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: Ketek
DA: Mon., Febr. 12, 2007

Sen. Chuck Grassley issued this comment regarding the announcement today by the Food and Drug Administration of label and indication changes for the antibiotic Ketek:

"The FDA's action today shows what transparency can do. When a spotlight was turned on the questionable way in which Ketek got approved by the FDA for certain sinus and lung infections, the FDA was held accountable. Last summer, the warnings on the drug label got stronger, and in December, the FDA sought expert advice from its advisory committees. Now the uses for Ketek are limited, and the public is safer and better informed . My goal through legislative reform and continued oversight is to make the FDA right its wrongs without delay, and to let the science prevail, whether it's for or against drug approval."

Sen. Grassley is scheduled to testify tomorrow before the House Energy and Commerce Subcommittee on Oversight and Investigations regarding drug safety. During the last year, Sen. Grassley has conducted extensive oversight of the way the Food and Drug Administration approved Ketek, even issuing a congressional subpoena for documents and directly confronting officials at the Department of Health and Human Services. Documents describing his oversight and findings follow this memo.

Sen. Grassley began his oversight of the FDA three years ago. He has put pressure on the drug safety agency to act with more independence and transparency than it now demonstrates in order to restore public confidence and strengthen public safety. He has called the FDA's relationship with the drug industry "too cozy" and criticized the way that agency leaders have acted to suppress scientific dissent regarding agency actions and drug-safety recommendations.

Last month, Sen. Grassley reintroduced his reform legislation with Sen. Chris Dodd to revamp and prioritize the post-market surveillance process within the Food and Drug

Administration (S.468) and to greatly expand public access to information about clinical trials regardless of the outcome of those trials through a clinical trials registry and results database (S.467). The senators authored nearly identical bills in the last Congress in the aftermath of the Vioxx and revelation of suicide risks with the pediatric use of antidepressants.

Previous documents:

For Immediate Release
Tuesday, Dec. 19, 2006

Grassley: Drug Safety Agency's Statements Under Scrutiny

WASHINGTON – Sen. Chuck Grassley, chairman of the Committee on Finance, has expressed concern that the Food and Drug Administration may have misled a joint advisory panel on the antibiotic Ketek. Grassley requested a transcript of the panel's proceedings as part of the committee's ongoing investigation of how the FDA handled data integrity problems with a pivotal Ketek safety study. Before the advisory panel met last week, Grassley issued a report showing the agency intentionally withheld key information from an advisory panel in January 2003 and dismissed concerns expressed by staff-level officials about presenting the troubled study to the advisory panel.

"It's unfortunate that the FDA misled its expert advisors and the public regarding Ketek once already," Grassley said. "Further scrutiny may show that some agency officials misled the public yet again. Convening the joint advisory panel was a step toward greater transparency and accountability, but the FDA appears to have taken another step back in the attempt."

The text of Grassley's latest letter follows here.

December 18, 2006

Via Electronic Transmission
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 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 prescription drugs regulated by the Food and Drug Administration (FDA), Department of Health and Human Services (HHS).

Last week, the FDA convened a joint meeting of the Anti-Infective Drugs Advisory Committee and the Drug Safety and Risk Management Advisory Committee (Joint Ketek Advisory Committee) to reconsider the risks and benefits of the antibiotic Ketek. As the Committee continues to investigate several allegations relating to the approval and post-market surveillance of Ketek by the FDA, I am troubled by a number of statements made on the record by agency officials, and other participants, before the Joint Ketek Advisory Committee, which appear to be factually inaccurate and/or misleading. It appears the FDA did not ensure that an expert advisory panel and the public received accurate information regarding Ketek. Pursuant to the Committee's ongoing investigation, I respectfully request a copy of the draft transcript of the proceedings of the Joint Ketek Advisory Committee as soon as a draft copy is made available to FDA. Please have your staff contact the Committee by no later than the end of this week, December 22, 2006, to identify the company that transcribed the Joint Ketek Advisory Committee proceedings and when FDA expects to receive a draft transcript. If you anticipate any difficulty in complying with the deadline, please immediately contact my Committee Staff.

Sincerely,
Charles E. Grassley
Chairman

For Immediate Release
Wednesday, Dec. 13, 2006

Grassley: Drug-Safety Agency Withheld Key Information From Expert Panel

WASHINGTON — As panelists prepare to meet regarding the risks and benefits of a relatively new antibiotic on the American market, Sen. Chuck Grassley said the Food and Drug Administration intentionally withheld key information from its own advisory panel in January 2003 about the integrity of a pivotal clinical trial used to support the safety of the drug and dismissed concerns expressed by staff-level officials before the advisory panel meeting.

Grassley has been conducting a lengthy review of the way the nation's drug-safety agency handled the approval and conducted post-market surveillance of the drug Ketek. Today, he released statements made by a number of members of the 2003 board in response to a survey he conducted about the FDA's posture on Ketek during those deliberations. Grassley reported his findings in a letter to the newly confirmed commissioner of the Food and Drug Administration. Grassley's letter report also includes detailed information about internal FDA communications and decisions that led to the agency's presentation of highly suspect information at that 2003 meeting.

"The Food and Drug Administration can't be in the business of misleading the public and hiding the truth," Grassley said. "I agree with these experts who say the agency was wrong for withholding information from them and to present a flawed study. The integrity of the agency is at stake. The new commissioner has promised to improve the way the FDA operates. If he lives up to his word, maybe something good will come out of this."

A newly formed FDA advisory panel will meet tomorrow and Friday to review the FDA's actions on Ketek, assess the risks and benefits of the drug, and make recommendations about the antibiotic's FDA-approved status. Grassley remains concerned that the FDA approved Ketek relying largely on foreign post-market data, reportedly an unprecedented step, after the pivotal safety study demanded by the agency proved to be useless for regulatory purposes.

A copy of Grassley's letter report is posted at http://finance.senate.gov.

M E M O R A N D U M

TO: Reporters and Editors
FR: Jill Kozeny, 202/224-1308
RE: Ketek
DA: June 29, 2006

Sen. Chuck Grassley issued the comment below in response to the announcement today about Ketek and a new bold warning label. Sen. Grassley has been investigating allegations about the FDA's handling of Ketek and failure to ensure the integrity of a pivotal study about the benefits and risks of this drug. The FDA continued to cite the study in safety information despite its own determination that the study was riddled with fraudulent information.

Grassley comment ---

"There are questions about whether this drug should stay on the market, and there's great legitimacy to those questions. Ketek is another example where the FDA accommodated a drug maker and turned a blind eye to serious safety concerns. The FDA has become a great facilitator, giving the drug makers what they want. What's happened with Ketek leaves little doubt that the FDA is incapable of taking the bold steps needed to protect Americans. Without that kind of commitment, giving drug safety equal footing with drug approval, Congress must act to make sure FDA understands where it has strayed from its mission."

Remarks of U.S. Sen. Chuck Grassley of Iowa
at the U.S. Department of Health and Human Services
Wednesday, June 14, 2006

Finance Committee staff investigators have been looking into the fraud that took place when the antibiotic drug Ketek was studied for safety and efficacy. This drug is on the market for adults despite all the questions about it. It's being studied in babies as young as six months old.

I came here today because I've been asking for a meeting with a special agent for the Food and Drug Administration and documents related to that agent's work on Ketek.

I'm fed up with resistance from the bureaucracy. It's been one excuse after another. Practices and policies have changed from one day to the next. Files available one day become "confidential" overnight. A line agent isn't allowed to tell his story, even though line agents have been made available in other cases. The agency says its employees will not be prohibited from cooperating with Congress, then instructs its employees not to cooperate with Congress. The agency won't provide a background briefing on past regulatory decisions.

None of the excuses for withholding information come anywhere near the importance of getting to the truth. Based on the run around that's gone on, I smell a cover up.

I came here today out of frustration, and after exhausting many other avenues, including formal letters of request, countless staff phone calls, a personal call from me to Secretary Leavitt and personal letters to Secretary Leavitt. I've only come in person to a federal agency one other time, when I went to the Pentagon in 1983. So I wish I didn't have to make this trip.

The FDA and the Department of Health and Human Services, in consultation with the Justice Department, are dug in. Sadly, that position will not help those taking Ketek now and the children already enrolled in the clinical trial.

Therefore, I've instructed my staff to look at a possible Finance Committee hearing. It's time to get all this out on the table and in the light of day. I'm committed to getting to the bottom on the questions and fulfilling my Constitutional responsibility to oversee the executive branch of government. Public safety and government accountability are at stake.

For Immediate Release
Tuesday, June 13, 2006

Grassley presses for information about antibiotic drug

WASHINGTON — Sen. Chuck Grassley said he will make a personal trip to the Department of Health and Human Services tomorrow for a meeting he requested with an FDA agent and to review documents about fraud that compromised a study on the safety of an antibiotic known as Ketek.

Grassley has been asking for information about Ketek from the Food and Drug Administration since April and said today that he's gotten fed up with resistance from the bureaucracy. "It's been one illegitimate excuse after another," he said. "The allegations of misconduct with this drug are as bad as any I've heard. I'm committed to getting to the bottom of the matter and fulfilling my Constitutional responsibility to oversee the executive branch of government."

Grassley said that he has asked the Secretary of Health and Human Services to gather the documents and make arrangements for him to meet with a special agent of the Food and Drug Administration at 12:30 pm, on Wednesday, June 14, in the offices of the Department of Health

and Human Services at 200 Independence Avenue, NW, in Washington.

A May 30 letter to Grassley from the Assistant Secretary for Legislation said that the Department of Health and Human Services had consulted with the Department of Justice and "is not able to make [line] agents available for interviews, but will make supervisory staff available to meet with Committee staff." Grassley said this assertion ignores historical precedent, including a recent event. Grassley's own Finance Committee staff interviewed two line agents from the FDA's Office of Criminal Investigations in November 2005.

Last week, the manufacturer of Ketek suspended its pediatric studies of Ketek. Previously, one of the main studies that supported approval by the Food and Drug Administration of Ketek for adults was found to be fraudulent. Even so, the agency continues to promote the study as evidence of the drug's safety.

Grassley's oversight of the Food and Drug Administration started two years ago when the drug safety agency tried to keep a lid on information about the dangers of antidepressants when used by children and teenagers. Since then, the senator has introduced legislation to improve post-market surveillance of drugs by the Food and Drug Administration and to require that information about clinical trials be publicly available. He also has urged the agency to make administrative reforms.

For Immediate Release
Tuesday, May 16, 2006

Senator says FDA should stop citing a fraudulent Ketek study, seeks access to information

WASHINGTON --- Sen. Chuck Grassley said it's "mystifying" that the Food and Drug Administration continues to provide information the agency knows is fraudulent about the safety of the antibiotic Ketek, and he's keeping the pressure on for more information about the FDA's initial approval and post-market surveillance of the drug.

In particular, Grassley is asking the drug-safety agency to allow one of its special agents who investigated and assisted in the prosecution of a fraud case involving a Ketek study to meet with Grassley staff investigators. Grassley is also seeking access to FDA documents, including emails, about Ketek.

"The FDA has an obligation to be forthcoming and open about its actions," Grassley said. "Serious allegations have been made about misconduct with the drug Ketek, and the public should not be mislead with statements about the safety of Ketek that cite a fraudulent study."

Grassley said his questions are part of his ongoing oversight of the Food and Drug Administration. "Congress has a constitutional responsibility to oversee the executive branch of government, and the FDA as a public agency has a responsibility to be responsive," he said.

The text of Grassley's second letter to the Acting Commissioner of the FDA about Ketek follows here, along with the text of his initial, April 27, letter.

May 16, 2006

Andrew C. von Eschenbach, M.D.
Acting Commissioner
U.S. Food and Drug Administration
5600 Fishers Lane
Rockville, MD 20857

Dear Dr. von Eschenbach:

The 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, including prescription drugs, under those programs.

The Committee continues to investigate extremely troubling allegations related to, among other things, the approval and post-market surveillance of telithromycin (Ketek) by the Food and Drug Administration (FDA). One of the most troubling allegations is that the FDA approved Ketek with full knowledge that some of the clinical safety data supporting its approval was beset by systemic data integrity problems. While the FDA takes its time negotiating with Sanofi-Aventis to decide what drug risk information the public should know, it is completely mystifying why a fraudulent clinical trial is referenced in safety information on the FDA's website. The American people deserve better. When will the FDA do the right thing and correct this information?

As Chairman of the Committee, I also respectfully request that your staff make immediate arrangements for my Committee staff to interview Special Agent , who successfully investigated and participated in the prosecution and sentencing of Dr. Maria Anne Kirkman Cambpell to nearly five years in prison for her fraud in Ketek Study 3014. In addition, provide a copy of all documents and communications related to Ketek and Study 3014 in the possession of Special Agent , including, but not limited to, all emails related to Ketek and/or the Committee's investigation of Ketek. Given the gravity of the Ketek allegations, I respectfully request that your staff contact my staff by no later than Thursday, May 18, 2006, to make arrangements for this interview and for the Committee to obtain the requested documents from Special Agent by no later than May 24, 2006. If you anticipate any difficulty in complying with this deadline, please immediately contact my Committee staff.

As you know, I requested that all FDA employees involved directly or indirectly with Ketek be immediately provided with a copy of my letter, dated April 27, 2006, to inform them of their right to speak and to cooperate with Congress. I also requested that all FDA employees should be informed that no documents, records, data or information related, directly or indirectly, to Ketek shall be destroyed, modified, removed or otherwise made inaccessible to the Committee. Further, if any FDA employee believes that he or she has been subject to retaliation

for meeting with Committee staff and/or for anything associated with the Committee's ongoing investigation of Ketek, the employee should contact the Committee immediately. Thank you for forwarding a copy of this letter to employees within the Center for Drug Evaluation and Research, however, I understand that it was not forwarded to the Office of Criminal Investigations, among others.

Accordingly, please advise Special Agent and all FDA employees within the Office of Criminal Investigations that they have the right to speak directly and independently to Congress, or to a Committee of Congress, without interference from the FDA if they wish, in accordance with 5 U.S.C. § 7211. Retaliation against these individuals, or any other FDA employees, who communicate with the Committee in reference to Ketek will not be tolerated. Such conduct is further punishable by 18 U.S.C. § 1505 and false statements and perjury are likewise punishable pursuant to 18 U.S.C. § 1001. Further, under 5 U.S.C. § 2302(b)(8), a federal employee authorized to take, direct others to take, recommend or approve any personnel action may not take, fail to take, or threaten to take any personnel action against an employee because of protected whistleblowing. Protected whistleblowing is defined as disclosing information which the discloser reasonably believes evidences: a violation of law, rule, or regulation; gross mismanagement; gross waste of funds; an abuse of authority; or a substantial and specific danger to public health or safety.

Please also note that P.L. 109-115 enunciates a government-wide prohibition on the use of appropriated funds to pay the salary of any federal official who prohibits or prevents or threatens to prevent or prohibit a federal officer or employee from contacting Congress, and "any punishment or threat of punishment because of any contact or communication by an officer or employee with a Member, committee or subcommittee."

Thank you in advance for your assistance.

Sincerely,
Charles E. Grassley
Chairman

For Immediate Release
Monday, May 1, 2006

Grassley slams FDA for citing fraudulent safety study

WASHINGTON — Sen. Chuck Grassley today released information about his ongoing investigation of the Food and Drug Administration regarding the drug-safety agency's initial approval and post-market surveillance of the antibiotic Ketek.

Grassley, who chairs the Senate Committee on Finance, said he is concerned about the FDA's complicity with the drug maker and subsequent failure to ensure the integrity of a pivotal study about the benefits and risks of this drug. He said he is also alarmed at the FDA's continued

reliance on the study as evidence of Ketek being safe, despite the FDA's own determination that the study is riddled with fraudulent information. Finally, Grassley said the stakes continue to grow when it comes to overseeing this antibiotic, since it is being studied in children as young as six months old.

"The allegations of misconduct in this case are as bad as I've heard yet," Grassley said. "It looks like the FDA caught the drug company red handed and let them get away with it. On top of that, the FDA failed to set the record straight and, in fact, continues to cite a discredited safety study as a principal reason to feel okay about using this drug."

The text of a letter Grassley sent last week to the Acting FDA Commissioner follows here.

April 27, 2006

Andrew C. von Eschenbach, M.D.
Acting Commissioner
U.S. Food and Drug Administration
5600 Fishers Lane
Rockville, MD 20857

Dear Dr. von Eschenbach:

The 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, including prescription drugs, under those programs.

As Chairman of the Committee, I am writing to inform you that the Committee has been investigating extremely troubling allegations related to, among other things, the approval and post-market surveillance of telithromycin (Ketek) by the Food and Drug Administration (FDA). The FDA approved Ketek, an antibiotic manufactured by Aventis Pharmaceuticals (Aventis), on April 1, 2004, for the treatment of community-acquired pneumonia, sinusitis, and acute exacerbation of chronic bronchitis. Several serious allegations related to Ketek have been brought to the attention of the Committee. Among the most troubling are allegations that the FDA approved Ketek despite unresolved questions about the drug's safety and efficacy and with full knowledge that some of the clinical safety data supporting its approval was beset by systemic data integrity problems.

Documents and information available to the Committee reveal that at least one of the "three principal sources of clinical data to assess the safety of telithromycin: Study 3014" was fraudulent, in whole or in part. In particular, a memorandum, dated March 25, 2004, prepared by the FDA's Division of Scientific Investigations (DSI) and entitled, "DSI Recommendations on Data Integrity," states unequivocally that Study 3014 involved "multiple instances of fraud" and that "the integrity of data from all sites involved in [the] study . . . cannot be assured with any degree of confidence." Additional allegations brought to the attention of the Committee assert

that FDA management:

1. accepted from Aventis the resubmission of a new drug application for Ketek, which included fraudulent data in support of approval of Ketek;
2. instructed FDA scientists preparing to appear before an advisory committee that they should present fraudulent data because discussing issues regarding data integrity and the conduct of the safety study would not be "productive";
3. presented fraudulent study data to an advisory committee tasked with recommending Ketek's approval or disapproval;
4. approved a pediatric clinical trial of Ketek, involving infants as young as six-months old, despite concerns related to known toxicities, including hepatic, visual, cardiovascular, and vasculitic adverse events; and
5. continued to knowingly cite fraudulent study data in publicly released safety information on Ketek.

Given that an advisory committee had recommended conducting Study 3014 in the first place, theses allegations are all the more outrageous. Specifically, in April 2001, Ketek was first brought before an advisory committee (the Anti-Effective Drugs Advisory Committee (AIDAC)) to consider the question: "Given the risks of cardiac and hepatic toxicity of [Ketek], does efficacy for [Ketek] in respiratory infections support its use for … community acquired pneumonia; acute exacerbation of chronic bronchitis; and acute sinusitis?" Based on continued concerns related to the toxicity of Ketek, AIDAC recommended that Aventis conduct a large clinical safety study. Accordingly, by letter dated June 1, 2001, the FDA asked Aventis to conduct just such a safety study:

It would be helpful . . . to assess further adverse events associated with [Ketek], particularly in patients at increased risk for potential drug related toxicity. . . . This study should include the monitoring and analysis of all adverse events, with particular attention to hepatic, visual, cardiovascular, and vasculitic adverse events. Investigations of any mortality outcomes by investigators should be conducted to evaluate optimally possible cardiac or liver toxicities or evidence of systemic vasculitis.

Aventis agreed to conduct a large safety study -- designated Study 3014 -- and subsequently submitted the results of Study 3014 to the FDA, despite allegedly knowing and not fully disclosing that the study was fraught with data integrity problems. When AIDAC reconvened to consider Ketek's risks and Study 3014, the safety study it had requested, the FDA presented data from Study 3014 without disclosing, in closed or open session, the fact that DSI and the FDA's Office of Criminal Investigation (OCI) were actively investigating both the integrity and conduct of the study. Without the benefit of this relevant information, AIDAC members voted to recommend approval of Ketek. The AIDAC board members would undoubtedly have been interested to know that the highest enrolling sites in Study 3014 were being investigated for major problems and that there appeared to be "significant under reporting of [adverse events]." For example, the principal investigator at the highest enrolling site was found to be enrolling patients when the clinic was closed and patient consent forms at the site

were found to have date modifications and signature inconsistencies. In August 2003, eight months after the AIDAC meeting, this particular investigator was indicted for falsifying study data, pleaded guilty in October 2003, and in March 2004 was sentenced to 57 months in jail.[1]

It is even more shocking that the FDA continued to cite Study 3014 in publicly released safety information for Ketek. Just a few months ago, on January 20, 2006, the FDA issued a Public Health Announcement (PHA),[2] following the publication of an article in the Annals of Internal Medicine, which reported that three patients experienced serious liver toxicity, one case required liver transplantation and one resulted in a patient death, following administration of Ketek.[3] Coincident with the PHA, the FDA also publicly released a document entitled, "Questions and Answers on Telithromycin (marketed as Ketek)" (Ketek Q&A), which stated, in pertinent part:[4]

> What information was known about liver problems related to telithromycin prior to approval?
>
> Based on the pre-marketing clinical data it appeared that the risk of liver injury with telithromycin was similar to that of other marketed antibiotics.
>
> Prior to approval, FDA looked extensively at the potential for hepatic toxicity in patients treated with Ketek. The data examined included a 25,000 patient controlled study, as well as information in nearly 4 million postmarketing prescriptions outside the United States. Ketek was the subject of two advisory committee meetings with input from a national expert on drug-induced liver disease. The committee concluded that the risk for hepatotoxicity from Ketek was similar to Augmentin and erythromycin which are other approved antibiotics. (emphasis added).

In this Ketek Q&A, the FDA cited the very study that DSI determined in March 2004 had "multiple instances of fraud" and that "the integrity of data from all sites involved in [the] study . . . cannot be assured with any degree of confidence." It defies explanation why the FDA would continue to cite Study 3014 in safety information for Ketek provided to the American public and do so without also disclosing that the advisory committee's recommendation came without knowledge that Study 3014 was fraudulent, in whole or in part. Please explain in detail why the FDA has continued to cite Study 3014 in its safety information for Ketek. Further, why would disclosing this information to AIDAC not be "productive"?

The Committee has also received equally serious allegations related to the post-market surveillance of Ketek. For example, there is presently an ongoing, FDA-approved pediatric clinical trial of Ketek, known as "TELI COM – Telithromycin in Children With Otitis Media."[5] Despite the known toxicities of Ketek, including evidence of hepatic, visual, cardiovascular, and vasculitic adverse events, the FDA is allowing Aventis to experiment with Ketek on children as young as six-months old. For example, my Committee Staff is aware of a report submitted to the FDA's Adverse Event Reporting System that details a suspected visual adverse event in a 15-month old girl participating in the pediatric trial. According to the report,

on three occasions the mother observed her baby girl have staring spells one day after taking Ketek. One time the staring spell lasted for 60 seconds. The investigator initially reported that the event was related to Ketek and "serious." According to subsequent addendums to the report, dated months later, the investigator downgraded this event -- it was later assessed to be "non-serious," not interpreted as a "visual event," and that a "staring spell is considered unexpected." Given that the Ketek label warns of severe cases of visual problems,[6] please advise the Committee what action has been taken to fully inform the parents of infants and children enrolled in this study about the risks and benefits of Ketek, including its known liver and visual toxicities.

Furthermore, as Chairman of the Committee, I respectfully request that your staff make immediate arrangements for my Committee staff to review documents and information related to Ketek and Study 3014 at the FDA, including, but not limited to, the administrative files within DSI, OCI, and the Office of Compliance. Given the gravity of the Ketek allegations, I respectfully request that your staff contact my Committee staff by no later than Friday, April 28, 2006, so that my Committee staff may travel to your offices as soon as possible to review the requested administrative files.

As Chairman of the Committee, I also respectfully request that senior FDA management officials be prepared to brief my Committee staff within three weeks of the date of this letter. To expedite this request, my staff will be available to travel to the FDA for the briefing. I respectfully request the attendance and participation of the following individuals at that briefing:

1. Director, Office of New Drugs (OND), Center for Drug Evaluation and Research (CDER)
2. Deputy Director, OND, CDER
3. Director, Office of Drug Evaluation IV (ODE IV), OND, CDER
4. Deputy Director, ODE IV, OND, CDER
5. Director, Division of Anti-Infective Drug Products, ODE IV, OND, CDER

Please advise these officials that they have the right to speak directly and independently to Congress, or to a Committee of Congress, without interference from the FDA if they wish, in accordance with 5 U.S.C. § 7211. Retaliation against these individuals, or any other FDA employees, who communicate with the Committee in reference to Ketek will not be tolerated. Such conduct is further punishable by 18 U.S.C. § 1505 and false statements and perjury are likewise punishable pursuant to 18 U.S.C. § 1001. Further, under 5 U.S.C. § 2302(b)(8), a federal employee authorized to take, direct others to take, recommend or approve any personnel action may not take, fail to take, or threaten to take any personnel action against an employee because of protected whistleblowing. Protected whistleblowing is defined as disclosing information which the discloser reasonably believes evidences: a violation of law, rule, or regulation; gross mismanagement; gross waste of funds; an abuse of authority; or a substantial and specific danger to public health or safety.

Please also note that P.L. 109-115 enunciates a government-wide prohibition on the use of appropriated funds to pay the salary of any federal official who prohibits or prevents or threatens to prevent or prohibit a federal officer or employee from contacting Congress, and "any

punishment or threat of punishment because of any contact or communication by an officer or employee with a Member, committee or subcommittee."

Finally, I respectfully request that all FDA employees involved directly or indirectly with Ketek be immediately provided with a copy of this letter to inform them of their right to speak and to cooperate with Congress. All FDA employees should be informed that no documents, records, data or information related, directly or indirectly, to Ketek shall be destroyed, modified, removed or otherwise made inaccessible to the Committee. Further, if any FDA employee believes that they have been subject to retaliation for meeting with Committee staff and/or for anything associated with the Committee's ongoing investigation of Ketek, the employee should contact the Committee immediately. Please also provide the Committee with a list of all FDA employees who were forwarded a copy of this letter.

Thank you in advance for your assistance.

Sincerely,
Charles E. Grassley
Chairman

[1] http://www.fda.gov/fdac/departs/2004/404_upd.html#fraud
[2] http://www.fda.gov/cder/drug/advisory/telithromycin.htm
[3] http://www.annals.org/cgi/reprint/144/6/415.pdf
[4] http://www.fda.gov/cder/drug/infopage/telithromycin/qa.htm
[5] http://www.clinicaltrials.gov/ct/show/NCT00315003?order=2
[6] http://www.fda.gov/cder/foi/nda/2004/21-144_Ketek_Prntlbl.pdf

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