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February 6, 1969

Mr. Robert M. Miller
Hercules, Inc.
Delaware Trust Building
Wilmington, Delaware

Dear Bob:

Following up on my letter of January 24 relative to recent developments in connection with the long awaited expectations of some action from the Food and Drug Administration as an aftermath to last February's National Conference on Indirect Food Additives, I have now noted that the story on the Food Protection Committee report that I discussed in my letter has been broken, at least in substantial part, in Food Chemical News. As far as I can tell, there is still no way to obtain official copies of the report entitled "Quantitative Guidelines for Toxicologically Insignificant Levels of Chemical Additives in Food" so that we could reproduce the material and send it to all of the members of our Committee. However, since we believe that the Food Chemical News coverage of the situation might well be of interest to everyone, we have obtained permission from the publisher in our usual way and are herewith enclosing reproductions of Pages 29 through 35 of the current issue so that all will have a chance to see this report on what is taking place.

While writing to the Committee on this subject, and in accordance with your recommendations, and those given us by Ralph Harding, we are also taking this opportunity to bring to everyone's attention an inquiry sent to the Society relative to the possibility of the development of suitable plastic containers which might be used for transporting tea from growing areas overseas to blending plants in North America. Towards the end of giving this business opportunity as widespread coverage as possible, we are herewith enclosing (1) a copy of a January 17 letter sent to the Society by Mr. R. E. Weiskopf of the Tea Association of the United States of America Inc., (2) a copy of Ralph Harding's interim response to that letter, and (3) a copy of your letter to

Mr. Weiskopf of February 4 indicating the action we would be taking on this matter.

I am reasonably sure that the members of our Committee will find all of this correspondence quite self-explanatory. As you have indicated to Mr. Weiskopf, while our Committee is not normally concerned directly with commercial opportunities such as this, we would expect that this widespread dissemination of the information may well lead individual companies to be in touch with the Tea Association as a matter of enlightened self-interest.

If you or any of the other members of the Committee have questions about any of these matters, we trust you will not hesitate to let us know.

Cordially yours,

Jerome H. Stickman

encls

cc SPI Food, Drug and Cosmetic Packaging Materials Committee

REPORT PEGS TOXICOLOGICAL INSIGNIFICANCE AT 0.1 P.P.M.

A report on "Quantitative Guidelines for Toxicologically Insignificant Levels of Chemical Additives in Food" developed for the Food Protection Committee has suggested that additives used for at least five years at a level up to 0.1 p.p.m. of the total diet are "toxicologically insignificant."

For additives which are used at a level higher than 0.1 p.p.m. in the diet and/or which have been commercially produced for less than five years, the Task Force recommended that "toxicologically insignificant" levels be determined by analogy with similar substances for which data are available.

"Negligible" Level of 1.0 p.p.m. Urged for Some Additives

An "insignificant" level of 1.0 p.p.m. in the diet was suggested for additives closely related to substances on which data are available, and which meet certain other criteria. For new additives and/or those used at more than 0.1 p.p.m. which are less closely related to analogous substances and which do not meet the criteria, the statement suggested "insignificant" levels based upon a stated fraction of the estimated safe level of analogous substances on which data is available.

The Food Protection Committee statement is broader than the field of indirect food additives, but this is where it will have its most immediate application. Later, there may be some attempt to apply the report to direct food additives used in small quantities on which there are relatively little data, but which experience indicate are safe.

The Committee was appointed soon after a national conference was held by the Food and Drug Administration with industry to discuss the possibility of easing regulation of indirect food additives (See FOOD CHEMICAL NEWS, Feb. 19, Pages 3, 10, and 18). Although the scope of the statement, which has been forwarded formally to the National Academy of Sciences-National Research Council, is broader than indirect additives, this is where it will have its most immediate application.

A proposal to exempt from testing data requirements indirect additives which migrate into food at no more than. 0.1 p.p.m. was made to FDA by Hercules' Dr. John P. Frawley. The proposal, which received widespread industry support, would exempt from the Food Additive Petition requirements indirect additives used at less than 0.2% by weight of the food container, without extraction studies.

In response to the Frawley proposal and the conference, FDA developed its own in-house proposal to ease regulation of indirect additives (See FOOD CHEMICAL NEWS, Aug. 19, Page 3). The FDA proposal would exempt indirect additives if they migrate at not more than 0.05 p.p.m. into specific foods, and would also exempt minor ingredients that are intended for repeated use - - such as rubber articles - - plus packaging components which are not expected to become com-

FDA held up action on its proposal in anticipation of the ad hoc Food Protection Committee group's report (See FOOD CHEMICAL NEWS, March 18, Page 21). The agency will now consider its in-house proposal in light of the "guidelines" in the statement.

FDA's proposal, as compared with the Frawley recommendation, was criticized late last year by Monsanto's George W. Ingle (See FOOD CHEMICAL NEWS, Nov. 18, Page 3). He hit the concept of exempting substances based on migration into specific foods, since this would entail extraction studies. He also said that 50 p.p.b. in a specific food is far less than half of 100 p.p.b.. in the total diet.

FDA May Revise Its Proposal

As a result of the Food Protection Committee statement, FDA may make some revision in its proposal. Although the 0.05 p.p.m. figure may change to a larger one, many FDA-ers still feel that exemptions should be tied to specific uses, rather than amounts in the total diet. They say informally that the total diet approach would leave FDA in the dark as to actual uses and amounts of indirect additives.

Although the Food Protection Committee report, at first glance, seems to endorse the Frawley proposal - - urging exemptions for substances which can migrate no more than 0.1 p.p.m. into the diet - - it has additional elements.

The Committee enunciated the theory of determining "insignificant" levels of substances which do not fall under the 0.1 p.p.m. cut-off by "analogy" to related substances on which data are available. This would apparently apply to substances on which there is little or no toxicological data but which are used at a level higher than 0.1 p.p.m. in the total diet, or newly-developed additives.

Analogy With Other Substances Urged to Determine Levels

For organic chemicals lacking toxicological data but closely related to substances on which data is available, a "toxicologically insignificant" level of 1.0 p.p.m. was suggested.

For organic chemicals with minimal data and less closely related structures, the task force suggested insignificant levels of either 1/10 or 1/20 of the lowest safe level of all the analogous substances on which data is available.

In addition, the statement proposed broader categories of substances to be excluded from the exemption than either the original Frawley proposal or the FDA in-house proposal. The broader exclusions are expected to be adopted by FDA.

After considering the Food Protection Committee statement, and perhaps making some revisions in its own proposal, FDA will consult with representatives of the food packaging industries before publishing a proposal in the Federal Register.

Late last year, Stein, Hall's Max Goldfrank urged FDA to call together an ad hoc industry advisory committee to consider a change in procedures (See FOOD CHEMICAL NEWS, Dec. 23, Page 6). At the national conference, FDA-ers seemed cool to an industry proposal for a permanent FDA-industry advisory committee on regulation of indirect food additives.

The long-smoldering issue of regulation of indirect additives came to the point of action because of FDA's proposed changes in its food additives procedural regulations. However, it is believed that FDA may propose the exemptions in the "good manufacturing practice" portion of the food additives regulations covering indirect additives. FDA-ers note that any change in the regulations could be subject to later amendment.

In suggesting the numerical cut-off for toxicological insignificance for "chemicals in commercial production," the report said:

> "In the absence of experience to the contrary, it is consistent with sound toxicological judgment to conclude, with respect to chemicals that have been in commercial production for a substantial period, e.g., 5 years or more, that are not heavy metals or their compounds, and that are not intended for use because of their biological activity, that a level of 0.1 p.p.m. in the diet of man is toxicologically insignificant."

In discussing "the application of experience," the statement said that aside from the "classes of compounds" that should be excluded from an exemption, "no commercial compound has been demonstrated to produce toxic reactions below a dietary concentration of 40 p.p.m." This calculation had previously been presented by Frawley.

The report continued that, "The criteria for insignificance will vary for different classes of compounds and may change with further research on compounds within classes." It said that, "Synthetic organic chemicals that are not manufactured specifically for their biological activity must be sharply distinguished from naturally occurring toxins or trace contaminants."

Calling for "quantitative assessment of toxicological insignificance," the group said "guidelines" are necessary for setting levels "for various classes of substances, based on available information concerning their safety or that of related compounds."

Except for the categories of compounds which would be excluded from the exemption, the report said:

> ". . . no single organic chemical that has advanced from the laboratory, through development, into general commercial use has been demonstrated to be toxic to experimental animals at a dietary level of 40 p.p.m. or less. Compounds that possess

greater toxicity have either been developed specifically for use as drugs or economic poisons or chemical warfare agents, etc., or were found to possess such biological activity during development and were diverted to these uses."

Both the Frawley proposal and the FDA in-house proposal would exclude from any exemption economic poisons and heavy metals. Also excluded would be potential carcinogens, which are barred under the Delaney Clause of the Food Additive Law.

The Food Protection Committee report would exclude "four general categories" of "compounds in commercial use that may have deleterious effects at low levels . . ." These are:

"(1) Certain impurities or contaminants of natural origin; (2) Certain essential nutrients and hormones; (3) Certain heavy metals and their compounds; and (4) Certain organic compounds employed for their biological activity.

"In the first category are such substances as aflatoxin, botulinus toxin, and tetrodotoxin, which are toxic at concentrations as low as 0.001 p.p.m. In categories 2, 3, and 4 is a large list of pesticides, pharmaceuticals, and anti-personnel agents that may have biological activity at levels as low as 0.1 p.p.m."

The theory of "analogy" was stated for substances used at levels higher than 0.1 p.p.m. or which are new and which lack toxicological data, but meet "special structural restrictions," intended to establish 1.0 p.p.m. as the insignificant level for these. The report explained that, "For many substances that are functionally effective in food at dietary concentrations above 0.1 p.p.m., but still much below any reasonable judgment as to their maximum safe level, there is need to arrive at estimates of toxicologically insignificant levels."

The statement said for these substances "it is justifiable to employ accumulated scientific experience, and to recognize their structural analogy to other chemicals whose metabolism or toxicity are known." The report explained:

"Reasoning by analogy may be used to arrive at conclusions of toxicological insignificance if: (1) The substance in question is of known structure and purity; (2) It is structurally simple; (3) The structure suggests that the substance will be readily handled through known metabolic pathways; and (4) It is a member of a closely related group of substances that, without known exception are, or can be presumed to be, low in toxicity. Substances that meet all these criteria may be presumed to be toxicologically insignificant at 1.0 p.p.m. or less in the human diet."

As examples of substances that are "structurally simple," the report named straight-chain or simply branched aliphatic alcohols, acids, and esters, linear polymers of ethylene or ethylene oxide, cellulose ethers, and mononuclear aromatic compounds containing only carbon, hydrogen, and oxygen, and equipped with one or more functional groups that include hydroxyl, carboxyl, aldehyde and keto.

The term "closely related" was defined as: "(a) Near members of a homologous series; (b) Geometric or positional isomers which would not be expected to present serious differences in chemical reactivity or steric effects; (c) Substances of identical basic structure or differing only by (a) or (b) above, and possessing additional functional groups readily accomodated by known metabolic mechanisms; (and) (d) Compounds readily metabolized into substances meeting the other criteria here listed."

Discussing "organic chemicals with minimal toxicological data and less closely related structures," the report suggested insignificant levels of 1/10 or 1/20 of the estimated safe level of analogous substances.

For substances "nearly, but not precisely" meeting the "special structural restrictions," the report said a level of insignificance may be established if:

> "(1) There are available adequate scientific studies that establish safe levels of similar magnitude for at least two analogous substances; (and) (2) The acute or subacute toxicity of the new substance and the analogous substances is of the same nature and degree.
>
> "A sound estimate of the safe level of the new substance that meets the two foregoing conditions is the lowest safe level of all the analogous substances that have been studied. If the safe levels for all the structurally analogous substances are essentially identical, 1/10 of the estimated safe level may be taken as a toxicologically insignificant level. In the event of an appreciable difference between the safe level of the analogous substances, the insignificant level should be taken as 1/20 of the estimated safe level."

The Committee said the quantitative levels it suggested as insignificant "are conservatively derived from accumulated toxicological experience," adding that, "They are intended to guide and stimulate - - not replace - - informed professional judgment." Noting that future evidence may change the situation, the group concluded that "in the light of today's knowledge, adoption of these principles will protect public health beyond any reasonable doubt and simultaneously allow greater attention to be devoted to more worthy projects of potential health significance."

Chairman of the Food Protection Committee Task Force which prepared the statement was University of Pittsburgh's Dr. Henry F. Smyth, Jr. Other members were Frawley, Jefferson Medical College's Dr. Julius M. Coon,

McCormick's Dr. Richard L. Hall, Food and Drug Research Laboratories' Dr. Bernard L. Oser, Food Materials' Arthur T. Schramm, and duPont's Dr. John A. Zapp, Jr. Also members were Dr. W. J. Darby, chairman of the Food Protection Committee, and Richard Henderson, chairman of the Industry Committee of the Liaison Panel.

Calling for "priorities," the panel said that, "If every chemical were required to be studied to the same extent as those used at levels close to their safe levels, scientific facilities urgently needed for pressing problems would be wasted on trivial questions without contributing meaningfully to the protection of public health." The report commented:

> "To insist that nothing can be assumed to be safe without direct experimental toxicological evidence leads to the dilemma that safety must be proved experimentally before the proof of safety can be considered unnecessary. This defeats the purpose of establishing criteria for insignificance. Thus, there is urgent need to arrive at more specific quantitative guidelines for setting dietary levels that can be considered toxicologically insignificant."

The group noted that a 1958 Food Protection Committee statement on "insignificant levels" made no attempt to define "toxicologically insignificant" in quantitative terms.

"When any particular use results in a dietary level well below the safe level, the possibility of hazard from use or misuse becomes so remote that regulatory activity to protect the public from the chemical in question is superfluous," the report said, adding, "Such low levels are so surely presumptive of safety that they may be properly termed 'toxicologically insignificant.'"

The statement noted that "the vast majority of the chemical entities that we consume are present naturally and unavoidably in foods," saying that "most of them are assumed to be toxicologically insignificant because: (1) They are present in foods at extremely low concentrations, (2) have been consumed by man for generations without apparent harm, and (3) are not related chemically to substances of known high toxicity."

Based on these criteria, the statement said, "there is a body of empirical knowledge deemed sufficient on which to base a judgment of the safety of virtually all of these substances at the levels found in food." The report added that, "The criteria are equally valid when applied to evaluation of safety for use of synthetic substances."

The task force endorsed a previous NAS-NRC Committee report which urged establishment of "negligible" residue tolerances for pesticides (See FOOD CHEMICAL NEWS, July 19, 1965, Page 3).

Discussing pesticide degradation products, the task force said most of these "are less toxic than the parent material," noting that "a few exceptions have been experienced, but even in these cases, the toxicity of the degradation products has been of the same order as that of the parent compound." The report concluded that, "Unless the safe level of the pesticide is below 1 p.p.m., dietary levels below 0.1 p.p.m. are insignificant and undeserving of laboratory investigation."

Noting the Delaney Clause which bans additives if they may cause cancer in animal tests, the task force said that, "Many properly qualified experts believe that flat prohibitions of this sort are scientifically untenable." However, the statement urged consideration regarding such substances of "the nature of the dose-response relationship and the physiologic, metabolic, or pathologic processes involved to insure against the possibility that the same effect might occur in man."

MRS. HITT SAYS NIXON WILL STRENGTHEN CONSUMER PROGRAMS

Assistant Health, Education and Welfare Secretary Patricia Reilly Hitt told the third annual Consumer Assembly in Washington last week that the Nixon Administration will strengthen rather than weaken Government consumer programs.

Mrs. Hitt, who is President Nixon's top woman in Government and served as his campaign co-chairman, indicated that a successor might be selected for Betty Furness, former President Johnson's Consumer Affairs Adviser. The staff of the President's Committee on Consumer Interests, which Miss Furness headed, has made four moves since the new Administration took over, and is no longer located in the prestigious Executive Office Building next to the White House.

Mrs. Hitt also indicated that the staff, many of whom have transferred to other agencies or left Government, may form the nucleus of a Government-wide consumer organization, that could be set up independently or in HEW, where she is in charge of the Office of Consumer Affairs.

Sen. Hart (D-Mich.) called upon the Assembly to support Miss Furness' proposal for a consumer version of the Federal Register which "would alert consumers to Government actions affecting them" (See FOOD CHEMICAL NEWS, Nov. 25, Page Page 3).

He also plugged his recommendation for an independent Consumer Council (See FOOD CHEMICAL NEWS, Jan. 27, Page 23) as a rival to Rep. Rosenthal's (D-N.Y.) Department of Consumers proposal and Esther Peterson's suggestion that the Consumer Federation of America take over the responsibility for representing all consumers.

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Tea Association of the United States of America, Inc.

January 17, 1969

Society of Plastics Industry, Inc.
250 Park Avenue
New York, New York

Gentlemen:

We are interested in knowing if you have facilities for investigating the possibilities of transporting tea in plastic containers from growing areas overseas to blending plants in North America.

For decades, even centuries, tea has been shipped in foil-lined wooden chests of various dimensions holding anywhere from 80 to 140 pounds of tea. While various substitute packaging has been tried, nothing has been completely satisfactory due to the combination of properties needed for transporting tea:

1. The package must be strong enough to withstand handling on the docks, an ocean voyage with possible transshipment, and rail or truck transportation at origin or destination, or both.

2. The package must be absolutely neutral in that it cannot give off odor or flavor to the tea which it contains. This is critical because tea picks up foreign odors and flavors very easily.

3. Either the plastic material or the package must "breathe", i.e. it cannot be air tight. The main reason for this is that when tea gets very warm in the course of transit it gives off moisture. This moisture must be allowed to escape or it will condense on cooling and ruin the tea.

4. The package cannot be too expensive, and must be rather easily manufactured or assembled in comparatively underdeveloped areas overseas.

Lately there has been some palletization of tea chests at overseas ports. For this operation, efforts are being made to standardize the package at 16" x 20" x 24". A strong plastic package could be a multiple of this, say 32" x 20" x 24".

To give you an idea of the possible volume involved, USA users import about 15 million chests per year, and Canadian users about 5 million. The ordinary wooden tea chest weighs about 15 pounds.

717 FIFTH AVENUE • NEW YORK, N. Y. 10022 • MUrray Hill 8-1577 • Cable: TEAFRONT

Tea Association of the United States of America, Inc.

We wonder if you or your industry members have had experience with other food or beverage products which would lend itself to tea. If so, we and our members would be glad to work with you in every way to develop a more suitable container for carrying tea worldwide.

Very truly yours,

TEA ASSOCIATION OF THE
UNITED STATES OF AMERICA, INC.

R Weiskopf

R. E. Weiskopf
Chairman - Traffic Committee

REW/jr

717 FIFTH AVENUE • NEW YORK, N. Y. 10022 • MUrray Hill 8-1577 • Cable: TEAFRONT

THE SOCIETY OF THE PLASTICS INDUSTRY, INC.
250 PARK AVENUE • NEW YORK, NEW YORK 10017 • 212/687-2675

RALPH L. HARDING, JR.
EXECUTIVE VICE PRESIDENT

January 30, 1969

Mr. R. E. Weiskopf
Chairman - Traffic Committee
TEA ASSOCIATION OF THE UNITED
STATES OF AMERICA, INC.
717 Fifth Avenue
New York, New York 10022

Re: Plastic Containers - Tea

Dear Mr. Weiskopf:

Your inquiry of January 17th is certainly intriguing. I am quite confident that some of our members can come forward with solutions for you.

I am referring your letter to the Chairman of our Food, Drug and Cosmetic Packaging Materials Committee - Mr. Robert M. Miller of Hercules. I am also sending copies to some of his associates.

One of us will be back in touch with you quite promptly.

Cordially,

Original Signed by
RALPH L. HARDING

RLH/jdg
cc: Messrs. C. L. Condit
J. H. Heckman
G. W. Ingle
R. M. Miller

HERCULES INCORPORATED

February 4, 1969

Mr. R. L. Weiskopf
Chairman - Traffic Committee
Tea Association of the United States of America, Inc.
347 Fifth Avenue
New York, New York 10022

Dear Mr. Weiskopf:

Re: Plastic Containers - Tea

As indicated in Mr. Ralph L. Harding's letter of January 30 to you, he has referred your most interesting inquiry of January 17 concerning plastic containers for transporting tea to me as the chairman of the Society of the Plastics Industry Food, Drug and Cosmetic Packaging Materials Committee.

Although our committee usually does not become involved directly with commercial affairs such as this, we find your potential use most intriguing and believe it should be brought to the attention of all our members. Accordingly, we have arranged to distribute your letter to the 135 committee members on our roster, with instructions to contact you directly if they have recommendations to offer. We will see that you receive a copy of our committee notice.

Thank you for your inquiry; you should be hearing from several of my associates shortly. Please let me know if there is anything further we can do.

Sincerely,

RMM

Robert M. Miller, Chairman
SPI Food, Drug and Cosmetic
Packaging Materials Committee

RMM:rbm

cc: R. L. Harding - SPI
C. L. Condit - SPI
J. H. Heckman
G. W. Ingle

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