing the statutory mandates of both components, and their important roles, and the necessity for maintaining a capable and trained internal investigational unit to conduct internal investigations, to provide a centralized investigative liaison between the Food and Drug Administration (FDA) and the Office of Inspector General (OIG), and to support the OIG's criminal investigations that involve FDA employees, the two components enter into this Memorandum of Understanding concerning the procedures they will observe in internal investigations involving FDA employees.

THE OFFICES

A. The Office of Inspector General

The Inspector General Act of 1978, Public Law 95-452, as amended by Public Law 100-504, 5 U.S.C. App., established the Office of Inspector General as an independent office within the Department of Health and Human Services (HHS). A major purpose of the OIG is to "conduct and supervise audits and investigations relating to the programs and operations of [HHS]." Section 2(1) of the Inspector General Act. The Act further provides that, "in carrying out the

duties and responsibilities established under this Act, each Inspector General shall report expeditiously to the Attorney General whenever the Inspector General has reasonable grounds to believe there has been a violation of Federal criminal law." Section 4(d).

B. *The Office of Internal Affairs*

The FDA, including its Office of Criminal Investigations (OCI), is a component of HHS and is responsible for implementing the Food, Drug, and Cosmetic Act, 21 U.S.C. § 321 et seq. and other statutes. The Office of Internal Affairs (OIA) which is staffed by special agents detailed from OCI, was authorized and established by the Secretary of HHS, within the FDA, Office of Commissioner, to conduct internal investigations of employee misconduct. 60 Fed. Reg. 4417 (January 23, 1995). The OIA Statement of Organization states that OIA "provides a centralized investigative liaison between FDA and [OIG]" and shall serve "as an FDA investigative resource to conduct internal FDA investigations and to support OIG investigations." *Id.*

PROCEDURES

1. FDA will continue to ensure that its Office of Internal Affairs (OIA) is properly equipped and supported and staffed with trained and experienced criminal investigators (1811-series), and will continue to refresh the OIA staff by assigning agents from FDA's Office of Criminal Investigations to the OIA for duty tours on a rotating basis.
2. The OIG will continue to staff its FDA investigations with trained and experienced criminal investigators (1811-series) and will endeavor to provide adequate resources for investigations so as to enable OIA to investigate promptly after allegations are made.

3. OIG and FDA's OIA shall have prompt access to all files and documents within the FDA relevant to their investigations, and the resulting open investigative files and documents of these investigative entities shall be disclosed outside the Department only to prosecutors and other law enforcement entities, consistent with applicable law and regulation and as necessary to accomplish the respective missions of the OIG and OIA.

4. When OIA receives an allegation of criminal misconduct or violation of the HHS standards of conduct by an HHS employee, OIA shall immediately notify the OIG in writing or by electronic mail. Similarly, when OIG receives an allegation of criminal misconduct or violation of the HHS standards of conduct by an FDA employee it shall, as appropriate with its role under the Inspector General Act, immediately notify OIA in writing or by electronic mail. This notification by the OIG should occur unless the OIG determines that the notification is inconsistent with its role under the Inspector General Act.

5. If, at any point during an investigation, OIA determines that a criminal violation has likely been committed by an FDA employee, OIA shall immediately notify the OIG in writing or by electronic mail. If at any point during an OIG investigation, OIG determines that a criminal violation by an FDA employee has likely occurred, but the OIG determines it will not investigate that violation, it will, as appropriate with OIG's role under the Inspector General Act, immediately notify the OIA in writing or by electronic mail.

6. In recognition of the availability and performance of the FDA OIA, as an existing, trained, equipped and supported investigative unit engaged in investigations of allegations of violative or illegal conduct by FDA employees, and to avoid the duplication of resources and effort that would result from dual focus on any particular investigation, both components anticipate that such investigations will be conducted expeditiously by FDA's OIA, subject to OIG's reservation

of the right in all cases to pursue a case jointly with OIA, or, after consultation with OIA, to replace OIA as the primary agency assigned to an investigation of an FDA employee. OIA will maintain an open file until it receives a final summary and disposition from the OIG on such cases. Any referral of an investigation by the OIG to the OIA will be made expeditiously, enabling OIA to begin any necessary investigation on current information. If OIA believes that its development of an investigation requires issuance of a subpoena duces tecum, it may request that the OIG pursue the case jointly with the OIA.

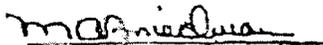
7. A headquarters OIG/OI supervisor will meet with the OIA Special Agent in Charge on a monthly basis for the purpose of examining all open investigations or cases, preliminary investigations, and any other informal investigative matters which in the judgment of OIA would be of interest to OIG. OIA will provide OIG with a report of all open investigations or cases, preliminary investigations, and any other informal investigative matters which in the judgment of OIA would be of interest to OIG. The outcome of all cases and investigations concluded during the course of the previous month will also be discussed at this meeting.

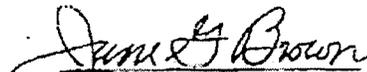
8. The OIA will provide reasonable notice to the OIG prior to any presentation to the Department of Justice of an investigation in order to allow OIG to participate in the presentation if OIG chooses.

This Memorandum of Understanding is entered into voluntarily by both OIG and FDA. It may be modified at any time by agreement of the parties and may be terminated upon thirty days prior written notice by either agency.

This Memorandum of Understanding shall become effective upon the date of signing by both parties and shall continue until it is modified or terminated.

Signed this 30th day of July, 1998


Michael A. Friedman, M.D.
Lead Deputy Commissioner
Food and Drug Administration


Judge Gibbs Brown
Inspector General

