

For Immediate Release  
Friday, March 6, 2009

Grassley asks for an accounting of contacts between FDA and device maker

WASHINGTON – Senator Chuck Grassley has asked the Food and Drug Administration and a medical device maker for information about their communication during the approval process of a new device for knee injuries.

Grassley said his inquiry is based on information provided to him, including emails that “make it look like the device maker was calling the shots and the FDA was going out of its way to accommodate the company.”

The text of Grassley’s letters is below. He has conducted oversight of the FDA for nearly five years and documented what he calls a “too cozy relationship” between the FDA and industry. “I hope this new example helps compel the new administration to name an FDA Commissioner committed to independent, scientific assessment on behalf of consumers. Congress needs to do its part, too, but the culture of the agency is set from the top down, and the next commissioner needs to be a reformer.”

March 6, 2009

Frank M. Torti, MD, MPH  
Acting Commissioner  
U.S. Food and Drug Administration  
5600 Fishers Lane  
Rockville, MD 20857

Dear Dr. Torti:

As Ranking Member of the United States Senate Committee on Finance (Committee), I have a responsibility to the more than 80 million Americans who receive health care coverage under the Medicare and Medicaid programs to oversee the proper administration of these programs and ensure that taxpayer dollars are appropriately spent on safe and effective drugs and devices.

Recently, I wrote to the Food and Drug Administration (FDA or Agency) regarding the Center for Device and Radiological Health’s (CDRH) handling of device reviews. In particular, I asked the FDA to respond to questions and provide information related to allegations of misconduct and retaliation within the Center’s Radiology Devices Branch.

In the course of my inquiries into those allegations, I have obtained documents that suggest FDA’s actions related to a particular device may have been influenced by the manufacturer, ReGen Biologics, Inc. (ReGen). In particular, emails provided to the Committee show that ReGen was involved in the convening of an FDA advisory panel for the review of the

company's Collagen Scaffold used in knee surgery. A consultant to the company made the following points in an email to FDA's Assistant Commissioner for Accountability and Integrity in October 2008:

The company has serious concerns about any involvement by CDRH and Dr. Schultz in the panel – given that you had to involve OCC to prevent Dr. Schultz from issuing a 3<sup>rd</sup> illegal NSE letter.

\* \* \*

We feel very strongly that you should run the panel meeting or somebody in the Commissioner's office and think that Dr. Torti should be involved in this process. I am concerned that things are moving very quickly and the company will not have the opportunity to have ANY input in the make up [sic] of the panel, who will run it, and what questions will be asked.

\* \* \*

Finally, if Dr. Schultz is allowed to run this panel and make the final decision – that is not fair or acceptable to us.

The Assistant Commissioner summarized the consultant's message in an internal email to Dr. Daniel Schultz, FDA attorneys and others, stating that the consultant "suggests several questions for the panel that ReGen thinks are legally acceptable, but he has voiced strong concern about having CDRH run the panel (because he thinks they are biased against ReGen) and asserts the company should have input into [sic] sits on the panel." See attached.

It appears, based upon the materials in my possession, that in response to ReGen's concerns, former Commissioner Andrew von Eschenbach became personally and actively involved in the matter. In a draft of his letter to the ReGen Chief Executive Officer (CEO), he stated that the "FDA has welcomed your [ReGen's] input into the structure and composition of this advisory committee in an effort to assure you of its effective and impartial deliberations." See attached. In addition, he stated that the FDA had "invited six temporary voting members to participate in the advisory committee, five of whom, per your [ReGen's] request, have sports medicine backgrounds. In selecting these temporary voting members, we have been mindful of the criteria you sent us regarding the types of experts that you believe are best qualified to evaluate the CS Scaffold." The draft letter also included the following statement regarding questions to be addressed by the advisory panel: "FDA will be the final arbiter of the meeting questions to the committee. However,...I am assured that your company has made ample contribution to their development."

After reviewing the draft letter, an FDA deputy chief counsel asked whether all sponsors are given the opportunity to provide such input regarding the composition of an advisory panel. The response he received was, "No, we do not give everyone that oppoprtnuity [sic]. I think that statement would cause significant problems [sic] for the agency." I understand the statement was ultimately removed from the final letter but its genesis is of great interest.

In addition, according to FDA's slide presentation to the Orthopaedic and Rehabilitation Devices Advisory Committee on the Collagen Scaffold on November 14, 2008, the FDA focused its clinical data presentation "on the approved IDE [investigational device exemption] protocol, JBJS [Journal of Bone and Joint Surgery] article, and clinical data provided in the 510(k) submission." An internal FDA email dated November 11, 2008, noted that the first author of the JBJS article is ReGen's Vice President of Scientific Affairs. Another listed author is a member of the ReGen Board of Directors. However, it was brought to my attention that FDA's slides did not mention that these two authors were affiliated with ReGen.

Furthermore, it appears that a potential panel member for the Orthopaedic and Rehabilitation Devices Advisory Committee may have been excluded from participation in the November 14, 2008 meeting to discuss the Collagen Scaffold as a result of ReGen's concerns. According to an internal FDA email dated May 6, 2008, the Assistant Commissioner stated, "I expect ReGen will want to make the case why [redacted] is biased against them. I explained to Michael [ReGen's consultant] last week that ReGen needs to do more than allege a bias based on [redacted] surgical specialty in meniscus replacements."

As I have stated in the past, I am concerned about the cozy relationship that sometimes exists between the FDA and manufacturers of the products regulated by the Agency. Thus I am very troubled that the documents that I presently have in my possession seem to suggest that the FDA allowed ReGen to play an active role in the make-up of the advisory panel, among other things. Furthermore, since the FDA Commissioner is not typically involved in regulatory decisions regarding an individual product, I am interested in the events that led to the former FDA Commissioner's personal involvement in the Agency's review of ReGen's device. Accordingly, I would appreciate FDA's response to the following questions and requests for information. Please repeat the enumerated question and follow with the appropriate response and documentation.

1. Are sponsors of pre-market approval applications and/or 510(k) submissions typically invited to contribute to the development of advisory panel questions and/or the structure and composition of an advisory panel that is reviewing their products? If it is not common for the FDA to obtain such input, please explain why it was appropriate to do so for the Collagen Scaffold.
2. According to an email dated October 31, 2008, former Commissioner von Eschenbach planned to "review the CVs of the SGEs [special government employees] over the weekend to be sure we have the right people" for the advisory panel reviewing ReGen's Collagen Scaffold.
  - a. Please describe in detail the circumstances under which the FDA Commissioner and/or staff from the Commissioner's office would become personally involved in the convening of an FDA advisory panel and/or other activities related to the review of a product application. Please include in your response a detailed description of the other types of review activities.

- b. Identify the number of times from January 2004 through the date of this letter that the FDA Commissioner and/or staff from the Commissioner's office have been personally involved in the convening of an FDA advisory panel to evaluate a specific product. Please identify the product(s) of interest and the center(s) overseeing the product(s).
    - c. Please identify the number of times from January 2004 through the date of this letter that the FDA Commissioner and/or staff from the Commissioner's office have been personally involved in other activities related to a center's review of a specific product. Please identify the product(s) of interest, the center(s) overseeing the product(s), and the activity(ies).
  3. If the FDA did disclose to the Orthopaedic and Rehabilitation Devices Advisory Panel the authors' affiliations with ReGen, please explain how and when that disclosure was made and how it was documented.
  4. When did ReGen first raise concerns about a particular physician's bias against the company? Please describe in detail and provide supporting documentation for why the FDA excluded that physician from participation on the Orthopaedic and Rehabilitation Devices Advisory Committee for the review of the Collagen Scaffold on November 14, 2008.
  5. Please provide a copy of all internal and external communications and other materials, including emails, memoranda, personal notes, and telephone notes, relating either directly or indirectly to ReGen and the FDA, the make-up of the Orthopaedic and Rehabilitation Devices Advisory Committee, and the development of the panel questions for the period of September 2007 through the date of this letter.

Thank you for your attention to this important matter. Please respond to the questions and requests set forth in this letter by no later than March 20, 2009.

Sincerely,  
Charles E. Grassley  
Ranking Member

March 6, 2009

Gerald E. Bisbee, Jr., PhD  
Chairman, President and Chief Executive Officer  
ReGen Biologics, Inc.  
411 Hackensack Avenue  
Hackensack, NJ 07601

Dear Dr. Bisbee:

As Ranking Member of the United States Senate Committee on Finance (Committee), I have a responsibility to the more than 80 million Americans who receive health care coverage under the Medicare and Medicaid programs to oversee the proper administration of these programs and ensure that taxpayer dollars are appropriately spent on safe and effective drugs and devices.

In the course of my inquiries into allegations of misconduct within the Food and Drug Administration's (FDA or Agency) Center for Device and Radiological Health (CDRH), I have obtained documents that suggest FDA's action related to a particular device may have been influenced by ReGen Biologics, Inc. (ReGen or Company). In particular, I am very troubled by the attached emails suggesting that the FDA allowed ReGen to play an active role in the make-up of an FDA advisory panel for the review of the company's Collagen Scaffold used in knee surgery and the development of panel questions, among other things.

In October 2008, a month before FDA's Orthopaedic and Rehabilitation Devices Advisory Committee was scheduled to convene, a consultant to the Company made the following points in an email to the FDA assistant commissioner for integrity and accountability (Assistant Commissioner):

The company has serious concerns about any involvement by CDRH and Dr. Schultz in the panel – given that you had to involve OCC to prevent Dr. Schultz from issuing a 3<sup>rd</sup> illegal NSE letter.

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We feel very strongly that you should run the panel meeting or somebody in the Commissioner's office and think that Dr. Torti should be involved in this process. I am concerned that things are moving very quickly and the company will not have the opportunity to have ANY input in the make up [sic] of the panel, who will run it, and what questions will be asked.

\* \* \*

Finally, if Dr. Schultz is allowed to run this panel and make the final decision – that is not fair or acceptable to us.

The Assistant Commissioner summarized the consultant's message in an internal email to Dr. Daniel Schultz, FDA attorneys, and others, stating that the consultant "suggests several questions for the panel that ReGen thinks are legally acceptable, but he has voiced strong concern about having CDRH run the panel (because he thinks they are biased against ReGen) and asserts the company should have input into [sic] sits on the panel." See attached.

It appears, based upon the materials in my possession, that in response to ReGen's concerns, former Commissioner Andrew von Eschenbach became directly and personally involved in the matter. In a draft of his letter to you, he stated that the "FDA has welcomed your

[ReGen's] input into the structure and composition of this advisory committee in an effort to assure you of its effective and impartial deliberations." In addition, he stated that the FDA had "invited six temporary voting members to participate in the advisory committee, five of whom, per your [ReGen's] request, have sports medicine backgrounds. In selecting these temporary voting members, we have been mindful of the criteria you sent us regarding the types of experts that you believe are best qualified to evaluate the CS Scaffold." The draft letter also included the following statement regarding questions to be addressed by the advisory panel: "FDA will be the final arbiter of the meeting questions to the committee. However,...I am assured that your company has made ample contribution to their development."

After reviewing that draft letter, an FDA deputy chief counsel asked whether all sponsors are given the opportunity to provide such input regarding the composition of an advisory panel. The response he received was, "No, we do not give everyone that oppoprtnuity [sic]. I think that statement would cause significant problemas [sic] for the agency." I understand the statement was ultimately removed from the final letter but its genesis is of great interest.

In addition, it was brought to my attention that a potential panel member for the Orthopaedic and Rehabilitation Devices Advisory Committee may have been excluded from participation in the November 14, 2008 meeting to discuss the Collagen Scaffold as a result of ReGen's concerns. According to an internal FDA email dated May 6, 2008, the Assistant Commissioner stated, "I expect ReGen will want to make the case why [redacted] is biased against them. I explained to Michael [ReGen's consultant] last week that ReGen needs to do more than allege a bias based on [redacted] surgical specialty in meniscus replacements."

I have been and continue to be concerned with the cozy relationship that sometimes exists between the FDA and manufacturers of the products regulated by the Agency. Accordingly, I would appreciate ReGen's response to the following questions and requests for information. Please repeat the enumerated question and follow with the appropriate response and documentation in accordance with the terms and conditions set forth in the attachment:

6. Please provide a list of all meetings and/or telephone calls between representatives of ReGen, including any third party contractors, and any FDA official/employee related directly or indirectly to the November 14, 2008 advisory panel meeting on ReGen's Collagen Scaffold. Please sort the list by date and provide the names of all participants at each event and a description of the subject matter discussed. This request covers the period of January 1, 2008 through December 31, 2008.
7. Please provide a copy of all documentation of communications, including but not limited to emails, memoranda, meeting notes, and telephone notes, related directly or indirectly to the Collagen Scaffold, between representatives of ReGen, including any third party contractors, the former Commissioner von Eschenbach and the following FDA officials: Dr. Frank Torti, Mr. William McConagha, Mr. Les Weinstein, Dr. Daniel Schultz, and Dr. Donna Bea Tillman. This request covers the period of September 2007 through the date of this letter.

8. Please provide a copy of all internal communications related to the November 14, 2008 FDA advisory panel meeting on the Collagen Scaffold, including but not limited to the structure, composition, and substance of the meeting and the development of the panel questions. This request covers the period of January 1, 2008 through December 31, 2008.
9. Please explain in detail why ReGen thought that Dr. Schultz was biased against ReGen.
10. State the date on which ReGen first raised concerns to the FDA regarding the participation of a specific physician on the Orthopaedic and Rehabilitation Devices Advisory Committee for the review of the Collagen Scaffold on November 14, 2008. In addition, please describe in detail the basis for which ReGen believed that the physician should be excluded from participation on that advisory panel.

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.

Sincerely,  
Charles E. Grassley  
Ranking Member