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October 27, 1967

To the Members of the SPI Food Packaging Materials Committee

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

Gentlemen:

The main purpose of this letter is to supply you with copies of some correspondence we have just received from Bob Miller of Hercules whereby Bob has advised us in detail about a set of comments filed by Dr. John Frawley in response to the Food and Drug Administration's Notice of Proposed Rulemaking referenced above.

As you will note, we are herewith enclosing (1) a copy of Bob's letter to us of October 24, (2) a copy of Dr. Frawley's letter to the Food and Drug Administration dated October 23, and (3) a copy of Dr. Frawley's latest article which appears in the August 1967 issue of Food and Cosmetics Toxicology, and which is directly referenced in his comments to FDA.

Generally speaking, we think you will find this material self-explanatory. Suffice it to say that we are most pleased to know about Dr. Frawley's filing and commend it to you. Indeed, we fully expect to add SPI's support to Dr. Frawley's recommendations in the comments we are now drafting, and agree with Bob Miller that it could be very helpful if as many of you as possible see fit to support the point of view expressed by means of your own letters to the FDA Hearing Clerk.

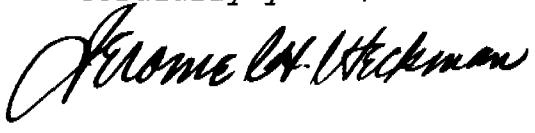
While writing to inform you about the Hercules filing, let us also take this opportunity to bring you up to date on our own efforts. We have already had one meeting with your special Procedural Regulations Subcommittee and have made considerable progress in drafting the SPI comments. We are now anticipating a mailing to the Subcommittee of a semi-final draft of the comments over this coming weekend, after which we shall probably have another meeting on November 1.

Our comments will be considerably more extensive than Dr. Frawley's. As a matter of fact, with all of the presently projected attachments, the comments could constitute a submission of more than 100 pages since, among other things, our plan is to use this opportunity to make such items as the ACS papers and our Guidelines comments a matter of more formal record with the Food and Drug Administration. In other words, since this is really our first opportunity to put all relevant documentation about the difficulties industry experiences with the Food Additives Amendment into a formal FDA docket which will be more conveniently subject to future reference and possible follow-up proceedings, we plan to submit everything we have to support our objections to the way in which the law is being administered.

In light of the way in which the Food and Drug Administration has limited the time available to submit comments, it is unlikely that we shall be able to pre-circulate our document other than to the Procedural Regulations Subcommittee. However, you may be assured that we shall send all Committee members copies of our final comments as soon as the filing has been completed.

We hope that this letter will serve to bring you up to date while we are continuing our work on this project but please do not hesitate to let us know if you have any questions, or desire any further interim information.

Cordially yours,



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HERCULES INCORPORATED

MEDICAL DEPARTMENT

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

October 24, 1967

Mr. Jerome H. Heckman
Keller and Heckman
1712 N Street, N. W.
Washington, D. C. 20036

Dear Jerry:

As we have discussed I am enclosing a copy of the letter we have sent to the Hearing Clerk of the Food and Drug Administration concerning the proposed changes in the Food Additives Procedural Regulations. We agree that the SPI Food Packaging Materials Committee should submit its comments and objections to the proposed regulations and are very much in favor of those to be submitted. However, since FDA has opened the door for comments on changes in the procedural regulations, we believe this is an excellent opportunity to present Dr. Frawley's proposal and try to bring it into the open. We believe his letter to the Hearing Clerk complements the SPI comments and does not conflict in any way.

As you know, Dr. Frawley's BIBRA paper containing his proposal was published in the August 1967 Food and Cosmetic Toxicology Journal and copies have been sent to the Hearing Clerk. We have received permission from the publisher to submit copies to members of the SPI Food Packaging Materials Committee. We also have submitted copies of the enclosed letter and the BIBRA paper to the American Paper Institute.

We would like to have the members of the SPI Food Packaging Materials Committee be informed of our letter to the Hearing Clerk as well as Dr. Frawley's paper and you indicated you could distribute them to the membership. If any individual or company member of the Committee shares our concern and agrees with this proposal, we would welcome supporting letters to the Hearing Clerk. The deadline for receipt of comments is November 6.

Sincerely,

Robert M. Miller

Robert M. Miller
Technical Services Administrator

RMM:vvh
Enclosure
cc: G. W. Ingle

HERCULES INCORPORATED

MEDICAL DEPARTMENT

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

many millions of dollars for research, the potential hazard from food packaging has been clearly defined as remote and in some cases nonexistent, and to continue to perpetuate this wasteful endeavor is beneath the dignity of a scientist and contrary to the best interest of public health.

As a first step toward elimination of this waste of our resources on predictably nonprofitable research, I conducted a review and analysis of as much of the biological and other research bearing on food packaging as I could obtain. I was assisted in this endeavor by scientists in industry and government who contributed published and unpublished reports for this review. In September 1966, I summarized my conclusion at a symposium on food packaging held by the American Chemical Society and in January of this year I presented more extensive evidence in support of my conclusion at the Annual Scientific Meeting of the British Industrial Biological Research Association in London. This latter presentation together with a complete documentation of supporting data has now been published in Food and Cosmetics Toxicology Journal, Volume 5, No. 3, page 293, 1967. Copies of these papers are enclosed.

The basic conclusion which can be drawn from our experience is that any material, suitable for use as a functional component in a food package or container, at a level of 0.2% or less cannot become a component of food at an unsafe level. Consequently, uses of such materials are generally recognized as safe and exempt from the Food Additives Amendment.

The overwhelming support which I have received from scientists in government, university, and industry, not only indicates the general concern of the scientific community, over the waste of scientific talent, but justifies the conclusion that these uses are exempt on the grounds that they are "generally recognized, among experts qualified by scientific training and experience---- to be safe."

Therefore, I encourage the Administration to concur with the scientific community on this conclusion and recommend that the Administration on its own initiative exempt food additive components used at 0.2% or less from the new administrative procedures. Specifically, this can be accomplished by publishing an amendment to Regulation 121.2500 to include a new subparagraph (2) (d) (5) as cited below. Such action will satisfy many of the objections already filed with the Hearing Clerk by others regarding the proposed changes in the Regulation.

The suggested change in subparagraph (2) (d) is presented below with the only change being the addition of subparagraph (5) as underlined.

(d) Substances that under conditions of good manufacturing practice may be safely used as components of articles that contact food include the following, subject to any prescribed limitation:

(1) Substances generally recognized as safe in or on food.
(2) Substances generally recognized as safe for their intended use in food packaging.
(3) Substances used in accordance with a prior sanction or approval.

(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

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.

present at 0·2% or less is safe beyond any reasonable doubt, and consequently, should not be subject to government regulations. When I first advanced this proposal, it was presented within the framework of existing legislation in my country, as a mechanism for correcting some of our mistakes. Tonight, I shall cast my remarks in a different vein, since your country has not yet committed itself to a regulatory procedure on packaging materials.

I do not pretend to be able to propose the best regulatory procedure for Great Britain. There are too many aspects of your business and government operations which I do not understand. However, I can review some of the evolutionary history of our regulatory procedure and suggest some ways to avoid the mistakes we have made.

According to the title of my lecture, I am scheduled to talk about scientific evidence and common sense. For no particularly good reason, I am going to reverse this order and address myself to the common-sense aspects of food-packaging regulations first.

It has always seemed axiomatic to me that in all matters of environmental health, the degree of hazard should define the degree of control. The amount of attention devoted to each problem should be in relation to the hazard. To distribute our limited efforts on any other basis is a form of gambling with public health.

Unfortunately, in this decade of doubt, the scientific community has little control over the area of its explorations. For the most part, the decision is made by national governments as to which area of environmental health should receive concerted attention and at least in the United States, these decisions are not always made on the basis of relative hazard to health. This certainly has been the case for food-packaging materials and it appears that many countries are prepared to follow in our footsteps.

In order to give a certain degree of perspective (which I believe is the foundation of common sense) in this matter, let us reflect on a few of the sources of environmental exposure to chemicals. Obviously the overwhelming majority of the chemicals to which we are exposed are the natural ones which constitute our diet. We tend to overlook these and seem to be content in assuring society that synthetic chemicals will not cause more disease than we already have. Reluctantly, I shall dismiss any further comments on these natural products except to note that it is refreshing to have Dr. L. Golberg and the BIBRA staff occasionally remind us of our prejudice.

If we restrict ourselves to a consideration of synthetic chemicals contributed to our environment, certain obvious sources come to mind: drugs, pesticides, food additives, air pollutants, water pollutants, cosmetics, occupational exposures, household chemicals and food-packaging. As I have already suggested, logically, the amount of time and attention devoted to each of these areas should be in relation to the hazard to health. Sometimes the hazard to health is difficult to evaluate until a significant amount of time and money has been invested. However, after the degree of hazard has been defined, we have the responsibility of accepting the facts and of adjusting our effort accordingly.

In recent years, in the United States, we have invested more industry, government and university time and money on food-packaging materials than on any environmental health problem other than pesticides and drugs. At the same time we have constructed a complex and restrictive maze of government controls which is too involved to be understood by the regulated industries. After 8 yr of effort we have now clearly demonstrated that the return on our investment has been negligible and that the health hazard is slight in comparison with other sources of chemical exposure. Consequently, I believe we have a responsibility to the public of restoring a more equitable balance to our programme. By an equitable balance, I do not mean that we should ignore all aspects of food packaging, but find some

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.

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

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.

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.

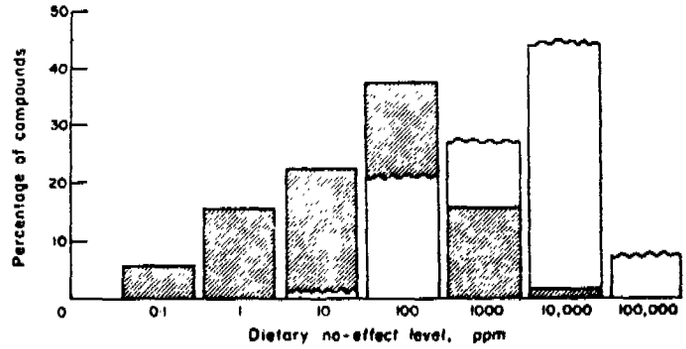

FIG. 1. Histogram showing distribution of "no-effect" levels in 2-yr chronic studies on 220 compounds. Shaded areas denote pesticides and heavy metals, and blank spaces other chemicals.

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

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[a] 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

[a]4% in paper.

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.

level of addition which will contribute no more than 0·1 ppm to the diet. Obviously, 100% of man's diet is not in contact with paper, or any other single type of food container. There are five major types of food container substrates, glass, metal, paper, plastics and regenerated cellulose. In addition, there is a significant portion of food which is not packaged or is packaged in bulk so that most of the individual units are never in contact with the container. It is impossible to get reliable figures revealing the percentage of the food-packaging market shared by each type. However, it is conservative to assume that no more than 25% of man's diet is in contact with any given type of food package or packaging additive.

Table 6 shows this final calculation of the maximum migration to the diet which would result from the use of a component at a level of 1% in the container (as directly measured from the rosin size experiments) and the maximum migration from a level in the container of 0·2%. Undoubtedly, this calculation is an exaggeration for most uses of packaging components which possess greater insolubility or which are used in substrates more resistant to penetration than paper. Nevertheless, it permits the conservative conclusion that any component of an article contacting food which is present in the article itself or its coating at a level of 0·2% or less by weight will contribute to the diet a level which can be of no possible public health significance. Consequently, such trivial uses should not be included on lists of components permitted in food packaging.

Table 6. *Calculation of maximum contribution to the diet*

Maximum total diet migration ...	2 ppm/each %
Maximum diet in contact ...	25%
Concn in package (%)	Maximum concn in diet (ppm)
1·0	0·5
0·2	0·1

As most of you know, I submitted this conclusion to the profession and to the industry in the United States last September. It was worded differently, by describing a level of 0·2% as GRAS*, because of the particular structure of our law. It has received overwhelming and gratifying support and only a few questions have been raised. Our own Food and Drug Administration has authorized me to tell you that they are giving it serious consideration, but could not reach a decision prior to this meeting.

At this point, I can only say that after 6 months, I am even more convinced that the conclusion is sound and conservative; and, that it offers a common-sense approach to a reduction in the extensive waste of time and money of both industry and government on problems which can be of no possible public health significance. From a regulatory point of view, I believe it offers one mechanism of avoiding preparation and constant modification of an omnibus permissive list which experience has shown becomes so unwieldy and complicated as to invite disregard. I do not believe that type of situation is in the best interest of the consumer, industry or government.

Now I have intentionally reserved for my closing remarks a discussion of the few questions and mental reservations about this proposal which have been raised by groups throughout the world. Perhaps, some of these points will answer some of the questions you would like to raise.

*Generally recognized as safe.

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).

I think the time necessary to accomplish this task would be time well spent and would be rapidly recovered in reduced administrative costs.

Let me close with this concept. Your country and mine have a limited number of competent specialists in the field of environmental health. There are many problems facing our society which are competing for their time and attention, as well as for financial support. Included are community air and water pollution, industrial exposures, household chemicals, pesticides, drugs, cosmetics, food additives, confined environments of space cabins and submarines and food-packaging. Having some professional responsibility in all of these segments, I am convinced that food packaging constitutes the least hazard to health of all of these. Yet in recent years it has commanded more time and attention than any other area other than drugs and pesticides. It is our moral and professional responsibility to invest our time and money in research which is likely to provide the greatest protection to health. I suggest that my proposal is a start toward restoration of a proper balance.

APPENDIX

No-effect levels established by 2-yr feeding studies

Compound	No-effect level (ppm)
Acrylamide[1]	40
Aldrin[2]	< 0·5*
Alkyl ketene dimer[3]	1000
Allethrin[4]	4000*
Amiben (2,5-Dichloro-3-aminobenzoic acid)[5]	10,000*
Ammonium sulphamate[6]	500
Antimony chloride[7]	<500†
Arsonic acid[8]	50*
l-Ascorbyl palmitate[9]	2500
Barium chloride[7]	2000†
Benzene hexachloride, technical (BHC)[7]	10*
α-Benzene hexachloride (α-BHC)[7]	10*
β-Benzene hexachloride (β-BHC)[7]	<10*
γ-Benzene hexachloride (γ-BHC)[7]	50*
δ-Benzene hexachloride (δ-BHC)[7]	<800*
Benzoic acid[10]	5000
Biurea[11]	7500
Butoxypolypropylene glycol (mol wt 800)[1]	640
Butylated hydroxyanisole (BHA)[10]	5000
Butylated hydroxytoluene (BHT)[12,13]	1000
Butyl 3,4-dihydro-2,2-dimethyl-4-oxo-1, 2*H*-pyran-6-carboxylate (Indalone)[14]	40,000
1,3-Butylene glycol[15]	30,000
2-(*p-tert*-Butylphenoxy) isopropyl 2′-chloroethyl sulphite (Aramite)[16]	100*
tert-Butylphenyl salicylate[1]	2000
Cadmium chloride[7]	<10†
Calcium disodium ethylenediamine-tetraacetate[1,17]	5000
Captan[4]	1000*
Carbarsone (*p*-Ureidobenzenearsonic acid)[18]	1000
Carboxymethylcellulose (CMC)[19]	10,000
β-Carotene[20]	1000
Catechol[21]	1250r
Chlorbenside (*p*-Chlorobenzyl *p*-chlorophenyl sulphide)[4]	20*
Chlorbenside, sulphone derivative[4]	20*
Chlordane[7]	2·5*
bis(*p-Chlorphenoxy*)*methane*[1]	300
p-Chlorophenyl *p*-chlorobenzene-sulphonate[1]	25*
Chlorpropamide[22]	1250
Chlortetracycline[22]	10,000
Citrus Red No. 2 (C.I. (1956) No. 12,156)[24]	500
Copper chromate[4]	500*
Cube[25]	50*
Cupric chloride[4]	500†
Dalapon[1]	300*
D & C Orange No. 5[26]	10,000
D & C Orange No. 10[26]	10,000
D & C Red No. 9[27]	500
D & C Red No. 10[26]	500
D & C Red No. 21[26]	10,000
D & C Red No. 27[26]	10,000
DDD (TDE)[4]	10*
DDT[7]	1*
Dehydroacetic acid[1]	1000
Diazinon[4]	0·75*
Dichlone[1]	<500*
1,1-*Dichloro*-2,2-*bis*(*p*-ethylphenyl)ethane (Perthane)[4]	100*

*Pesticide
†Heavy metal

r—Tumours at higher levels.

Appendix (contd)

Compound	No-effect level (ppm)
2,4-Dichloro-6-*o*-chloroanilino-s-triazine (Dyrene)[4]	5000*
2,4-Dichlorophenoxyethyl sulphate, sodium salt[1]	200*
4,4′-Dichloro-*α*-trichloromethyl-benzhydrol (Kelthane)[4]	20*
Dicyandiamide[19]	2500
Dieldrin[3]	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[1]	1300
Di-*n*-hexyl azelate[20]	5000
Di-isobutyl adipate[1]	5000
Dilauryl thiodipropionic acid[21]	30,000
Dimethyl carbate[14]	10,000
2,4-Dimethyl-2-methylene-1,2,4-thiadiazolidine-5-thione[1]	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[22]	600*
3,5-Dinitro-*o*-toluamide[1]	62*
Diphenyl[4,23]	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)[24]	2000
Dodecyl gallate[10]	350
Dodine[4,25]	50*
Endosulphan[4]	30*
EPN[4]	5*
Epoxidized soybean oil (Paraplex G-60)[26]	25,000
Epoxidized soybean oil (Paraplex G-62)[26]	5000
4-Ethoxyphenylurea (Sucrol, dulcin)[27]	<1000
Ethoxyquin[4]	120*
Ethyl acrylate[28]	100
Ethyl 4,4′-dichlorobenzilate[4]	50*
2-Ethyl hexanediol-1,3[14]	40,000
2-Ethylhexyl diphenyl phosphate (Santicizer 141)[29]	1250
Ethyl phthalyl ethyl glycolate[1]	5000
Fast Green FCF[40]	10,000
FD & C Blue No. 1[41]	5000
FD & C Blue No. 2[41]	1000
Ferbam[4]	200*
Glycerol[42]	100,000
Glycerol monostearate[43]	250,000
Gum guaiac[44]	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[1]	50,000
Hydroquinone[21]	10,000†
d-Isoascorbic acid[21]	10,000
d-Isoascorbyl palmitate[21]	2500
Isopropyl *N*-(3 chlorophenyl) carbamate (CIPC)[48]	2000*
4,4′-Isopropylidene bis(2-Isopropyl-phenol)[1]	1000
Light Green SF Yellowish[40]	10,000
Malathion[4]	100*
Maleic hydrazide[4]	20,000*
Maneb[4]	25*
Melamine–formaldehyde resin (Parez 607)[18]	50,000
Mercaptobenzothiazole[4]	120*
Mercury acetate[7]	2·5*
Methoxychlor[7,49]	200*
O-Methyl-*O*-(4-*tert*-butyl-2-chlorophenyl) methylphosphoroamidothioate (Ruelene)[1,50]	30*
O-Methyl-*O*-(2,4-dichlorophenyl) isopropylphosphoramidothioate[3]	10*
Methyl *p*-hydroxybenzoate[21]	20,000
Methyl methacrylate[28]	100
Methyl naphthaleneacetic acid[7]	2500*
Methylpolysiloxane[1]	3000
Methyl salicylate[52]	10,000
Monuron[4]	250*
1-Naphthyl-*N*-methyl carbamate[1]	200*
α-Naphthylthiourea[48]	50*
Nicotine[4]	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[21]	10,000
Phenyl mercuric acetate[7]	0·1*
o-Phenylphenol[60]	2000*
Pimaricin[61]	500
Piperonyl butoxide[6]	700*

Appendix (contd)

Compound	No-effect level (ppm)
Polyacrylamide (Separan AP30)[69]	10,000
Polyacrylamide (Separan NP10)[69]	10,000
Polyethylene glycol (mol wt 200)[1]	40,000
Polyethylene glycol (mol wt 400)[1]	20,000
Polyethylene glycol (mol wt 1500)[1]	2000
Polyethylene glycol (mol wt 1540)[1]	40,000
Polyethylene glycol (mol wt 4000)[1]	40,000
Polymerized turpentine resin[5]	2000
Polyoxyethylene(20)sorbitan monolaurate (Tween 20)[63]	50,000
Polyoxyethylene(20)sorbitan monooleate (Tween 80)[63]	50,000
Polyoxyethylene(20)sorbitan monopalmitate (Tween 40)[63]	50,000
Polyoxyethylene(20) sorbitan monostearate (Tween 60)[64]	50,000
Polyoxyethylene(20)sorbitan tristearate (Tween 65)[63]	50,000
Polyoxyethylene(8)stearate (Myrj 45)[64]	20,000
Polyoxyethylene(40)stearate (Myrj 52)[64]	50,000
Ponceau 3R (C.I. (1956) No. 16,155)[66]	5000
Ponceau SX (C.I. (1956) No. 14,700)[66]	50,000
Potassium bromate[68]	627
1-*n*-Propoxy-2-amino-4-nitrobenzene (P-4000)[67]	<1000
Propyl gallate[51]	10,000
Propyl *p*-hydroxybenzoate[51]	20,000
Pyrethrum[7]	1000*
Rosin, disproportionated[46]	500
Rosin, fully dimerized[46]	500
Rosin, partially dimerized[46]	500
Rotenone[7]	2*
Saccharin[57]	10,000
Selenium[7]	<3*
Sodium alginate[67]	50,000
Sodium alkylbenzenesulphonate[68]	5000
Sodium bisulphite[69]	500
Sodium chromate[70]	300*
Sodium cyclamate[57]	10,000
Sodium 2,2-dichloropropionate[1]	300
Sodium dioctyl sulphosuccinate[71]	5000
Sodium hexametaphosphate[68]	5000
Sodium lauryl glycerylsulphonate[78]	5000
Sodium lauryl sulphate[71]	10,000
Sodium lauryl trioxyethylene sulphonate[73]	5000
Sodium monofluoracetate[7]	<5*
Sodium nitrate[78]	10,000
Sodium β-sulphopropionamide[1]	10,000
Sodium tripolyphosphate[68]	5000
Sorbic acid[10]	50,000
Sorbitan monopalmitate (Span 40)[63]	50,000
Sorbitan monostearate (Span 60)[64]	50,000
Sorbitan tristearate (Span 65)[63]	50,000
Sulphenone (*p*-chlorophenyl phenyl sulphone)[4]	100*
Tall oil rosin, pale[46]	2000
Tartar emetic (Potassium antimonyl tartrate)[4]	<500†
Tartaric acid[74]	12,000
Tartrazine[75]	10,000
Terpene polychlorinates (Strobane)[4]	50*
Tetradifon[4]	300*
Thiodipropionic acid[81]	30,000
Thiourea[76]	500*
Thiram[4]	200*
Toxaphene[7]	25*
2,4,5-Trichlorophenoxyethyl sulphate, sodium salt[1]	200
Tri(polynonylphenyl) phosphite (Polygard)[77]	3300
Tylosin[78]	10,000
Vinyl chloride–vinyl acetate copolymer[79]	120,000
Vinylidene chloride–vinyl chloride copolymer[1]	50,000
Wood rosin, dark[46]	500
Wood rosin, fully hydrogenated[46]	500
Wood rosin, hydrocarbon insoluble residue[46]	500
Wood rosin, pale[46]	2000
Wood rosin, partially hydrogenated[46]	2000
Yellow AB[80]	500
Yellow OB[80]	500
Zineb[4]	500*
Ziram[4]	250*

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