

and the Assistant Secretary for Health have taken final action in the following case:

Timothy R. Smith, Ph.D., Michigan State University: Based on the findings of Michigan State University, the respondent's admission, and analysis conducted by ORI in its oversight review, the U.S. Public Health Service (PHS) found that Timothy R. Smith, Ph.D., former Postdoctoral Fellow, Department of Biochemistry and Molecular Biology at Michigan State University, engaged in scientific misconduct in research supported by National Institute of General Medical Sciences (NIGMS), National Institutes of Health (NIH) grant P01 GM57323, entitled "Oxygen utilizing membrane heme proteins."

Specifically, PHS found that Dr. Smith falsified and fabricated data involving research into the physical interaction of prostaglandin endoperoxide synthase-2 (PGHS-2) with cell membranes, and the effects of arachidonate and nonsteroidal anti-inflammatory drugs (NSAIDs) on PGHS-2 structure.

Dr. Smith committed scientific misconduct by falsifying and fabricating data for the following tables and figures in his 2000 doctoral dissertation and in a paper in the *Journal of Biological Chemistry* (275:40407-40415, 2000) entitled "Arachidonic Acid and Nonsteroidal Anti-inflammatory Drugs Induce Conformational Changes in the Human Prostaglandin Endoperoxide H₂ Synthase-2 (Cyclooxygenase-2)" (*JBC* paper):

I. *JBC* paper Table II, entitled "Comparison of inter-residue distances as determined by EPR spectroscopy and as calculated from the x-ray crystal structures" (and corresponding Dissertation Table 6 entitled "EPR determined and X-ray crystal modeled inter-nitroxide distances of PGHS-2 MBD mutants");

II. *JBC* paper Table III entitled "Changes in inter-nitroxide differences between PGHS-2 holoenzyme and the apoenzyme, and the arachidonate, flurbiprofen, and SC58125 complexes" (and corresponding Dissertation Table 7), entitled "Relative changes in inter-nitroxide distances for NSAID and arachidonate complexes compared to the unliganded enzyme";

III. *JBC* paper Figure 4 (binding curves) (and corresponding Dissertation Figure 20 entitled "Binding curves for the association of heme, flurbiprofen and arachidonic acid with PGHS-2 double mutants");

IV. Dissertation Table 8 entitled "EPR determined inter-nitroxide distances for

NSAID and arachidonate complexes of PGHS-2 MBD mutants;"

V. Dissertation Table 9 entitled "Relative changes in inter-nitroxide distances for NSAID and arachidonate complexes compared to the unliganded enzyme;"

VI. Dissertation Table 10 entitled "Kinetic properties and NSAID sensitivities of PGHS-2 active site mutants;"

VII. Dissertation Table 12 entitled "Relative PGHS-2 protein incorporation of PGHS-2 into liposomes of varying composition;"

IX. Dissertation Table 13 entitled "EPR determined inter-nitroxide distances for detergent solubilized and liposome reconstituted PGHS-2 mutants;" and

X. Dissertation Figure 27 entitled "Lipid and activity profile of sucrose gradient fractions."

The research misconduct was significant for several reasons. First, the *JBC* paper was novel in that it reported that binding of arachidonate and NSAIDs induced structural changes in PHS-2. For the naturally occurring fatty acid arachidonate, this had not previously been shown. These results could be interpreted as having important implications for understanding the catalytic mechanism of this enzyme. In addition, a considerable expenditure of other researchers' time and resources was prompted by using results generated from the falsified and fabricated data in the *JBC* paper.

Dr. Smith has entered into a Voluntary Exclusion Agreement (Agreement) in which he has voluntarily agreed:

(1) to exclude himself from serving in any advisory capacity to PHS including but not limited to service on any PHS advisory committee, board, and/or peer review committee, or as a consultant for a period of three (3) years, beginning on October 27, 2003;

(2) to exclude himself voluntarily from any contracting or subcontracting with any agency of the United States Government and from eligibility or involvement in nonprocurement programs of the United States Government defined as "covered transactions" in the debarment regulations at 45 CFR part 76 for a period of three (3) years, beginning on October 27, 2003. During the three (3) year period of voluntary exclusion, PHS grant funds may be used to pay for page charges for any written work currently being prepared for submission and/or publication on which Dr. Smith is listed as an author only if (i) such written work is unrelated to the misconduct

findings described in the Agreement, (ii) Dr. Smith is not listed as first author, and (iii) the publication does not state that Dr. Smith was supported by a PHS grant. Dr. Smith must certify that all data supporting such written work is true and accurate to the best of his knowledge; and

(3) to submit a letter within 30 days of notification of this action to *JBC* requesting retraction of the following paper: Smith, T., McCracken, J., Shin, Y.K., & DeWitt, D. "Arachidonic Acid and Nonsteroidal Anti-inflammatory Drugs Induce Conformational Changes in the Human Prostaglandin Endoperoxide H₂ Synthase-2 (Cyclooxygenase-3)." *J. Biol. Chem.* 275:40407-40415, 2000. Dr. Smith agreed that the retraction will state that he alone was responsible for the falsification and fabrication of the results and will specifically list the falsified figures delineated on page 1 of the Agreement (Findings I, II, and III). Dr. Smith must submit a draft of the retraction letter for ORI approval prior to sending it to *JBC*. This requirement for retraction will be noted on the ALERT System until Dr. Smith sends a copy of the retraction letter to ORI.

FOR FURTHER INFORMATION CONTACT:
Director, Division of Investigative Oversight, Office of Research Integrity, 1101 Wootton Parkway, Suite 750, Rockville, MD 20852, (301) 443-5330.

Chris B. Pascal,

Director, Office of Research Integrity.

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DEPARTMENT OF HEALTH AND HUMAN SERVICES

Administration for Children and Families

Head Start Survey Under Emergency Review by the Office of Management and Budget (OMB)

Title: Survey of Salaries and Other Compensation of Head Start Grantees and Delegate Agencies Nationwide.

OMB No. New request.

Description: A committee of the U.S. House of Representatives requested that the Secretary of Health and Human Services conduct a review of the financial management of Head Start grantees nationwide. The House Education and the Workforce Committee is interested in knowing the salaries and benefits of the top 25 Head Start executives and the amount of their salary and benefits financed using Federal Head Start dollars. To be responsive to the House of

Representatives, the Head Start Bureau has prepared a survey form to be mailed to and completed by all Head Start

grantees and delegate agencies within 30 days. The Head Start Bureau will then compile the results and forward

the requested information to the Committee.

Instrument	Number of respondents	Number of responses per respondent	Average burden hours per response	Total burden hours
Completion of HSB Survey (new web-based form)	2700	1x only	.5	1,350
Retrieval and submission of existing IRS Form 990, SF424, and PIR data	2700	1x only	8.5	22,950

Estimated Total Burden Hours: 24,300 hours.

Additional Information: The Administration for Children and Families is requesting that OMB grant a 30-day approval for this information collection under procedures for emergency processing by December 8, 2003. A copy of this information collection, with applicable supporting documentation, may be obtained by calling the Administration for Children and Families, Reports Clearance Officer, Robert Sargis at (202) 690-7275. In addition, a request may be made by sending an e-mail request to: rsargis@acf.hhs.gov.

Comments and suggestions about the information collection described above should be directed to the following e-mail address at the Office of Information and Regulatory Affairs, Office of Management and Budget, Paper Reduction Project: Lauren_Wittenberg@omb.eop.gov.

Dated: November 6, 2003.

Robert Sargis,

Reports Clearance Officer.

[FR Doc. 03-28437 Filed 11-12-03; 8:45 am]

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DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration

[Docket No. 2001B-0431]

International Conference on Harmonisation; Final Recommendations on the Revision of the Permitted Daily Exposures for Two Solvents, N-Methylpyrrolidone and Tetrahydrofuran, According to the Maintenance Procedures for the Guidance Q3C Impurities: Residual Solvents; Availability

AGENCY: Food and Drug Administration, HHS.

ACTION: Notice.

SUMMARY: The Food and Drug Administration (FDA) is announcing final recommendations to revise the permitted daily exposures (PDEs) for

two solvents, n-methylpyrrolidone (NMP) and tetrahydrofuran (THF), according to the maintenance procedures for the guidance for industry entitled "Q3C Impurities: Residual Solvents." The final recommendations were reached under the auspices of the International Conference on Harmonisation of Technical Requirements for Registration of Pharmaceuticals for Human Use (ICH).

DATES: Submit written or electronic comments on guidance documents at any time.

ADDRESSES: Submit written comments on the analyses and recommendations to revise the PDEs for NMP and THF to the Division of Dockets Management (HFA-305), Food and Drug Administration, 5630 Fishers Lane, rm. 1061, Rockville, MD 20852. Submit electronic comments to <http://www.fda.gov/dockets/ecomments>. Submit written requests for single copies of the documents to the Division of Drug Information (HFD-240), Center for Drug Evaluation and Research, Food and Drug Administration, 5600 Fishers Lane, Rockville, MD 20857; or the Office of Communication, Training and Manufacturers Assistance (HFM-40), Center for Biologics Evaluation and Research, 1401 Rockville Pike, Rockville, MD 20852-1448, FAX 888-223-7329. Send two self-addressed adhesive labels to assist the office in processing your requests. See the **SUPPLEMENTARY INFORMATION** section for electronic access to documents and maintenance procedures.

FOR FURTHER INFORMATION CONTACT:

Regarding the Q3C guidance: Robert Osterberg, Center for Drug Evaluation and Research (HFD-520), Food and Drug Administration, 5600 Fishers Lane, Rockville, MD 20857, 301-827-2120; or Andrew Shrake, Center for Biologics Evaluation and Research (HFM-345), Food and Drug Administration, 1401 Rockville Pike, Rockville, MD 20852-1148, 301-402-4635.

Regarding the ICH: Michelle Limoli, Office of International Programs (HFG-1), Food and Drug

Administration, 5600 Fishers Lane, Rockville, MD 20857, 301-827-0864.

SUPPLEMENTARY INFORMATION:

I. Background

In recent years, many important initiatives have been undertaken by regulatory authorities and industry associations to promote international harmonisation of regulatory requirements. FDA has participated in many meetings designed to enhance harmonisation and is committed to seeking scientifically based, harmonized technical procedures for pharmaceutical development. One of the goals of harmonisation is to identify and then reduce differences in technical requirements for drug development among regulatory agencies.

ICH was organized to provide an opportunity for tripartite harmonisation initiatives to be developed with input from both regulatory and industry representatives. FDA also seeks input from consumer representatives and others. ICH is concerned with harmonisation of technical requirements for the registration of pharmaceutical products among three regions: The European Union, Japan, and the United States. The six ICH sponsors are the European Commission; the European Federation of Pharmaceutical Industries Associations; the Japanese Ministry of Health, Labour, and Welfare; the Japanese Pharmaceutical Manufacturers Association; the Centers for Drug Evaluation and Research and Biologics Evaluation and Research, FDA; and the Pharmaceutical Research and Manufacturers of America. The ICH Secretariat, which coordinates the preparation of documentation, is provided by the International Federation of Pharmaceutical Manufacturers Associations (IFPMA).

The ICH Steering Committee includes representatives from each of the ICH sponsors and the IFPMA, as well as observers from the World Health Organization, the Canadian Health Protection Branch, and the European Free Trade Area.