Committee Correspondence

re FDA Procedural Regulations

Food, Drug, and Cosmetic Chemicals

The B.F.Goodrich Co.
500 S. Main St.
Akron, Ohio 44318

December 8, 1967

Mr. Morgan M. Hoover
Manufacturing Chemists' Association, Inc.
1825 Connecticut Avenue, N.W.
Washington, D.C. 20009

Dear Morgan:

In response to your letter of December 4, 1967, with respect to the carcinogenic question, I am in agreement with your thinking to leave the matter rest on the basis of our November 3 statement.

Very truly yours,

W.E. McCormick

mj
cc: W.A. Knapp
V.H. Knoop

TELEPHONE HUDSON 3 6126

Manufacturing Chemists' Association, Inc.

(FOUNDED 1872)

1825 CONNECTICUT AVENUE, N. W.
WASHINGTON, D. C. 20009

December 4, 1967

Mr. W. E. McCormick
The B. F. Goodrich Company
500 S. Main Street
Akron, Ohio 44318

Dear Bill:

In answer to your letter of November 24 re the separate statement endorsing Jack Frawley's specific proposal, Bill Knapp called after receiving his copy of my November 17 letter to you to say that he is willing to withdraw his request for the separate statement because the MCA statement to the HEW Hearing Clerk dated November 3 accomplishes the objective in large measure.

Your suggestion that I or my source contact Jack Frawley to discuss the carcinogenicity question raises a problem because the source wishes to remain anonymous and I do not have the necessary detailed background.

I do not think that this is worth spending much more time on since we already have gotten the main point across in the November 3 statement, the proponent is now satisfied without the separate statement, and there were three negative votes anyway. Do you agree?

Sincerely yours,

Morgan M. Hoover

MMH:sjg

cc: W. A. Knapp
V. H. Knoop

Food, Drug, and Cosmetic Chemicals

The B.F.Goodrich Co.
500 S. Main St.
Akron, Ohio 44318

November 24, 1967

Mr. Morgan M. Hoover
Manufacturing Chemists' Association, Inc.
1825 Connecticut Avenue, N.W.
Washington, D.C. 20009

Dear Morgan:

This refers to your letter of November 17. I am still in favor of the MCA's endorsing Frawley's statement and it appears as if the majority of the Committee feel likewise.

I, of course, do not know the basis for your source's comment regarding the carcinogencity question, and it may be that the results are equivocal. I feel that you and/or your source should immediately contact Jack Frawley and discuss it before making the final presentation. If for any reason after your discussion it appears undesirable to do so, then we should not.

Very truly yours,

W.E. McCormick

mj
cc: V.H. Knoop
W.A. Knapp

TELEPHONE HUDSON 3-6126

Manufacturing Chemists' Association, Inc.

(FOUNDED 1872)

1825 CONNECTICUT AVENUE, N. W.
WASHINGTON, D. C. 20009

November 17, 1967

Mr. W. E. McCormick
The B. F. Goodrich Company
500 S. Main Street
Akron, Ohio 44318

Dear Bill:

The replies to my letter of November 2 to the FDCCC requesting advice re MCA's support of Dr. Frawley's specific proposal show eight in favor, three not in favor, one no objection, one not involved.

Most of the replies did not go into any detail. However, one set of comments in particular makes me question the advisability of our going beyond what we submitted on November 3 in support of Dr. Frawley's concept. This particular set of comments says that even at 0.2% evidence of carcinogenicity has been detected. Why this apparently was not reported before is a mystery to me. The same source said LD-50's and 30-day feeding studies are needed for new compounds.

Please advise as to how you wish to handle this matter.

Sincerely yours,

Morgan M. Hoover

MMH:sjg

cc: V. H. Knoop
W. A. Knapp

November 13, 1967

Mr. Morgen M. Hoover
Manufacturing Chemists' Association, Inc.
1825 Connecticut Avenue, N.W.
Washington, D.C. 20009

Dear Mr. Hoover:

Pursuant to letter ballot requested in letter of November 2, I wish to cast my vote in favor of endorsement of the Frawley proposal. This would not eliminate difficulties in compliance where petition is required but it would eliminate the necessity for petitions on a substantial number of substances. It appears to be a move in the right direction.

Sincerely yours,

Original Signed
W. A. Knapp

W. A. Knapp

WAK:dmk

cc: Mr. William E. McCormick, The B.F. Goodrich Company,
500 S. Main Street, Akron, Ohio 44318

ATLAS CHEMICAL INDUSTRIES, INC.

WILMINGTON, DELAWARE 19899

November 3, 1967

Hearing Clerk
Department of Health, Education and Welfare
Room 5440
330 Independence Avenue, S.W.
Washington, D.C.20201

Dear Sir:

Comments on Proposed Rule-making
21 C.F.R., Part 121, Federal Register
Volume 32, No. 152, Pages 11443 - 6

Atlas Chemical Industries, Inc., hereinafter referred to as Atlas, is a manufacturer of food additives and has in the past filed many food additive petitions for both direct and indirect additives. Atlas expects to file additional food additive petitions and hence is an interested person.

Atlas supports the comments filed or about to be filed by the Manufacturing Chemists Association.

In addition, Atlas makes the following comments with respect to the proposed regulation.

Section 121.50(e)I, B, 2 and 5, and Section 121.50(e) II, B, 1st paragraph and subparagraph 2, require an estimate of the maximum as well as the average quantity of the food additive to be expected in the total daily diet of the consumer. It is respectfully submitted that estimates of the maximum quantity, for both direct and indirect food additives, will be relatively meaningless and that this requirement should be deleted. The meaningful figures and the Department of Agriculture tables are average consumption figures and, where feasible, these have been used in the Atlas petitions that establish the average quantity of the food additive to be expected from all of the approved uses.

The safety factor of 100 is designed not only to take care of the species difference between animals and humans, but also to take care of the different dietary patterns of humans. In

some cases, of course, as, for example, infants, it may well be that the average will also be the maximum in the sense that the infant may only be consuming one food. A discussion of the safety factor of 100 and its applicability is more fully set forth in the comments filed by the Manufacturing Chemists' Association and will not be repeated here.

Section 121.50(e) II, A, 1, b, Description of the additive, subparagraphs iv, v, vi, and vii, regarding manufacturing processes, specifications, reproducibility and stability data are objectionable in that they do not exclude this type of data where this data is unnecessary for one reason or another. For example, present regulation 121.51(c) A, in the second paragraph, says some of these types of information shall be supplied "When the chemical identity and composition is not known,". It is suggested that this qualification be applied to all these subparagraphs. Examples would be petitions for new uses for additives already included in the Food Additive Regulations, Food Chemicals Codex, U.S.P., N.F., etc.)

Section 121.50(e) II, A, 2, a, relates to indirect additives and recognizes two types, namely those added for functional use in production and those in food contact surfaces. This comment relates to the latter.

As a practical matter and for purposes of clarity, the petition framework should recognize that there are at least two aspects of food contact surfaces which are not necessarily amenable to uniform treatment. The first of these is the basic substrate of the contact surface, such as cellophane, polyethylene, etc., and the ingredients used in making it. The second constitutes the large group of adjuvants used in or on the basic substrate.

In existing food additives Subpart F relating to food additives resulting from contact with containers or equipment, these two types of additives from food contact surfaces are treated in at least three different manners.

Some of the regulations define only the basic substrate leaving the definition of suitable adjuncts to other regulations in Subpart F. Examples of such regulations are 121.2510 Polyethylene and 121.2521 Vinyl Chloride-Propylene Copolymer.

A second type of regulation defines the composition of the basic substrate and also in the same regulation lists optional adjuvants that may be incorporated in or added to the basic substrate. An example of this type of regulation is 121.2522 Polyurethane Resins. Or such a regulation may list the adjuvants and also provide for the use of other adjuvants included in any other regulation as safe for use as a component. Such a regulation is 121.2507 Cellophane. See 121.2507(b)(3).

A third type of regulation lists classes of adjuvants that may be in or on any of the approved food contact surfaces. Such a regulation is 121.2541 Emulsifiers and/or Surface Active Agents.

Section II, A, 2, b, and particularly portions of subparagraphs iii, iv and v are confusing and inapt in that they tend to treat the adjuvants for food contact surfaces in terms of the food contact surfaces. For example, subparagraph iii requires "Manufacturing process, including for food contact surfaces the raw materials and their specifications that encompass the basic resin polymer and the adjuvants (such as plasticizers, stabilizers, preservatives, fillers, colorants, catalysts, etc.) along with the analytical technique used to check the specifications***." If it be assumed that the basic substrate is an approved food contact surface, as it will be in many instances where a new adjuvant is proposed, it is not believed that this information should be required for the basic food contact surface or substrate.

If it can be said that subparagraph iii is not applicable to a new adjuvant, we then turn to subparagraph iv which reads in part, "Specifications for the additive(s) in food contact surfaces, including their identities, the minimum content of the desired component(s), and the limitations or impurities including total heavy metals, monomers, catalyst residues, etc.**** Data from a suitable number of representative production batches of the food contact surfaces shall be included to establish the range of impurities and by-products to be expected and to show that the proposed specifications can be met." (Emphasis ours.)

It is submitted that data from representative production batches of the food contact surfaces are not appropriate to show that the specification for the adjunct additive can be met. If the requirement that data from a suitable number of representative production batches is kept (see above comment regarding subparagraphs iv, v, vi and vii under A, Identity, 1, Direct Additive (b) Description of the Additive), it would seem that this should be "representative batches of the additive(s)".

It is noted in this connection that Atlas also supports the Manufacturing Chemists' Association position that at the time a food additive petition is filed, there may not have been any "production" batches of the additive and that the word "production" should be deleted.

Again in subparagraph v. we find the requirement

> "Reproducibility of the food contact surfaces including the production controls and tests employed to assure that a reproducible product will be manufactured."

If this requirement is to be retained (see above comment regarding subparagraphs iv, v, vi, and vii under A, Identity, 1, Direct Additive (b) Description of the Additive), it should not be applicable to adjuvants particularly for adjuvants for substrate food contact surfaces that have already been approved in the regulations.

In Section 121.50(e) II, D, Methods, subparagraph 4, it appears that the specifications for food contact surfaces referred to are no different than those referred to in A, 2, b, iii, and iv, which require the analytical methods for each specification. This would appear to be duplication of information on the "tests" or "analytical methods."

Respectfully submitted,

ATLAS CHEMICAL INDUSTRIES, INC.

By Kenneth E. Mulford
Assistant to the President

KEM:HP
Submitted in Quintuplicate
CERTIFIED MAIL -
RETURN RECEIPT REQUESTED

CC:
Dr. Morgan H. Beaver
Dr. James Hulse
Dr. G. F. Vincent
Dr. W. A. Knapp ✓

TELEPHONE HUDSON 3-6126

Manufacturing Chemists' Association, Inc.

(FOUNDED 1872)

1825 CONNECTICUT AVENUE, N. W.
WASHINGTON, D. C. 20009

November 2, 1967

TO: Food, Drug, and Cosmetic Chemicals Committee

SUBJECT: MCA Support of Dr. Frawley's Proposal re Indirect Food Additives

Gentlemen:

Your chairman requests that you advise me by November 15 whether or not you favor MCA support of Dr. Frawley's specific proposal as submitted to HEW in his letter of October 23. A copy of this letter was mailed to you from this office on October 30.

The MCA statement regarding FDA's proposed food additives procedural regulations as prepared by Dr. Knapp's task group, to be filed by November 6, endorses Dr. Frawley's concept only, not the specific proposal.

If you are willing to support the specific proposal, a supplemental communication to the hearing clerk can be made.

Please be sure to reply one way or the other.

Sincerely yours,

Morgan M. Hoover

MMH:sjg

HOFFMANN-LA ROCHE INC.

NUTLEY • NEW JERSEY • 07110

October 30, 1967

Dr. William A. Knapp
Allied Chemical Corporation
P. O. Box 405
Morristown, New Jersey 07960

Dear Doctor Knapp:

I have received Mr. Hoover's letter dated October 23, 1967, enclosing a copy of the comments which MCA has prepared for filing with FDA with respect to the Food Additives Procedural Regulations. The time and work on the part of the committee that obviously went into the drafting of these comments is certainly appreciated.

As Mr. Hoover requested, we have reviewed the draft of the MCA position and have set forth our comments below. We have added several ideas which were not contained in the letter to you of September 25th. We would appreciate your considering these for incorporation into the final MCA comments filed with FDA. The comments are as follows:

(1) With respect to Section 121.7(a)

We suggest the addition of a new subsection (4) as follows:

"Where the conditions of use or characteristics of a new drug or antibiotic drug which substance is also a food additive provide adequate protection of the public, such conditions or characteristics may be considered as being acceptable, practical regulatory methods."

We believe the addition of this paragraph is essential to provide in the regulations the flexibility necessary to permit the approval of a New Drug Application and promulgation of a regulation without requiring assay methodology in those cases where assay methodology will not contribute further to the protection of the public. An example of when such flexibility would be needed is when the drug is used on animals at a time when the animals are at a stage of life or in a condition which is not suitable for the production of food.

Another example would be when the drug substance itself consists of several components, one of which is metabolized more rapidly than the other. To be an effective regulatory method in this case, regulatory methodology would be needed only for that component which is present for the longest period of time.

Still another example might be in cases where a substance is to be given to animals as an antidote. In such cases usage and distribution would be limited. Also, in these cases the animals would not likely be fit for food production and potential hazards to the public would be strictly limited.

To require methodology in such cases would impose undue burdens upon the industry and restrict the development of substances for these uses, thereby adversely affecting the public interest.

(2) <u>With respect to Section 121.50(f)</u>

We suggest that there may be an internal inconsistency between the wording of the proposed revision of this regulation and the discussion of that wording immediately following.

In the proposed rewording of this section it is stated that a general summary of the toxicological basis on which the Food Regulation is based is "not considered

l or entitled to protection" as a trade secret. the last sentence on page 17 it is stated that ary of the toxicological data is not necessary ment purposes and "should not under any circum- released as public information unless the peti- ents". We agree with the general intent of the ence.

ition, we suggest that it may be unadviseable to alternative you suggest on page 18 permitting wal of the petition prior to publication. We do hat it would be desirable to provide the Agency eans of forcing the petitioner to withdraw his consent to have the information published.

Very truly yours,

Philip J. Franks
General Attorney

eorge P. Vincent
Mathieson Chemical Corp.)

ames Hulse
. Pfizer & Co.)

organ M. Hoover
facturing Chemists' Assn., Inc.)

TELEPHONE HUDSON 3-6126

Manufacturing Chemists' Association, Inc.

(FOUNDED 1872)

1825 CONNECTICUT AVENUE, N. W.
WASHINGTON, D. C. 20009

October 30, 1967

TO: Members of the Food, Drug, and Cosmetic Chemicals Committee

SUBJECT: Dr. Frawley's Proposal re Indirect Food Additives

Gentlemen:

I am enclosing a copy of Dr. Frawley's letter of October 23, 1967 to the HEW Hearing Clerk (along with a copy of his BIBRA talk) for your information in the event you intend to submit an individual company set of comments re FDA's proposed changes to the Food Additives Procedural Regulations.

Dr. Knapp's task group has referred to Dr. Frawley's proposal in its draft sent to you with my covering letter of October 23. This draft also mentions "it is expected that many of these (MCA) companies will also submit their comments directly to the Food and Drug Administration." The task group plans to reference the BIBRA paper.

Sincerely yours,

Morgan M. Hoover

MMH:sjg

Enclosures

Copy to: Dr. J. P. Frawley

States, the term toxicological insignificance has real meaning and significance. I believe it is a sound scientific principle which must be preserved and eventually I hope will be restored in my country. It is this principle which I believe is the very crux of intelligent common-sense regulation of food-packaging materials.

Let us take stock. Experience has taught us that most uses of food-packaging materials are safe beyond any reasonable doubt. Experience has also taught, at least in the United States, that an "omnibus" permissive list not only diverts the energies of our corporations, government and universities into predictably unprofitable research, but can lead to some, if not general disregard for the law. This leaves us with the conclusion that some mechanism should be found for subjecting to a permissive list only those uses of packaging materials which pose a potential hazard to health; that is, constructing a "non de minimis list" or "relevant" list.

Here is where I invite each and everyone of you to sit down and define those uses which can be assumed to be safe. As I stated earlier this exercise sounds like fun, but it is just plain hard work. I am not certain that my solution is the best, but I assure you it is the result of many hours of reflection and analysis. In its briefest form, I believe that any chemical suitable for use in food-packaging is safe for man at a level of 0·1 ppm in the total diet. Extrapolating this dietary concentration to a practical and meaningful guideline for regulatory purposes, use of a chemical in a container at a level of 0·2% or less will contribute less than 0·1 ppm to man's diet.

On the surface, this may not appear to propose a major improvement, but application of this guideline would permit deletion of 75% of the citations in the United States regulations and I am certain would permit more efficient use of manpower, in establishing permissive lists in other countries.

I do not ask that you accept this conclusion on faith. So, as briefly as possible, I should like to review the scientific basis for this conclusion.

First of all, what level of a compound, which is suitable for use in food packaging, but of unknown toxicity, can be assumed to be safe in the human diet? I know of no better approach to answering this question than to examine our toxicological experience and tabulate the experimentally determined safe level for all the compounds which have been studied. Because 90-day toxicity studies are generally considered inadequate for calculation of safe levels and because only a small number of these are published, I decided to review as many 2-yr chronic toxicity studies as I could find and to tabulate the "no-effect" level confirmed for each.

I can make no claim that I have found every 2-yr chronic toxicity study which has been conducted. I can only claim that I have tabulated the "no-effect" levels from every chronic study which I could find, without any selection or rejection except irradiated foods. In total, I was able to locate 2-yr chronic toxicity studies on 220 different substances (see Appendix), and although this may seem like a modest number, it represents between 4 and 7 million pounds in toxicological research. Last September I had been able to locate only 143 such studies, but with the co-operation of many of my colleagues in the field of toxicology, I estimate that I now have collected about 90% of all such studies which have been conducted.

Table 1 presents the distribution of "no-effect" levels for all of the 220 compounds.

It is apparent from Table 1 that a small percentage of compounds will be extremely toxic—having a "no-effect" level in experimental animals below 1 ppm, but that the majority will exhibit no toxic effect even at 100 ppm. Only 19 of the 220 compounds demonstrated

HERCULES INCORPORATED

MEDICAL DEPARTMENT

[illegible] HERCULES TOWER • 910 MARKET STREET • WILMINGTON, DELAWARE 19899 • (302) 656-9811

October 23, 1967

Hearing Clerk
Department of Health, Education, and Welfare
Room 5440
330 Independence Avenue, S. W.
Washington, D. C. 20201

Re: Food and Drug Administrations' Proposed Food Additives Procedural Regulations (32 Fed. Reg. 152, p. 11443)

Dear Sir:

I wish to concur with the stated objective of the Food and Drug Administration that the Procedural Food Additive Regulations should be revised "to expedite their scientific review," and to reduce the "unnecessary burden that wastes the time and efforts of both Administration and industry scientists." Having been a scientist in the Administration, as well as in industry, I share the concern of the Administration over the increasing use of your experts on nonproductive assignments. This concern is one which scientists inside and outside government consider to be a major threat to a continued unblemished record of consumer health protection currently shared by the Administration and the industry.

However, after careful review of the proposed changes in the procedural regulations for food additives, I have concluded that the Administration has overlooked one of the major obstacles to efficient and effective use of industry and Administration scientists, because no recognition has been given to the inherent safety of certain uses of incidental food additives and no procedure has been provided to eliminate such uses from the same exhaustive scientific evaluation and administrative review required of more hazardous applications. If we are to provide the public the degree of protection to health which we are morally and legally dictated to provide, we must find some mechanism for expending our limited resources, both manpower and finances, in a manner appropriate to the relative risk. Under the current regulations and the proposed revisions, no opportunity is provided for this.

In the field of food packaging I do not think we should direct any criticism toward any individual or group for failure to incorporate such provisions into the existing regulations adopted in 1959. At that time the potential health hazard from food packaging was poorly defined and scientists in industry and government, including myself, were unwilling to assign a lower risk to any use of a food packaging component. However, after many years and

Therefore, if we exclude heavy metals and pesticides from our consideration, experience has indicated that only a very occasional (fewer than 1 out of 100) commercial compound will have a "no-effect" level below 100 ppm and that an infinitely small number will exhibit any toxicity at 10 ppm or less.

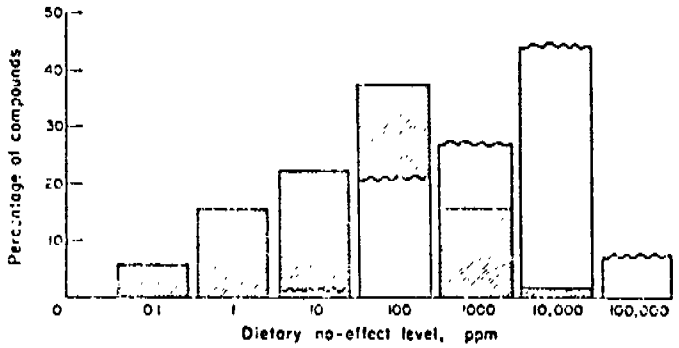

FIG. 1. Histogram showing distribution of "no-effect" levels in 2-yr chronic studies on 220 compounds. Shaded areas denote pesticides and heavy metals, and blank spaces other chemicals.

Now if we apply the conventional 100-fold margin of safety to these experimentally determined "no-effect" levels, all 132 of the non-pesticidal chemicals are safe for man's diet at a dietary concentration of 0·1 ppm or higher. Many of these materials are used at much higher levels in food, but had we assumed that they were all safe at 0·1 ppm and permitted their use up to that level without toxicity studies, we would have been correct in 100% of the cases and would not have exposed the public to any health hazard.

For accuracy, I should point out that in the above calculation I have dealt only in orders of magnitude. If these "no-effect" levels are subdivided into small groups as 10, 30, 100 or 300 ppm, it can be concluded that all were safe to animals at 30 ppm. Moreover, I did not take into consideration the larger food consumption per kg of body weight of rats and dogs versus man. Combined, these additional calculations show that the 0·1 ppm level in the human diet provides less than 1/1000th the mg/kg/day intake of the most toxic of the 132 compounds. Some may argue that I have been unnecessarily conservative, and perhaps I have been.

Now let me consider briefly the other aspect of our problem—migration to food—and attempt to develop some guidelines which will tell us which uses may contribute more than 0·1 ppm to the diet of man, and which uses cannot.

First of all, it is obvious to everyone that any major component of a food container must be assumed to possess the capability of migrating to food at a level in excess of 0·1 ppm, unless proven otherwise. However, it is equally obvious, that some uses will not contribute 0·1 ppm to the diet. Our problem is to find this dividing line.

Undoubtedly, this dividing line is different for each type of substrate. It will be different for films than for bottles. It will be different for one polymer than for another. We could establish a whole series of levels for each food-packaging substrate and its intended use, but most of these differences are not sufficient to justify complication of regulations.

Therefore, in order to determine the level of addition which would contribute less than 0·1 ppm to the diet with all types of substrates, I selected the substrate which is the most permeable and susceptible to extraction by food, namely, paper. In addition I have selected

(4) Substances permitted for use by regulations in this Subpart F.

(5) Substances used at a level of no more than 0.2% by weight of the container or no more than 0.2% by weight of the coating or other surface treatment, provided these substances are not heavy metals, as defined in Food Chemicals Codex, or pesticides, as defined in the Federal Insecticide, Rodenticide and Fungicide Act.

Addition of this new subparagraph to regulation 121.2500 appears logical because it automatically incorporates the other restrictions of good manufacturing practice to the food packaging uses of these trace components; for example, that the amount used in the container shall not exceed that which is "reasonably required to accomplish the intended physical or technical effect," that the purity shall be "suitable for its intended use" and that the uses shall not violate any other provision of the Federal Food, Drug and Cosmetic Act.

I submit this proposal for your careful study and consideration and recommend its adoption.

Sincerely,

John P. Frawley, Ph.D.
Chief Toxicologist

JPF/eaw

Attachments

HERCULES

food, sugar, doughnuts, ground beef, butter, bacon, sausage, to name just a few) and analysed each sample at several different storage intervals and temperatures. For our purposes, I have selected only the uncoated and unwaxed paper and only the maximum migration levels obtained for the 18 commodities packaged in these uncoated papers under typical commercial storage conditions. Admittedly this gives unrealistically high values for rosin size which are not typical of industry practice, but for our present purposes, the worst case must be presented.

Table 4. *Calculation of maximum migration of rosin size* to total diet*

Commodity group	Percentage of diet	Average migration (ppm)	Contribution to total diet (ppm)
Milk products	31	3·1	1·0
Vegetables	20	2·0	0·4
Meats	18	38·2	6·9
Fruits	13	0·5	0·1
Grain products	10	3·5	0·4
Sugar	5	0·2	0·0
Butter, oils	3	32·8	0·9
		Total ...	9·7

*4% in paper.

Table 3 shows the maximum migration value for 18 food commodities at various typical storage times and temperatures when exposed to paper containing an average of 4% rosin size. It is obvious from some of these values that high levels of migration can occur with some foods, whereas other foods contain much less rosin size. The data in Table 3 can be quickly considered since the individual values are of no great significance, but the composite of these values can be helpful. Table 4 shows the average consumption of these various commodity groups in the US†, the average migration to that commodity group and a calculation of the maximum level of rosin size in the average total diet, if 100% of the diet were packaged in uncoated paper containing 4% rosin size. Undoubtedly there are some differences in dietary habits between our countries, but I doubt that they would significantly alter the calculation.

As I mentioned previously, three different sizing levels were used in these studies. Table 5 shows the final dietary calculations for the same foods, under the same conditions for paper containing 2 or 1% rosin size. The extrapolation is remarkably good. The last column shows the migration in ppm expressed on the basis of a unit of 1% rosin size in the paper or container. For each per cent addition to the container, man's diet would contain a maximum of 2 ppm of the additive, if the entire diet was in contact with that container.

One further calculation is necessary in order to arrive at a realistic determination of the

Table 5. *Maximum migration of rosin size to diet*

Level of size in paper (%)	Migration (ppm)	ppm/%
4	9·7	2·4
2	4·4	2·2
1	1·9	1·9

†U.S. Department of Agriculture Dietary Evaluation of Food Used in Households in U.S., 1961.

Fd Cosmet. Toxicol. Vol. 5, pp. 293–308. Pergamon Press 1967. Printed in Great Britain

*BIBRA Annual Scientific Meeting**

Scientific Evidence and Common Sense as a Basis for Food-Packaging Regulations

J. P. FRAWLEY

Hercules Incorporated, Wilmington, Delaware 19899, USA

I am honoured by your invitation to meet with you tonight and to discuss with you some of the problems associated with assuring the safety of food-packaging materials. However, I am equally humbled by my own inadequacies to discuss our subject matter as expertly as it deserves.

Unfortunately for all of us, there is no individual who can be considered an expert on all aspects of food packaging. Although essentially all of the individual components used in food packaging originate in a chemical plant, the technology for formulating and converting these materials into useful containers varies with every substrate, whether it is plastics, paper or metal. Moreover, the marketing relationship between producer, formulator, converter and the food industry is notably different for each segment of this complex industry. Consequently, it is a formidable task to become an expert for even one aspect.

Each of you here this evening possesses expert knowledge in one or more aspects which I wish I had. It is unfortunate that telepathic communication has not reached my level of intellectual development, so I could benefit from your experience. In fact, the only thought waves reaching me suggest that many of you should be delivering this lecture rather than I. Therefore, if you will consider me to be a substitute speaker, you may be a little more tolerant towards my remarks.

When was the last time you sat down in the solitude of your study and attempted to write out a geometrical proof that the shortest distance between two points is a straight line? Most of us would have a difficult time doing it today because, as you recall, it is not susceptible to proof. It must be accepted. Indeed, some of the most difficult things in life to prove are the obvious ones.

A number of months ago, I sat down to try to prove something which was obvious to me—that there are some uses of food-packaging materials which cannot involve any hazard to health of the consumer of food. I had no preconceived idea of the end point I would reach, but it seemed like it would be fun. Sometimes now I wish I had resisted the temptation and invested my time in some other form of recreation.

My main exercise was to try to determine a level of use of any food-packaging component which could be considered safe regardless of its degree of toxicity. Many of you know the conclusion I reached; namely, that any component of a food container or coating which is

*Editor's note: This paper was delivered to the Fifth Annual Scientific Meeting of the British Industrial Biological Research Association (BIBRA), held in London on 25 January 1967. The Annual Scientific Meeting, instituted in 1962, provides an opportunity for members and guests of the Association to receive an address from an eminent toxicologist on a topic related to BIBRA's field of interest. Previous speakers have been Professor H. C. Hodge, Dr. A. J. Lehman, Professor L. J. Goldwater and Dr. J. M. Barnes.

The most frequent comment is a concern that despite our toxicological experience to date, we cannot assume that the next compound will not be toxic at 0.1 ppm. The same basic concern has been expressed in another way, by expressing doubt that toxicity data from 2-yr chronic studies represent a valid cross-section of chemicals, since some of the more toxic ones are rejected by short-term toxicity tests.

It is, of course, possible that some chemical may be synthesized at some time in the future which would be toxic at 0·1 ppm in the diet. However, it is almost impossible for such a compound to become an intentional component of a food container. For a compound to be toxic for man at 0·1 ppm presumes that it will be as toxic or more toxic than any commercial pesticide. For it to be used as a component of a food container presumes that it must be manufactured, packaged, distributed, and in other ways handled several times before contacting the food. It is inconceivable that a compound as toxic as this could pass through so many hands, in an industry not accustomed to handling highly toxic substances, without revealing its toxicity through injury to personnel. Once recognized, safe handling of such a compound would require such extreme industrial hygiene precautions as to be incompatible with converting operations and food-packaging practices. It seems to me that in order to produce an unsafe food package, due to incorporation of a toxic ingredient at a level of 0·2% or less, it would require a deliberate or intentional act on the part of a manufacturer to poison the public, without at the same time poisoning his own workers. No amount of legislation or regulation can protect against such insanity.

It has been suggested by a few of my colleagues that the extreme toxicity of such materials as aflatoxin rules out an assumption that any chemical is safe at even one part in a thousand million unless it has been tested. I believe that such an assumption is valid, if we limit our discussion to certain uses or industries. Again, I believe common sense tells us that it is inconceivable that anyone could manufacture millions of pounds of aflatoxin, or any substance of extreme toxicity and distribute it for use as a stabilizer in plastics or wet-strength resins for paper without finding out that it was too toxic for that industry. No company can afford to lose customers that way.

Accidental contamination with aflatoxin or other extremely toxic substances is another matter, but this is outside the considerations of a permissive list. Whether a permissive list contains 200 or 20,000 substances, accidental contamination is no more or less likely. Quality control, inspection, and personal attention to details in manufacture are all necessary ingredients to the prevention of contamination of any product.

A few individuals have questioned the validity of my estimate that no more than 25% of the diet will be in contact with the same packaging substrate or chemical. In rare circumstances, of course, some individuals may eat canned foods almost exclusively and some may eat fresh or unpackaged food almost exclusively. These variations in dietary habits, along with other intraspecies differences have been taken into consideration as part of the basic concept of our 100-fold margin of safety. Moreover, as mentioned above, the conservative calculations used above provide a 1000-fold margin of safety.

The principal objection to this proposal in the United States has been administrative. Adoption of this proposal would obviate the need for many of our packaging regulations and would suggest a complete rewriting of Subpart F. For example, the "general adhesives" and "defoamer in paper manufacture" regulations would be replaced by a statement of good manufacturing practice that adhesives should not contact the food (as is already provided despite the fact that thousands of chemicals are enumerated) and that defoamers may be used only prior to and during sheet-forming process (as is also already provided).

common-sense approach to allow us to concern ourselves with potential hazards and not with predictably safe practices.

It is to this assignment that I applied myself last summer—to try to develop a scientific basis for a start, and only a start, towards a common-sense approach to food-packaging regulation. However, before proceeding with the scientific evidence I have collected and the conclusions I have drawn, I have made two statements which require documentation. First, that the return on our investment has been negligible and second, that our regulatory scheme has been too complex to serve its intended purpose.

Following enactment of our law, the major task facing the industry was evaluation of current industry practices. Many of you are familiar with some of the larger research programmes undertaken by different segments of the industry, for example, the petroleum wax studies by the American Petroleum Institute, the can enamel studies by the can producers and the rosin product studies by Hercules. Many other programmes which received less publicity were conducted on regenerated cellulose, polyethylene and other polymers, paper coatings and wet strength resins, to mention only a few. The net result of this investment of millions of pounds has been that more than 90% of the prior industry practices have been confirmed as safe, through a combination of low toxicity and low migration, and have been endorsed by our Food and Drug Administration (FDA), by inclusion on our permissive list. This general endorsement of the vast majority of industry practices testifies to the fact that most uses of packaging materials are inherently safe.

However, before sufficient facts were accumulated to confirm the low degree of hazard associated with packaging materials, we had committed ourselves to an "omnibus" permissive list, containing every conceivable chemical which might even remotely come in contact with food. We now have 94 separate food-packaging regulations or lists dealing with different uses of packaging chemicals, from 967 ingredients* for adhesives to 8 ingredients for zinc-silicon dioxide matrix coatings. These regulations contain over 43,000 words, about 10,000 words more than the regulations for all intentional food additives. In 1966 alone, the 8th yr of the law's existence, over 200 new uses of packaging chemicals were approved and published in our *Federal Register*. Even a superficial examination of these regulations reveals that the vast majority of these words are devoted to the enumeration of thousands of chemicals for one or more specific uses under which most cannot migrate to food at an unsafe level, regardless of their degree of toxicity. Unless you work with these regulations on a daily basis, are familiar with the multiple cross-references and have sufficient technical training to understand what chemicals are covered by some of the vague generic terms, it is almost impossible to determine the approved uses of a given chemical. We have created a complex maze of regulations, too lengthy and involved to be understood by most of the regulated industry, with the unanticipated result of a growing apathy towards correct interpretation.

This type of "omnibus" permissive list came about in the United States at the insistence of some segments of industry, coupled with a change in interpretation of our laws by the FDA—a change which revoked the long-established principle of *de minimis non curat lex* (the law does not concern itself with trifles) by claiming that the law does not recognize any level of a chemical as insignificant. This denial of the existence of a toxicologically-insignificant level or biological zero is analagous to a denial of the existence of night, on the grounds that you cannot prove the absence of light. In all countries outside the United

*967 does not count the numerous reaction products cleared for one or more of these chemicals. If these are counted, the number exceeds 3800.

Appendix (contd)

Compound	No-effect level (ppm)
2,4-Dichloro-6-*o*-chloroanilino-*s*-triazine (Dyrene)[4]	5000*
2,4-Dichlorophenoxyethyl sulphate, sodium salt[3]	200*
4,4′-Dichloro-α-trichloromethylbenzhydrol (Kelthane)[4]	20*
Dicyandiamide[29]	2500
Dieldrin[2]	0·5*
O,O-Diethyl *O*-3-chloro-4-methyl-1-oxo-2*H*-1-benzopyran-7-yl phosphorothioate (Co-Ral)[4]	2*
Di(2-ethylhexyl) phthalate[31]	1300
Di-*n*-hexyl azelate[30]	5000
Di-isobutyl adipate[3]	5000
Dilauryl thiodipropionic acid[21]	30,000
Dimethyl carbate[14]	10,000
2,4-Dimethyl-2-methylene-1,2,4-thiadiazolidine-5-thione[2]	100*
Dimethyl phthalate[14]	20,000
3,5-Dimethyltetrahydro-1,3,5,2*H*-thiadiazine-2-thione (Mylone)[21]	<10*
O,O-Dimethyl-*O*-(2,4,5-trichlorophenyl) phosphorothioate (Ronnel)[4]	10*
3,5-Dinitrobenzamide[32]	600*
3,5-Dinitro-*o*-toluamide[1]	62*
Diphenyl[1,33]	500*
Diphenylamine[4]	100*
3-(2-Diphenylyloxy)-1,2-epoxypropane[1]	2000
Distearyl thiodipropionic acid[21]	30,000
Diuron[4]	125*
Dodecyl benzene sodium sulphonate (Santomerse no. 3)[34]	2000
Dodecyl gallate[10]	350
Dodine[1,35]	50*
Endosulphan[4]	30*
EPN[4]	5*
Epoxidized soybean oil (Paraplex G-60)[36]	25,000
Epoxidized soybean oil (Paraplex G-62)[36]	5000
4-Ethoxyphenylurea (Sucrol, dulcin)[37]	<1000
Ethoxyquin[4]	120*
Ethyl acrylate[38]	100
Ethyl 4,4′-dichlorobenzilate[4]	50*
2-Ethyl hexanediol-1,3[16]	40,000
2-Ethylhexyl diphenyl phosphate (Santicizer 141)[39]	1250
Ethyl phthalyl ethyl glycolate[3]	5000
Fast Green FCF[40]	10,000
FD & C Blue No. 1[41]	5000
FD & C Blue No. 2[42]	1000
Ferbam[4]	200*
Glycerol[43]	100,000
Glycerol monostearate[43]	250,000
Gum guaiac[14]	5000
Gum rosin, pale[45]	500
Heptachlor epoxide[4]	0·5*
2-Heptadecyl glyoxalidine acetate (Glyodin)[4]	210*
n-Heptyl-*p*-hydroxybenzoate[46]	1500
1-[5-(3a,4,5,6,7,7a-Hexahydro-4,7-methanoindanyl)]-3,3-dimethylurea (Herban)[3]	500*
Hydroxyethylcellulose[47]	10,000
Hydroxypropylmethylcellulose[3]	50,000
Hydroquinone[21]	10,000r
d-Isoascorbic acid[21]	10,000
d-Isoascorbyl palmitate[21]	2500
Isopropyl *N*-(3 chlorophenyl) carbamate (CIPC)[44]	2000*
4,4′-Isopropylidene bis(2-Isopropyl-phenol)[1]	1000
Light Green SF Yellowish[10]	10,000
Malathion[4]	100*
Maleic hydrazide[4]	20,000*
Maneb[4]	25*
Melamine-formaldehyde resin (Parez 607)[9]	50,000
Mercaptobenzothiazole[4]	120*
Mercury acetate[7]	2·5*
Methoxychlor[3,10]	200*
O-Methyl-*O*-(4-*tert*-butyl-2-chlorophenyl) methylphosphoroamidothioate (Ruelene)[1,10]	30*
O-Methyl-*O*-(2,4-dichlorophenyl) isopropylphosphoramidothioate[1]	10*
Methyl *p*-hydroxybenzoate[51]	20,000
Methyl methacrylate[38]	100
Methyl naphthalenecacetic acid[7]	2500*
Methylpolysiloxane[1]	3000
Methyl salicylate[52]	10,000
Monuron[4]	250*
1-Naphthyl-*N*-methyl carbamate[1]	200*
α-Naphthylthiourea[53]	50*
Nicotine[1]	62
Nordihydroguaiaretic acid[21]	2500
Nylon (Zytel)[54]	100,000
Octadecylamine[55]	500
Octyl gallate[10]	350
p-tert-Octylphenoxy-polyethoxy ethanols (Triton X-405)[56]	14,000
Parathion[4]	1*
Petrolatum[57]	50,000
Petroleum wax no. 2[58]	100,000
Petroleum wax no. 8[58]	100,000
Petroleum wax no. 12[58]	100,000
Petroleum wax no. 15[58]	100,000
Petroleum wax no. 20[58]	100,000
Phenacetin[59]	630
Phenol[22]	10,000
Phenyl mercuric acetate[7]	0·1*
o-Phenylphenol[50]	2000*
Pimaricin[61]	500
Piperonyl butoxide[4]	700*

Table 1. *Distribution of "no-effect" levels in 2-yr chronic studies*

"No-effect" level (ppm)	All compounds (220)
<1	5
<10	19
<100	40
<1000	101
<10,000	151

any toxic effect below 10 ppm. We might conclude that the odds of detecting a toxic effect at 10 ppm from any "unknown" compound are approximately 1 in 10.

Let us now look at Table 1 a little more closely and examine the nature of these 19 compounds which had a "no-effect" level at 10 ppm or less. Table 2 shows the same information as Table 1, except two additional columns have been added which subdivide these 220 compounds into two categories: (1) a "heavy metals and pesticides" category and (2) an "all other compounds" category. I believe this breakdown is worthy of careful examination. The most apparent conclusion is that all 19 of the compounds, which were toxic below 10 ppm, were pesticides and heavy metal compounds. Equally significant is the fact that 39 of the 40 compounds, which had "no-effect" levels below 100 ppm in experimental animals, were also pesticides or heavy metal compounds. The only compound in the "all other compounds" category which was toxic below 100 ppm was acrylamide.

Table 2. *Distribution of "no-effect" levels in 2-yr chronic studies*

"No-effect" level (ppm)	All compounds (220)	Heavy metals and pesticides (88)	Others (132)
<1	5	5	0
<10	19	19	0
<100	40	39	1
<1000	101	72	29
<10,000	151	86	65

It is obvious that the degree of toxicity of pesticides and heavy metals (which were used as pesticides at one time) is quite different from that of other commercial chemicals. This should represent no surprise because pesticides are synthesized, screened and selected for their toxicity to one or more forms of life before becoming commercial products. This contrast is more clearly shown by Fig. 1 which depicts the distribution of "no-effect" levels for the two categories of chemicals. It is obvious that the average toxicity of a pesticide is about 100 times as great as the average for other chemicals.

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an additive which is very readily extracted from its substrate, namely, rosin size. This combination of substrate and additive, I believe, represents the most extreme case of migration and values determined from rosin sized paper should represent a maximum for any component of any packaging media. Indeed, such data would be excessive for most uses of packaging components.

In our initial efforts to study the migration of rosin size from paper, we used typical simulated solvents: various aqueous solutions, hexane, maize (or corn) oil, etc. This was wasted effort because, in water and oil, the extraction was a direct function of time and temperature and did not plateau until essentially 100% of the rosin size was extracted and the integrity of the paper sheet was destroyed. Nevertheless a century and a half of experience has shown paper to be a satisfactory packaging material. Although these studies clearly demonstrated that rosin sized paper would be an appropriate choice for developing maximum migration data, they contributed nothing to the evaluation of safety of rosin size which was our principal motive at that time.

As a consequence of this failure of the simulated solvents test to help define the amount actually migrating to food, we prepared radioactive samples of rosin size, incorporated them into typical commercial paper and paperboard at known levels, packaged a wide variety of food in contact with these paper samples at typical package ratios, stored them at typical storage temperatures for typical storage times and determined the rosin size content of each food by counting the radioactivity.

The study was far more extensive than I shall describe, because we used several types of paper (greaseproof, waxed, unwaxed, etc.), containing three different levels of rosin size, 24 different types of food (water, ice-cream, oysters, apricots, green beans, dry breakfast

Table 3. *Maximum migration of rosin size* from uncoated paper under typical storage conditions*

Food	Temperature (°F)	Time (days)	Migration (ppm)
Milk products			
Water	34	14	5·9
Ice-cream	10	28	0·3
Vegetables			
Green beans	34	7	1·3
Green beans	72	14	4·1
Lettuce	34	7	2·4
Potatoes	72	28	0·2
Meats			
Ground beef	34	5	8·7
Chicken	34	3	7·2
Beefsteak	34	7	4·9
Sausage	34	5	124·0
Fruits			
Apricots	72	28	0·1
Apples	72	28	1·2
Grain products			
Puffed rice	72	14	5·8
Wheaties	34	28	7·0
Flour	72	28	0·2
Doughnuts	72	3	0·9
Others			
Sugar	72	28	0·2
Butter	34	14	32·8

*4% in paper.

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ATLAS CHEMICAL INDUSTRIES, INC.

WILMINGTON, DELAWARE 19899

October 27, 1967

Dr. William A. Knapp
Allied Chemical Corporation
P. O. Box 405
Morristown, N. J. 06960

Dear Dr. Knapp:

This refers to Morgan Hoover's letter of October 23 and the proposed MCA comments on the new food additive regulations.

I assume that Morgan Hoover can supply you with some standard paragraphs identifying the Manufacturing Chemists Association, the number of members, etc., for inclusion at some point, possibly after the first paragraph of your covering letter.

I think it is an interesting idea to use this opportunity to initiate discussion of Dr. Frawley's proposal.

With respect to the actual comments, I believe your committee has done an excellent job. I have the following suggestions.

On page 2, Section 121.9(c), third sentence, I suggest that "except wherein parts of a master file are incorporated in petitions by reference" be deleted. If this happens to be a confidential portion of the master file, it should still be kept confidential except for court suits, etc.

I have some difficulty with Section 121.50(e)I.B.2. commencing on page 7. The proposed amendment language at the top of page 7 still includes for direct food additives "where possible or practical, an estimate of the maximum quantity to be expected in the daily diet of the consumer." However, in the paragraph at the bottom of page 9 you urge that as to direct additives a petitioner need only estimate the average quantity of the direct food additive to be expected in the total daily diet of the consumer.

It seems to me that your first request should entirely eliminate the estimate of the maximum quantity using the argument at the bottom of page 9 and the top of page 10.

You could then say that if FDA insists on some maximum quantity, this should be only where it was possible or practical.

The same applies to Section 121.50(e)I.B.5. on page 10 and to Section 121.50(e)II.B. on page 15.

I note that after treating Section 121.9(c) on page 2, you again come back to this section at the bottom of page 18. I can understand the reason for this but suggest that on page 2 at the end you might say "and particularly the last paragraph on page 18."

Very truly yours,

Kenneth E. Mulford
Assistant to the President

KEM:HP
CC: Dr. G. P. Vincent
Mr. James Hulse
Mr. M. M. Hoover

COMMITTEE CORRESPONDENCE

Manufacturing Chemists' Association, Inc.

Committee: Food, Drug, and Cosmetic Chemicals

Address Writer Care Of:
The B.F.Goodrich Co.
500 S. Main St.
Akron, Ohio 44318

Subject:

Date: October 27, 1967

MAK 10/30/67

Dr. William A. Knapp
Allied Chemical Corporation
P.O. Box 405
Morristown, New Jersey 07960

Dear Bill:

I have just reviewed your proposed letter to be submitted to FDA on the procedural regulations. My compliments to you and the other members of your sub-committee for a fine job. This was not easy to do, but you have done it very thoroughly.

Very truly yours,

W.E. McCormick

mj
cc: G.P. Vincent
James Hulse
M.M. Hoover
V.H. Knoop ?

Food, Drug, and Cosmetic Chemicals

The B.F.Goodrich Co.
500 S. Main St.
Akron, Ohio 44318

October 26, 1967

wtf 10/30/67

Dr. John P. Frawley
Hercules Incorporated
910 Market Street
Wilmington, Delaware 19899

Dear Jack:

I have today received your letter of October 24, and its attachments. I have also received in the same mail, the letter that has been proposed for MCA's submission to FDA on the procedural regulations. You may recall at the last FDCC Committee meeting in Washington, I appointed a small sub-committee to collate the criticisms of these proposed regulations from the other committee members, and to formulate a position. Dr. William A. Knapp chaired this sub-committee and he has just completed this project. He has included in the proposed position, reference to your publication and basic philosophy of excluding those components present in quantities less than 0.2%.

? So far as the RMA is concerned, official objections to the proposed regulations have been given to FDA several weeks ago. They did not, however, include-so far as I am aware-any reference to your 0.2% idea.

Very truly yours,

W.E. McCormick

mj
cc: M. M. Hoover
W. A. Knapp

Tele one: 515 228-3241

SALSBURY LABORATORIES Charles City, Iowa, 50616

October 27, 1967

Dr. William A. Knapp
Allied Chemical Corporation
P. O. Box 405
Morristown, New Jersey 07960

Dear Dr. Knapp:

We have received and reviewed the draft of comments of the MFA concerning Procedural Regulations covering organization and handling of FAPs as published in the Federal Register of August 8, 1967, page 11443 et seq.

We have noticed no disagreements with basic philosophy as evidenced in this draft. Thank you for the opportunity of reviewing this material.

Sincerely,

Thomas K. Shotwell, Ph.D.
Government Relations Manager

mac

cc: Dr. George P. Vincent
Mr. James Hulse
Mr. Morgan M. Hoover

TELEPHONE HUDSON 3-6126

Manufacturing Chemists' Association, Inc.

(FOUNDED 1872)

1825 CONNECTICUT AVENUE, N. W.
WASHINGTON, D. C. 20009

October 23, 1967

TO: Members of the Food, Drug, and Cosmetic Chemicals Committee

SUBJECT: MCA Comments re Proposed Revision to FDA Procedural Regulations

Cover letter not included

Gentlemen:

I am enclosing the draft of the comments prepared by Dr. Knapp's task group, along with the draft of the accompanying letter, for your review.

To meet the filing deadline of November 6, you are asked to send any comments you may have to Dr. Knapp (copies to Dr. Vincent, Mr. Hulse and to me) to be received by Monday, October 30.

Dr. Knapp suggests that, because of time problem, you limit your comments to disagreement with basic philosophy, if you have such. The task group has not included some of the comments already received that they felt appeared to be of a relatively minor nature.

Addresses are as follows:

Dr. William A. Knapp, Allied Chemical Corporation, P.O. Box 405, Morristown, New Jersey 07960.

Dr. George P. Vincent, Olin Mathieson Chemical Corporation, 1730 K Street, N.W., Washington, D. C. 20006.

Mr. James Hulse, Chas. Pfizer & Co., 235 E. 42nd Street, New York, New York 10017.

Sincerely yours,

Morgan M. Hoover

MMH:sjg
Enclosur

D R A F T

Hearing Clerk
Department of Health, Education and
Welfare
Room 540
330 Independence Avenue, S.W.
Washington, D. C. 20201

Dear Sir:

Pursuant to the proposed Procedural Regulations covering organization and handling of Food Additive petitions as published in the Federal Register of August 8, 1967, page 11443 et seq., we respectfully submit herewith comments of the Manufacturing Chemists' Association prepared with the assistance of its Food, Drug and Cosmetic Chemicals Committee.

Before proceeding with question and comment on wording and intent of the proposed regulation we would like to take this opportunity to express what we feel are basic difficulties in the administration of Section 409 of the Food, Drug and Cosmetic Act, particularly with relation to indirect additives.

Although the direct additives area of this section are probably of greatest concern to ~~manufacturing~~ chemical producers chemists, we are also intimately concerned with components of packaging materials, both basic polymers and adjuvants, which may fall within the purview of the Act if meaningful migration occurs.

Much uncertainty arises in the determination of what constitutes meaningful migration. Administration policy notwithstanding, we maintain that the act of testing for migration is not in itself evidence that the additive may reasonably be expected to migrate. Modern analytical techniques will detect minute quantities of materials which may or may not be identifiable as coming from a packaging material but which may reasonably be expected to be toxicologically insignificant. We do not believe that it was the intent of Congress to control these very small amounts of relatively non-toxic migrants which usually can be detected from most packaging materials.

The plastic package of today and the adjuvants therein do produce migrants but at quite low levels and from which no deleterious effect has yet been demonstrated. We submit that the vast majority of adjuvants added in small quantity to packaging materials do not migrate in quantities which are toxicologically significant and should be exempt from exhaustive safety evaluation prior to marketing. ~~In this connection, we refer you to the presentation of Dr. John P. Frawley before the September, 1966 meeting of the American~~

Chemical Society. In this he reaches the conclusion that " . . . any component of an article contacting food which is present in the article or its coating at a level not exceeding 0.2% by weight is generally recognized as safe provided it is not a heavy metal or pesticide." We submit that a practical solution might be to establish a realistic level for the components of a packaging material below which there need be no concern with migration, provided, of course, that the materials are known not to be highly toxic.

The purpose of this discussion is to urge that administrative policy be established and regulatory provision made for rapid acceptance of food additives which are present in packaging material in small quantity (e.g., <0.2%), or which would not be expected to be found in significant quantities (e.g., 0.1 ppm) in the daily diet.

The comments submitted herewith represent, in substance, comments submitted to the Manufacturing Chemists' Association by many of its member companies. It is expected that many of these companies will also submit their comments directly to the Food and Drug Administration. We respectfully urge the Commissioner to carefully evaluate our position on the proposed regulations and ask that appropriate changes be made in any final regulations that may issue. We strongly

urge that, in finalizing any regulations in this area and in evaluating the existing food additive regulations, especially those dealing with indirect food additives, that careful consideration be given to the substantive problems we have discussed regarding the administrative treatment and handling of these materials.

§121.7 Food additives for use in feed and drinking water of animals and food additives that are also new drugs, certifiable antibiotic drugs and/or pesticides.

§121.7 (a) (3)

We strongly urge that this Section be revised to delete the word "chemical." The limitation of acceptable assay methods to "chemical assays" is an unnecessary and illogical restriction as there may be practical biological, physical, or other methods which technically cannot be defined as chemical assays. To limit acceptable assay methods to chemical assays would unduly restrict the constant search by quality control personnel for better and more practical methods of assay, some of which may be better than chemical methods. We point out that neither Sections 505 nor 409 of the Federal Food, Drug, and Cosmetic Act require that assay methods relating to food additives be limited to chemical assay methods.

§121.9 Food additive master files.

§121.9 (a)

We request that the words "submitting or intending to submit a food additive petition" be deleted from the first sentence of this Section. In many instances, the person submitting a food additive master file is doing so for the benefit of another company or person; he, himself, may not intend to submit a food additive petition.

The last sentence of this same paragraph appears to limit the use of these master files to use in food additive petitions. Many materials are used as adjuncts in connection with foods, drugs, colors and pesticides.

In view of the voluminous nature of many of these master files, it is believed that one master file should suffice for all of these fields.

§121.9 (c)

We strongly urge that this subparagraph be deleted from the proposed regulation. Master files are submitted voluntarily and represent a confidential relationship between the Food and Drug Administration and industry. We believe that this relationship should remain, ~~except wherein parts of the master file are incorporated in petitions by reference~~. For our comments on the confidentiality of analytical methods and toxicological data in a food additive petition, please refer to §121.50 (f).

§121.50 Content and form of food additive petitions.

§121.50 (a)

It is requested that the third sentence of this Section be amended to read as follows:

> Any published information used in support of the petition shall be submitted in reprint form, if available, or other suitable photocopy, and, in the event that the published material is readily available to FDA, references can be made to the publications in lieu of furnishing reprints or photocopies.

Under the existing regulation 121.51 "reprints or photostatic copies" of published information are permissible. We submit that the proposed regulations, restricting the petitioner to reprints is not practical and quite often will be impossible to meet. In some instances, reprints are not available for a number of reasons. We urge, therefore, that either reprints or

other suitable photocopies be allowed to support the food additive petition. In addition, where the published material is from a journal or other source readily available to FDA, the petitioner should be authorized to merely cite the journal or other source. This procedure is presently being used in the new drug and certifiable antibiotic areas (§130.37) and should also be adopted in connection with food additive petitions.

It is also requested that the sixth sentence which refers to unpublished scientific studies be amended to read as follows:

> All original unpublished scientific studies supplied in the petition shall include identification and a description of the qualifications including educational background and experience of the technical and professional personnel who are responsible for assuring the accuracy and reliability of such studies. This information need only be furnished for the person or persons who are the responsible head of the laboratory or scientific unit conducting the studies.

We point out that in many instances, it would be impractical to list the identity and qualifications of all the various technicians, chemists, toxicologists and other scientists or technical personnel who participated in the unpublished study presented in the petition. We point out that in regard to new drug applications §130.4 (c), subsection 2.8 (b) requires that the detailed educational and background information need only be given for the person responsible for assuring that the drug has the safety,

identity, strength, etc., which is claimed by the application. We submit that this information should only be required for the person responsible for the scientific studies presented in support of the food additive petition.

§121.50 (b)

Section 121.50 (b) provides for the incorporation by reference of previous submissions where the previous submission ". . . is in a food additive master file kept current by the petitioner, or is in another form of submission not over 10 years old."

We do not understand the intent or meaning of this 10 year limitation. By implication, one could conclude that any data over 10 years old is deemed to be unreliable unless in a master file kept current. We suggest that many submissions whether part of master files (formerly designated "master files" or now designated "food additive master files"), petitions, new drug applications, or data leading to prior sanctions or approvals are of permanent value regardless of age. For example, detailed toxicological studies submitted in 1950 which led to a prior sanction or approval are still valid in many cases and data in food additive petitions filed since the effective date of the Food Additives Amendment may still be valid although over 10 years old.

The net effect of such a 10-year limit on submissions other than master file submissions is to force petitioners to establish master files for intentional or incidental food additive products. We see no justification for imposing this added burden on a petitioner whose formal petition filing should constitute an adequate file record.

The only burden petitioner should have in connection with the reference to data already on file with FDA is a requirement of an accurate description in sufficient detail to provide adequate identification thereof and a statement reaffirming the current validity of any conclusions therein.

For the above reasons, we would suggest deletion of the 10-year limitation for submissions other than those in a "master file kept current."

§121.50 (c)

This section prescribes paper size, line spacing, typing margins, hole punchings, etc., which must be used in connection with petitions. There are many reasons which would make compliance difficult. Some are the following:

(1) Except for legal purposes, the vast majority of U.S. business establishments use only 8-1/2" x 11" paper for correspondence, report writing, etc. It is difficult to obtain any other size from most stationers except on special order at extra cost. Carbon paper of different size presents similar difficulties.

(2) Photoreproduction papers are likewise of 8-1/2" x 11" dimension requiring hand trimming to bring to size prescribed.

(3) It is often desirable for the sake of completeness to include past studies rather than incorporate same by reference. The proposed regulation would require retyping of thousands of pages of text and photoreduction of graphs or pictures to bring to proper size.

(4) As noted in comments on §121.50 (a) above, reprints or photoreproductions of journal articles are usually not of the prescribed size and would require photoreduction or enlargement at needless and great expense.

(5) Similarly, reports of outside investigators (toxicologists, consultants, analysts, etc.,) are all on paper of 8-1/2" x 11" dimension and would require retyping or other reproduction to the size prescribed.

(6) File cabinets, file folders, record boxes, ring binders, etc., are made to accommodate 8-1/2 x 11" paper. While 8" x 10-1/2" paper can be used in these storage containers, 10% of storage space therein is wasted.

(7) To the best of our knowledge, the vast majority of prior submissions have been on 8-1/2" x 11" paper. If §120.9 (b) means that master files must be converted to 8" x 10-1/2" paper "as if it were a portion of a petition" the task would be an impossible burden.

For the reasons stated above and probably additional complications not yet conceived, it is suggested that paper size requirement be deleted. Further, it is requested that double spacing be suggestive rather than obligatory or the requirement modified by "where practical." The retyping of large amounts of available material now in single space does not appear to be a reasonable requisite for food additive petitions.

§121.50 (e) I.B.2.

We request that this Section be amended to read as follows:

> USE. The purpose which the additive is to serve, including, if a direct additive, an estimate of the average quantity of the direct food additive to be expected in the total daily diet of the consumer, and where possible or practical, an estimate of the maximum quantity to be expected in the daily diet of the consumer. The bases for such estimates will be provided in this summary.

The introductory summary of use information required in this Part B for both direct and indirect additives is not practical as applied to indirect additives. Incidental or indirect food additives, whether food packaging or processing materials, do not lend themselves to meaningful estimates of either the average or the maximum levels that might be expected in the total daily diet. Food processing and packaging materials, unlike many direct food additives, generally can be used for across-the-board food contact use, thus coming into contact with countless types of foods under a variety of industrial processing and packaging use situations. Indeed, the petitioner for an indirect food additive in most cases will have no way of knowing all of the many packaging uses that the additive could be used for. We submit, therefore, that estimates of either the average or maximum quantities that might become part of the total daily diet will always be relatively meaningless figures; as such, this information should not be required for indirect additives.

We do not suggest the deletion of this requirement for indirect additives without pointing out that FDA has adopted and is presently following the philosophy that the 100-fold safety factor (100 times the no-effect level found in animals) adequately ensures the safety of indirect food additives and can logically be relied upon to take care of multiple variables such as diverse use and consumption. The text "Appraisal of the Safety of Chemicals in Foods, Drugs, and Cosmetics," published by the Association of Food and Drug Officials of the United States in 1959, was written by FDA staff members. This publication relates the sensitivity of man to various species of animals and reports that the highest ratio is that man is ten times as sensitive as the rat or cat. The safety factor of 100, then, provides another multiple ten-fold difference to protect man from possible adverse effects of a food additive.

The use of the factor of 100 was also endorsed by the Joint FAO/WHO Expert Committee on Food Additives. In the Second Report of this Committee, in the section entitled "Procedures for the Testing of Intentional Food Additives to Establish Their Safety for Use" (See WHO Technical Report Series No. 144, page 17,1958), the Committee concluded:

> "From these various investigations a dosage level can be established that causes no demonstrable effect in the animals used. In the extrapolation of this figure to man, some margin of safety is desirable to allow for any species difference in susceptibility, the numerical differences

> between the test animals and the human population exposed to the hazard, the greater variety of complicating disease processes in the human population, the difficulty of estimating the human intake and the possibility of synergistic action among food additives.
>
> "It will be useful to try to define here the standard daily dietary dose. This is taken to be the amount of the food additive that might be expected to be consumed by an average adult eating a normal diet as determined from some appropriate dietary survey. It should be assumed in these calculations that all the foods likely to be treated with the additive will contain it at the level proposed.
>
> "It is inescapable that some arbitrary factor must be applied in order to provide an adequate margin of safety. Where the maximum ineffective dose in animals is calculated in g/kg body-weight, a margin of safety of the order of 100 has been widely used. In the absence of any evidence to the contrary, the Committee believes that this margin of safety is adequate."

In addition to the deletion of the requirement of an estimated quantity of daily consumption of an indirect additive, we urge that as to <u>direct additives,</u> a petitioner need only estimate the average quantity of the direct food additive to be expected in the total daily diet of the consumer. It should be realized that an estimate of the average quantity will be a somewhat arbitrary figure, but an estimate of the maximum anticipated consumption will be even less meaningful. Again, we point out that the safety factor of 100 in judging the safety of the

particular direct food additive on the basis of animal toxicity studies was designed to take care of the variations in consumption by individual consumers.

§121.50 (e) I. B. 5.

For consistency with this entire Section 121.50, we request that the phrase "daily diet" be used wherever reference is made to the "diet of the consumer."

In addition, we request that the reference to "several species of test animals" in the second sentence be amended to read "in test animals." As a practical matter, normally only two species of test animals are required by FDA.

With respect to the third sentence of this Section, we strongly urge that it be amended to read:

> The margins of safety between the no-effect level in the most sensitive species of test animals and, with respect to direct food additives, the average level ~~as well as~~ and the maximum level, where practical to determine, likely to occur in the total daily diet of the consumer should be stated, taking into consideration previously approved food additive uses for the substance and any toxicologically comparable substance. (Underlined language is new).

To support our request that the requirement for estimating average and maximum quantities of food additives to be consumed in a daily diet be limited to direct additives we refer to our comments on Section 121.50 (e) I. B. 2. In addition, we urge that the consideration given to "comparable substances" be limited to those substances that are known to be "toxicologically comparable."

It is well known that many substances are comparable from the standpoint of their effect or use in food but are not comparable from a safety or toxicity or chemical viewpoint.

§121.50 (e) II (A) (1) (b)

We find this subsection confusing in that several terms used therein appear to be descriptive of the same thing, namely, the chemical specifications for the food additive. Thus, "complete quantitative composition" (b.i.), "food grade specifications" (b.v.), and "reproducibility" (b.vi), all, we believe, mean substantially the same thing and would be best covered by the term "food additive specifications" or "food grade specifications." We submit that either of these terms adequately describes "complete quantitative composition" and "reproducibility" and request these items be deleted.

§121.50 (e) II. A. 1. b. iv.

It is requested that this subsection in describing food additives be amended to read:

> iv. Brief description of manufacturing process(es) and a listing of raw materials and their specifications.

We believe that a "brief description" of manufacturing process(es) should suffice for the purposes of evaluating the safety of the food additive petition by FDA. Detailed processing information would serve no real purpose. We would point out that once a petition is approved and a food additive regulation is published, any manufacturer may produce the additive using any manufacturing process

known, so long as the food additive meets the product specifications established in the applicable regulation and the manufacturer adheres to good manufacturing practice. The question arises as to whether petitioner would be bound to the process described in his petition. If so, the developer of the new facet of food technology would be placed at a severe disadvantage. We believe that the structure of §409 (b) of the Act, which details the requirements for a petition, supports the argument that production process information should be required only in special situations and not as a matter of routine.

In this regard, §409 (b) (2), subsections A through E thereof, lists the basic statutory requirements of data that must be included in a petition. No reference is made to production process information. A separate subsection of §409 (b), namely, (b) (3), deals with the problem of supplying, upon request of the Secretary, "a full description of the methods used in and the facilities and controls used for the production of such additive." Thus, we believe it was the intent of Congress to provide that the Secretary have the right to require such information where relevant because of special circumstances, but not merely as a matter of routine in every petition. Otherwise, a separate section (b) (3) would be meaningless since the requirement of production process information would have been listed in subsection (b)(2) of §409.

Finally, we also urge that the proposed requirement in this subsection for detailing the analytical techniques used to check the raw material specifications be deleted.

The important consideration is the final product specification and validation of the analytical methods used for the final product. In special situations, at the request of FDA, the description of specific analytical techniques could be provided to FDA but certainly they should not be required as a routine matter.

§121.50 (e) II. A. 1. b. v.

We request that the third sentence in this section be revised to delete the word "production" prior to the word "batches." Very often, at the time that the food additive petition is submitted no production batches have been prepared. Thus, it would be impossible for a petitioner to submit data from production batches. Data from either laboratory batches or controlled pilot plant batches should be sufficient to show the range of impurities and by-products to be expected and to show that the proposed specifications can be met.

§121.50 (e) II. A. 2. a. vi.

Deletion of this requirement is suggested. Methods presently available for determining molecular weight distribution of polymeric substances are generally complex and difficult to reproduce. We submit that extractive limitations for polymeric materials in selected solvents adequately reflect low molecular weight fractions which may be suspect toxicologically and that molecular weight distribution adds little to the appraisal of safety.

§121.50 (e) II. A. 2. b. iii.

Please refer to our comments on §120.50 (e) II. A. b. iv. with respect to requirements for manufacturing processes and analytical techniques used to check raw material specifications.

With respect to the specific wording of this paragraph, it is presumed that "adjuvants" referred to therein refers only to such adjuvants as are incorporated in the basic polymer polymerization and not to adjuvants in a resin formulation. To our knowledge, the final resin formulation has not been the subject of a petition nor is it intended that they should be. Such formulations are comprised of the basic resin to which may be added GRAS materials, adjuvants listed under the basic resin regulation and adjuvants otherwise permitted under Subpart F. as in regulations of the types represented by §121.2511, §121.2527 and §121.2541 as examples.

§121.50 (e) II. A. 2. b. iv.

As in §121.50 (e) II. A. 1. v. we submit that production batches are normally not available at the time of petitioning. Hence the word "production" should be deleted.

§121.50 (e) II. A. 2. b. v.

As in comment on §120.50 (e) II. A. 1. b. above, we submit that product specificationsas given in §121.50 (e) II. A. 2. b. iv. of the proposed regulation are the proper measure of reproducibility.

§121.50 (e) II. B.

For the reasons set forth in our comments under Section 121.50 (e) I. B. 2., we ask that the second sentence be amended to read:

> The petitioner shall furnish, if a direct additive, an estimate of the average quantity of the direct food additive to be expected in the total daily diet of the consumer, and where possible or practical, an estimate of the maximum quantity to be expected in the daily diet.

§121.50 (e) II. B. 1.

We strongly urge that the first sentence be amended so that the data required need only be given "if reasonably practical or possible to determine." This qualification should apply to all the data sought in this Section. We point out that the use information and specifications provided in the petition are designed to ensure the expected tolerable and safe level of the additive. The analytical methods are designed to measure the levels of the additive in a particular food or class of foods. The requirement in this proposed Section for showing the fate of the additive in food, conversion information, and possible reaction with other components of the food, is not necessary and very often, cannot be readily determined. As a practical matter, where final assays do not show an acceptable level of the direct additive, a petition is not likely to be approved by FDA.

§121.50 (e) II. B. 2.

Although migration data using actual and simulated foods will determine extent of transfer of a food additive in terms of milligrams per square inch of food contact surface under conditions of use, we submit that it will not provide information from which the average or maximum daily dietary intake can be calculated for reasons stated in §121.50 (e) I. B. 2. above. Accordingly, comments there are equally applicable to this subsection.

§121.50 (e) II. D. 2.

This subsection requires that in the case of the food additive needing a tolerance the regulatory method (analytical procedure) ". . . be satisfactory for application to the raw, processed, and/or finished food." This requirement is presumably intended for direct additives or those substances incidentally present in a final food product because of addition for functional use elsewhere in the production operation. We trust that this subsection is not intended to cover indirect additives as represented by extractives migrating from packaging materials. These extractives are multicomponent in character and in many cases it would be extremely difficult if not impossible to determine accurately amounts of individual components in food per se. Accordingly, it is suggested that this requirement be limited to direct additives and incidental additives (those substances incidentally present in a final food product because of addition for functional use elsewhere in the food production operation).

§121.50 (f)

For the reasons set forth below we request that this Section be amended to read:

> Data in a petition regarding any method or process entitled to protection as a trade secret will be held confidential and will not be revealed unless it is necessary to do so in a regulation, and the petitioner approves of such regulation or in the alternative chooses to withdraw his petition, or in an administration hearing preliminary to any judicial proceedings under the Act. The analytical methods which do not reveal confidential processing information and the general summary of the toxicological basis on which a food additive regulation is based, as such general summary was presented and so designated in the petition, are not considered confidential or entitled to protection as trade secrets. Detailed descriptions of toxicological studies and the raw data of such studies will be considered confidential and entitled to protection from general disclosure. (Underlined language is new.)

It is our unified belief that {in-process} analytical methods and toxicological data should be entitled to protection as are trade secrets and remain confidential. The development of toxicological data and analytical methods are two of the most costly aspects of food additive petitions. While knowledge of {final product} analytical techniques may be necessary for enforcement purposes by FDA, and as such, ultimately disclosed in an enforcement action, no real need is seen for authorizing general public disclosure of such knowledge. Toxicological data, ~~and even a summary thereof~~, is not necessary for enforcement purposes and should not under any circumstances be released as public information, unless the petitioner consents to such release

Arguments that disclosure of methodology and toxicological information are necessary to permit non-FDA experts to evaluate such methods and toxicological data are rebuttable as there are other means available to the FDA for substantiating this information as it appears in the food additive petition.

If it is deemed necessary to publish information concerning analytical methods in a regulation, the petitioner should be given the opportunity, prior to publication, to decide whether he wishes to have such information published or wishes to withdraw his petition.

We take particular note of the fact that Section 301 (j) of the Federal Food, Drug, and Cosmetic Act makes it an offense for any person to use to his own advantage or reveal to other than the secretary or officers or employees of the department or to courts under certain circumstances any information acquired under Sections 404, 409, 505, 506, 507, 704 or 706 concerning any method or process which as a trade secret is entitled to protection. We believe that the arbitrary designation of analytical methods and toxicology as non-confidential ~~is in fact an attempt to usurp the~~ function of the courts and goes beyond the authority granted to FDA by the legislature.

We must strongly request that Section 121.9 (c) be deleted, since the development of methodology may be a major expense involved in the development of a marketable food additive and in addition, we see no reason that the toxicological information in support of a food additive petition, also developed at a major expense to the petitioner, be released for public disclosure. If this request is not honored, we would ask that this Section be amended in accordance with the language set forth above.

§121.51 (c)

If further information or sample is requested by FDA "a reasonable time in advance of 180 days, but is not submitted within such 180 days after filing the petition, the petition will be considered withdrawn without prejudice." It is suggested that "reasonable time in advance of 180 days" is too indefinite and that "180 days" implies that if added data are required the petitioner has no hope for a regulation within the 90 days provided by Section 409 (c) (2) of the Food, Drug and Cosmetic Act and little hope of obtaining a regulation within the statutory limit of 180 days. While we would hope that request for sample and/or additional data be made within 45 days after date of filing,a limit of 90 days would appear equitable. It must be recognized that the time required to provide information or sample may vary from days to months depending upon nature of the request. The petitioner should not be penalized by withdrawal of petition when, in fact, notice in advance of 180 days is not adequate to fill request.

§121.51 (d)

It is respectfully requested that petitioner be provided an opportunity to review language of a proposed regulation prior to publication in the Federal Register if it differs from that proposed by petitioner (§121.50(e)II.F.) and that this subsection be so revised.

Pg 17 to Howe

October 24, 1967

FDCC Subcommittee on FDA Procedural Regulations

TO: Dr. George P. Vincent

Mr. James W. Hulse

Photoprints of Eastman letter of October 11 and attachment thereto are enclosed. I do not believe comments of Mr. Bernard Astill will affect our brief but believe you should have complete file of comments.

Original Signed
W. A. Knapp

W. A. Knapp

WAK:dmk
Encl.

October 20, 1967

Mr. Morgan M. Hoover
Food, Drug and Cosmetic Chemicals
Committee
Manufacturing Chemists' Association, Inc.
1825 Connecticut Avenue, N.W.
Washington, D.C. 20009

Dear Morgan:

Enclosed herewith are original and one copy of drafts of (1) comments on FDA proposed Procedural Regulations and (2) letter of transmittal to Hearing Clerk. In the final document we believe it may be more suitable to follow transmittal comments with comments on proposed regulation in letter proper rather than as attachment but to avoid re-typing and further delay we request that it be sent to the full committee in present form.

To meet the deadline of November 6 we request that committee review immediately and return any further comments by Monday, October 30th, with copies to you and subcommittee members. We assume that MCA staff review can be made simultaneously.

We also assume that MCA office will type final submission and, if necessary, deliver to Hearing Clerk unless you advise differently.

Sincerely yours,

Original Signed
W. A. Knapp

W. A. Knapp

WAK:dmk
Encls.
cc: Dr. G. P. Vincent
Mr. J. W. Hulse

...ich FDCC file

October 13, 1967

FDCC Subcommittee on FDA Procedural Regulations

TO: Dr. George P. Vincent

Mr. James W. Hulse

Attached second draft of comments on FDA Procedural Regulations includes, I believe, all comments not definitely deleted at our last meeting.

I suggest a meeting in latter part of week of October 15th and that Dr. Vincent mention date which might coincide with his weekly visit to New York.

Very truly yours,

Original Signed
W. A. Knapp

W. A. Knapp

WAK:dmk
Encl.
cc: Mr. Morgan Hoover

P.S: Mr. Hoover:
These drafts to you to indicate we are working. Suggest they be destroyed whenever final draft is produced.
WAK

October 4, 1967

FDCC Subcommittee on FDA Procedural Regulations

TO: Dr. George P. Vincent
Mr. James W. Hulse

The attached compilation of comments of FDA Procedural Regulations includes more points of discussion than were agreed to at our last meeting because on reconsideration I felt that the MCA commentary should include all questions we could not ourselves resolve. Also, I felt it would be easier to delete than to compose language at our next meeting now set for Wednesday, October 11 at Morristown if we find no opportunity to meet earlier.

Will you please contemplate tone of introductory remarks to FDA.

Very truly yours,

W. A. Knapp

WAK:dmk
Encl.
cc: Mr. Morgan Hoover

TELEPHONE HUDSON 3-6126

Manufacturing Chemists' Association, Inc.

(FOUNDED 1872)

1825 CONNECTICUT AVENUE, N. W.
WASHINGTON, D. C. 20009

JAMES R. CARNES
SECRETARY-TREASURER

October 11, 1967

Mr. M. C. Stone
Assistant Secretary
Tennessee Eastman Company
Kingsport, Tennessee 37662

Dear Mr. Stone:

Thank you for your letter of October 6 which gives us your comments on the Proposed Food Additives Procedural Regulations.

These should be of considerable interest to the task group within the MCA Food, Drug, and Cosmetic Chemicals Committee which is preparing our comments. So I am sending them along to the chairman of this task group, Dr. William A. Knapp of Allied Chemical, along with his copy of this letter. As you probably know by now, the deadline for filing comments has been extended 30 days until November 6.

Sincerely yours,

J. R. Carnes

JRC:sjg

cc: W. A. Knapp ✓

OCT 9 - 1967

DEPARTMENT OF HEALTH, EDUCATION, AND WELFARE
FOOD AND DRUG ADMINISTRATION
WASHINGTON, D.C. 20204

October 6, 1967

FHR

Mr. F. H. Carman
Manufacturing Chemists' Association, Inc.
1825 Connecticut Avenue, N. W.
Washington, D.C. 20009

Dear Mr. Carman:

Dr. Goddard has asked us to reply to your letter of September 18, 1967, which requests an extension of time for filing comments on the proposed food additive procedural regulations published in the FEDERAL REGISTER of August 7, 1967.

We believe that the proposed revision will aid in the preparation of petitions so that the resultant FDA reviews can be completed more rapidly and with fewer requests to petitioners for clarification of submitted material. Comments so far received have responded favorably to the more detailed descriptions provided by the proposal.

In order to permit your members additional time, we are extending the time for comments for another 30 days or until November 6, 1967.

A notice to this effect will appear in the FEDERAL REGISTER shortly.

Sincerely yours,

J. K. Kirk
Associate Commissioner
for Compliance

ASI 00001791

Pfizer

CHAS. PFIZER & CO., INC.

ESTABLISHED 1849

235 EAST 42nd STREET

NEW YORK, N.Y. 10017

LEGAL DIVISION

October 4, 1967

See first draft of collected comments for amendments

Dr. William Knapp
Allied Chemical Corporation
P.O. Box 405
Morristown, New Jersey 07960

Dear Dr. Knapp:

As agreed upon at our recent meeting, I have drafted comments on numerous sections of the proposed food additive regulations which prompted comment from many member companies of the FDCC Committee.

I have attempted to incorporate the comments of the member companies, following the guidelines agreed upon at our meeting. On those sections where you agreed to draft comments, I have so indicated this fact.

I think that one area we should take a further look at is the area dealing with indirect additives and the many requirements for same in the body of the petition. If at all possible prior to our next meeting, you might discuss the quite detailed requirements for indirect additives with a member of the committee that is more directly concerned with indirect additives than are either your company, Dr. Vincent's, or Pfizer.

I hope this draft will be helpful to you and that we can soon put together a final draft.

Very truly yours,

James W. Hulse

James W. Hulse

JWH:mw
Enclosure

cc : G. P. Vincent, Olin Mathieson
M. Hoover, MCA

INDU TRIAL CHEMICALS DIVISION
Corporation
RESEARCH LABORATORY • P. O. BOX 405 • MORRISTOWN, NEW JERSEY 07960
TEL. (201) 538-8000

October 4, 1967

FDCC Subcommittee on FDA Procedural Regulations

TO: Dr. George P. Vincent
Mr. James W. Hulse

The attached compilation of comments of FDA Procedural Regulations includes more points of discussion than were agreed to at our last meeting because on reconsideration I felt that the MCA commentary should include all questions we could not ourselves resolve. Also, I felt it would be easier to delete than to compose language at our next meeting now set for Wednesday, October 11 at Morristown if we find no opportunity to meet earlier.

Will you please contemplate tone of introductory remarks to FDA.

Very truly yours,

Bill

W. A. Knapp

WAK:dmk
Encl.
cc: Mr. Morgan Hoover

Allied Chemical Corporation

INDUSTRIAL CHEMICAL DIVISION

RESEARCH LABORATORY • P. O. BOX 405 • MORRISTOWN, NEW JERSEY 07960
TEL. (201) 538-8000

September 18, 1967

TO: F.D.C.C. Sub-Committee on F.D.A. Procedural Regulations

Gentlemen:

Attached are comments submitted to S.P.I. Food Packaging Materials Committee for consideration in connection with new F.D.A. Procedural Regulations. The language therein is from one committee member to another and will require revision if presented to F.D.A.

As I see our situation it will be very difficult, if not impossible, to submit comments by October 7 deadline, if they are to be approved by the full committee via letter ballot.

As discussed with you, Jim, we will hold meeting in your office as shortly after September 26 as is convenient for Dr. Vincent, possibly September 28 or 29. This, of course, presumes that we will have some comments from members to discuss.

Morgan Hoover expects to issue letters today: (1) to F.D.A. requesting extension and (2) to committee members requesting comments by September 25.

Very truly yours,

W. A. Knapp

WAK: dmk
Attachment
cc: Mr. M. Hoover, M.C.A., 1825 Connecticut Ave. N.W. Washington, D.C. 200C
Mr. J. W. Hulse, C. Pfizer & Co., 235 East 42nd St., N.Y. 10017
Dr. G.P. Vincent, Olin Mathieson Chem. Corp. 1730 K. St. N.W.
Washington, D.C. 20006

TELEPHONE HUDSON 3-6126

Manufacturing Chemists' Association, Inc.

(FOUNDED 1872)

1825 CONNECTICUT AVENUE, N. W.
WASHINGTON, D. C. 20009

September 18, 1967

TO: Members of the Food, Drug, and Cosmetic Chemicals Committee

SUBJECT: Proposed Revised FDA Food Additives Procedural Regulations

Gentlemen:

At the September 12, 1967 meeting of the FDCC Committee, it was voted unanimously to prepare a recommendation as to what MCA should do regarding the notice of Proposed Rule Making sent to you on August 11 which appeared in the Federal Register, Vol. 32, No. 152 - August 8, 1967 (21 CFR Part 121).

In line with this, your chairman requests that you review this notice immediately and mail your comments no later than Septemb r 25 (Monday) to the chairman of the task group appointed to handle this matter: Dr. William A. Knapp (Allied Chemical Corporation, P.O. Box 405, Morristown, New Jersey 07960) with copies to task group members James Hulse (Chas. Pfizer & Co., 235 E. 42nd Street, New York, New York 10017) and Dr. George P. Vincent (Olin Mathieson Chemical Corporation, 1730 K Street, N.W., Washington, D. C. 20006). Please send a copy to me also.

It is planned to send the recommendation of the task group to the full committee for letter ballot.

It is most important that your comments be sent in promptly so as to give the task group time to prepare a recommendation and ballot the committee prior to the deadline of October 7. We are requesting an extension of time, but of course have no way of knowing whether or not it will be granted.

As you can see, there is very little time for the task group to do its work and for a letter ballot to be made.

Sincerely yours,

Morgan M. Hoover

MMH:sjg