

DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Rockville MD 20857

DATE: March 25, 2008

TO: Randall W. Lutter, Ph.D.
Deputy Commissioner for Policy
Food and Drug Administration

THROUGH: Vince Tolino /s/
Director, Ethics and Integrity Staff
Office of Management Programs
Office of Management

Michael F. Ortwerth, Ph.D. /s/
Deputy Director, Advisory Committee Oversight and Management Staff
Office of Policy, Planning, and Preparedness

FROM: Igor Cerny, Pharm.D. /s/
Director, Advisors and Consultants Staff
Center for Drug Evaluation and Research

SUBJECT: 712(c)(2)(B) Conflict of Interest Waiver for Thomas Kosten, M.D.

I am writing to request a waiver for Dr. Thomas Kosten, a temporary voting member of the Anesthetic and Life Support Drugs Advisory Committee, from the conflict of interest prohibitions of section 712(c)(2)(A) of the Federal Food, Drug, and Cosmetic Act . Waivers under section 712(c)(2)(B) may be granted by the appointing official where "necessary to afford the advisory committee essential expertise" and where the individual has made a disclosure to FDA of the financial interests at issue. We have determined that you are the appointing official for purposes of section 712(c)(2)(B). Therefore, you have the authority to grant Dr. Kosten a waiver under section 712(c)(2)(B).

Section 712(c)(2)(A) prohibits Federal executive branch employees, including special Government employees, from participating in any particular matter in which the employee or an immediate family member has a financial interest that could be affected by the advice given to the FDA with respect to the matter. Because Dr. Kosten is a special Government employee, he is under a statutory obligation to refrain from participating in any deliberations that involve a particular matter having a direct and predictable effect on a financial interest attributable to him.

The function of the Anesthetic and Drug Support Drugs Advisory Committee is to review and evaluate available data concerning the safety and effectiveness of marketed and investigational human drug products for use in anesthesiology and surgery and make appropriate recommendations to the Commissioner of Food and Drugs

Dr. Thomas Kosten has been asked to participate in the May 5, 2008, meeting to discuss New Drug Application (NDA) 22-272, oxycodone hydrochloride controlled-release tablets (trade name OxyContin), Purdue Pharma L.P., and its safety for the proposed indication of management of moderate to severe pain when a continuous, around-the-clock analgesic is needed for an extended period of time. This is a purportedly less abusable formulation of OxyContin. Dr. Kosten has also been asked to participate in the May 6, 2008, meeting to discuss supplemental New Drug Application (sNDA) 21-947/s-005, fentanyl buccal tablet (tradename Fentora), Cephalon, Inc., and its safety for the proposed indication of breakthrough pain in opioid tolerant non-cancer patients with chronic pain.

These matters are coming before a joint meeting of the Anesthetic and Life Support Drugs and the Drug Safety and Risk Management advisory committees. These issues are particular matters involving specific parties.

Dr. Thomas Kosten has advised the Food and Drug Administration (FDA) that he has a financial interest that could potentially be affected by his participation in the matter described above. Dr. Kosten owns stock in _____, _____ subsidiaries, _____, manufacture competing products to OxyContin and Fentora.

As a temporary member to the Anesthetic and Life Support Drugs advisory committee, Dr. Kosten could become involved in matters that could affect his financial interests. Under section 712(c)(2)(A), he is prohibited from participating in such matters. However, as noted above, you have the authority under section 712(c)(2)(B) to grant a waiver permitting Dr. Kosten to participate in such matters if necessary to afford this committee essential expertise.

For the following reasons, I believe that it would be appropriate for you to grant a waiver to Dr. Kosten that would allow him to participate fully in the matter described because his voting participation is necessary to afford the committee essential expertise.

First, Dr. Kosten's interest in _____ is not so substantial as to preclude his participation in the meeting. Dr. Kosten owns a moderate number of shares in _____.

Second, it is important to consider that _____ subsidiaries are two of more than thirty competing firms for the OxyContin meeting and two of seventy competing firms for the Fentora meeting.

Third, the committees' determinations and subsequent FDA actions concerning the OxyContin and Fentora is not likely to cause _____ stock to rise or fall

significantly or affect the viability of the firm. _____ is a highly diversified company with over _____ subsidiaries and 2007 revenue of approximately \$_____.

Fourth, the uniqueness Dr. Kosten's qualification justifies granting this waiver. According to the review Division, Dr. Kosten is a well-recognized leader in the field of addiction medicine. Dr. Kosten is Professor of Psychiatry and Neuroscience at Baylor College of Medicine and Research Director of the VA national Substance Use Disorders Quality Enhancement Research Initiative (QUERI). Dr. Kosten's extensive knowledge of addiction medicine and years of experience in the research and treatment of addiction is valuable to the committees' discussion of the complex interface of opioid use in the treatment of chronic pain and the problems associated with its misuse, abuse, and diversion.

Fifth, the difficulty of locating a similarly qualified individual without a disqualifying financial interest to serve on the committee also justifies granting this waiver. It has been exceedingly difficult to find addiction medicine experts with experience in conducting clinical trials of opioids and other treatments for chronic pain and yet have not had any involvement with the sponsors of the products at issue or any of the competing products. Of the six addiction medicine experts contacted, four accepted the offer to represent the agency's interests, with two declining due to scheduling conflicts. Of the four, two of the interested parties disclosed conflicts of a significant nature that would result in recusal. The division feels that a minimum of two leading physicians in the field of addiction medicine is required at the meeting in order to provide a fair and balanced discussion of this very controversial area of medicine and drug development. Consequently, the division requests that a waiver be granted for Dr. Kosten to participate as there has been a genuine effort to secure individual participation and representation with minimal conflict of interest. A reduction in the number of addiction medicine experts in the committee will render much of the discussion useless, and may call into question the validity of any committee recommendations to the Agency.

Moreover, the Federal Advisory Committee Act requires that committee memberships be fairly balanced in terms of the points of view represented and the functions to be performed by the advisory committee. Also, the committee's intended purpose would be significantly impaired if the agency could not call upon experts who have become eminent in their fields, notwithstanding the financial interests and affiliations they may have acquired as a result of their demonstrated abilities. I believe that Dr. Kosten's participation in the committees' deliberations will contribute to the diversity of opinions and expertise represented on the committees.

Accordingly, I recommend that you grant Dr. Thomas Kosten a waiver that would allow his voting participation in all official matters concerning the safety of (1) New Drug Application (NDA) 22-272, oxycodone hydrochloride controlled-release tablets (trade name OxyContin), a purportedly less abusable formulation sponsored by Purdue Pharma L.P., for the proposed indication of management of moderate to severe pain when a continuous, around-the-clock analgesic is needed for an extended period of time; and (2) supplemental New Drug Application (sNDA) 21-947/s-005, fentanyl buccal tablet (tradename Fentora), Cephalon, Inc., for the proposed indication of

