Robert BRADY

C·T·F·A
The Cosmetic, Toiletry and Fragrance Association

E. Edward Kavanaugh
President

STATEMENT OF THE
COSMETIC, TOILETRY AND FRAGRANCE ASSOCIATION, INC.
TO THE
PENNSYLVANIA HOUSE JUDICIARY COMMITTEE
CONCERNING
HOUSE BILL 873

May 25, 1989

1110 Vermont Avenue, NW • Suite 800 • Washington, DC 20005 • (202) 331-1770 • Telex 89-2673

STATEMENT OF THE
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My name is Robert Brady. I am now a partner at the Washington law firm of Patton, Boggs & Blow. From 1975-1981 I was an attorney at FDA, and from 1981-1983 I was Executive Assistant to the Commissioner of Food and Drugs. Subsequent to that, I became General Counsel and the Executive Vice President of CTFA, leaving that organization last fall. I appreciate this opportunity to present CTFA's views in opposition to House Bill 873, which would prohibit use in the State of Pennsylvania of various animal testing procedures that are essential to ensure the safety of consumer products.

CTFA is the national trade association representing the cosmetic, toiletry and fragrance industry. The Association has an active membership of some 250 companies, which manufacture or distribute the vast majority of the finished cosmetic and personal care products marketed in the United States. CTFA also includes some 250 associate member companies from related industries, such as manufacturers of raw materials and packaging materials.

CTFA understands the concerns for animal welfare that prompted introduction of this bill. We share those concerns. Nevertheless, providing safe products to our customers has been, and must continue to be, our fundamental responsibility.

The cosmetics produced by our industry include not only the makeup preparations often thought of as "cosmetics," but also toothpastes, mouthwashes, shampoos, deodorants, sunscreens, shaving creams, and a wide variety of similar personal care products that are used daily by virtually everyone. The welfare of millions of people depends on the safety of these products. The magnitude of our safety concerns is illustrated by the fact that over nine billion cosmetic products are distributed in the United States every year.

We have a moral and legal responsibility to ensure that our products are safe for consumer use. That responsibility compels us to oppose this bill. We simply must use the most scientifically accurate and acceptable safety testing methods available. Given the present state of scientific knowledge, we must include animal safety testing as part of our program of assuring safe personal care products to consumers.

The tests that would be outlawed by this bill -- eye irritancy tests, including the Draize eye irritancy test, and acute toxicity tests, including the LD_{50} test -- are accepted scientific procedures to assess the safety of cosmetic products for human use. Proponents of the bill argue that alternative, non-animal tests can replace animal testing and that animal tests are not required for regulatory purposes. Both arguments are false.

THERE ARE NO ACCEPTABLE ALTERNATIVES TO REPLACE ANIMAL TESTING

At this time, there are no alternatives that can eliminate the need for animal testing. As noted by the Federal Food and Drug Administration (FDA) only last month:

> "[M]any years of further research and broad advances on all fronts of toxicological, medical, and related scientific disciplines will be required to replace animal testing methods with non-animal techniques."[1]

Since the FDA is responsible for regulating the safety of cosmetics, as well as such other products as foods, drugs, and medical devices, its position on animal testing is particularly pertinent. For the last three years, the State of Maryland has considered -- and rejected -- legislation similar to House Bill 873. During the course of that legislature's examination of this issue, Maryland Senator Walter Baker, by letter dated February 17, 1988, asked the FDA explicitly whether any non-animal alternative tests exist to replace the tests that would have been banned by the Maryland proposal. The FDA's reply was unequivocal:

> "At the present time and in the foreseeable future, the answer is no. The Agency is aware that there are many potential non-animal replacement tests which are in various stages of evolution but none have been accepted for such use by the scientific community at the present time. This response applies specifically to the Draize eye irritancy test and to all other acute toxicity tests of which the Agency is aware."[2]

The FDA's position on this issue is supported by recognized experts in the field. For example, testifying before the Maryland House Judiciary Committee in 1987, Dr. Alan Goldberg, Director of the Johns Hopkins Center for Alternatives to Animal Testing, stated that "no single method developed to date, nor anticipated in the near future, will provide a <u>replacement</u> for eye irritancy testing in intact animals." Dr. Goldberg emphasized that to eliminate animal testing at this time would "constitute an abrogation of the toxicologist's responsibility to ensure safety and will pose a risk to human health that government, industry and the public will find unacceptable."[3]

ANIMAL TESTING DATA ARE NEEDED FOR CONSUMER SAFETY

The Federal Food, Drug and Cosmetic Act bans the sale of any cosmetic that "bears or contains any poisonous or deleterious substance which may render it injurious to users ... under such conditions of use as are customary or usual."[4] The FDA, which enforces the Act, has issued regulations providing that each ingredient used in a cosmetic and each finished cosmetic product must be adequately substantiated for safety before it is marketed. If there is inadequate safety substantiation, the product must be labeled "Warning--The safety of this product has not been determined."[5] No reputable manufacturer would market a product whose safety has not been adequately substantiated.

The vast majority of scientific and regulatory experts agree that animal testing data are required to meet the safety criteria imposed by the federal law. For example, when asked whether animal tests are necessary to establish the safety of cosmetic products, FDA Commissioner Frank Young said, "Yes." He added:

> "The FDA cannot permit the use of any potentially harmful substance in humans prior to preliminary testing in animals to provide reasonable assurance that it is not injurious to humans. Since certain tests should never be carried out in human beings and since at the present time there are no adequate alternatives, whole animal testing remains unavoidable."[6]

Commenting on the Draize eye irritancy test, Commissioner Young stated in the same letter that the test is "currently the most valuable and reliable method for evaluating the hazard or safety of a substance introduced into or around the eye."

Commissioner Young reiterated that position in a December 1988, letter to a legislator from the State of New Jersey, which last year considered -- and rejected -- legislation to ban use of the Draize eye irritancy test. Dr. Young stated that:

> "The Draize eye irritancy test remains the most valuable and reliable method for evaluating the hazard or safety of a substance introduced into or around the eye. This will continue to be the case for the foreseeable future in spite of significant progress in some areas of the development of alternatives to the Draize test. We must never lose sight of the fact that the objective of testing is confirmation of the safety of the product. This determination must be accomplished using the best methods available." [7]

The FDA clearly recognizes the need for animal safety testing. To quote from a statement issued by the agency on April 17, 1989:

> "The FDA position is that the use of animal tests by industry to establish the safety of regulated products is necessary to minimize the risks from such products to humans." [8]

The FDA identifies various animal tests that should be conducted to evaluate the safety of color additives. Other federal government agencies use animal testing data to carry out their safety programs. As an example, the Occupational Safety and Health Administration worker right-to-know standard specifically references a number of commonly used animal test protocols as the basis for identifying hazards in the workplace. Similarly, under the Federal Hazardous Substances Act, which covers many household products, regulations have been issued as a guide for identifying the hazards that must be labeled on consumer products. To determine whether a consumer product is corrosive or an irritant to the skin and eye, pertinent regulations refer to data that

are developed in a specific animal test protocol.[9] The Environmental Protection Agency similarly relies on animal test results in evaluating the safety of products under its jurisdiction.

ANIMAL DATA ARE INVALUABLE IN CASES OF PRODUCT MISUSE

In addition to being essential to help ensure that new cosmetic product formulations are safe under normal conditions of use, animal testing procedures are invaluable in the treatment of cases involving misuse of products. Unfortunately, the deliberate or accidental misuse of even the safest of products can pose a serious risk to consumers. This risk is of particular concern in connection with young children. In fact, the FDA reports that 90 percent of the cases of accidental ingestion involve children three years or less of age.[10]

To evaluate such cases and to make specific recommendations for treatment, it is often necessary to rely on animal testing data, including skin and eye irritancy test results. It is for this reason that both the Consumer Federation of America and the American Association of Poison Control Centers last year adopted resolutions that oppose the type of legislation now before you.

WE ARE COMMITTED TO THE SEARCH FOR ALTERNATIVES TO ANIMAL TESTING

Cosmetic companies have sponsored more research into alternatives to animal testing than any other industry. We have taken many positive steps to hasten the time when alternative, scientifically valid, and reliable safety substantiation methods can replace the need for animals.

In March 1988, for example, CTFA, in cooperation with the Battelle Memorial Institute (Battelle), launched the In Vitro Alternative Evaluation Program. This program is evaluating a number of promising non-animal testing procedures that are currently being used by CTFA member companies as screening assays and that could potentially serve as alternatives to the animal eye irritation safety test. The companies involved in the program include: Avon Products, Beiersdorf AG, Colgate-Palmolive, The Dial Corporation, Gillette, Johnson & Johnson, Estee Lauder, Noxell, Procter & Gamble, and Revlon.

Scientists believe that it will be impossible to develop one single in vitro (test tube) test that will be effective for all types of cosmetics. The program, therefore, is being conducted in phases, with each phase concentrating on one range of products. During Phase I, participants have studied ten prototype alcohol-containing products: pump hair spray, cologne, hair setting/styling lotion, sun block, deodorant, perfumed skin lotion, after shave lotion, freshener, mouthwash, and light cologne. Each of these is being tested at 12 separate facilities using one or more of the 12 basic in vitro tests being evaluated in Phase I. A list of the initial tests and sponsors is attached to this testimony. A final report on Phase I is expected to be published by the fall of 1989.

Arrangements for subsequent phases of the In Vitro Alternative Evaluation Program are already underway. Phase II will concentrate on oil-in-water emulsion cosmetics. Additional classes of formulations will be studied in subsequent phases until there is sufficient information to provide the necessary background data to begin the formal validation process for those tests shown to be effective and reliable.

The In Vitro Alternative Evaluation Program is designed to lead to the eventual validation of a battery of screening tests that can be mixed and matched as needed to cover the total range of cosmetic, toiletry, and fragrance products. Until that ultimate goal is reached, the program will provide companies with information enabling them to employ some of the in vitro tests in their current safety screening procedures and thereby reduce the number of animals necessary for safety testing.

Dramatic progress is being made in the development and use of alternative tests to reduce the use of animals. Recent announcements by individual companies demonstrate that progress. It is important to note, however, that there are more than 80 categories of cosmetics and more than 5,000 individual products marketed by the industry. A non-animal screening mechanism that may apply to the formulations of a particular company may not be suitable for another company's product line. The In Vitro Alternative Evaluation Program is a major step the industry is taking to determine whether particular alternative tests may have widespread applicability to general product categories.

In addition to supporting the In Vitro Alternative Evaluation Program, the cosmetic industry has allocated millions of dollars to other programs searching for acceptable alternatives to animal testing. Since 1981, for instance, CTFA and its members have contributed more than three million dollars to establish and maintain the Johns Hopkins Center for Alternatives to Animal Testing.

The Johns Hopkins Center is a national center for development of alternative testing methodologies. It supports a research grants program, symposia, and workshops that attract recognized investigators, scientists, and regulators from around the world. In addition to researching alternatives to the Draize test, it supports the development of in vitro alternative methods to measure inflammatory response, cytotoxicity, acute toxicity, and cell or organ specific responses that may be used as alternatives to whole animal tests in the future.

The Center has legitimized worldwide the scientific pursuit of alternatives to animal testing. Its procedures have achieved international recognition and have served as the model for two similar programs established in Germany and Switzerland. We are proud of our part in its creation and our contributions to its success.

Besides the Johns Hopkins Center, cosmetic industry members have supported other programs in the search for alternative tests. Among these has been a $1.5 million project conducted at Rockefeller University. In addition, during the past two years, CTFA members have spent more than three million dollars on their own in-house efforts to develop alternative procedures.

Our companies are committed to phasing out the use of animals as soon as non-animal alternative tests are available and found acceptable by the scientific community and governmental regulatory agencies. We are making progress in our search for such tests, but as the FDA has stated:

> "[M]any years of further research and broad advances on all fronts of toxicological, medical, and related scientific disciplines will be required to replace animal testing methods with non-animal techniques." [11]

WE ARE COMMITTED TO MINIMIZING ANIMAL USE AND DISCOMFORT

Until scientifically valid and reliable non-animal alternatives can eliminate the need for animals, the cosmetic industry is committed to reducing animal use and discomfort to the greatest possible extent. Evidence of this commitment can be seen in two industry programs.

The CTFA Cosmetic Ingredient Review (CIR) program is a key element in the industry's efforts to minimize animal use. CIR has reduced the need for animal testing by establishing an industry-wide mechanism to share ingredient safety data.

CIR's mission is to collect, evaluate, and publicize all available published and unpublished safety data on cosmetic ingredients. By offering the data maintained in an ingredient data bank to any company -- member or non-member -- that requests it, the CIR plays an important role in reducing duplicative animal testing.

The cosmetic industry has also conducted research into modifying the Draize eye irritancy test to make it less painful. A special CTFA task force has evaluated variations, such as reducing the volume of material applied, diluting the concentrations of ingredients used, using local anesthetics, and reducing the number of animals used in the test. These techniques are designed to minimize discomfort and ensure that these modifications do not affect the validity of test results.

Let me emphasize that, as important as this work is, we do not consider it to be a substitute for our search for true alternatives to the use of animals in safety testing.

SUMMARY

The cosmetic industry is genuinely concerned about animal welfare. We have taken impressive steps to minimize animal use, and we are among the leaders in the search for reliable alternatives to animal testing. We are committed to continuing these efforts to phase down and phase out the use of animals in safety testing.

At the same time, the safety of human consumers is and will continue to be our primary concern. We have a moral and legal responsibility to ensure that our products are safe for human use. The animal testing procedures that would be outlawed by House Bill 873 are currently essential to meet that responsibility.

For these reasons, we respectfully request that this bill not be reported out of committee.

Thank you for your attention.

NOTES

1. April 17, 1989, statement of the U.S. Food and Drug Administration to the Maryland Governor's Task Force to Study Animal Testing.

2. February 29, 1988, letter from Dr. Frank E. Young, Commissioner of Food and Drugs, U.S. Food and Drug Administration, to Maryland Senator Walter M. Baker.

3. Testimony before Maryland House Judiciary Committee, March 18, 1987, pages 2-3. (Emphasis added)

4. 21 U.S.C. §361.

5. 21 U.S.C. §361, 21 C.F.R. §740.10.

6. February 29, 1988, letter from Dr. Frank E. Young, Commissioner of Food and Drugs, U.S. Food and Drug Administration, to Maryland Senator Walter M. Baker.

7. December 19, 1988, letter from Dr. Frank E. Young, Commissioner of Food and Drugs, U.S. Food and Drug Administration, to New Jersey Assemblyman John A. Villapiano.

8. April 17, 1989, statement of the U.S. Food and Drug Administration to the Maryland Governor's Task Force to Study Animal Testing.

9. See 16 CFR Part 1500.

10. March 17, 1989, letter from Heinz, J. Eiermann, FDA Division of Colors and Cosmetics.

11. April 17, 1989, Statement of the U.S. Food and Drug Administration to the Maryland Governor's Task Force to Study Animal Testing.

C·T·F·A
The Cosmetic, Toiletry and Fragrance Association

E. Edward Kavanaugh
President

CTFA In Vitro Alternative Evaluation Program
Participants and Test Procedures
April 1989

Avon Products, Inc.
- In Corporate Facility:
  - Neutral Red Uptake
  - Kenacid Blue R Uptake
- At Fund for the Replacement of Animals in Medical Experiments (FRAME):
  - Highest Tolerated Dose
  - Neutral Red Uptake
  - Kenacid Blue R Method for Protein
- At Ohio State University:
  - Tetrahymena Motility Assay

Beiersdorf AG
- In Corporate Facility:
  - HET-CAM Procedure
  - Neutral Red Uptake
  - Protein Determination
  - RBC-Test System

Colgate-Palmolive Company
- In Corporate Facility:
  - Chorioallantoic Membrane Vascular Assay (CMVA)
  - Chorioallantoic Membrane Assay (CAM)

The Dial Corporation
- In Corporate Facility:
  - SIRC Cell Cytotoxicity Test

Gillette Medical Evaluation Laboratories
- In Corporate Facility:
  - EYTEX™ and/or EYTEX-MPA™

Johnson & Johnson Baby Products Company
- In Corporate Facility:
  - Dual Dye Staining Procedure

Estee Lauder, Inc.
- In Corporate Facility:
  - MTT Assay - Mitochondrial Activity
  - Neutral Red Assay - Cell Viability
  - Total Cell Protein - Kenacid Blue R

Noxell Corporation
- At North American Science Associates, Inc.:
  - Agarose Diffusion Method

The Procter & Gamble Company
At IIT Research Institute:
Chromium-51 Release Assay

Revlon, Inc.
In Corporate Facility:
Highest Tolerated Dose (HTD/NR-90)
Neutral Red Absorption
Protein Determination

INDEX TO EXHIBITS SUPPLEMENTING
TESTIMONY OF ROBERT P. BRADY FOR
THE COSMETIC, TOILETRY AND FRAGRANCE ASSOCIATION

PENNSYLVANIA HOUSE BILL 873
MAY 25, 1989

U.S. Food and Drug Administration
Statement to the Maryland Governor's Task Force
to Study Animal Testing - April 17, 1989

As commonly noted by opponents of animal testing, current laws administered by the Food and Drug Administration (FDA) do not require the use of animal testing for cosmetics. The FDA position is that the use of animal tests by industry to establish the safety of regulated products is necessary to minimize the risks from such products to humans.

Although the Federal Food, Drug, and Cosmetic Act does not require that cosmetic manufacturers or marketers test their products for safety, the FDA strongly urges cosmetic manufacturers to conduct whatever toxicological or other tests are appropriate to substantiate the safety of the cosmetics. If the safety of a cosmetic is not adequately substantiated, the product may be considered misbranded and may be subject to regulatory action unless the label bears the following statement: Warning--The safety of this product has not been determined.

The FDA feels strongly that animal testing should derive the maximum amount of useful scientific information using the minimum number of animals necessary. Consideration should be given to the use of validated and accepted alternative methods to whole animal testing. Attempts should be made to eliminate or minimize the degree and duration of suffering in the animals that are used. Pain-relieving medication, including anesthetics, should be considered and employed when such drugs will not interfere with the nature and purpose of the testing. Euthanasia of moribund animals should be considered and employed when the procedure will not interfere with the nature and purpose of the testing.

We share the concern about the use of animals in toxicological testing and agree that, within the limits of scientific capability, more humane methods be used for testing the safety of regulated products. However, we also know that many procedures intended to replace animal tests are still in various states of development and that it would be unwise for us to urge manufacturers not to do any further animal testing or to reject data obtained from such tests. There appears to be little chance of much "replacement" of animal testing in the foreseeable future, but it is certainly realistic to expect progress in the areas of "reduction" and "refinement." Developments in these areas will result in a reduction in the numbers of animals required and less distress for those animals that are used.

Much of the attention concerning animal testing has been focused upon the LD50 test and the Draize eye irritancy test.

Some have mistakenly thought that FDA requires use of the "classical" LD50 test to establish levels of toxicity. Not so. FDA has no requirements for LD50 test data obtained by using the classical, statistically-based test. Attached is a copy of the LD50 test policy statement as published in the Federal Register. However, some type of animal acute toxicity testing needs to be done to determine the safety or toxicity of regulated products.

With respect to the Draize test, it is the FDA position that the Draize eye irritancy test is currently the only meaningful and reliable method for evaluating the hazard or safety of a substance introduced into or around the eye. As far as alternatives to the Draize test are concerned, tissue and cell culture techniques are very useful to study the actions of substances when research scientists wish to answer questions specifically directed to certain cell types or tissues. However, the responses and results of a tissue or cell culture alone cannot, at the present time, be the basis for determining the safety of a substance. Any human or animal organ is a complex biological system, and the effect of a substance on a specific cell or tissue in culture may differ significantly from the effect observed in a specific organ system or in the animal as a whole.

Although most require more research for validation, some in vitro studies are useful as screening tools to indicate relative toxicity or safety of a substance coming into contact with the eye. The agency has provided industry with the following guidance relating to the use of in vitro methods to support the safety of products subject to eye irritancy testing:

(1) Because no one wishes to sacrifice animals unnecessarily and because the proper use of in vitro studies can reduce the total number of animals used in the development of a product, it is appropriate for industry to develop and use in vitro tests.

(2) Because of their inherent over-simplification of the physiology and response of the whole animal system, in vitro tests are not total replacements for the Draize eye irritancy test and probably can never be.

(3) A quick and inexpensive test, despite its inability to detect everything, can be used early on in the development phase of a product to eliminate chemical candidates that fail to pass, thus reducing the number of chemicals or formulations that would need to be tested eventually in animals.

(4) It is conceivable that in vitro tests, based in part on prior calibration with animal tests, could also be used as a final safety test in those situations where only a minor change in an inactive ingredient is made and where prior experience enables one to draw the scientific conclusion that the in vitro test is capable of detecting any likely changes due to reformulation.

(5) Since FDA has no testing requirements for the premarketing of cosmetics, we have not developed testing protocols for that purpose. The four statements above represent our considered, informed opinion on the science. They should not be construed as regulatory dicta.

Immunochemical and biochemical techniques are being substituted for animals to determine the potency and purity of some biological products. There is excellent potential for developing acceptable alternatives to the use of animals or their reduction in test numbers for some purposes. As an example, in the Federal Register for February 19, 1988, the FDA announced the availability of a guideline for use of the Limulus Amebocyte Lysate (LAL) Test as an end-product endotoxin test for human injectable drugs (including biological products), animal injectable drugs, and medical devices. The guideline is intended to inform manufacturers of acceptable methods of validating the LAL test before using it as an alternative to the official rabbit pyrogen test.

As it stands now, many years of further research and broad advances on all fronts of toxicological, medical, and related scientific disciplines will be required to replace animal testing methods with non-animal techniques. Various scientific efforts are under way to reach this goal. Let us hope the time will come when the safety of regulated products can be predicted without the need for animal testing.

In the final analysis, the research and testing required for the approval of a product is based upon the characteristics and the use of the product. The design and execution of the supporting documentation for the safety and effectiveness approval of a product must be worked out on a case-by-case basis with the scientific staff of the FDA.

EXHIBIT 2

DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administra
Rockville MD 20857

February 29, 1988

The Honorable Walter M. Baker
Chairman, Judicial Proceedings Committee
Senate of Maryland
James Senate Office Building, Room 300
Annapolis, Maryland 21401-1991

Dear Mr. Baker:

The agency has the following comments regarding its position with respect to the animal testing issues addressed in your letter of February 17, 1988. The Food and Drug Administration is concerned that its position on this subject is clear and fully understood. Our response to your specific questions follows.

1. In your opinion, does there exist any non-animal alternative test methodologies to replace the Draize irritancy test and the other acute toxicity tests? In particular, can the CAM test serve as a replacement to the Draize test?

At the present time and in the foreseeable future, the answer is no. The agency is aware that there are many potential non-animal replacement tests which are in various stages of evolution but none have been accepted for such use by the scientific community at the present time. This response applies specifically to the Draize eye irritancy test and to all other acute toxicity tests of which the agency is aware.

With respect to the chorioallantoic membrane (CAM) assay, it is the agency position that at the present time there is not sufficient data to establish the validity of the CAM assay as a replacement for the Draize eye irritancy test.

2. Is the use of these animal tests, including the Draize eye irritancy test, necessary to establish the safety of cosmetic products under the regulatory control of FDA?

Yes. The Draize eye irritancy test is currently the most valuable and reliable method for evaluating the hazard or safety of a substance introduced into or around the eye. Many shampoos (particularly baby shampoos), hair conditioners, and other cosmetics get into the eye by accident, no matter how carefully they are used. Tissue and cell culture techniques (alternatives to whole animals) are very useful to study the actions of substances when research scientists wish to answer questions specifically directed to certain cell types of a tissue or of an organ as, for example, the eye. However, the responses and

results of a tissue or cell culture test alone cannot, at the present time, be the basis for determining the safety of a substance. Any human or animal organ is a complex biological system, and the effect of a substance on a specific cell or tissue in culture may differ significantly from the effect observed in a specific organ system or in the animal as a whole.

The FDA cannot permit the use of any potentially harmful substance in humans prior to preliminary testing in animals to provide reasonable assurance that it is not injurious to humans. Since certain tests should never be carried out in human beings and since at the present time there are no adequate alternatives, whole animal testing remains unavoidable.

The agency trusts that you find these answers useful and that they specifically answer your questions. We will be pleased to respond to any further questions that you might have on this public safety issue. Thank you for contacting us on this difficult issue.

Sincerely yours,

Frank E. Young, M.D., Ph.D.
Commissioner of Food and Drugs

EXHIBIT 3

DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Rockville MD 20857

DEC 19 1988

The Honorable John A. Villapiano
State of New Jersey
General Assembly
Hall of Records
Main Street
Freehold, New Jersey 07728

Dear Mr. Villapiano:

I write to respond to your October 28 letter regarding the status of the development of alternatives to the Draize eye irritancy test.

I wish to reiterate that the Draize eye irritancy test remains the most valuable and reliable method for evaluating the hazard or safety of a substance introduced into or around the eye. This will continue to be the case for the foreseeable future in spite of significant progress in some areas of the development of alternatives to the Draize test. We must never lose sight of the fact that the objective of testing is confirmation of the safety of the product. This determination must be accomplished using the best methods available.

At this stage of the development of alternatives, the results would indicate that no single method will replace the Draize test. The direction of much of the current work is toward a test or group of tests suitable for a specific chemical type or product class. A central issue in the development of alternative methods is that of verification and validation of methods. This process is highly complex and specific to the method under consideration. Validation of a test method must show that the proposed method accurately predicts eye irritation, that the test produces similar results in other laboratories, and that results are reproducible within the same laboratory.

Several activities of current interest should be mentioned. The use of the chorioallantoic membrane (CAM) of a developing chick embryo to test for potential irritants has received much attention. Reports indicate that the Colgate-Palmolive Company is making significant improvements in this method.

The Eyetex System, which is being privately developed to test for eye irritancy, is based upon aggregation of a mixture of macromolecules. This system is currently being evaluated by agency scientists and scientists in the private sector.

In addition, both the Soap and Detergent Association and the Cosmetic, Toiletry and Fragrance Association have active programs to evaluate non-animal test systems for predicting eye irritancy. A joint government-industry workshop was held on September 14, 1988 to consider the direction to be taken by these programs. Results presented at this workshop indicate that tests will need to be established for individual classes of chemicals because of their variation in physical characteristics and biological activity.

Although tissue and cell culture techniques are very useful to study the actions of substances when research scientists wish to answer questions specifically directed to certain cell types of a tissue or of an organ, they cannot, at the present time, be the basis for determining the safety of a substance.

The agency trusts that you find this information useful. If you have any further questions on this issue, please contact Dr. Richard Bradbury of our Center for Veterinary Medicine at 301/443-4557.

Sincerely yours,

Frank E. Young, M.D., Ph.D.
Commissioner of Food and Drugs

EXHIBIT 4

DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administra
Washington DC 20204

March 17, 1989

Ms. Anita Curry
102 West Greenway Blvd.
Falls Church, VA 22046

Dear Ms. Curry:

This is in reference to your recent letter regarding the use of live animals for testing of cosmetics. You expressed concern that this kind of testing causes unjustified pain and suffering and recommended that cosmetic companies be forced to use other, non-animal methods for determining product safety.

We share your concern about the use of animals in toxicological testing and agree with you that, within the limits of scientific capability, more humane methods be used for testing the safety, or harmfulness, of cosmetic products. However, we also know that many procedures intended to replace animal tests are still in various stages of development and that it would be unwise for us to urge manufacturers not to do any further animal testing or to reject data obtained from such tests.

Cosmetic manufacturers test their products by various chemical, microbiological and toxicological methods to assure their integrity and safety under ordinary conditions of use as well as anticipated misuse. The LD50 test, for example, is carried out to determine whether or not a cosmetic may be toxic when ingested by accident. If toxic, a child would need to ingest only about two ounces or less of product to experience serious adverse effects, and ninety percent of the reported cases of accidental ingestion involve children of three years or less of age.

The LD50 test data are rarely submitted to us because the submission of cosmetic safety testing information to the FDA is voluntary on the part of cosmetic manufacturers. These data are usually given to poison control centers, hospital emergency rooms, and physicians. Quite often, the information is also made available to parents of children that may have swallowed a cosmetic product.

Another example is the testing of shampoos or other cosmetics in the eyes of rabbits by the method of Draize. It is currently the most valuable and reliable method for determining the harmfulness, or safety, of a substance

introduced into the eye; and many shampoos, hair conditioners, and other cosmetics get into the eye by accident, no matter how carefully they are used. Tissue and cell culture techniques are very useful to study the action of chemicals when research scientists wish to answer questions specifically directed to certain cells of an organ as, for example, the eye. However, the results of a tissue or cell culture test alone cannot be the basis for deciding on the safety of a substance, at least not at the present time. Any human or animal organ is a complex biological system, and the effect of a chemical on a specific cell or tissue in culture may differ significantly from the effect experienced in the entire system.

Some testing may be performed in humans. We do not believe however, that anyone would condone the testing of potentially harmful substances in humans prior to some initial animal testing that could reasonably assure absence of injury; and certain tests could never be carried out in human subjects. Animal testing, therefore, remains at present unavoidable.

Today, most tests are carried out by using only the smallest number of animals necessary to assess consumer safety. In the case of the LD50 test, for example, only enough rodents are used to distinguish between nontoxic, toxic and highly toxic materials. We fully support this modification and have repeatedly been encouraging cosmetic firms to adopt it as an alternative to the original method which requires substantially more animals.

As it stands now, many years of further research and broad advances on all fronts of toxicological, medical and related scientific disciplines will be required to replace animal testing methods with non-animal techniques. Various scientific efforts are under way to reach this goal. Let us hope the time will come when the safety of cosmetics can be predicted without the need for animal testing.

We trust you find this information useful.

Sincerely yours,

Heinz J. Eiermann
Director
Division of Colors and Cosmetics

EXHIBIT 5

UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
WASHINGTON, D.C. 20460

OFFICE OF
PESTICIDES AND TOXIC SUBSTANCES

Honorable Walter M. Baker
Chairman
Judicial Proceedings Committee
Senate of Maryland
James Senate Office Building
Annapolis, Maryland 21401-1991

Dear Mr. Baker:

It is important that the Maryland Legislature understand the position of the Environmental Protection Agency (EPA) regarding eye irritancy and acute toxicity testing. I have the following responses to the questions you posed in your March 4 letter:

(1) In your opinion, does there exist any non-animal alternative test methodologies to replace the Draize eye irritancy test and other acute toxicity tests?

Although there are non-animal test systems which screen for various aspects of ocular and acute toxicity, none of them has been validated to ensure that it accurately mimics responses in the intact animal. As a consequence, there is no consensus within the scientific community to proceed with any one or combination of alternative tests.

Until the time that such tests are available, there are still means of promoting animal welfare. EPA is currently reviewing ways to reduce the usage of experimental animals in acute toxicity testing of chemical substances. We took steps in 1984 to limit animal consumption, and are about to revise testing guidance again. The Agency is also about to investigate modification of the Draize test which will ameliorate some of the discomfort from chemical application. Finally, we are planning a meeting with other regulatory agencies and the public concerning the steps needed to validate alternative tests and make them acceptable to the scientific community. All of these measures demonstrate our commitment to test methods that reduce or obviate animal usage and suffering.

(2) Is the use of these animal tests, such as the Draize eye irritancy test, necessary to establish the safety of consumer products under the regulatory control of EPA?

Acute toxicity and ocular testing are necessary steps in the evaluation of chemical substances that are used by the public and workers. Without animal tests this Agency would be unable to fulfill the charge given us by Congress through several statutes to protect human health from unreasonable risks. Some chemicals under the purview of EPA produce adverse effects following acute contact with the eyes, skin, respiratory tract or gastrointestinal system, and appropriate cautionary measures are needed to mitigate these consequences.

At this time, we at EPA oppose legislation that would ban eye and acute toxicity testing. Such action would be at variance with Federal mandates and would leave regulatory agencies without scientifically acceptable means of evaluating these toxicities.

Sincerely yours,

John A. Moore
Assistant Administrator
for Pesticides
and Toxic Substances

EXHIBIT 6

U.S. CONSUMER PRODUCT SAFETY COMMISSION

WASHINGTON, D.C. 20207

Honorable William S. Horne
Chairman, Judiciary Committee
House of Delegates
121 T. H. Lowe Bulding
Annapolis, Maryland 21401-1991

Dear Mr. Chairman:

The Federal Hazardous Substances Act (FHSA), 15 U.S.C. Sec. 1261-1276, administered by the Commission, requires cautionary labeling for hazardous household products other than food, drugs, cosmetics, pesticides, alcoholic beverages, firearms and tobacco. Among the hazards addressed by FHSA are toxicity and irritancy, which are defined in the Code of Federal Regulations (16 C.F.R., Sec. 1500.3(b)(5)-(9) and 16 C.F.R. Sec. 1500.3(c)(1)-(5)). Neither the FHSA nor the regulations expressly require product testing on animals to determine the hazard posed by consumer products. This can be determined on the basis of prior human experience, existing animal test data, or expert opinion. In those instances when these other sources of information are inadequate and animal testing is necessary, the FHSA and the regulations (16 C.F.R. Sec. 1500.40-42) prescribe how such testing shall be performed. The Commission's policy on animal testing is described in the enclosed Federal Register notice. The policy substantially reduces the number of animals used in these tests and alleviates pain and suffering in animals that are used.

The answer to specific questions raised in your letter dated March 4, 1988, are as follows:

1. The Commission actively participates and monitors the progress in the area of alternatives to animal testing. At the present time we do not believe that an adequate non-animal replacement exists for either the Draize eye irritation test or other acute toxicity tests. The non-animal tests presently under development are not yet at a stage where they can be validated prior to their incorporation into regulatory testing protocol.

2. In those instances when existing animal test data, human experience or expert knowledge is inadequate to determine toxicity, acute toxicity tests such as Draize eye irritation test are necessary to facilitate the appropriate labeling of hazardous consumer products. The objective is to enable the consumer to safely use and store household chemical products and, when necessary and appropriate, to provide instructions for first aid treatment in the case of accidents. Failure of manufacturers to determine the hazards associated with their product and failure to appropriately inform the public of this hazard, even if it requires animal testing, could increase the number and severity of injuries to persons because they were not adequately warned of the danger.

3. During the last few years, there has been substantial progress in the development of several non-animal test methods as potential substitutes for the Draize eye irritation test. Some of these tests are being evaluated by an ad hoc committee composed of the Soap and Detergent Association, the Cosmetics, Toiletries and Fragrance Association, the Consumer Product Safety Commission, the Environmental Protection Agency, and the Food and Drug Administration. A workshop is planned for the fall of 1988 to discuss and evaluate the substitute tests available. The issues involved include whether these non-animal tests have potential as screening tools, or as partial or complete replacements for the Draize eye irritation test. These tests then need to be successfully validated by several laboratories, using a wide range of test products, a process that may require several years before being incorporated into the regulations.

The Office of the General Counsel of the Commission wants to point out, as it did last year, that another factor that may be relevant to the consideration of these bills is that the courts have held state statutes to be invalid if they conflict with, or impair the operation of, federal statutes. That Office knows of no case involving any conflict between the statutory scheme embodied in the FHSA and state prohibitions on animal tests, but it is possible that a court would find such a law to be preempted by the federal statute.

We hope these responses address your concerns. If you require additional information, please let me know.

Sincerely,

Andrew G. Ulsamer, Ph.D.
Associate Executive Director
Directorate for Health Sciences

EXHIBIT 7

Consumer Federation of America

CFA Policy Resolution--adopted February 6, 1988

CFA opposes efforts to outlaw the use of animals for the purpose of testing the safety of consumer products, such as household substances, drugs and cosmetics. Outlawing animal testing would have a chilling effect on biomedical research and would make it impossible to determine the adverse effects of many chemical ingredients used in thousands of consumer products. CFA supports laboratory guidelines and standards to promote the humane treatment of animals and believes that alternative non-animal tests should be developed.

EXHIBIT 8

AMERICAN ASSOCIATION OF POISON CONTROL CENTERS, INC.

Anthony S. Manoguerra, Pharm.D.
President, AAPCC
San Diego Regional Poison Center
225 Dickinson Street, H925
San Diego, California 92103

Resolution - Use of Animals in Safety Testing of Consumer Products

Be it resolved that the American Association of Poison Control Centers (AAPCC) supports the safety testing of consumer products to determine the toxicity of these products prior to their introduction to the marketplace. This information is important for poison centers to use to evaluate emergency medical situations involving inappropriate exposures in humans.

The AAPCC opposes legislation that would limit the humane use of animals to provide acute or chronic toxicity data until such time as reliable, non-animal alternatives exist to provide such data.

Approved by a unanimous vote of the Board of Directors on March 11, 1988.

Anthony S. Manoguerra

Anthony S. Manoguerra, Pharm.D.
President

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EXHIBIT 9

March 3, 1988

The Honorable Walter M. Baker
Chairman, Senate Judicial Proceedings Committee
Room 300
James Senate Office Building
Annapolis, Md. 21404

Re: Senate Bill 395

Dear Chairman Baker:

I have been involved in the practice of Emergency Medicine for the past 14 years. Most recently, I have been in private practice in a community hospital in Bethesda. During my career I have been involved in clinical and laboratory research using both human and animal subjects. I have been a member of editorial boards of scholarly medical journals where part of my responsibility was to be sure that the subjects of the publication had been properly cared for- be they animal or human. I have taught and practiced Emergency Medicine, extensively. The prospect of passage of House Bill 1162 terrifies me.

In my career, I have had occasion to treat hundreds of patients of all ages who have injected, ingested, splashed, spilled or in some way come into contact with a potentially toxic substance. Frantic phone calls from mothers wanting to know if their child will be harmed from eating their lipstick or from drinking daddy's aftershave lotion are not at all uncommon. It is reassuring to them to have a physician tell them not to worry. It is reassuring to me, as the physician, to be able to read about the potential toxin in a textbook or the Poisindex, or to hear from the regional poison control center that there is no danger. The data on which these calming words are based come not from the mistakes of dozens of other parents but from the carefully constructed and humanely performed scientific studies often done on animals.

As a doctor and a scientist, I am not willing to accept anything other than a rigidly controlled study in making my life and death decisions. Unfortunately, in most circumstances we have no acceptable alternative to animal subjects in the performance of these studies. When we do, I will be supporting the animal rights proponents. I will attempt to attend your hearing on this bill, but if I am not able, I would appreciate your reading my letter at the public hearing. Thank you.

Sincerely,

Robert J. Rothstein, M.D.
8600 Old Georgetown Rd.
Bethesda, Md. 20814

EXHIBIT 10

NATIONAL CAPITAL POISON CENTER

202/784-2

GEORGETOWN UNIVERSITY HOSPITAL
3800 RESERVOIR ROAD, N.W. WASHINGTON, D.C. 20007

March 8, 1988

The Honorable Walter M. Baker
Chairman, Senate Judicial
Proceedings Committee
Room 300
James Senate Office Building
Annapolis, MD 21404

Re: Senate Bill 395

Dear Chairman Baker:

I am writing in strong opposition to the above-referenced bill. My opinion is based on my experience as Director of the National Capital Poison Center, Assistant Director of the Emergency Department of Georgetown University Hospital, member of the Board of Directors of the American Association of Poison Control Centers, and chairperson of the National Data Collection Committee of the American Association of Poison Control Center. Last, but certainly not least, I am the mother of an active toddler.

I have personally treated or evaluated the case reports of literally hundreds of thousands of children who have ingested household chemicals and cosmetics. The fact that few children die of these exposures is a result of research--including animal research--conducted over the years in industrial, government, academic, and clinical settings. My ability to assess the potential severity of a poisoning and guide the treatment of a poisoned patient relates directly to the quality of available research. Put another way, my ability to provide a safe home environment for my own three-year-old is dependent of research which indicates the potential severity of a product when accidentally misused.

In the poison center, lack of available animal testing data on a particular product or chemical means that a human, usually a child, in fact becomes the experimental animal. Children are most likely to be poisoned by products in and around their homes; more than ninety percent of all poisonings occur in a residential setting. I reject the notion that children, victims of their own natural curiosity, should be experimental subjects for toxicity testing.

The Food and Drug Administration, Consumer Product Safety Commission, and Environmental Protection Administration agree that there are no validated alternatives to the use of animals for the testing of cosmetics and household products. This is a position with which I totally agree.

I strongly urge that you vote against Senate Bill 395 and against any legislation that would ban the use of animals for toxicity testing of cosmetics and household products. I respectfully request that this letter be read as testimony at your public hearing, as a previous commitment prevents me from testifying in person.

Sincerely,

Toby L. Litovitz, M.D.

EXHIBIT 11

PRINCE GEORGE'S HOSPITAL CENTER

One Hospital Drive Cheverly, Maryland 20785 (301) 341-3300

March 9, 1988

The Honorable William S. Horne
Chairman, House Judiciary Ciommittee
Room 121
Lowe House Office Building
Annapolis, Maryland 21404

re: House Bill 1162

Dear Chairman Horne:

I am the medical director of emergency services at Prince George's Hospital Center. I am writing to you to make you aware of my opposition to House Bill 1162. I have been affiliated with Prince George's Hospital Center since 1980 and I have treated a large number of patients during that period of time who have ingested toxic household products and some who have been injured by the application of a cosmetic. On many occasions I have directly benefited in the treatment of these patients by my ability to receive information from the poison control center concerning toxicity level of various products that patients have either purposely or inadvertently used.

I am afraid that without the benefit of data obtained from tests on live animals, my ability to effectively treat my patients would be severely hampered. Since there is at this time no appropriate alternative to the use of animals to test product safety, then I feel that the issue of human safety should take precedence. Ultimately the real issue that we are discussing here is human safety. If you or any member of your committee has ever had a family member or a loved one admitted to a hospital in critical condition, then you most likely have witnessed that this person was treated with a variety of medications that made have indeed been life-saving. Please remember that these medications were also tested with the use of live animals. If these tests had not been allowed in the past or if they are not allowed in the future you can be sure that the medical care of not just thousands of faceless people but indeed the lives of your very families will be in jeopardy. Therefore, I would stongly urge that you vote against any legislation that would ban the use of animals for testing cosmetics and household products.

I hope to attend your hearing on this bill. However, if I do not attend I would resepectfully request that you read my letter at the public hearing. Once again, as an emergency medicine physician, I have seen on countless occasions how information obtained from testing using live animals can be vital in the treatment of my patients.

Respectfully,

Lawrence Blob, M.D.

LB/ls

EXHIBIT 12

HOLY CROSS HOSPITAL

1500 FOREST GLEN ROAD SILVER SPRING, MARYLAND 20910 301/565/0100

March 9, 1988

The Honorable Walter M. Baker
Chairman, Senate Judicial Proceedings
Committee
Room 300
James Senate Office Building
Annapolis, Maryland 21404

RE: Senate Bill 365

Dear Chairman Baker:

I am a board certified emergency physician. I have practiced emergency medicine in the state of Maryland for the past fifteen years.

It is not uncommon to see patients coming to our emergency department after having ingested household and cosmetic products or getting these substances in their eyes. I rely on the local poison center for information on the potential toxicity and appropriate management of these cases.

Dr. Toby Litovitz, the Director of the National Capital Poison Center informs me that data from animal testing is imperative for ensuring continual accurate advice from her facility.

I need the best and most accurate advice available when treating emergency patients. Until it can be scientifically proven without a doubt that alternatives to animal testing are just as valid as the standard tried and true methods, I strongly recommend that you not prematurely abandon these tests and potentially place my emergency patients at risk. Thank you for your consideration.

Respectfully,

Philip N. Buttaravoli, M.D.
Chairman, Department of Emergency Medicine

PB/ldd

EXHIBIT 13

SINAI HOSPITAL OF BALTIMORE

March 10, 1988

The Honorable William S. Horne
Chairman, House Judiciary Committee
Room 121
Lowe House Office Building
Annapolis, Maryland 21404

RE: House Bill 1162 Animal Testing

Dear Chairman Horne;

I am writing you to express my strong opposition to House Bill 1162. Currently, I am the Associate Chief of the Department of Emergency Medicine at Sinai Hospital of Baltimore, and a medical consultant to the Maryland Poison Center. I am regularly called upon to treat, or consult on the treatment of patients who have ingested potentially toxic household products, or who have been injured by the application of a cosmetic.

These types of ingestions and exposures are not unusual, according to the 1986 Annual Report of the American Association of Poison Control Centers National Data Collection System, Cleaning substances were reported to be the most common group of substances involved in human poison exposures, involving 104,546 or 9.2% of all reported cases. Similarly, cosmetics were involved in 80,214 or 7.1% of all cases.

At the present time, there are no verified alternatives to the use of animals for evaluating the toxicities of household products and cosmetics. Without the toxicity data from animal experiments, I am concerned that human patients will experience unnecessary morbidity (and possibly mortality) from products which have not been tested. Additionally, the treatment of patients who have had potentially toxic exposures to these products will be made much more difficult. Therefore, I would strongly urge that you vote against any legislation that would ban the use of animals for testing cosmetics and household products.

I regret that I am unable to attend your hearing on this bill. If at all possible, please read my letter at the public hearing.

Respectfully,

Steven Grufferman MD

Steven Grufferman, M.D., FACEP
Associate Chief,
Emergency Medicine
Consultant,
Maryland Poison Center

SG

vedere at Greenspring, Baltimore, Maryland 21215-5271
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