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Ralph Nader, Founder

April 25, 1994

David Kessler, M.D., J.D.
Commissioner, Food and Drug Administration
Parklawn Building
5600 Fishers Lane
Rockville, MD, 20857

Dear Dr. Kessler,

Based on evidence summarized in an April 4, 1994 FDA memo, the summary of which we have obtained, it is imperative that you immediately refer the case of Upjohn and Halcion to the Justice Department for criminal prosecution because of a clear pattern of withholding information from the FDA and misleading the agency concerning its top-selling sleeping pill. The Summary of Findings in this memo concludes that **"the firm has engaged in an ongoing pattern of misconduct with Halcion."**

Based on information obtained during an FDA inspection of the firm from December 1991 through March 19, 1992 which was abruptly stopped before the investigators were finished (this inspection is the subject of the April 4, 1994 FDA memo), such a referral to a Grand Jury was considered at an FDA ad hoc meeting on May 12, 1992 but was, inexplicably, rejected.

Some of the most damaging conclusions described in the "Endorsement" or the Summary of Findings of the April 4, 1994 memo include:

* "Study 321 (1 mg level), conducted at a prison in Jackson, MI, reflected serious adverse reactions, 30% of which were not reported to the FDA in the [new drug application] submission. Handwritten corrections to the original tabulations were omitted in the final report. Responsible management was aware of serious side-effects." The memo also states that Upjohn's "characterization of the omission as merely 'transcription errors' is also false and misleading." This study used 1 mg doses of Halcion, originally approved in Holland and for which approval was sought in the U.S. Currently, doses up to 0.5 mg are still approved in the U.S.

* "Upjohn sought approval at the 1 mg level even though information shows that there was an awareness that the dose was too high and caused serious side-effects in significant numbers." The memo also stated that "[s]tatements from two ex-employees of Upjohn support the contention that the firm knew full well that the 1 mg dose was too high." One of the former Upjohn employees told FDA investigators that "perhaps even the .5 mg dose was too high."

* "The firm [successfully] attempted to gain approval for long-term use of the drug even though available evidence indicated that long-term use was both dangerous and medically untenable." **"It appears that Upjohn misrepresented the data [to FDA] in order to persuade FDA reviewers to waive the proposed 14 day duration of use limit."** An internal Upjohn memo, uncovered by the FDA investigators, stated that "... a 14 day limit could reduce projected sales by 50% over a 10 year period." Another memo stated that "if we are unsuccessful in appealing the 14 day upper limit, it will be necessary to redo the analysis omitting protocols 6045, 6047 and 6065." FDA investigators described this as "perhaps the most incriminating evidence found at Upjohn because it shows that the firm chose to disregard the potential harm of inappropriate use, in order to gain additional sales."

In fact, Upjohn was successful in appealing the 14 day limit and, until December 1991, almost 10 years after FDA approval, the labeling for the drug allowed use for up to 1 month. The memo points out, with reference to the approval for dangerously long periods of time, that "Patients involved in some of the publicized criminal cases had been on Halcion for long periods of time."

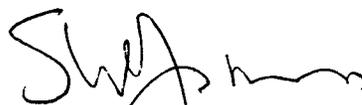
* Another Upjohn memo "discussed a strategy for pressuring FDA into approving Halcion" and stated that "If my sources are anywhere near correct, the **FDA will never approve Halcion without tremendous pressure. We have the people willing to exert the pressure but we must orchestrate it.**"

* Upjohn formed a Product Support Committee "to defend negative publicity about the drug and to suppress publication of unfavorable data and silence critics." This included "attempts to discredit reports by [British psychiatrist] Ian Oswald, prevent publication of an adverse article in the New England Journal of Medicine, provide misleading data to a Boston study group who subsequently sent a flawed letter to Lancet,.... published misleading data that omitted the results of study 321 and furnished misleading data to Japan and France."

If a team of FDA investigators, handicapped by the absence of subpoena power because of deficiencies in FDA enforcement authority, can find so much "misconduct", having to depend on the cooperation of some company officials, consider what might become known when a Justice Department criminal investigation is launched. It is inexcusable and irresponsible that you, FDA General Counsel Margaret Porter and other FDA officials chose to abruptly halt this investigation which had yielded so much valuable information and

even more irresponsible not to have referred the case to the Justice Department which has much more authority and resources to get to the bottom of this scandal. In addition, it is unfortunate that the FDA -- unlike its British counterpart which has permanently banned Halcion, stating that had it known at the time of approval what it eventually learned, they would never have approved the drug -- is still wallowing in its series of Upjohn-inspired regulatory mistakes and, to the endangerment of Americans, still allows the drug on the market. As you know, we petitioned the FDA to ban Halcion almost two years ago, and the FDA has failed to take meaningful action to protect the American public. I look forward to a prompt response to this letter.

Sincerely,

A handwritten signature in cursive script, appearing to read 'Sidney M. Wolfe'.

Sidney M. Wolfe, M.D.
Director, Public Citizen's
Health Research Group