DEPARTMENT OF HEALTH & HUMAN SERVICES Public Health Service

Food and Drug Administration
Rockville MD 20857

DATE: February 20, 2007

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

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

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

SUBJECT: Conflict of Interest Waiver for Kenneth Saag, M.D.

I am writing to request a waiver for Kenneth Saag, M.D., a member of the Arthritis Drugs Advisory Committee, from the conflict of interest prohibitions of 18 U.S.C. §208(a). The appointing official may grant waivers under section 208(b)(3) where "the need for the individual's services outweighs the potential for a conflict of interest created by the financial interest involved" and where the individual has made a disclosure of the financial interests at issue. We have determined that you are the appointing official for purposes of section 208. Therefore, you have the authority to grant Dr. Saag a waiver under 18 U.S.C. §208(b)(3).

Section 208(a) prohibits Federal executive branch employees, including special Government employees, from participating personally and substantially in matters in which the employee, or any other person whose interests are imputed to the employee under 18 U.S.C. §208, has a financial interest. Since Dr. Saag is a special Government employee, he is under a statutory obligation to refrain from participating in an official capacity in any particular matter having a direct and predictable effect on a financial interest attributable to him, his spouse, minor child, or general partner; an organization or entity for which he serves as an officer, director, trustee, general partner, or employee; and, a person with whom he is negotiating for, or has an arrangement concerning, prospective employment.

Dr. Saag has been asked to participate in all official matters concerning the safety and efficacy of New Drug Application (NDA) 21-389/21-772, proposed trade name, Arcoxia (etoricoxib), a non-steroidal, anti-inflammatory, cyclooxygenase-2 (COX-2) enzyme inhibitor, manufactured by Merck & Company, Inc., for the proposed indication of the relief of the signs and symptoms of osteoarthritis. This matter is a particular matter involving specific parties.

The function of the Arthritis Advisory Committee, as stated in its Charter, is to review and evaluate available data concerning the safety and effectiveness of marketed and investigational human drug products for use in the treatment of arthritis, rheumatism, and related diseases, and to make appropriate recommendations to the Commissioner of Food and Drugs.

Dr. Saag has advised the Food and Drug Administration that he has financial interests that could potentially be affected by his participation in the matter at issue. **Dr. Saag is a member of ———'s National Osteoporosis Board. He also lectures for ——— on osteoporosis, and serves as a member of their Speaker's Bureau. Osteoporosis is unrelated to the product, issues, and competing products coming before the committee. ——— is the sponsor of ————————.**

In addition, Dr. Saag serves as a consultant for two of the competing firms, ——— and———, concerning their osteoporosis agents.

As a member of the Arthritis Drugs Advisory Committee, Dr. Saag potentially could become involved in matters that could affect his financial interests. Under 18 U.S.C. §208(a), he is prohibited from participating in such matters. However, as noted above, you have the authority under 18 U.S.C. §208(b)(3) to grant a waiver permitting Dr. Saag to participate in such matters as you deem appropriate.

For the following reasons, I believe that it would be appropriate for you to grant a waiver to Dr. Saag, which would permit him to participate in the matter previously described.

First, Dr. Saag's interests are not so substantial as to preclude his participation in this matter. He receives low to moderate compensation for these activities.

Second, the uniqueness of Dr. Saag's qualifications justifies granting this waiver. Dr. Saag's expertise in rheumatology and preventive medicine gives him the unique qualification of knowledge spanning both clinical rheumatology and safety from a public health perspective that will be valuable to the committee as it discusses the risk-benefit profile for Arcoxia (etoricoxib).

Third, 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 qualified rheumatologists who have not had any involvement with the product, competing products, or the affected firms. The Division searched and polled a number of current special Government employees and Federal employees at the National Institutes of Health (NIH) for their availability. The search yielded no individual with comparable experience and the Division was unable to find anyone as qualified as Dr. Saag who was available to participate. Therefore, we request to use the services of Dr. Saag who will serve as the only representative on the panel with expertise in both rheumatology and preventive medicine to discuss the risk-benefit profile for Arcoxia (etoricoxib). Dr. Saag's participation in this meeting will ensure the level of expertise and objectivity required to provide advice and recommendations required to discuss the clinical significance of several endpoints related to NSAID and COX-2 toxicities.

Finally, 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. Dr. Kenneth Saag is an Associate Professor of Medicine in the Division of Clinical Immunology and Rheumatology at the University of Alabama at Birmingham. Dr. Saag is experienced in

population-based investigations, working with large databases, survey research, and quality indicator development. He has served on the National Institutes of Health (NIH) and Arthritis Foundation study sections, Institute of Medicine (IOM) Committees, national committees to develop both arthritis and osteoporosis guidelines, the Musculoskeletal Workgroup of the Cochrane Collaboration, the National Committee for Quality Assurance (NCQA) work group on Arthritis Quality Indicators, the American Medical Association (AMA) Physician Consortium for Performance Improvement on Osteoarthritis of the Knee, and the National Institute of Arthritis and Musculoskeletal and Skin Disease (NIAMS) Work Group on Epidemiology, Education, and Health Services Research. I believe his participation will contribute to the diversity of opinions and expertise represented on the committee and will provide a foundation for developing advice and recommendations that are fair and comprehensive.

Accordingly, I recommend that you grant Kenneth Saag, M.D., a waiver that will permit him to participate in all official matters concerning the safety and efficacy of New Drug Application (NDA) 21-389/21-772, proposed trade name, Arcoxia (etoricoxib), a non-steroidal, anti-inflammatory, cyclooxygenase-2 (COX-2) enzyme inhibitor, manufactured by Merck & Company, Inc., for the proposed indication of the relief of the signs and

symptoms of osteoarthritis. I believe that such a waiver is appropriate because in this case, the need for the services of Dr. Kenneth Saag outweighs the potential for a conflict of interest created by the financial interests attributable to him.

CONCURRENCE: /s/ 2/28/07

Vince Tolino
Director, Ethics and Integrity Staff
Office of Management Programs
Office of Management

Date

DECISION:

X Waiver granted based on my determination, made in accordance with section 18 U.S.C. §208(b)(3), that the need for the individual's services outweighs the potential for a conflict of interest created by the financial interests attributable to the individual.

_____ Waiver denied.

/s/ 3/9/07

Randall W. Lutter, Ph.D.
Associate Commissioner for Policy and Planning
Food and Drug Administration

Date