ONE HUNDRED TENTH CONGRESS

U.S. House of Representatives
Committee on Energy and Commerce
Washington, DC 20515–6115

JOHN D. DINGELL, MICHIGAN
CHAIRMAN

March 6, 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:

Under Rules X and XI of the Rules of the United States House of Representatives, the Committee on Energy and Commerce and its Subcommittee on Oversight and Investigations are investigating the ability of the Food and Drug Administration (FDA) to protect the American public from excessive risks associated with prescription drugs.

Early last year, the Committee became aware of troubling signs of safety problems in connection with a class of drugs known as Erythropoiesis-Stimulating Agents (ESAs), which are designed to prevent the need for blood transfusions in cancer and dialysis patients suffering from anemia. Since then, we have been increasingly alarmed by clinical study reports that indicate ESAs, also known as erythropoietin (EPO) products, cause increased blood clots and mortality, and may even enhance disease progression.

The Data Safety Monitoring Boards of a number of ESA clinical studies have recommended suspension of their studies because of heightened risk of harm to patients. In April 18, 2007, letters to this Committee, Johnson & Johnson, and Amgen listed 10 ESA clinical studies that were terminated or suspended because of unanticipated harm to patients: BEST Study; PR00–03–006; LEGACY Study; CHOIR Study; PR00–27–024; PR01–04–005, GOG 191; RTOG–99–20; EPO–CAN–20; DAHANCA 10; and Roche's study NH19960.

As a result, FDA issued a "black box" label warning last year on all drugs in the ESA class, citing heart and cancer risks and urging their use in the lowest dose possible that still helped patients avoid blood transfusions. Nevertheless, these drugs continue to be prescribed for indicated as well as off-label use. Indeed, Johnson & Johnson and Amgen, the manufacturers of

manufacturers of these drugs, continue to invest millions of dollars into lobbying and marketing campaigns that misrepresent the risks associated with ESAs.

Furthermore, the dramatic findings of a recent meta-analysis of ESA data published in the Journal of the American Medical Association (JAMA) raise serious concerns about the risk profile of the entire class of ESA products, including Aranesp and Procrit. In the February 27, 2008, issue of JAMA, Charles L. Bennett, M.D., Ph.D., *et al.* found that even when used as directed, ESAs put cancer patients at nearly 57 percent increased risk of blood clots. Study researchers also reported that ESAs increase the risk of death in cancer patients by about 10 percent. The meta-analysis also discusses results of experiments that indicate use of ESAs could actually *enhance* cancer growth at the same time that doctors are using other drugs to control the disease.

We applaud the past efforts of FDA officials who have insisted on science and evidence-based decisions respecting use of ESA drugs. The analysis published in JAMA, however, along with the 10 clinical studies halted by Data Safety Boards and other negative safety data, suggest a need for reconsideration of the risk/benefit profile of this potentially dangerous class of drugs.

We urge FDA to use the scheduled Oncologic Drugs Advisory Committee meeting on March 13, 2008, to seriously reconsider the overall safety of ESAs and address the question of whether any demonstrable benefits of these drugs offset the evidence of increased mortality, blood clots, and tumor promotion.

Most importantly, we encourage FDA to act with due haste to avoid further endangering patients who may have been steered toward these drugs by aggressive marketing practices, including the use of misleading direct-to-consumer advertisements and recommendations from physicians who personally profit from the sale of these drugs.

Should you have any questions regarding these requests, please contact us or have your staff contact Joanne Royce or Paul Jung with Committee on Energy and Commerce 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