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October 8, 2008

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

Dear Dr. von Eschenbach:

The Committee on Energy and Commerce and its Subcommittee on Oversight and Investigations have been investigating the ability and commitment of the Food and Drug Administration (FDA) to protect Americans from unsafe food and drugs. During the course of the drug safety inquiry, the Committee is aware that, following on the heels of disclosures regarding gross improprieties at Ranbaxy Laboratories, the entire production of another generic drug manufacturer has been recalled. Apparently, on August 1, 2008, Actavis Totowa, LLC, a generic drug manufacturer headquartered in Iceland, that operates a plant in Little Falls, New Jersey (formerly Amide Pharmaceuticals), recalled its entire product line from that plant—some 66 products, many of which are controlled (scheduled) drugs.

The FDA press release insisted that products at other Actavis Totowa locations are not suspect even though on February 8, 2008, another Actavis subsidiary, Actavis South Atlantic LLC, formerly known as Abrika Pharmaceuticals Inc., recalled fentanyl transdermal patches because of a dangerous manufacturing defect. Further, the Little Falls, New Jersey, plant was the production source of a serious Class 1 recall of digoxin on May 9, 2008. That drug was recalled

> "due to the possibility that tablets with double the appropriate thickness may have been commercially released. These tablets may contain twice the approved level of active ingredient than is appropriate. Digitek is used to treat heart failure and abnormal heart rhythms….Death can also result from excessive Digitalis intake."

Recalls of this seriousness causes us to question whether FDA was deceived regarding the current good manufacturing practices (cGMPs) of this company, or did FDA simply fail to conduct adequate and timely inspections of these facilities. A more important question is whether FDA permitted additional products from this firm onto the market while the agency knew or should have known about the breakdown of manufacturing practices at Actavis or its subsidiaries.

Accordingly, for all FDA-regulated products that Actavis has received approval to sell into domestic commerce since January 1, 2003, or that Actavis imports into this country from abroad regardless of approval date, please provide:

1. All documents that convey preapproval inspection assignments;

2. All documents that describe the tasks undertaken and all findings by the investigators during the preapproval inspections, including any Notice of Inspectional Observations (form 483s), or Establishment Inspection Reports (EIRs);

3. All documents relating to any "for cause" inspection of the Actavis firm, its subsidiaries, or its active pharmaceutical ingredient (API) suppliers;

4. A list of all API suppliers and any 483s, EIRs, or other documents that describe the tasks undertaken and the findings of inspections of those suppliers;

5. A list of all laboratories performing bioequivalence studies, noting which Actavis drug substances were tested, when they were tested, and the results;

6. Any 483, EIR, or comparable document that would describe inspections of the laboratories that performed bioequivalence testing for Actavis or its subsidiaries; and

7. A list of FDA personnel that conducted or reviewed each inspection listed above.

Please provide all of the requested documents no later than <u>two weeks after the date of this letter</u>. To arrange for a rolling production of these documents or to answer any questions relating to these requests, please contact David Nelson, Joanne Royce, or Paul Jung with the Committee staff at (202) 226-2424.

Sincerely,

John D. Dingell
Chairman

Bart Stupak
Chairman
Subcommittee on Oversight and Investigations

cc: The Honorable Joe Barton, Ranking Member
Committee on Energy and Commerce

The Honorable John Shimkus, Ranking Member
Subcommittee on Oversight and Investigations