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Joan Claybrook, President

August 6, 2009

Margaret A. Hamburg, M.D.
Commissioner, Food and Drug Administration
Department of Health and Human Services
5630 Fishers Lane, Room 1061
Rockville, MD 20852

Dear Dr. Hamburg,

We are filing the enclosed petition for reconsideration of the FDA decision concerning propoxyphene, Docket No. FDA-2006-P-0270, for two reasons.

The first is because the decision to deny the relief requested in our petition was clearly made well before you took over, arguably even before the 1/30/09 advisory committee meeting, as evidenced by FDA documents prepared for that meeting. In the introduction to the FDA documents for the meeting, Dr. Bob Rappaport, Director, Division of Anesthesia, Analgesia and Rheumatology Products of CDER stated that: "In addition, FDA and SAMHSA representatives will present the data supporting the efficacy and safety of propoxyphene documented in the NDAs for these products and in the medical literature, as well as adverse event data from FDA's Adverse Event Reporting System (AERS) and from SAMHSA's Drug Abuse Warning Network (DAWN)."[1]

In a recent New England Journal of Medicine editorial written by you and principal deputy FDA commissioner Dr. Joshua M. Sharfstein[2], entitled *The FDA as a Public Health Agency*, you confirmed the agency's "overriding purpose....of protecting the public health." You went on to say that "Some benefits are not worth the risk" and concluded by pointing out that "the public must trust the agency to base its decisions on science."

We fully agree with this, but see CDER's decision on propoxyphene as a refutation of these important principles which you espouse: Protecting the public health, benefits not worth the risk and basing decisions on science.

The second reason, then, has to do with the failure of the FDA to consider all the available scientific evidence in its 7/7/09 denial of our petition, entirely omitting key information and misrepresenting other evidence in order to justify the conclusions it reached.

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[1] Division Director Memo: FDA Documents for 1/30/09 Advisory Committee Meeting
[2] N Engl J Med 360;24: 2493. June 11, 2009

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Such evidence, all known to the agency prior to the decision, includes information not presented by the FDA at the meeting, inaccurate FDA conclusions concerning safety, efficacy and the benefit risk balance of propoxyphene at the meeting and in FDA's response to our petition, and events and new information since the meeting but prior to the decision was issued. In addition, we address the recently-proposed FDA remedy---new labeling and warnings — which, for the reasons explained more fully in the petition for reconsideration, are inadequate to address the concerns raised in our petition.

Former FDA Commissioner Dr. Donald Kennedy, joining us in this petition for reconsideration, had the following criticism of the FDA decision:

"As Commissioner of the FDA in 1978, I received a petition from the Health Research Group (HRG) that urged me to initiate proceedings to ban Darvon and its formulations in combination with over-the-counter analgesics. The evidence offered considered the involvement of propoxyphene in a number of Drug Abuse Warning Network reports involving deaths of persons having taken these drugs, often in combination with alcohol or other abused drugs. The HRG petition also pointed to evidence that propoxyphene itself, in amounts equivalent to that used in the combinations, was less effective than the combined drugs required to be ordered by prescription. At the time, I judged that numbers of persons, including elderly patients suffering from arthritis, depended on the Darvon compounds — and that a ban could be harmful for that cohort.

That was over three decades ago. Now actions in the United Kingdom and the European Union have taken account of new efficacy studies that confirm earlier doubts about the need for propoxyphene, and have enhanced the estimates of risks associated with this opioid drug. Indeed, the results of its withdrawal from the British market demonstrate that the risks of continued use substantially outweigh the benefits of continued availability — especially considering that now propoxyphene is available in a wider variety of generic forms. Accordingly, I would have made a different decision today."

We know that you will be involved in an independent review of this petition for reconsideration of the FDA decision and sincerely hope that you will recognize the urgency of beginning the process of removing propoxyphene from the market, as is being done in more and more of the world. This is the right public health decision and is based on the best scientific evidence and experience.

Sincerely,

Sidney M. Wolfe, MD, Director, Health Research Group at Public Citizen

Steven Karch MD, Forensic Toxicologist, Author of *Pathology of Drug Abuse*
Donald Kennedy, Ph.D, President Emeritus, Stanford University., Former Commissioner, FDA and former Editor-in Chief, Science Magazine
Jerry Avorn, MD, Professor, Harvard Medical School, Director of Division of Pharmacoepidemiology and Pharmacoeconomics, Department of Medicine, Brigham and Women's Hospital
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