

6/22/92

JUN 21 1992

The Honorable Ed Towns
Chairman, Congressional
Black Caucus
House of Representatives
Washington, D.C. 20515

Dear Mr. Chairman:

This is in response to your letter of May 18, 1992, concerning the Over-the-Counter (OTC) drug 2% Hydroquinone.

The status of 2% hydroquinone for OTC availability continues to be under review by the Food and Drug Administration (FDA). On May 20, 1992, the Agency met with the industry to discuss additional, safety data and information related to this issue. Because of your interest, we have enclosed a copy of the minutes of this meeting. Also we have forwarded a copy of your correspondence to FDA's Center for Drug Evaluation and Research, Office of OTC Drug Evaluation so that the factors you have raised on OTC availability of hydroquinone will be considered before a final decision is made.

Our final decision on hydroquinone skin bleaching products is pending completion of our review of the data. We want to thank you for taking the time to express your concerns on this matter.

We hope this information is helpful. If we can be of further service, please let us know.

Sincerely yours,

Marc J. Scheineson
Associate Commissioner
for Legislative Affairs

Enclosure
As stated above

78N-0065

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John Conyers, Jr., MI '65
 William Clay, MO '69
 Louis Stokes, OH '69
 Ronald V. Dellums, CA '71
 Charles B. Rangel, NY '71
 Cardiss Collins, IL '73
 Harold Ford, TN '75
 Julian C. Dixon, CA '79
 William H. Gray, PA '79
 Mervyn M. Dymally, CA '81
 Gus Savage, IL '81
 Major R. Owens, NY '83
 Edolphus Towns, NY '83
 Alan Wheat, MO '83
 Charles A. Hayes, IL '83
 Mike Espy, MS '87
 Floyd H. Flake, NY '87
 John Lewis, GA '87
 Kweisi Mfume, MD '87
 Donald M. Payne, NJ '89
 Craig A. Washington, TX '90
 Barbara-Rose Collins, MI '91
 Gary Franks, CT '91
 Eleanor Holmes-Norton, DC '91
 William Jefferson, LA '91
 Maxine Waters, CA '91

Congressional Black Caucus
Congress of the United States
 H2-344 House Annex #2
 Washington, D.C. 20515

202 — 226-7790

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May 18, 1992

RECEIVED
 MAY 27 PM 2:41
 CONGRESSIONAL BLACK CAUCUS

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

Dear Dr. Kessler:

I understand that the Food and Drug Administration is reviewing the regulatory status of 2% Hydroquinone as the active ingredient in over-the-counter products designed to treat hyperpigmentation.

It is my understanding that several proposed regulatory modifications have been drafted for consideration at your upcoming meeting without benefit of consultation and recommendation by physicians and dermatologists serving the African-American patients who are virtually the exclusive consumers of these products. Additionally, we are concerned that correlations to limited study in developing countries have been transposed in this instance to develop conclusions which:

- 1) are derived from product used at strengths hundreds of times stronger than considerations available in the United States; and
- 2) have seen limited scientific study through rat experimentation where ingestion of this topical product was forced at grossly toxic levels in contradiction to all directions and warnings on packaging in this country.

As Chairman of the Congressional Black Caucus, I am sharing this communication with the Chairman of our Health Braintrust, Congressman Louis Stokes, who works extensively with health care providers across the nation.

I believe that the medical evidence assembled from over fifty years of use by tens of millions of American consumers indicates that these products are safe and effective in the form in which they are

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available in this country.

Further, these products serve an important role by allowing African-Americans to treat the very common instances of hyperpigmentation caused by acne scars, razor bumps, mosquito bites, and other skin irritations. The availability of these products on an over-the-counter basis provides African-Americans with a low cost option for responsible self-medication.

I hope your agency considers these factors in your review.

Sincerely,

A large, stylized handwritten signature in black ink, appearing to read 'Ed Towns'.

Ed Towns, M. C.
CBC Chairman

SEARCHED 11-10-22

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

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

Donald Dobbs

M E M O R A N D U M

DEPARTMENT OF HEALTH AND HUMAN SERVICES
PUBLIC HEALTH SERVICE
FOOD AND DRUG ADMINISTRATION
CENTER FOR DRUG EVALUATION AND RESEARCH

DATE:

FROM: Director
Monograph Review Staff (HFD-810)

SUBJECT: Material for Docket No. 78 W - 0065

TO: Dockets Management Branch (HFA-305)

- The attached material should be placed on public display under the above referenced Docket No.
- This material should be cross-referenced to Comment(s) No. _____.



William E. Gilbertson, Pharm. D.

Attachment