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FROM: T. G. Grumbles
DATE: February 3, 1989

Interoffice Communication

SUBJ: NEW ACGIH TLV BOOKS

VISTA

Enclosed is a copy of the 1988-89 TLV Book for your reference. Additional copies, if needed, may be obtained from ACGIH in Cincinnati.

Tom dlj

T. G. Grumbles

dlj
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To Paul Warner
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Date 2/6 TGG: JCL: MMG: AJO: RE
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FYI - latest intan on
Chemistry Data requirements
for INDIRECT Food Additive
petitions.

TGG

VVV 000006722

RECOMMENDATIONS FOR CHEMISTRY DATA

FOR

INDIRECT FOOD ADDITIVE PETITIONS

THESE RECOMMENDATIONS WERE DEVELOPED TO ASSIST PETITIONERS IN THE PREPARATION OF THE CHEMISTRY PORTION OF PETITIONS FOR INDIRECT FOOD ADDITIVES. THE LAW, REGULATIONS AND SPECIFIC LETTERS TAKE PRECEDENCE OVER THESE INFORMAL RECOMMENDATIONS.

THIS EDITION SUPERSEDES THE INDIRECT ADDITIVE GUIDELINES ISSUED IN MARCH, 1976.

DIVISION OF FOOD CHEMISTRY & TECHNOLOGY
CENTER FOR FOOD SAFETY & APPLIED NUTRITION
FOOD & DRUG ADMINISTRATION
DEPARTMENT OF HEALTH & HUMAN SERVICES
WASHINGTON, D.C. 20204

SEPTEMBER, 1988

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I. Indirect Food Additive Petitions

Section 409(a) of the Federal Food, Drug and Cosmetic Act (the Act) states that use of a food additive shall conform to a regulation prescribing the conditions under which the additive may safely be used. The definition of food additives (Section 201(s)) includes substances used in the processing, packaging, holding, and transporting of food that have no functional effect in the food but which may reasonably be expected to become components of food. These latter substances are known as indirect food additives. Specific regulations are established to cover the safe use of indirect food additives. These regulations are set forth in Title 21 of the Code of Federal Regulations (21 CFR) parts 175-179. In addition to the specific regulations, 21 CFR 174.5 lays out general safety requirements for all indirect food additives.

Anyone intending to use an additive that does not conform to an existing regulation must file a petition proposing the issuance of a new regulation. Section 409(b)(2) of the Act sets forth the statutory requirements for such a petition. These requirements include descriptions of the following: (1) the identity of the additive, (2) proposed conditions of use of the additive, (3) technical effect data, (4) methods for the analysis of the additive, and (5) full reports of investigations made with respect to the safety of the additive. These requirements are described in greater detail in 21 CFR 171.1. This section also specifies the format of the petition.

These recommendations for indirect food additive petitions are intended to amplify and explain the statutory chemistry requirements for indirect food additive petitions.* (Phrases in quotations are taken from the Act, as amended January, 1980.) Considering that the science and technology of food-packaging and food-contact articles as well as the scientific basis for evaluating exposure to indirect food additives are continually evolving, these recommendations will be periodically updated to address new developments for these areas. For indirect food additive applications that are not explicitly covered by these recommendations, appropriate information should be developed in collaboration with FDA.

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* Separate recommendations pertaining to sanitizer formulations and direct food additives are available upon request from the Division of Food and Color Additives (HFF-330), Food and Drug Administration, 200 C Street, SW, Washington, DC 20204.

A. Identity.

"The name and all pertinent information concerning such food additive, including, where available, its chemical identity and composition."

Identity information is necessary to specify uniquely the additive for which a regulation is sought and to identify substances that may migrate into food. These substances include not only the petitioned additive itself, but also impurities in the additive that have no functional.

Information identifying the food additive should be as complete as possible with respect to the name, composition, and method of manufacture of the additive. Such items include:

1. Chemical Name. The IUPAC or Chemical Abstracts name is acceptable.

2. Common or Trade Names. Common and/or trade names should not, however, be the only means of identification of materials. The Food and Drug Administration does not maintain a dictionary of commercial names. Identifying materials in this manner may cause delays in processing the petition.

3. Chemical Abstracts Service (CAS) Registry Number, where possible. CAS Registry Numbers for new compounds and assistance with nomenclature can be obtained by writing to the Director of Nomenclature, Chemical Abstracts Service, Ohio State University, Columbus, Ohio 43210. A copy of appropriate CAS listings should be provided for the additive and, in some instances, materials used in its synthesis.

4. Chemical Formulae, Structures and Molecular Weights for Single Compounds or Components of Commercial Mixtures. For polymers submit the weight average or number average molecular weight, the molecular weight distribution and the methods for their determination. If the molecular weight is not readily obtainable, furnish other properties of the polymer that are functions of the molecular weight, such as intrinsic or relative viscosities or melt flow indices.

5. Composition. A full description of the composition is needed to compile a list of potential migrants to food.

Provide the following information:

a. A complete description of the manufacturing process, including purification procedures. Submit the chemical equations for the principal reactions.

b. A list of reagents, solvents, catalysts, purification aids, etc., used in the manufacturing process, the amounts or concentrations used, and their specifications.

c. Chemical equations for known or likely side reactions occurring during manufacture. Include catalyst degradation reactions, if known.

d. Concentrations of all major impurities together with the supporting analytical data or calculations. In the case of polymers, include concentrations of residual monomers.

Those data and information unavailable for public disclosure as specified in 21 CFR 171.1(h)(2) should be so noted.

6. Properties. Submit the physical and chemical specifications of the additive. Provide data that can uniquely characterize the additive. In most cases an infrared spectrum is sufficient, but occasionally other properties, such as visible and ultraviolet absorption spectra or nuclear magnetic resonance spectra, are more useful. Properties that can affect migration potential, such as solubilities of additives in food-simulating solvents, and, in the case of polymers, glass transition temperatures, and possible ranges for densities and melt flow indices, should be reported.

7. Analyses. If the additive is a component of an otherwise regulated material, e.g., an antioxidant in a regulated polymer, provide analytical methods for determining the additive in that material. Supporting analytical data should be submitted. Refer to Section D.3. of these guidelines.

B. **Use**

"A statement of the condition of the proposed use of such additive, including all directions, recommendations, and suggestions proposed for the use of such additive..."

Clearly state the proposed use of the additive - for example, as a wet strength agent used in the manufacture of paper and paperboard. The following specific information is needed:

1. The maximum use level of the additive and the types of food-contact articles in which it may be used. For indirect additives "use level" refers to a concentration of a substance in the food-contact article, not in the food itself. State the range of possible uses -- films, molded articles, coatings, etc., and, if known, report the maximum thickness and/or weight per unit area of these articles. Migration levels in food are related to the levels of the additive in the food-contact material. A method for analysis of the additive in the food-contact article should be submitted to provide a means of ensuring that the maximum use level is not exceeded.

2. Types of food (with examples) that will be in contact with the additive and the maximum temperature and time conditions of food contact. Classifications that may be helpful are given in 21 CFR 176.170(c), Table 1 (Types of Raw and Processed Foods) and Table 2, which lists various conditions of use. These tables are not intended to be all inclusive, however.

Migration into food is dependent on the nature of the matrix in which the additive is used, the chemical structure of the additive, the type of food in contact with the additive and the temperature and time of food contact. It is important that specific use information be provided so that appropriate extraction protocols can be devised (Section D).

3. Draft of proposed regulation. The petition should contain a draft of the proposed regulation that should include, where applicable, limitations on maximum level of use, types of food and conditions of use. Select the content and format of the draft regulations using examples from the indirect food additive regulations, which appear in 21 CFR, Parts 175 through 179.

C. <u>Intended Technical Effect</u>

"All relevant data bearing on the physical or other technical effect such additive is intended to produce, and the quantity of such additive required to produce such effect."

Present data to show that the additive will have the intended technical effect and that the proposed use level is the minimum level reasonably required to accomplish the intended technical effect [21 CFR 171.1(c)]. For an indirect food additive, "technical effect" refers to the effect on the food package or processing equipment, not on the food. An example would be the effect of an antioxidant on a particular polymer. In the case of a new food-contact polymer, present data that demonstrate the particular properties of the polymer that are useful for food contact applications. This information is frequently present in available product technical bulletins.

In cases where the use level of an additive is self-limiting, provide supporting data.

D. Migration & Analytical Methodology

"A description of practical methods for determining the quantity of such additive in or on food, and any substance formed in or on food, because of its use."

A petitioner shall provide information sufficient to permit estimation of the daily intake of the additive. From analyzed or estimated levels of an additive in food or food-simulating solvents, the Division of Food Chemistry and Technology (DFCT) calculates the concentration of the additive expected in the daily diet. A more complete discussion of this topic is given in Section E and Appendix IV of these guidelines.

From a given concentration in the daily diet, the estimated daily intake (EDI) is calculated as the product of that concentration and the total food intake, assumed to be 3000 grams per person per day (solids and liquids). A concentration in the daily diet of 2 ppm corresponds to an EDI of $2 \times 10^{-6} \times 3000$ gms or 6 mg/person/day.

Both the concentration in the daily diet and the EDI are used in the safety evaluation of an additive. The concentration in the daily diet helps to determine the type of animal feeding studies required to establish the safety of the additive under the proposed conditions of use. The Division of Toxicology calculates an acceptable daily intake (ADI) based on the results of the feeding studies. If the EDI is lower than the ADI, use of the additive can be permitted. If this is not the case, the petitioner can sometimes obtain a regulation by limiting the proposed uses, which in turn reduces the EDI.

The concentration of an additive in the daily diet may be calculated from measured levels in food or in food-simulating solvents. Although FDA has always accepted reliable analyses of additives in real foods, in practice many analytes are difficult to measure in food. Alternatively, petitioners may submit extraction data obtained with food-simulating solvents, that can reproduce the nature and amount of extraction of the indirect additive by food. Because an additive may contact many different foods having varying processing conditions and shelf lives, it is necessary that the submitted extraction data simulate the most severe temperature/time conditions to which food will be exposed while in contact with the food-contact article containing the additive.

Before undertaking extraction testing, the petitioner should carefully consider the potential uses of the additive. If, for example, use at temperatures no higher than room temperature is anticipated, it makes little sense to conduct extraction experiments that simulate high temperature food contact because such experiments would lead to elevated levels of the additive in the food simulants and, consequently, to increased toxicity testing requirements. In some cases where the use level of the additive is low, it may be possible to dispense with extraction testing altogether by calculating worst-case migration. The following example illustrates this approach: Consider an adjuvant added prior to the sheet forming operation in the manufacture of paper. If it is found by analysis or calculation that the final concentration in paper cannot exceed 1 ppm and the basis weight of the finished paper is 50 pounds/3000 ft^2, or 50 mg/in^2, then the maximum weight of additive per unit area of paper is $1x10^{-6}$ x 50 mg/in^2 = 0.000050 mg/in^2. If all the additive migrates into food and 10 grams of food is in contact with 1 square inch of paper (DFCT's usual assumption), the maximum concentration in food would be 5 parts per billion. Since the resulting daily intake of the additive would be quite low, extraction experiments would ordinarily not be required.

When it is necessary to carry out extractions, however, standard procedures should be followed to ensure reproducibility, to allow for comparisons with data obtained from different laboratories with different additives, and most importantly to allow for comparisons with the migration studies in the literature that have been carried out using real foods.

1. Design of the Extraction Experiment

a. Extraction Vessel. When use is anticipated with one particular package, such as a beverage bottle, packages may be filled with food-simulating solvents and extracted. For more general uses or when the package surface area does not produce sufficient extractives for adequate characterization, an extraction cell should be used in which a specimen of known surface area is extracted by a known volume of solvent. The recommended two sided extraction cell is described in an article by Snyder, R.C., and Breder, C. V. (1985, J. Assoc. Off. Anal. Chem., 68 (No. 4), 770). Although this specific cell may not be universally applicable, the essential features of the cell are now recommended by DFCT. These are:

(1) Polymer plaques of known surface area and thickness (generally twice the maximum anticipated thickness) are separated by inert spacers (such as glass beads) so that solvent flows freely around each plaque. Exposure to the solvent is two-sided.

(2) The cell is subjected to mild agitation to minimize any localized solubility limitation that might result in mass-transfer resistance in the simulant phase.

(3) Headspace is minimized, and gas-tight and liquid-tight seals are maintained. (Minimum headspace and gas tightness are of lesser importance if the migrant of interest is non-volatile.)

For applications in which use of such a cell design is not suitable, such as laminate constructions, the petitioner should devise an alternative cell. FDA would be glad to comment on any such cell.

b. Extraction Sample. Some important considerations are the following:

(1) Formulation: Use the highest proposed concentration of the additive in preparing formulations for extractions. Information which characterizes resin samples used in testing should be provided. This should include the concentrations and identities of other components that may be

present, the chemical composition of the resin (including comonomer content where appropriate), molecular weight range, density, and melt flow index. If the formulation is plasticized, the most highly plasticized formulation should be used for testing.

(2) Sample Thickness & Surface Area: Report both the thickness and surface area of the sample extracted. When a sample is extracted by immersion, the surface area of both sides can be used to calculate mg/in^2 if the sample is of sufficient thickness that the initial additive concentration at the center of the plaque is unaltered by migration that occurs from both sides of the plaque.

Practically, DFCT considers migration to be independent from both sides if the sample thickness is at least 0.05 cm (20 mil or 0.020 in) and not more than 25 percent of the additive has been extracted at the end of the experiment. If either of these conditions is not met, the surface area of only one side should be used in the calculation. In such a case, the final regulation may have to limit maximum film thickness.

(3) Degree of Polymerization: If the additive is a polymer or will be used in a polymer, extract the polymer with the lowest average molecular weight.

c. Volume of Extracting Solvent. The volume should ideally reflect the volume-to-specimen surface area ratio expected to be encountered in actual food packaging. A ratio of 10 mL/in^2 is acceptable. In general, other ratios may be acceptable if migration levels do not approach concentrations reflecting the partition limit. Precipitation of the additive from solution or a cloudy solution are indications that this limit is being reached. The volume-to-surface area ratio should always be reported.

d. Extraction Conditions. Previous test protocols recommended the following four food simulants:

Distilled Water	Non-acid foods, pH above 5.0
3% Acetic Acid	Foods with pH 5.0 or below
8 or 50% Ethanol	Foods containing alcohol
Heptane	Fatty foods

Recent studies have demonstrated that migration into certain aqueous foods is higher than would be predicted from migration into water or 3% acetic acid. Addiionally, it has been shown that migration into an exaggerated migration into fatty foods by factors varying over several orders of magnitude depending on the particular polymer. Additional discussion on this subject is found in Appendix II, 1. WE NOW RECOMMEND THE FOLLOWING FOOD-SIMULATING SOLVENTS:

Aqueous & Acidic Foods. (176.170(c), Table I. Food Types I, II, IVB, VIB, VIIB)	8% Ethanol is the recommended solvent. In certain specific applications, e.g., if the polymer or adjuvant is acid sensitive or if transesterification occurs in ethanol solutions, separate extractions with water and 3% acetic acid may be required.
Alcoholic Foods. (Food Types VIA, VIC)	8 or 50% Ethanol. Actual alcohol concentration may be substituted (see discussion Appendix II).
Fatty Foods. (Food Types III, IVA, V, VIIA, IX)	If possible, use a food oil (corn oil or HB307, a mixture of synthetic triglycerides, is recommended).

In many cases, analysis of the migrant in food oil will not be practicable, and simple solvents must be used. There does not appear to be one solvent that will effectively simulate a food oil for all polymers. A list of various polymers and their fatty-food simulants appears in Appendix I of these recommendations. For other polymers the petitioner should consult with DFCT concerning use of a fatty-food simulant.

e. Temperature & Time of Extraction. Conduct extractions under the most severe conditions of temperature/time for which a regulation is requested (Appendix II). If the intended application of the packaging material involves contact with food at temperatures higher than room temperature, conduct the extractions at the highest expected temperature for the maximum time period. In many instances, the short time periods of elevated temperature-food contact are immediately followed by extended periods of storage at ambient temperatures. For such applications, the extraction protocols are intended to simulate the extraction that may occur during the entire food contact scenario. Test conditions and use-temperature limits should not exceed the temperature at which the material is functional. Should inspection of test plaques or articles following extraction testing reveal that the test samples have been softened and deformed as a result of the high test temperatures, the test material will probably be considered unacceptable for such use temperatures and the migration results will be considered invalid. Selected protocols are given in Appendix II; however, depending on the particular food-contact application, a specific protocol may be devised in consultation with DFCT.

For room-temperature applications, the appropriate extraction temperature is 120°F. Short-term accelerated testing at this temperature permits an estimation of the migration that may occur over an extended shelf life at room temperature. For refrigerated or frozen food applications, the extraction temperature is 70°F.

In general, plastic articles should be extracted for ten days at 120°F for room-temperature applications. For polymers, such as polyolefins, that are used with food at temperatures above their glass transition

temperatures, the migration values at ten days will be used to calculate the concentration in the daily diet.

Studies of temperature dependence of migration have generally shown that migration levels after ten days at 120°F are roughly equivalent to levels after extended time periods (6-12 months) at 70°F.

For polymers, such as polyethylene terephthalate, that are used with food at temperatures below their glass transition temperature, a change in temperature generally produces a smaller change in migration rate. Therefore, migration data obtained over ten days at 120°F should be extrapolated to 30 days (if migration is observed to follow a predictable time relationship) in order to better approximate levels expected after extended time periods at 70°F. The petitioner may wish to carry out extractions for 30 days to avoid uncertainties in extrapolation. Of course, if a petitioner provides appropriate data that demonstrate that a different extrapolation period is more appropriate for a given additive/polymer combination, such information may be used for evaluating additive exposure.

For restricted uses where the maximum shelf life and food-contact temperature of an article are known, it is always possible to carry out extractions for the maximum shelf life under temperature conditions approximating expected use. Petitioners may want to consult DFCT before undertaking such tests.

Extractions should be done in triplicate. Portions of the extracts should be analyzed at intervals during the experiment. Recommended times for a ten-day extraction are 2, 24, 96, and 240 hours. A solvent blank should be determined on a portion of the solvent using a test cell identical to that used for the extractions, but without exposure to the food-contact surfaces.

It is important to realize that the appropriate extraction conditions for a new food additive are <u>not</u> those described in 175.300, 176.170 or other sections in 21 CFR. These published "end-test" extractions are quality control test methods that are intended to permit the determination of whether a particular product

is in compliance with the specifications of already-regulated materials. They generally bear no relation to migration testing required for evaluating probable exposure to a new food additive.

Selected extraction protocols for conditions of use, specific polymers and other food-packaging materials appear in Appendix II of these recommendations.

2. Characterization of Extracts & Data Reporting

Extracts should be analyzed for the migrants resulting from the petitioned use. If the petition is for a polymer, the amount and nature of total extractives should be determined. Ordinarily, the total amount is determined by weighing. The nature of the extractives, which may include monomers, oligomers, adjuvants, catalyst residues, etc., is determined by any suitable chemical or physical test, such as UV-visible spectroscopy, atomic absorption spectroscopy, or gas or liquid chromatography. The quantitation limit and selectivity of the method(s) should be indicated. If quantitation of individual migrants is not possible, it is necessary (at the very least) to show the distribution of the extractives between organic and inorganic fractions by solvent fractionation (e.g., the fraction of the total extractive residue that is soluble in chloroform).

Extracts from unregulated polymers should be analyzed for constituent monomers. Alternatively, monomer concentrations may be calculated using the known residual level in the polymer, assuming that all of the residual monomer migrates into food and that ten grams of food is in contact with one square inch of food-contact article.

If the petition is for an adjuvant, not for a new polymer, it is normally necessary to analyze the extracts only for the adjuvant. Occasionally, however, it may be necessary to quantitate in the extract impurities or decomposition products present in the additive in addition to the additive itself. An example would be the presence of carcinogenic impurities in the additive.

Report results in terms of milligrams of substance extracted per square inch (mg/in^2) of surface area. Although migration amounts are often expressed in terms of either mg/dm^2 or mg/in^2, DFCT prefers the non-standard unit mg/in^2 to facilitate conversion to concentration in food. If ten grams of food are in contact with one square inch of

packaging surface, migration of 0.01 mg/in^2 corresponds to a concentration in food of 1 ppm. For specialized food contact applications where an assumed ratio of 10 g food per in^2 is not appropriate, appropriate information should be provided.

3. Analytical Methodology

Submit the following for each method:

a. Complete description of the method. A reprint of the journal, or text article should describe the method in sufficient detail so that it could be carried out by an experienced analytical chemist. The procedure's accuracy, precision, selectivity and lower quantitation limit should be described. Statements describing the quantitation limit should accompany the description.

b. Standard curves. The standard curve, or calibration curve, should be obtained by analyzing a prepared medium spiked with several known amounts of analyte to obtain concentrations both greater than, and less than, the concentration of extracted analyte. The prepared medium may be the pure solvent, a solution of known ionic strength, etc. It is important that the data points from which the standard curve is derived bracket the concentration of the migrant in the extract. An analyte concentration of 1 ppm determined from a standard curve obtained from concentrations of 10, 15 and 20 ppm would be unacceptable.

c. Examples of adequately identified spectra or chromatograms. In the special case where the absence of a substance is to be demonstrated at a certain level, spectra or chromatograms of the extracts and extracts spiked at the claimed limit of detection should be submitted.

d. Examples of calculations relating the data obtained from instrumental methods to the reported levels (milligrams of migrant(s) per square inch of surface area extracted). Such calculations provide the reviewer with an internal check on the reported method.

e. Validation of the analytical methods. Validation of the method's intended use, the determination of

accuracy and precision, usually involved replicate analyses of appropriate matrices spiked with known amounts of the additive at levels similar to the levels encountered in the migration studies and determination of the percentage recovery of the spiked additive.

In many cases where a polymer adjuvant is the subject of interest, extracts of the same polymer formulated without the adjuvant may serve as the matrix for spiking and recovery measurements. However, other validation procedures may be appropriate depending on the particular analysis. For example, analysis of the same extract by two completely independent analytical methods would be acceptable validation. Similarly, the method of standard additions is an acceptable alternative in certain cases, such as metal analyses by atomic absorption spectrometry. In this case, the matrix should be spiked at two separate concentrations (at least) in addition to the unspiked concentration, and the linearity of the standard addition curve verified by calculation of the least squares correlation coefficient.

The usual validation procedure consists of spiking/recovery studies. Recovery is defined as the difference between measured analyte levels in the spiked matrix and the unspiked matrix. Percent recovery is the recovery divided by the spiking level times 100, i.e., if "a" is the measured level in the unspiked solution, "b" is the measured level in the spiked solution and "c" is the spiking level, then percent recovery equals $\frac{b-a}{c} \times 100$.

Spiking and recovery experiments should be performed using three (3) sets of triplicate samples of the matrix to be spiked with each set spiked at a separate level (See Appendix III). The spiking levels should be one-half (1/2) times the analyzed concentration of the additive, one (1) times the concentration, and two (2) times the concentration. In the event that no compound is detected, the detection limit for the method should be determined. For quantifiable levels of the additive, acceptable recoveries should meet the following criteria:

For levels in food or food-simulating solvents lower than 0.1 ppm, recoveries should average 60-110% and the relative standard deviation should not exceed 20%. For levels in food or food-simulating solvents greater than or equal to 0.1 ppm, recoveries should average 80-110% and the relative standard deviation should not exceed 10%. (If 0.001 mg of a substance is extracted from one square inch of packaging material into 10 grams of food or food-simulating solvents, the estimated concentration in food is 0.1 ppm.)

Samples must be spiked before the analytical workup. In the case of substances extracted from packaging materials into food-simulating solvents, the extracts should be spiked after the time of maximum extraction, e.g., 240 hours. It is important that extracts be spiked, not the pure food simulating solvents. Spiking of pure solvents instead of extracts is probably the most common deficiency in the validation section of indirect food additive petitions.

To eliminate variability arising from individual samples, triplicate analyses may be done on a homogeneous composite (a blend of the triplicate samples) where practicable. (This applies to the validation procedure only, where precision resulting from the analytical method itself is being evaluated.)

Representative spectra or chromatograms from validation analyses of spiked and blank samples should be submitted. Spectra or chromatograms of the "blank" are necessary so that the absence of interferences may be verified.

An illustrative example appears in Appendix III.

E. Exposure

"In determining .... whether a proposed use of a food additive is safe, the Secretary shall consider .... the probable consumption of the additive and of any substance formed in or on food because of the use of the additive."

Migration data developed following procedures outlined in Section D are intended to provide estimates of the highest level of migration to food that might result from the additive. DFCT estimates probable exposure to the additive by combining data on migration with information on use of materials that may contain the additive.

1. Calculation of Exposure

As briefly discussed at the beginning of the previous section, the safety evaluation of an indirect additive depends on the probable consumption of the additive (or any compound resulting from use of the additive). Probable consumption of an indirect additive depends on potential levels in food (i.e., migration values) and on the fraction of a person's diet that is likely to contact packaging materials containing the additive.

DFCT uses the term Consumption Factor (CF) to describe the portion of the diet likely to contact specific packaging materials. The CF is the ratio of the weight of food contacting a specific packaging material to the weight of all food packaged. CF values for both packaging categories (e.g., metal, glass, polymer and paper) and specific food contact polymers are summarized in Tables I and II of Appendix IV, respectively. These values were derived using information on the types of food consumed, the types of food contacting each packaging surface, the number of food-packaging units in each food-packaging category, the distribution of container sizes, and the ratio of the weight of food packaged to the weight of the package. These values may, however, be modified as new packaging information is received.

Additionally, before migration levels can be combined with CF values to derive estimates of probable consumption, it is necessary to know the nature of the food that will likely contact the packaging material. High migration values into fatty food will be of little importance in estimating probable exposure if the packaging material is used exclusively to package aqueous food. To account for the variable nature of food contacting each packaging material, food-type distribution factors (f_T's) have been calculated for each packaging material to indicate the fraction of the food contacting each material that is aqueous, acidic, alcoholic and fatty. Appropriate f_T values for both packaging categories and polymer types appear in Tables I and II of Appendix IV.

When DFCT computes exposure to an adjuvant, the petitioned adjuvant is assumed to capture the entire market for which it is petitioned. While this approach is conservative, it reflects both uncertainties about likely market penetration as well as limitations in the data surveyed. Thus, if a company petitions for the use of an antioxidant in

polystyrene, it is assumed that the antioxidant will be used in all polystyrene manufactured for food contact. In certain cases where an adjuvant is petitioned for use in only a part of a resin category, DFCT may employ a CF for the coverage that is sought that is lower than the CF for the whole resin category. If a stabilizer is petitioned for use only in rigid and semirigid polyvinyl chloride (PVC), a CF of 0.055 rather than 0.11 could be used in estimating exposure since only about 50% of all PVC food-contact surfaces could contain the stabilizer. However, because the types of food that rigid and semirigid PVC contact may be different from that contacted by the whole resin category, additional data for calculating appropriate f_T values would be necessary before exposure could be estimated.

The concentration of the additive in food contacting the packaging material, <M>, is derived by multiplying the appropriate f_T values by the migration values for simulants representing the four food types. This, in effect, scales the migration value from each simulant according to the actual fraction of food of each type that will contact packaging material containing the additive.

$$\langle M \rangle = f_{\text{aqueous and acidic}}(M_{\text{8\%Ethanol}}) + f_{\text{alcohol}}(M_{\text{50\%Ethanol}}) + f_{\text{fatty}}(M_{\text{food oil}})^{*}$$

* Or appropriate fat simulant

The concentration of the additive in the diet is obtained by multiplying <M> by CF. The estimated probable daily intake (EDI) for the additive is then determined by multiplying the dietary concentration by the total weight of food consumed by an individual per day using the following equation (see Appendix IV for sample calculations):

$$\text{EDI} = 3000 \text{ gm/person/day} \times \langle M \rangle \times \text{CF}$$

When new products are introduced, they will initially be treated as replacement items for existing technology. Again, conservative estimates will be based on the assumption that the new product will capture the entire market. For example, the retortable pouch was initially treated as a replacement for coated metal cans and was

assigned a CF of 0.17. As additional information on actual use of the retortable pouch became available to DFCT, the consumption factor was lowered to 0.05.

In order to compensate for the inherent limitations of any survey, a minimum CF has been chosen for estimates involving low consumption items. Initially, the minimum CF that will be used in any exposure estimate will be 0.05. Although this number appears to be quite conservative for certain polymers such as nylons and polycarbonates, lower CF values will be applied only as we obtain more data on the amount of food likely to be in contact with such polymers.

The approach outlined above is designed to deal with the majority of petitioned uses for polymers and adjuvants in food packaging. If the petitioned polymer or adjuvant is already regulated for other uses, the cumulative exposure including these uses must also be estimated (see Appendix IV). The above approach will not, however, be used for estimating dietary concentrations for components of repeat use items and materials used on food processing equipment. Exposure in these cases will continue to be based on the amount of food contacted during the lifetime of the article.

2. Exposure Information for Indirect Food Additive Petitions

Exposure estimates will, in general, be made by DFCT using the aforementioned procedures and accompanying data. DFCT considers the procedures and data contained herein as a first step in reflecting realistic probable exposure. More refined exposure estimates may be possible with industry input. For instance, suggestions for subdividing packaging or resin categories could reduce the calculated exposure by lowering the CF for the category. The division of PVC into rigid and plasticized categories is one example. Another example would be the division of polymer coatings for paper into subcategories, such as polyvinyl acetate polymer coatings, styrene-butadiene polymer coatings, etc. If a compound is to be used solely in styrene-butadiene coatings for paper, use of the CF for polymer coated paper (0.21, Appendix IV, Table 1), would be a gross exaggeration.

In the cases where the nature of the coverage sought in a regulation may require more detailed information or where a petitioner may feel that exposure will be overstated by

simply selecting CF and f_T values presented in Appendix IV, data of the following type may be submitted to FDA to facilitate calculations of CF and f_T values for materials likely to contain the additive:

a. Estimates of the total amount of food in contact with the packaging material determined using either:

(1) package unit data (number of units and their size distribution).

or

(2) pounds of packaging material produced for food contact, container size distribution, and ratios of weight of food packaged to weight of package.

b. Characterization of the foods that might contact the food package and the likely food-type distribution factors.

c. Information that would demonstrate that only a fraction of a resin category would be affected by the coverage sought.

d. Technological limitations that could affect the type of food contacted or the fraction of the diet that might be contacted.

II. Inquiries Regarding Compliance with Food Additive Regulations

FDA receives numerous letters and other inquiries requesting an opinion concerning the compliance of formulations and individual components to be used in the preparation of articles intended for producing, manufacturing, packaging, processing, transporting, holding, or cooking food. Often the information submitted is not sufficient to permit a decision on the food additive status of the material in question. To avoid delay, include the following information in the initial letter:

A. Formulations

The additive must be identified by chemical name. If available, the structural formula and Chemical Abstracts Service Registry Number should also be submitted. Food additives are not listed in the regulations under trade names, nor does FDA maintain a list of such names. Therefore, FDA cannot review materials identified only by trade names. If the additive is a formulation, the individual components should be identified as above. In addition, the weight percentages in the formulation should be reported.

To facilitate review, the specific regulation section numbers that authorize the use of the additive or its components under the desired conditions of use should be listed, if the section numbers are known. Because regulations frequently contain limitations on maximum use level of an additive, maximum temperature of use and type of food with which it may be used, this information should be provided unless it is known that such information is unnecessary for evaluation. (Some regulations contain no specific limitations.)

B. Individual Components

Provide the following information:

1. Chemical identity and specifications for all raw materials used in the manufacture of the item.

2. A complete description of the manufacturing process.

3. The chemical reactions of the manufacturing process and actual byproducts.

4. Specifications for the finished material.

5. Most severe conditions of use: time-temperature conditions, types of foods to be contacted, and type of usage (single and/or repeated use).

6. For unregulated additives, estimate the level that may migrate to food either by calculating the concentration in food assuming 100% migration or by submitting available extraction data with supporting description of the analytical method. However, if the suitability of a given extraction procedure is uncertain, it is best to consult with DFCT before conducting extraction studies.

APPENDIX I

FATTY-FOOD SIMULANTS FOR PARTICULAR POLYMERS

A food oil is considered by DFCT to be a worst-case fatty food. If contact with fatty foods is anticipated, DFCT recommends that experiments intended to evaluate potential migration to all fatty foods be conducted using a food oil as the food-simulating liquid. If an extensive data base is developed comparing migration to fatty foods and a food oil, the appropriateness of using a food oil as a worst-case fatty food may be reconsidered. Corn oil and the synthetic triglyceride HB307 are preferred for use as liquid fats because an extensive migration data base has been developed using these materials. Since analysis of these oils for additive migration may not always be practicable, the use of solvents that simulate the action of these liquid fats is sometimes necessary. While it seems unlikely that one solvent will be found that simulates the action of a food oil for all food contact polymers, the following list presents polymers for which adequate data exist to support the use of these solvents as fatty-food simulants. The recommendation of these solvents is based upon studies done in FDA's own laboratories, at the National Bureau of Standards, and by Arthur D. Little, Inc. under contract to FDA. For polymers other than those listed below, DFCT should be consulted before extraction experiments are undertaken.

1. Polyolefins complying with 177.1520 and ethylene-vinyl acetate copolymers complying with 177.1350 ---------- 95% ethanol

2. Rigid polyvinyl chloride ---------- 50% ethanol

3. Polystyrene and rubber modified polystyrene ---------- 50% ethanol

Previous test protocols recommending the use of heptane as a fatty-food simulant have permitted the division of heptane migration levels by a factor of five (5) to account for the aggressive nature of heptane relative to a food oil. Recent studies mentioned above show that the exaggeration effect of heptane relative to a food oil varies over orders of magnitude depending on the polymer extracted. In some cases, division of heptane results by five underestimates migration into a food oil. Therefore, although DFCT may continue to accept heptane extraction data, migration values will not be divided by any factor unless there is adequate justification.

Even though heptane exaggerates migration, it can be a useful fatty-food simulant due to the ease of analytical workup for those systems where very low migration is anticipated, such as for inorganic adjuvants or certain highly cross-linked polymers.

Absolute or 95% ethanol has been found to be an effective fatty-food simulant for polyolefins, but appears to exaggerate migration for other food-contact polymers.

APPENDIX II

SELECTED EXTRACTION PROTOCOLS

1. General Protocols Corresponding to Conditions of Use

The following extraction protocols are intended to simulate most anticipated end-use conditions by food-contact articles. If expected use conditions are not adequately simulated by these protocols, appropriate test protocols should be developed in consultation with DFCT. Since test conditions for Use Condition A have traditionally only involved testing at 250°F, all uses where expected food-contact temperatures exceed 250°F should be the subject of special protocol development.

These protocols reflect DFCT's increased understanding of processes affecting additive migration. As new information becomes available to DFCT on factors affecting additive migration (e.g., diffusion during high temperature food contact or on correlations between migration levels to food simulants and levels in food), these test protocols may be subject to revision. Periodic up-dates of test protocols will be made available to reflect revisions.

These test protocols are based primarily on the premise that additive migration to aqueous and fatty foods is typically diffusion controlled within the polymer, strongly affected by the temperatures encountered during food contact, and further modified by the solubility of the additive within the foods. Therefore, DFCT recommends that migration testing with food simulating solvents be conducted at the highest temperatures expected during food contact. If testing with food-simulating solvents at the highest temperatures is not practicable, alternative test protocols to those presented below should be developed in consultation with DFCT. In the case of food contact at room temperature and below, migration experiments are conducted at temperatures that accelerate the migration process in order to avoid excessively long extraction periods that would be necessary to simulate long term food contact (see discussion in D.1.e.).

Because water is a poorer solvent than aqueous foods for many organic migrants, 8% ethanol is now recommended as an aqueous food simulant. It not only provides greater solubility for organic migrants, but detailed migration studies with water, 8% ethanol, and aqueous foods have shown that the proportion of under-estimates can be reduced when 8% ethanol is used as the

food-simulating solvent. This solvent will be used for evaluating indirect additive migration to aqueous, acidic, and low alcohol foods, except when the acidity of the food is expected to lead to significantly higher levels of migration. In those instances, 3% acetic acid should be used as the simulant for acidic food. Since 8% ethanol is intermediate in alcohol concentration between wine and beer and migration levels to wine and beer are expected to be nearly identical to 8% ethanol values, test results developed with 8% ethanol will be used to evaluate exposures and support clearances for alcoholic beverages with up to 13 volume % ethanol.

As noted in Appendix I, migration to fatty foods is evaluated using a pure liquid fat as a worst-case fatty food. Aqueous ethanol solutions are recommended as fatty-food simulants when analytical limitations with a liquid fat preclude sensitive analyses.

A. High temperature, heat sterilized or retorted over (212°F)

8% Ethanol	--	250°F for two hours
50% Ethanol	--	160°F for two hours
Food Oil (corn oil or HB307)	--	250°F for two hours
or		
50% or 95% Ethanol*	--	250°F for two hours

* Depends on food-contact layer, see Appendix I

After extraction for two hours at elevated temperatures, the extractions should be continued at 120°F to a total of 240 hours. Extracts should be analyzed at the end of the initial two hour period, and after 24, 96 and 240 hours.

B. Boiling water sterilized. The protocol remains the same except that the highest extraction temperature is 212°F.

C. Hot filled or pasteurized above 150°F. Solvents should be added to the test samples at 212°F, held for 30 minutes, and then be allowed to cool to 120°F. The extraction cells should then be maintained at 120°F for ten days with samples taken for analysis after the intervals indicated for the previous protocols.

If the maximum hot fill temperature will be lower than 212°F, solvents may be added at this lower temperature, but the ensuing regulation will have a hot fill temperature limitation.

D. Hot filled or pasteurized below 150°F. The protocol is analogous to that for C except that all solvents should be added to the test samples at 150°F and held for 30 minutes before cooling to 120°F.

E. Room temperature filled and stored (no thermal treatment in the container). Extractions should be conducted for 240 hours at 120°F. Extracts should be analyzed after 24, 48, 120 and 240 hours.

F. Refrigerated storage (no thermal treatment in the container). The protocol is identical to that for E except that the temperature of extraction is 70°F.

G. Frozen storage (no thermal treatment in the container). The protocol is identical to F except that the time of extraction is five (5) days.

H. Frozen or refrigerated storage: Ready-prepared foods intended to be reheated in container at time of use:

8% Ethanol	--	212°F for two hours
50% or 95% Ethanol* or Food Oil (corn oil or HB307)	--	212°F for two hours

* Depends on food-contact layer. See Appendix I.

2. <u>Adjuvants for Polyolefins</u>

For use with all polyolefins regulated in 177.1520, extractions should be carried out on three polymers:

a. High density polyethylene (HDPE)

b. Low density polyethylene (LDPE) complying with 177.1520(a)(2)

c. Polypropylene (PP) or propylene copolymers complying with 177.1520(a)(3)(i)

The exact protocol depends on the condition of use. Refer to Section 1 of this appendix. If the most rigorous applications correspond to those of Section 1.A, the extraction temperature for LDPE should be at the highest temperature at which the polymer remains functional (ca. 212°F).

In general, under identical extraction conditions, levels of migrants from LDPE are higher than corresponding levels from HDPE or PP. Extractions done solely on LDPE (complying with 177.1520(a)(2)) are, therefore, sufficient to provide coverage for all polyolefins. In such a case the consumption factor for all polyolefins (CF = 0.33) will be used instead of the individual consumption factor for LDPE (see Appendix IV). However, it is usually to the petitioner's advantage when seeking coverage for all polyolefins to extract HDPE and PP as well as LDPE so that the calculated concentration in the daily diet and the EDI are lower.

3. Adjuvants for Other Polymers.
Adjuvants for More than One Polymer.

The corresponding general protocols for extraction of other polymers are the same as those in Section 1 of this appendix. Consult Appendix I for the recommended fatty-food simulant.

If a regulation without limitation to specific polymers is sought, the petitioner may obtain such broad coverage by extracting LDPE complying with 177.1520(a)(2). The exact protocol depends on the anticipated conditions of use (refer to Section 1 of this appendix). If the most rigorous applications correspond to those of Section 1.A., the extraction temperature should be at the highest temperature at which the polymer remains functional (ca. 212°F). The consumption factor for all polymers (Appendix IV, CF = 0.79), will be used with the migration data to calculate the concentration in the daily diet. In general, a lower calculated concentration in the daily diet will result if a series of representative polymers are separately extracted and individual consumption factors are applied (refer to the examples in Appendix IV). Consult with DFCT to determine which representative polymers should be extracted.

4. Articles Intended for Repeated Use

The article should be extracted with 8% and 50% ethanol and a liquid fat such as corn oil or the synthetic triglyceride HB307 for 240 hours at the highest intended temperature of use. Extracts should be analyzed for additive migration after 8, 72,

and 240 hours. The petitioner should also provide estimates of the weight of food contacting a known area of repeat-use article in a given time period as well as an estimate of the average lifetime of the article. Together with the extraction data, this should allow calculation of migration to all the food processed during repeated use over the lifetime of the article.

In the case of an adjuvant in a repeat use article, it is strongly recommended that the petitioner calculate an average level in food by assuming complete extraction over the lifetime of the article and dividing by the quantity of food processed. It may be that this calculated concentration is sufficiently low that extraction studies will be unnecessary.

5. Coatings for Cans (21 CFR 175.300)

The extraction protocol is usually that outlined in Section 1.A of this appendix for high temperature, heat sterilized or retorted products. If broad coverage is sought for all types of coatings, consult with DFCT to determine which particular coatings should be extracted. For use conditions less severe than retort sterilization at 250°F, extraction protocols should follow the test conditions outlined in Section 1.B-G of this appendix which most closely approximate the most severe expected use conditions.

6. Uncoated & Clay-Coated Papers with Latex Binders

These papers are intended for contact with food at temperatures less than 120°F for short periods of time. The protocol is the following:

8% Ethanol	120°F for 24 hours
50% Ethanol, heptane	120°F for 24 hours
or	
Food Oil	120°F for 24 hours

When total nonvolatile or chloroform-soluble extractives are determined for a paper coating, do not subtract the corresponding extractives from uncoated paper as a blank correction.

In the event that the paper disintegrates in a particular solvent, the above protocol may be modified with DFCT approval.

7. Specially Treated Papers

This class includes such types as fluoropolymer- and silicone-treated papers that have oil-resisting and heat-resisting properties. The exact protocol depends on the particular uses anticipated. It is recommended that the petitioner either devise a protocol and submit it to DFCT for comment or request DFCT comment about appropriate test conditions.

8. Adhesives (21 CFR 175.105)

For use at room temperature or below, no extraction data are necessary. High temperature applications are discussed in Section 9.

9. Laminates & Coextrusions

Components of multilayer structures used above room temperature (120°F) are the subject of two regulations. One covers laminates used in the temperature range 120°-250°F (21 CFR 177.1395) and the other covers laminate structures used at temperatures of 250°F and above (21 CFR 177.1390). Layers not separated from food by "functional barriers" during expected use must be listed in these regulations unless they are regulated elsewhere for the intended use conditions (21 CFR 177.1395(b)(2) and 21 CFR 177.1395(e)). While test protocols presented in 1.A-1.H may be appropriate for evaluating the level of migration from non-food contact layers of some laminate structures, end uses which differ considerably from these guidelines should be the subject of special protocol development in consultation with DFCT.

10. Boil-in-bags.

The protocol is the same as that employed in Use Condition C.

11. Ovenable & Microwaveable Trays.

The protocols are dependent on the end-use conditions expected for the package during food contact. In many instances, the package is only intended to hold ready-prepared food during periods of reheating in the container. For those uses where the temperature of the package and food are essentially identical and do not exceed 250°F, extraction testing should follow test protocols outlined in 1.H. If the temperature of the package exceeds 250°F as a result of high temperature oven use or as a result of other technologies that cause high temperature heating

of the package (e.g., microwave heat susceptors) then extraction testing will need to simulate the times, temperatures, and extent of migration expected during such food-contact scenarios. Appropriate protocols should be developed in consultation with DFCT.

12. Colorants for Plastics (21 CFR 178.3297)

Colorants are treated in a manner identical to other indirect food additives. Extraction conditions should correspond to the most severe anticipated use conditions.

13. Dry Foods with Surface Containing No Free Fat or Oil (21 CFR 176.170(c), Table 1, Food Type VIII)

Although recent studies have shown migration of certain adjuvants into dry foods, at the present time no migration testing is required. If, however, the additive is expected to become a component of food as a result of its proposed use, test protocols should be developed in consultation with DFCT.

APPENDIX III

ILLUSTRATIVE EXAMPLE OF VALIDATION OF ANALYSES FOR AN INDIRECT FOOD ADDITIVE

Polyethylene film containing a new non-polar antioxidant was extracted with water, and the extract was analyzed for antioxidant. Extractions were carried out in separate cells each containing 100 in^2 of film. The extracts from the different cells were analyzed at various time intervals. Validation experiments were carried out with extracts from the longest time period, 240 hours. Following water extraction, each solution was extracted with hexane, the hexane solution concentrated, and a known aliquot injected into a gas chromatograph.

To validate the migration results, an additional nine separate water extractions could have been run for 240 hours and the extracts spiked in triplicate with the additive at three levels corresponding to one-half (1/2), one (1) and two (2) times the average migration value found earlier for the regular 240 hour extractions. Instead, the petitioner decided to carry out one large extraction using enough film and solvent for twelve analyses. After 240 hours, the extract was divided into twelve equal solutions. Three solutions were analyzed and found to contain antioxidant at an average level equivalent to 0.00080 mg/in^2. This value corresponds to 0.080 ppm in food if it is assumed that 10 grams of food contacts one square inch of film. Of the remaining nine solutions, three solutions were spiked at concentrations corresponding to 0.00040 mg/in^2, three were spiked at 0.00080 mg/in^2 and three were spiked at 0.00160 mg/in^2. Each solution was extracted with hexane, concentrated and analyzed by GC. Measured antioxidant levels in the three solutions spiked at a concentration corresponding to 0.00040 mg/in^2 were 0.00110 mg/in^2, 0.00105 mg/in^2 and 0.00112 $mg/^2$. The recoveries of spiked antioxidant, obtained by subtracting 0.00080 mg/in^2, are 0.00030 mg/in^2, 0.00025 mg/in^2 and 0.00032 mg/in^2, respectively, and the corresponding percent recoveries are 75.0%, 62.5%, and 85.0%. The average percent recovery is 74.2%, and the relative standard deviation is 15.2%. These numbers are within the limits specified for a concentration in food of 0.080 ppm (percent recovery 60-110%, relative standard deviation not exceeding 20%). If the corresponding percentages for the other two spiking levels are also within these limits, the validation would be acceptable. The actual validation procedure used will, or course, depend on the particular type of analysis.

APPENDIX IV

CONSUMPTION FACTORS & FOOD-TYPE DISTRIBUTION FACTORS/EXAMPLE OF EXPOSURE ESTIMATE CALCULATIONS

This appendix summarizes data used by DFCT for evaluating exposure to food packaging components. An example of how DFCT uses these data is also presented. A more complete discussion of the source of these data and their use in exposure calculations is presented in part I.E.

Table I

Package Category	CF**	Food-Type Distribution (f_T)			
		Aqueous	Acidic	Alcoholic	Fatty
Glass	0.08	0.08	0.36	0.47	0.09
Metal - Polymer Coated	0.17	0.16	0.35	0.40	0.09
Metal - Uncoated	0.03	0.54	0.25	0.01*	0.20
Paper - Polymer Coated	0.21	0.55	0.04	0.01*	0.40
Paper - Uncoated	0.10	0.57	0.01*	0.01*	0.41
Polymer	0.41	0.49	0.16	0.01*	0.34

* 1% or less

** As discussed in text, a minimum CF of 0.05 will be used initially for all exposure estimates.

TABLE II

Polymer	CF	Food-Type Distribution (f_T)			
		Aqueous [a]	Acidic [a]	Alcoholic	Fatty
Acrylonitrile	0.05[b]	0.01[c]	0.01[c]	0.01[c]	0.97
Acrylics, Phenolics, etc.	0.15	0.17	0.40	0.31	0.12
EVA	0.05[b]	0.30	0.28	0.28	0.14
Ionomers	0.05[b]	0.01[c]	0.01[c]	0.01[c]	0.97
Polycarbonates	0.05[b]	0.97	0.01[c]	0.01[c]	0.01[c]
Polyesters	0.05[b]	0.01[c]	0.97	0.01[c]	0.01[c]
Polyolefins [d]	0.33	0.67	0.01[c]	0.01[c]	0.31
Polystyrene	0.08	0.67	0.01[c]	0.01[c]	0.31
PVC	0.11	0.01[c]	0.23	0.27	0.49
PVDC	0.05[b]	0.01[c]	0.01[c]	0.01[c]	0.97
Wax	0.05	0.47	0.01[c]	0.01[c]	0.51
Cellophane	0.05[b]	0.05	0.01[c]	0.01[c]	0.93

a When 8% ethanol is used as the food simulant for aqueous and acidic foods - the recommendation in these guidelines, the food-type distribution factors for aqueous and acidic foods should be summed.

b The minimum CF is 0.05. In certain cases a lower CF may be used when adequate data are available.

c 1% or less

d The CF for polyolefins is currently subdivided as follows:

Polyolefin	CF
LDPE	0.18
HDPE	0.13
PP	0.02

If polyolefin coverage only involves PP, a minimum CF of 0.05 is used.

Examples of Exposure Estimate Calculations

The following hypothetical examples are intended to illustrate the calculation of the concentration of an indirect additive in the daily diet (CF x <M>, i.e., the fraction of food in the diet contacting the packaging material times the average concentration of the additive in the food contacted) and its EDI (mg/person/day).

Example 1

The petitioner is seeking coverage for use of a new antioxidant at a maximum level of 0.25% by wt. in polyolefins contacting food at or below room temperature (Section 1.E, F, and G, Appendix II). Appropriate migration values from LDPE reported to FDA for the three food simulating solvents are given below:

Solvent	M (ppm)
8% aq. Ethanol	0.060
50% aq. Ethanol	0.092
HB307	7.7

Since the petitioner used a solvent volume to exposed surface area ratio of 10 mL/in^2, solution concentrations are essentially equivalent to food concentrations. The CF and food-type distribution value (f_T) for polyolefins are given in Table II. The <M> for the antioxidant would be calculated as follows:

$$\langle M \rangle = (f_{aqueous}+f_{acidic})(M_{8\%\ Ethanol})+f_{alcohol}(M_{50\%\ Ethanol})+ f_{fatty}(M_{HB307})$$

$$= 0.68(0.060)+0.01(0.082)+0.31(7.7)$$

$$= 2.4 \text{ ppm}$$

The concentration of the antioxidant in the daily diet resulting from the proposed use would be:

$$CF \times \langle M \rangle = 0.33 \times 2.4 \text{ ppm}$$

$$= 0.80 \text{ ppm}$$

If there were no other regulated or proposed uses, then the EDI would be calculated using the above value:

$$EDI = 3000 \text{ gms/person/day} \times 0.80 \times 10^{-6}$$

$$= 2.4 \text{ mg/person/day}$$

Example 2

In a subsequent petition, the company sought additional coverage for the same antioxidant in polycarbonate and polystyrene resins. Each polymer would contact food at or below room temperature (Section 1.E, F, and G, Appendix II). Migration estimates are given below:

Solvent	Polycarbonate	Polystyrene	Impact Polystyrene
8% Ethanol	0.020 ppm	0.020 ppm	0.020 ppm
50% aq. Ethanol	0.025	0.035	0.22
HB307	0.033	0.15	6.2

The concentration of the antioxidant in the daily diet resulting from each of the proposed uses is calculated below. For polystyrene, the higher migration levels for impact polystyrene is used in the calculation.

Polycarbonates

$$CF \times \langle M \rangle = 0.05[0.98(0.020)+0.01(0.025)+0.01(0.033)]$$

$$= 0.001 \text{ ppm}$$

Polystyrene

$$CF \times \langle M \rangle = 0.08[0.68(0.020)+0.01(0.22)+0.31(6.2)]$$

$$= 0.16 \text{ ppm}$$

The total concentration of the antioxidant in the daily diet resulting from the additional uses given in this petition is approximately 0.16 ppm.

Their contribution to the EDI is calculated below:

$$EDI = 3000 \text{ gms/person/day} \times (0.16 \times 10^{-6})$$

$$= 0.48 \text{ mg/person/day}$$

The cumulative exposure from the previously regulated use and the additional proposed uses would be 2.9 mg/person/day.

TGG: JCL: MMG: AJG: RF
XF: Acme Desk

TO: Distribution

FROM: T. G. Grumbles
DATE: February 6, 1989

SUBJECT: Responsible CARE Information Meeting

VISTA

Interoffice Communication

Below is the agenda for the subject meeting to be held Tuesday, February 7, from 3:00 - 4:00 P.M. in Conference Room 3B.

Agenda

Purpose: 1) Introduce the CMA Responsible CARE program elements and proposed communication plan.
2) Introduce VISTA's Draft Environmental Policy Statement

	Item	Resp.	Time
1.	Introduction & Purpose	RDG	5 min.
2.	Review of Responsible CARE	TGG	15 min.
	a) Elements b) VISTA obligations c) Proposed Communication Plan		
3.	Present VISTA Environmental Policy Statement	TGG	20 min.
	a) Elements b) Specific impact of each element		
4.	Discussion	All	15 min.
5.	Review Action Items	TGG	5 min.

T. G. Grumbles

/bh

Distribution: JRB, RDG, JJW, NCF, RTF, GGD, JDB, RVD

cc: MSR

VVV 000006762

TGG: JCL: MMG: AJG: BF
XF: DGK

TO: New Product Development/Product Liability Team

FROM: T. G. Grumbles
DATE: February 8, 1989

Interoffice Communication

SUBJ: PHASE II OBJECTIVE STATEMENT

VISTA

Attached is the draft objective statement for Phase II of our process improvement, existing products. This is the product of Jeff Fenton, Malcolm McMullen, Bill McClain and I.

Please review and let me know if you have comments. This will be reviewed in detail at our next team meeting.

T. G. Grumbles

dlj
.508

Attachment

Distribution: Jeff Fenton-Ponca City, Harry Garrison-OKC, Rick Flammer, J. J. Hall, Malcolm McMullen, John McCulley, W. L. McClain

VVV 000006763

Introduction

Vista has recently improved our processes on new product development so that regulatory liability and product liability is minimized. However, while new product development is the most risky, Vista also is responsible for its existing products and processes. We must be sure that the design, production, sale, transport, and use of all Vista products is in compliance with all pertinent regulations and is handled with due consideration of product liability issues. Problems in any of these areas can result in liabilities for Vista.

Charter

The Product Liability Team recommends that by September 30, 1989 consideration be given to the following areas:

* Existing products defects review prioritization model
* Toll processor quality control
* Ex-plant storage and distribution
* Common tarrier qualification
* Customer complaint/health allegations - tracking and follow-up

This will be accomplished by the establishment of teams in each of the above areas.

The team's goal will be to analyze and evaluate present processes and procedures, recommend and document appropriate new procedures. The team will provide the basis for continuous improvement of the production and distribution of existing products to minimize potential product liability incidents and exposures while assuring compliance with all applicable governmental standards, rules, and regulations.