

Tab A

Memorandum of Meeting
May 20, 1992
Potomac Room, Parklawn Building

Between: Food and Drug Administration Representatives

Susan Alpert, M.D., Division of Anti-Infective Drug
Products (HFD-520)
Donald Dobbs, Biologist, OTC Drug Policy Staff
(HFD-820)
Michael D. Kennedy, Director, OTC Drug Policy Staff
(HFD-820)
Murray M. Lumpkin, M.D., Director, Division of Anti-
Infective Drug Products (HFD-520)
Robert Osterberg, Ph.D., Division of Anti-Infective
Drug Products (HFD-520)
Gerald M. Rachanow, P.D., J.D., Deputy Director,
Monograph Review Staff (HFD-811)
Ella L. Toombs, M.D., Division of Anti-Infective Drug
Products (HFD-520)
Michael Weintraub, M.D., Consultant, Office of OTC Drug
Evaluation (HFD-800)
Judith L. Weissinger, Ph.D., Assistant Director
(Pharmacology), Office of Drug Evaluation II
(HFD-502)

and

Nonprescription Drug Manufacturers Association (NDMA)
Hydroquinone Task Force Representatives

George Andrassy, Vice President, Research and
Development, DEP Corporation
Michael Bento, Oglivy Adams & Rinehart
Peter A. Burke, Ph.D., Vice President, Research and
Development, Kiwi Brands Inc.
Mario de la Guardia, Sr., President, Carson Products
Thomas B. Fitzpatrick, M.D., Ph.D., Professor,
Department of Dermatology, Harvard Medical School,
Massachusetts General Hospital
Eugene H. Gans, Ph.D., President, Hastings Associates
Clyde Hammond, Sr., President, Summit Laboratories,
Inc.
John Hazlin, Director of Marketing, DEP Corporation
Thomas O. Henteleff, Esquire, Kleinfeld, Kaplan, &
Becker
Harry Hess, Director of Research, J. Strickland &
Company
John A. Kenney, Jr., M.D., Professor of Dermatology,
College of Medicine, Howard University
Howard I. Maibach, M.D., Department of Dermatology,
University of California School of Medicine
Terry Michael, Oglivy Adams & Rinehart

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John O'Donoghue, Ph.D., VMD, Director of
Toxicological Sciences Laboratory, Health and
Environmental Laboratories, Eastman Kodak Company
Madhu Pathak, M.B., Ph.D., Massachusetts General
Hospital
Jonah Shacknai, Chairman and Chief Executive Officer,
Medicis Pharmaceutical Corporation
R. William Soller, Ph.D., Senior Vice President and
Director, Science & Technology, NDMA
Lorna C. Totman, Ph.D., Director of Pharmacology and
Toxicology, NDMA
Daniel E. Wieneke, Vice President, Operations, E.T.
Browne Drug Company, Inc.
Gary M. Williams, M.D., Director of Medical Sciences,
American Health Foundation

Others present:

G. Clay, GD Searle & Co
Elizabeth Dorsey, King and Spalding
Elisabeth Embley, F-D-C Reports
George Ford, Eastman Chemical Company
Craig Richardson, D&S
Sania N. Rodriguez, Hyman, Phelps and McNamara
Kathy Schrode, Bristol-Myers Squibb
Ritashona Simpson, Research Associate, New York City
Department of Consumer Affairs
Millicent Yim, Kleinfeld, Kaplan and Becker
Jeff Zimmer, Washington Drug Letter

Background:

NDMA requested this feedback meeting to discuss recent data regarding the safety of OTC skin bleaching drug products containing hydroquinone.

Discussion:

Dr. William Soller opened the meeting with a brief introduction and purpose statement.

Dr. Thomas Fitzpatrick presented a brief overview of hydroquinone. He discussed the importance of hydroquinone when treating certain skin disorders. He stated that he has never seen a safety problem with the use of two to three percent hydroquinone and knows of no alternative skin bleaching agent. He recommends that his patients use OTC skin bleaching products twice daily and that they only use skin bleaching products with a total sun block (at least SPF 15).

Dr. John Kenney discussed clinical benefits of hydroquinone. He addressed problems that African Americans have with hyperpigmentation due to external forces such as blemishes, insect bites, bruises, etc. He indicated that OTC skin bleaching products are economically feasible for poor people (particularly minorities) who cannot afford a dermatologist's office fee and recommended that the drug remain available OTC to help these people. Dr. Kenney has prescribed five percent hydroquinone for years and stated that he has never observed a case of ochronosis over many years of practice.

Dr. William Soller discussed the association of hydroquinone with exogenous ochronosis. He indicated that the published literature contains a total of 14 domestic cases of medically-diagnosed hydroquinone-associated ochronosis from 1976 to 1992. Over this time, companies estimate that over 160 million units of 1-4% hydroquinone skin bleaching products have been sold in the United States. Over this same time period, 17 domestic reports of skin darkening associated with the use of hydroquinone skin bleaching products have been reported to companies marketing these products. Only one of these reports (Howard, 1990) is medically diagnosed in the domestic literature as hydroquinone-associated exogenous ochronosis. Three domestic cases relating to adverse effects of hydroquinone have been reported to FDA's Spontaneous Reporting System. Gerald Rachanow requested that NDMA ask the American Academy of Dermatology to survey its members on the occurrence of hydroquinone-associated exogenous ochronosis in their practices. This would help the FDA to better evaluate the severity of hydroquinone-associated exogenous ochronosis in the United States. Dr. Kenney mentioned that he has not seen any cases and has surveyed his colleagues, with a few reporting one or two cases. He felt that this was a very minimal problem in the United States.

The majority of cases of hydroquinone-associated exogenous ochronosis have been reported in South Africa. Dr. Howard Maibach explained that the South African experience differs from the United States experience in a number of ways, including: units sold/year; a more extensive use pattern in South Africa; higher concentration of hydroquinone used; use of alcoholic vehicles; no use of a sunscreen; other ochronotics in the product (e.g., resorcinol and phenol). Dr. Maibach discussed formulation considerations and how they relate to the percutaneous absorption of hydroquinone. Bucks et al. (a 1989 study) and other dermal absorption and toxicity studies performed on hydroquinone were discussed. The absorption rate has been reported as 3 ug/cm² per hour.

Dr. John O'Donoghue discussed the chronic health effects testing of hydroquinone (Tab A). The oral bioassay studies performed by the National Toxicology Program (1989) and Shibata et al. (1991)

were reviewed and a series of nine discussion points pertaining to the significance of the bioassay results were addressed.

Dr. Lorna Totman presented an outline of NDMA's research program to further the understanding of hydroquinone's toxicity. Dr. Totman gave a brief overview of the studies proposed by NDMA and a projected timeline for their completion (Tab B).

Dr. William Soller presented voluntary labeling guidelines (dated May 1992) proposed by the industry members of the NDMA Hydroquinone Task Group (Tab C). The guidelines represent a combination of labeling language proposed by the agency and new language proposed by the Hydroquinone Task Group. Gerald Rachanow asked when these guidelines would be implemented. Dr. Soller and Jonah Shacknai replied that they would be implemented as soon as possible, most likely when the next printing of new packaging occurs.

Ritashona Simpson read a statement from Mark Green, Commissioner, New York City Department of Consumer Affairs (Tab D).

After considerable discussion between FDA personnel and NDMA Task Group representatives, the meeting was adjourned.

Donald Dobbs

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