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PLAINTIFF'S EXHIBIT CMA-293

Manufacturing Chemists' Association, Inc.

(FOUNDED 1872)
1825 Connecticut Avenue, N. W.
WASHINGTON 9, D. C.

MINUTES OF MEETING
LABELS AND PRECAUTIONARY INFORMATION COMMITTEE
AMERICAN CYANAMID OFFICES
ROOM 570 - TIME AND LIFE BUILDING
NEW YORK CITY

WEDNESDAY & THURSDAY
MAY 24 & 25, 1961

The meeting came to order at 9 A.M. on Wednesday, May 24, 1961.

PRESENT

Chester L. French, Chairman	Mallinckrodt Chemical Works
Edward J. Hogan, Vice Chairman	Allied Chemical Corporation
Robert H. Dewey	Commercial Solvents Corporation
Fred Ebersole	General Aniline & Film Corporation
J. T. Gormally	Pennsalt Chemicals Corporation
James W. Hammond	Humble Oil & Refining Company
Edward J. Masek	Diamond Alkali Company
Harry H. McIntyre	The Dow Chemical Company
George E. Merryman, Jr.	Union Carbide Canada Limited
J. A. Mooney	Food Machinery and Chemical Corporation
Thomas W. Nale, M.D.	Union Carbide Corporation
John F. Osterritter, M.D.	Celanese Corporation of America
Richard F. Philpitt	Olin Mathieson Chemical Corporation
C. Boyd Shaffer	American Cyanamid Company
G. Robert Sido	Monsanto Chemical Company
F. D. Sparre	E. I. du Pont de Nemours & Co., Inc.
Ralph G. Troup	J. T. Baker Chemical Company
N. E. Wendt	American Potash & Chemical Corporation
N. G. White	Shell Chemical Company
James D. Kittelton, Secretary	Manufacturing Chemists' Association, Inc.

GUESTS

Raymond M. Asher (May 24 Only)	Monsanto Chemical Company
A. G. Cranch, M.D. (May 24 Only)	Celanese Corporation of America
L. George Hoth (May 24 Only)	The Borden Chemical Company
Carl MacLagan (May 24-25)	The Borden Chemical Company
Frederick J. Rich (May 24 Only)	U. S. Industrial Chemicals Co.
R. B. Schaefer (May 24 Only)	Pennsalt Chemicals Corporation
George Scriba (May 24-AM Only)	Union Carbide Corporation
Don P. Smoot (May 24-25)	Stauffer Chemical Company
A. F. Zeller (May 24 Only)	Olin Mathieson Chemical Corporation

ABSENT

James T. Fuess	Eastman Organic Chemicals Dept., Distillation Products Industries, Division of Eastman Kodak Company
Sanford J. Hill	E. I. du Pont de Nemours & Co., Inc.

Dr. French welcomed the guests who were present and said that this LAPI Committee meeting was being held to formulate MCA policy on the proposed regulations under the Federal Hazardous Substances Labeling Act. Dr. French emphasized that he would welcome the comments of guests, but would prefer that there not be extended discussion on the various points.

I. CSMA POSITION ON PROPOSED REGULATIONS UNDER FEDERAL HAZARDOUS SUBSTANCES LABELING ACT

The Chairman said that he would begin the meeting by asking Mr. Sparre to briefly review CSMA's attitude on the proposed regulations. Mr. Sparre emphasized that he believed, if possible, MCA's attitude should be consistent with that of CSMA.

Mr. Sparre said that CSMA was of the opinion that the scope of the definition of "container" goes far beyond the definition contained in the Act itself.

CSMA also finds the various sections on "prominence and conspicuousness" to be especially objectionable. Mr. Sparre said that CSMA reason for this position is that the Act did not contemplate this amount of specificity. The Act did not contemplate that the requirements set out in the proposed regulations would be the only way that prominence and conspicuousness could be

accomplished. The FDA regulations in effect declare that putting the precautionary information on the main panel represents conspicuousness, the use of the boarder, contrast and Gothic type of a certain print size, legibility.

Mr. Sparre said that CSMA is also strongly opposed to the 5 gram rule which the regulations would establish for the definition of "toxic." If the level is set at 5 grams, many products will be pulled in which are not really toxic. Manufacturers will thus have to apply to FDA for an exemption and this will then really mean that FDA is licensing hazardous household products.

CSMA has had considerable discussion concerning the methods set out in the regulations for determining toxic substances, irritants and flammable substances. The opposition to the methods stated is that the regulations provide for no alternatives.

CSMA also finds that the definition of "substantial personal injury or illness" is quite objectionable. Dr. Klarmann, in his talk at the recent CSMA meeting, emphasized CSMA's opposition to this. In his talk he stated the following:

> "If the criterion by which a substantial injury or illness is to be judged is nothing more than an indisposition resulting from eating a little soap, it is difficult to see how anything (other than soap) would be excluded that has an LD_{50} within the range of 5 grams or less per kilogram.
>
> "This appears to establish yet another standard which could apply conceivably to substances even less toxic (than those having an LD_{50} of 5 grams)....and one apparently devoid of any rational limitation of the area encompassed."

Mr. Sparre said that CSMA believes that the section of the proposed regulations declaring certain substances to be highly toxic has listed the wrong section of the law as a basis. However, a more serious objection is that no percentages have been specified in the regulation for mixtures of the six substances.

CSMA also believes that the Commissioner may not have sufficient information to show that the five substances listed in section 191.6 are "strong sensitizers."

Mr. Sparre emphasized that CSMA feels that FDA by drafting such broad regulations has now, in effect, created a licensing regulation, requiring manufacturers to petition for exemptions under 191.62 and 191.63.

At this point in the meeting the LAPI Committee considered strategy to be used concerning the proposed FDA regulations. It was agreed that since these regulations affect many chemical manufacturers, it would be well to have them make their views known to FDA. CSMA has urged its 450 members to make their views known to the Food and Drug Administration.

Mr. Sparre's remarks were supplemented by Mr. McIntyre and Mr. Hammond who were also present at the recent CSMA Precautionary Labeling Committee meetings. Mr. McIntyre emphasized that at the present time there is not a really satisfactory method for testing flammable solids.

Mr. Scriba urged that MCA write the Executive Contacts of its member companies urging them to file comments with FDA on the regulations. This letter would refer to the regulations previously distributed with MCA's General Bulletin. It could also emphasize, in a general way, the sections of the proposed regulations which are especially objectionable. Mr. Kittelton will discuss this matter with MCA staff members after returning to Washington.

II. LAPI COMMITTEE RECOMMENDATIONS CONCERNING PROPOSED REGULATIONS UNDER FEDERAL HAZARDOUS SUBSTANCES LABELING ACT

A. Preparation of Brief:

The Committee considered the matter of the brief to be filed by MCA with the Hearing Clerk and were of the opinion that MCA Counsel should do this after policy is established by the LAPI Committee. The Secretary emphasized that the Committee would have to be of considerable technical aid in the preparation of the brief.

Following this,

It was moved, seconded and voted

THAT, The LAPI Committee recommends to MCA that the necessary brief on the proposed Hazardous Substances Labeling Regulations outlining the MCA position be drawn up by MCA Counsel for presentation to the FDA Hearing Clerk.

This motion was adopted unanimously.

B. Consideration of Proposed Regulations:

191.1 Definitions

1. Section 191.1 (c) "Containers" - The Committee carefully considered this section and took a number of votes. The only change which was voted was to delete the last sentence.

Reasons given for this action were that the sentence is inconsistent with the first sentence. It was the consensus of the Committee that the definition as drafted is confusing, since it gives at least three different interpretations of what is meant by "container." (See also point 13.)

2. Section 191.1 (d) "Prominently and Conspicuously" - The Committee carefully considered this wording and were of the opinion that it should be revised to read:

"'Prominently' in section 2 (p)(2) and 'Conspicuously' in section 2 (p)(1) and (p)(2) of the act means that the required information should be visible and noticeable to the purchaser or user. Some factors affecting a warning's prominence or conspicuousness are: Location on the label, size and style of type and contrast of printing against background and other printed matter on the label. Also bearing on the effectiveness of a warning might be the effect of the package contents if spilled on the label. The label when possible should be of such construction and finish as to withstand reasonably foreseeable spillage through foreseeable use. (Sec. 191.101)"

The Committee's reasons for its actions were that the first part of the definition introduced a new concept of "Understandability" into the regulation which does not appear in the law.

The second sentence of the definition was changed since it was believed the rewording states all of the various factors affecting prominence rather than only a few as in the proposed FDA regulations.

3. Section 191.1 (e) - "Highly Toxic Substances" - Dr. Nale pointed out that the amount mentioned in Section 191.1 (3)(2) of "2 milligrams per liter by volume or less of mist or dust" was in error and should be 0.2 milligrams instead. However, it was pointed out that the figure of 2 milligrams is in the statute. It was the consensus of the Committee that an attempt should be made to have this changed.

Reasons justifying this action are cited in Dr. Nale's memorandum of May 19th, attached to these minutes as Appendix A.

4. Section 191.1 (f) - "Toxic Substances" - The Committee agreed with Dr. Nale's position that the amounts for the concentrations should be changed as follows:

191.1 (f)(1) - change 5 grams to 1 gram.
(2) - change 20,000 parts to 2,000 parts.
- change 200 milligrams to 20 milligrams. (However if the statute is changed, this would be 2 milligrams)
191.1 (f)(3) - 2 grams will be left as it is in the regulation.

Reasons justifying this action are also found in Dr. Nale's memorandum of May 19th. The Committee also believed that these requirements, if adopted, could lead to extensive over-labeling.

It was agreed that at the end of 191.1 (f)(3) the following should be added:

"or by any method which is the practical equivalent thereof."

This is discussed more fully below.

5. Section 191.1 (g) & (h) - "Irritants and Corrosive"; Sections 191.11 and 191.12 - "Methods of Testing Primary Irritant Substances" and "Test for Eye Irritants"

The Committee agreed that Section 191.1 (g)(2) should be revised to read:

"(2) The term 'primary irritant' means a substance that is not corrosive and that the available data of human experience indicate is a primary irritant; or which is a primary irritant when tested by the method described in Section 191.11 or by a method which is the practical equivalent thereof."

The Committee also agreed that Section 191.1 (g)(3) should be changed in a similar fashion to read:

"(3) Eye irritants - A substance is an irritant to the eye mucosa if the available data on human experience indicate that it is an irritant for the eye mucosa or is an irritant to the eye mucosa when tested by the method described in Section 191.12, or by any method which is the practical equivalent thereof."

A similar change would be made in Section 191.1 (h) "Corrosive" to read:

"(h) Corrosive - A corrosive substance is one that causes visible destruction or irreversible alterations in the tissue at the site of contact. A test for a corrosive substance is whether, by human experience, such tissue destruction occurs at the site of application, or is a corrosive when tested by the method described in Section 191.11 or when tested by any method which is the practical equivalent thereof."

Dr. Shaffer agreed to send the Secretary the necessary changes in Sections 191.11 and 191.12 which will be necessitated by the changes set out above.

6. Section 191.1 (j) (1) & (2) - "Extremely Flammable Substances" and "Flammable Substances"; Section 191.14 and 191.15 -"Methods for Determining Flammability"

It was agreed that "liquid" should be added before flammable in the titles and in the sections of these two definitions.

The Committee believed that Section 191.1 k(1) should read "ignites and burns" in the same way as Section 191.1 k(2).

The Committee also agreed that it would be desirable to refer Sections 191.14 and 191.15 to the National Fire Protection Association for their opinion. Mr. McIntyre will do this on behalf of the Committee

7. Section 191.1 (l) - "Extremely Flammable and Flammable Contents of Self-Pressurized Containers"

The Committee agreed that this section should be left to CSMA.

8. Section 191.1 (m) - "Substances That Generate Pressure" - It was agreed that Section 191.1 (m) (3) should read "2 days or less" to be consistent with Section 191.1 (m)(2).

9. Section 191.1(o) - "Accompanying Literature" - This section was thoroughly discussed by the Committee and it was agreed that it was written too broadly and in some respects was ambiguous. The definition as drafted goes beyond the language of the statute or the intent of the statute.

Following this discussion,

It was moved, seconded and voted

THAT, The LAPI Committee recommends that Section 191.1(o) be strongly opposed and be amended so that "accompanying literature means any literature in or on, or attached to the product."

10. Section 191.1(p) - "Substantial Personal Injury or Illness" - The Committee agreed that the example in this section of a child eating soap is a very poor one. The Secretary read comments made by Dr. Klarmann on this section and were in agreement with Dr. Klarmann's statements. Dr. Nale also mentioned that a common antidote is to advise drinking soapy water.

11. Section 191.1(r) - "Reasonably Foreseeable Handling or Use"- The Committee considered this and agreed that it would be desirable to use the entire language of the House Report. This section then would read as follows:

> "This includes the reasonably foreseeable accidental handling or use, not only by the purchaser or intended user of the product, but by others in the household, especially children, who are prone to swallow or tamper with household aids left within their reach."

12. Section 191.101 - "Placement, Conspicuousness, Contrast"; Section 191.102 - "Warning Statements"; Section 191.104 - "Arrangement of Label Statements"

The Committee next considered the important matter of "prominence and conspicuousness" and it was pointed out by Mr. Sparre that the methods set out in the above-listed sections for achieving "prominence and conspicuousness" are not the only methods contemplated by the statute.

Mr. Sparre said that CSMA wishes to have Sections 191.101, 191.102(b) and 191.104 deleted. Mr. Sparre reviewed some suggestions he had for amending these sections. The Committee believed that Mr. Sparre's suggestions were excellent and asked him to write them up for use in MCA's brief.

Following this discussion,

> It was moved, seconded and voted
>
> THAT, The LAPI Committee believes that rather than the regulations being so specific as to type size and other requirements, the regulations on prominence and conspicuousness should be stated in general language along the lines set out by Mr. Sparre."

This motion was passed unanimously.

13. Section 191.62 - "Exemption from Full Labeling Requirements" - The Committee was strongly of the opinion that the definition of container was too broad and could include many types of containers used for research, investigational, laboratory and manufacturing activities.

The Committee agreed that MCA should immediately request a regulation exempting such products in accordance with the following language:

> A hazardous substance in a container intended for research, investigational and other laboratory uses only or for manufacturing use only, shall be exempt from the requirements of this Act, provided that the label on such container bears:
>
> 1. A statement clearly indicating the manufacturer's intended use such as "FOR LABORATORY USE ONLY," "FOR EXPERIMENTAL USE ONLY," "FOR MANUFACTURING USE ONLY" or a practical equivalent; and
>
> 2. Adequate instructions and precautionary statements for the guidance of those intended users who are trained and experienced technicians and who may reasonably be expected to utilize such a substance properly to the extent that the hazards are known to the manufacturers, packers, distributors or sellers.

C. Appointment of Subcommittees

The Chairman announced that he was appointing a subcommittee to aid in the preparation of the MCA statement on the proposed regulation under the Federal Hazardous Substances Labeling Act. The subcommittee named consists of Dallas Sparre as chairman with Messrs. Gormally, Philpitt and Kittelton as members.

The Chairman also announced that he was appointing a subcommittee to consider carefully the scientific methods set out in the proposed regulations. Under point (5) above, it will be necessary to make certain changes in Sections 191.11 and 191.12 and the subcommittee will do this. The subcommittee will consist of Dr. Boyd Shaffer as chairman with Drs. Nale, Osterritter and White as members.

5.0 REVISION OF MANUAL L-1

A. Part I

1. Mr. Troup began a review of Part I page by page. The first point discussed was whether there was a sufficient explanation of the relationship of the Manual to the new Federal Hazardous Substances Labeling Act. Mr. Masek's recent letter was discussed and the consensus of the Committee was that no change was needed in the draft of the Manual concerning this point. It was agreed, however, that the footnote concerning the Federal Hazardous Substances Labeling Act would be deleted.

2. The Committee next considered the definition of "poison" on pages 8 and 9 and agreed that when and if a change is made in the Federal Hazardous Substances Labeling Act of "2 milligrams or less per liter of mist, fume or dust" to "0.2 milligrams or less per liter of mist, fume or dust," a similar change should be made in the poison definition.

3. Mr. Troup said that the Revision Subcommittee believes that a note at the top of the table should be added emphasizing that the table does not include all precautionary statements which might be necessary under all circumstances. It may be necessary to change the wording of some of the statements and also to add statements in certain circumstances.

4. The Secretary was asked to consult with the Secretary of the MCA Packaging Committee concerning the container, handling and storage statements appearing on pages 22 and 23.

5. Mr. McIntyre read to the Committee wording which he had drafted concerning the part of the Manual covering the labeling of aerosol containers. The Committee agreed that this wording was better and Mr. McIntyre's draft will be substituted for the material now appearing on page 23.

6. It was agreed that the section on "MCA Precautionary Labeling Activity" would be moved to precede page 5 of the Manual.

B. Part II

1. Acetic Anhydride

It was agreed that the contact statement would be

revised to read, "In case of contact, immediately remove contaminated clothing and flush skin or eyes with plenty of water for at least 15 minutes; for eyes get medical attention."

2. Anhydrous Ammonia

The Secretary reported the results from a letter ballot which he had conducted concerning the changes in the label for Anhydrous Ammonia. The Secretary said that all MCA members not represented on the LAPI Committee oppose the change of the signal word from "WARNING" to "DANGER." Mr. Kittelton emphasized that MCA had received another letter from the Agricultural Ammonia Institute concerning this proposed change.

There was considerable discussion concerning this label and Dr. White emphasized that human experience with the agricultural application had been very good. The same point was made the previous day by Dr. Shaffer. The Committee discussed this point and it was emphasized that the label appearing in Part II was for industrial use of Anhydrous Ammonia and not specifically for agricultural ammonia.

Following this discussion,

It was moved and seconded

THAT, The LAPI Committee reconsider its previous action of changing the signal word on the label from "WARNING" to "DANGER."

The vote on the motion was 6 ayes and 8 nays. Thus, the motion was defeated and the previous action of the LAPI Committee in revising the Anhydrous Ammonia label stands.

The Secretary emphasized to the Committee that any action of the LAPI Committee was subject to Board approval or reversal. Since there has been considerable conflict concerning this label the MCA staff will review the LAPI Committee's action on the label.

3. Benzyl Chloride

It was agreed that "Stabilized" should be added in parenthesis after the name of this chemical.

4. Beryllium Oxide Powder

Mr. Wendt said that he wondered why the LAPI Committee had added a poison to this label. Dr. Nale said that the action was taken on the basis of human experience and not because Beryllium Oxide Powder met the definition of poison in the Manual.

5. Butyl Acetate (normal)

The Committee agreed that this label should read: "Same label as AMYL ACETATE (Mixed Isomers)".

6. Butyl Alcohol (normal or secondary)

WARNING! LIQUID CAUSES EYE BURNS

Keep away from heat and open flame.
Avoid contact with eyes.
Avoid prolonged breathing of vapor.
Use with adequate ventilation.
Avoid prolonged or repeated contact with skin.
In case of contact with eyes, immediately flush with plenty of water for at least 15 minutes.

7. Butyllithium (normal)

It was agreed that the following statement would appear in parenthesis after the name of the chemical: "(25% or less in hydrocarbon solvents)". It was also agreed that the precautionary measure, "Keep away from heat, sparks and open flame," should appear as the second precautionary measure.

8. Calcium Cyanide and Cyanides, Inorganic

The Committee voted to change the statement of hazard from "Hazardous Solid" to "Poisonous Solid."

The same change would be made in the label for Cyanides, Inorganic, with the statement, "May be fatal if swallowed" deleted.

9. Decaborane

It was agreed to change the word "agents" to "materials" in the statement "Keep from contact

with oxidizing agents...."

The Secretary also agreed to check on the number of the Safety Data Sheet for Boron Hydrides.

10. Pentaboranes

The Committee agreed that the contact statement for this product should be changed to read, "In case of contact, immediately wash skin with soap and plenty of water; flush eyes with water for at least 15 minutes. Get medical attention. Remove and wash clothing before reuse."

11. Sodium Hydrosulphite

The Committee agreed to change the last precautionary measure to read, "In case of fire, smother with SODA ASH, DRY SAND or CARBON DIOXIDE. Dispose by flushing away with a LARGE VOLUME of water under adequate ventilation."

12. Sodium Sulfide

It was agreed that the second precautionary measure should be amended to read, "Do not breathe dust or gas."

13. Titanium Trichloride, Anhydrous

It was agreed that the contact statement should be amended to read, "In case of contact, immediately remove with dry cloth followed by flushing with plenty of water for at least 15 minutes; for eyes flush with plenty of water for at least 15 minutes; get medical attention. Remove contaminated clothing and wash before reuse."

The Committee discussed the advisability of adding a statement along the following lines to the label for TITANIUM TRICHLORIDE, ANHYDROUS and VANADIUM TETRACHLORIDE: "Do not poke, dig or scoop compacted damp powder from container with any tool whatsoever."

It was agreed that Mr. Wendt would review this language and submit a final draft of it to the Revision Subcommittee.

C. Part III

1. Calcium Cyanide

The Committee agreed to change the precautionary measures as in Part II to read, "Poisonous Solid" and "Liberates Poisonous Gas."

2. Cyanides, Inorganic

As in Part II, the Committee agreed to delete the precautionary statement, "May Be Fatal If Swallowed" and to substitute, "Poisonous Solid."

3. Hydrocyanic Acid, Liquid

The Committee agreed to delete "Liquid" from the title of this chemical. Mr. Sparre also agreed to investigate whether the statement "USE ONLY IN A CLOSED SYSTEM" should be retained.

4. Nicotine Sulfate Solution (40% Nicotine)

The Committee agreed to change the precautionary statement, "Absorbed Through Skin" to "Absorption Through Skin Harmful."

5. Parathion

Mr. Sparre said that he would consult Dr. Shaffer concerning the treatment listed under Parathion before the Manual is printed.

6. Pentachlorophenol, (Oil Solutions)

It was agreed that the precautionary statement reading, "Absorbed Through Skin" would be changed to "Absorption Through Skin Harmful."

7. Toxaphene

The Committee agreed to change the precautionary statement "May Be Harmful By Absorption Through Skin" to read, "May Be Harmful By Skin Absorption."

The Committee agreed that the printer should be reminded that at the end of the Manual the following should appear, "Printed in the United States of America."

James D. Kittelton

James D. Kittelton, Secretary
Labels and Precautionary
Information Committee

Minutes Subject to Approval
June 7, 1961

JDK:jmb

Attachment

COPY

APPENDIX A

MAY 19, 1961

Comments by Dr. Thomas W. Nale on Proposed Definitions and Procedural and Interpretative Regulations
HAZARDOUS SUBSTANCES

191.1 Definitions.

(e) Highly toxic substances.

(2) Inhalation. It is unfortunate that the Act as passed refers to 2 milligrams per liter by volume or less of mist or dust. In the original draft it was 0.2 milligram. As a matter of fact, 2 milligrams per liter is more nearly equivalent to 2,000 parts per million instead of 200 parts per million. Two milligrams of mist or dust per liter of air is an extremely dense cloud. This concentration may be excluded by the Act, for it is unlikely to be encountered by man. Such concentrations are almost impossible to attain in laboratory inhalation equipment. It is our impression that almost all dust except coarse particles of insoluble mineral dust and wood flour will reach the lungs and kill at this concentration (2 mg./l.) within an hour's inhalation. If accurate studies are conducted, most dry solid household preparations may be classed as poisons by inhalation.

(f) Toxic substances.

We would question the use of such strigent factors as 100-fold safety factors which the Food and Drug Administration has been accustomed to using in reference to food additives. This Act covers household products, not food additives.

		Factor
(1)	Oral, 50 mg. to 5,000 mg.	100
(2)	Vapor, 200 p.p.m. to 20,000 p.p.m.	100
	Dust, 2 mg. to 200 mg.	100
(3)	Skin, 200 mg. to 2,000 mg.	10

(f) (1) According to this definition, all compounds that kill rats within 14 days by peroral administration at 5 grams per kilogram or less are considered toxic. This is not necessarily true. Table salt has an LD50 of 4.54 gm./kg. and by this definition should be labeled in the same manner as a toxic substance.

Volume is important in considering toxic effects. At 5 gm./kg., a 50-kilogram individual would have to swallow 250 grams the substance; a 10-kilogram child, 50 grams.

(f) (2) This is entirely too high a concentration because all concentrations up to and including the lower explosive limits of 1.5 to 2 per cent by volume (15,000 - 20,000 p.p.m.) must be free of harm to animals. This means that only inert gases such as Freons and nitrogen are likely to escape being labeled. It would seem to be more in order for the upper limit for toxic substances to be 2,000 p.p.m. for vapor.

We are informed that 200 milligrams of dust per liter of air (20,000 mg./cubic meter) is beyond the capability of the laboratory to achieve. This is in the range of the explosive concentration for certain dusts. It is unfortunate that someone without a knowledge of dust exposure studies put in a 100-fold safety factor which cannot be applied.

(f) (3) The safety factor of 10 is not too unreasonable for skin penetration, but from a practical viewpoint, it would be preferable for the upper limit to be one gram per kilogram.

(g) Irritants.

Reference is made to a specific test method which is spelled out in 191.11. This is not the only acceptable method for testing skin irritation. Many practical industrial toxicology laboratories have different test methods which give adequate results and which are based upon years of experience. The Act covers household chemicals, not cosmetics.

The Act refers to contact with normal living tissue, not abraded skin. Laboratories cannot abrade the skin of live, unanesthetized rabbits in a reproducible manner. It is our impression that the irritation test can be adequately done by the uncovered application to intact skin. There certainly seems to be no need to utilize a patch and then a rubber sleeve over the abdomen of the animal. Even water under these circumstances will macerate a rabbit's skin. Many of our solvents which are not irritating under usage will cause skin burns if held to the skin by a patch test.

Consideration should be given to the extensive experience in use and handling of many solvents by industry. Many of these same solvents are in household products. These human exposures in industry are much more accurate indications of skin irritation than animal experimentation. There should also be consideration of the proposed application and usage. If usage does not involve skin contact or at most involves very brief contact, a specific product would not be an irritant. Many solvents are not irritants on casual

contact, but prolonged and repeated contact can have a defatting action on the skin and a resulting irritation.

Physical properties influence skin irritation. For example, when two compounds equally irritating are applied to the skin, a high melting solid will be less hazardous than a fluid to the individual whose hands must contact it.

There still seem to be many methods for determining skin irritation potential besides the elaborate test procedure described under 191.11.

191.10 Method of testing toxic substances.

(a) Acute dermal toxicity (single exposure).

There is no objection to this test except that we question the necessity to make epidermal abrasions on some of the test animals. A rubber dam is specified. Such a dam will not withstand all solvents, etc., any more than polyethylene, Vinylite, and Saran, to mention several others.

We also question the necessity to test unctuous materials as described under item (d). Such materials can be tested readily at 2 gm./kg. under an impervious sheeting without the involved procedure suggested.

191.12 Test for eye irritants.

It is unreasonable to specify the use of six rabbits to test a single compound for eye injury. Nor is it necessary to use one eye of each rabbit as a control. This test is an endeavor to find out whether a specific chemical injures a specific tissue, the cornea of the eye. Normal albino rabbit eyes are selected on the basis of absence of grossly visible staining by a 5 per cent aqueous solution of fluorescein sodium, flushed with distilled water 20 seconds after application. After a 2-hour interval, 0.005 ml. of the undiluted test material is applied to the center of the cornea while the lids are retracted. 18 to 24 hours later the eye is examined in strong daylight, then stained with fluorescein, and the injury is scored. It is not felt that repeated observations of the eye at 48 and 72 hours are necessary.

The Department is quite specific regarding certain animal test methods and has ignored others. Those specified are ones currently being used by the Food and Drug Administration in respect to cosmetics, etc. No reference is made to test methods for inhalation

studies or specific directions for determination of the single acute oral LD_{50} dosages.

We have in this country many industrial toxicology laboratories that are perfectly competent to evaluate toxicity, etc., of household products by their own test procedures. The Department should certainly recognize this fact and not tie down all toxicity studies to the specific test methods it prescribes.

191.1 Definitions.

(p) Substantial personal injury or illness.

The legal advisors should be able to handle this question. Whoever prepared this definition for substantial personal injury or illness certainly threw Webster's out the window. Substantial injury is certainly more than "wholly insignificant or negligible injury or illness."

These comments are based upon advice and help received from Dr. H. F. Smyth, Jr., and Dr. C. P. Carpenter. I also had reviewed comments by Dr. J. A. Zapp.

(signed)
Thomas W. Nale, M. D.

Copied by MCA
June 7, 1961