An Agricultural Law Research Article

Regulating Carcinogens in Food: A Legislator's Guide to the Food Safety Provisions of the Federal Food, Drug, and Cosmetic Act

Part II

by

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color even upon a finding of carcinogenicity or some more acute hazard. By contrast, the agency can suspend, without even publishing a proposal or seeking comments, the use of a *provisionally listed* color whose safety comes into question.[198]

D. *Indirect Constituents of Food*

The Food, Drug, and Cosmetic Act separately recognizes three other categories of added food constituents that are not intended ingredients but become components of food through their intended use in food production, processing, or distribution. The three classes are: (1) so-called "indirect" or "incidental" food additives, such as packaging materials that migrate to food; (2) animal drugs that can leave residues in tissues (meat, milk, or eggs) consumed as human food; and (3) pesticide residues on raw agricultural commodities and in processed foods.[199] The levels at which these indirect constituents occur typically are much lower than the levels at which most intended ingredients are used. The first two categories are subject to some version of the Delaney Clause. The statutory standards for tolerances for pesticide residues, however, do not accord decisive weight to a finding that a pesticide induces cancer.

1. *Indirect food additives*

As many as 10,000 substances[200] are used in proximity with food—in food packaging, in equipment used to process or store food, in compounds used to clean such equipment—in ways that permit small amounts to migrate to and become a part of the food. Such constituents of food are ordinarily not "unavoidable" in the sense that mercury contamination of swordfish is unavoid-

198. *See* Certified Color Mfrs. Assn. v. Mathews, 543 F.2d 284 (D.C. Cir. 1976).

199. The FDA estimates that there may be as many as 10,000 indirect food additives (including indirect GRAS and prior sanctioned substances). *Food Additives Hearings, supra* note 159, at 57. As of September 1978, the EPA had set tolerances for the residues of 268 pesticides on one or more raw agricultural commodities. Of the total of 5,984 individual EPA tolerances, 940 are for chemicals suspected of causing cancer. SUBCOMM. ON OVERSIGHT AND INVESTIGATIONS OF THE HOUSE COMM. ON INTERSTATE AND FOREIGN COMMERCE, 95TH CONG., 2D SESS. CANCER-CAUSING CHEMICALS IN FOOD 33 (Comm. Print 1978). At least 143 pesticides and animal drugs are known to leave chemical residues in meat and poultry, but the USDA monitors only 46 of these substances occurring in edible animal tissue. *Id.* at 24. In this context, "pesticide residues" include only pesticides purposely used on crops for which they are approved, and not residues that may find their way into the food supply through drift to other crops or persistence in the environment.

200. *Food Additives Hearings, supra* note 159, at 57 (statement of Sherwin Gardner, Acting Commissioner of Food and Drugs).

able. Apparently, swordfish that contain no measurable amounts of mercury cannot be found, but most foods can either be packaged in materials that do not migrate in detectable amounts or can be marketed without packaging. Avoidance of the contaminant in the latter case does not require giving up the food.

The full requirements of the Food Additives Amendment apply to substances that migrate to food from food-contact surfaces. Section 201(s) of the Act defines a food additive as

> *any substance the intended use of which results or may reasonably be expected to result, directly or indirectly, in its becoming a component* or otherwise affecting the characteristics *of any food* (including any substance intended for use in producing, manufacturing, packing, processing, preparing, treating, packaging, transporting, or holding food).[201]

A migrating food contact material can escape the food additive classification if it is generally recognized as safe or if it is the subject of a prior sanction, and some established packaging materials fall within these exceptions.[202] The procedures for obtaining, or withdrawing, FDA approval are identical for indirect and direct food additives, and the basic statutory criteria for approval are the same. Accordingly, an indirect food additive must be shown, with reasonable certainty, to be safe, and no weight may be accorded the economic benefits of its use. Similarly, the Delaney Clause squarely applies to indirect food additives and prohibits the use, in applications likely to result in migration to food, of any substance shown to induce cancer in experimental animals. While application of the Delaney Clause to direct ingredients and animal drugs has proved controversial, its expanding application to indirect food additives is likely to prove the most disruptive.

Most materials used in packaging and other food-contact applications would never be considered for use as food ingredients because their chemical structure, or experimental evidence, suggests they are probably toxic. This is clearly true for the many varieties of packaging materials synthesized from hydrocarbon sources. Furthermore, rapid improvements in chemical analysis

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201. 21 U.S.C. § 321(s) (1976) (emphasis added).

202. For example, although acrylonitrile polymers in beverage containers are classified as food additives, some meat product wrappings made from acrylonitrile copolymers have a prior sanction and thus are not classified as food additives. 21 C.F.R. § 181.32 (1978). Some other packaging materials, such as sorbose and acacia, are generally recognized as safe and thus are not subject to regulation as food additives. *See* 21 C.F.R. §§ 186.1330 (acacia), .1839 (sorbose) (1978).

have permitted scientists to measure increasingly small quantities of substances migrating from food contact applications.[203] This development has made it possible to detect traces in food of packaging materials that once were thought incapable of migration. Improvements in analytical chemistry thus irresistibly enlarge the category of compounds that are potential food additives—and are subject to the Delaney Clause.[204]

A recent decision of the Commissioner of Food and Drugs, if upheld on judicial review, may accelerate this development.[205] The decision affects the use[206] of acrylonitrile copolymers to manufacture beverage containers. The FDA initiated proceedings to revoke existing food additive regulations for four such containers, because of (1) evidence that residual acrylonitrile monomer is likely to migrate into the beverages at levels higher than anticipated, and (2) recent experimental data that raise serious questions about the material's safety.[207] The manufacturers contended that improved fabrication methods would produce a bottle containing so little residual acrylonitrile monomer that no migration could be detected. The Commissioner rejected this contention as unpersuasive. He ruled that a material in packaging can be pre-

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203. In 1958, 50 parts per million was the smallest amount of material detectable. Today, analytical chemistry can detect parts per trillion. *See* Lyons, *Up-to-Date Technology, Out-of-Date Regulations,* N.Y. Times, Dec. 31, 1978, at § 4 at 6E, col. 1. For a more detailed discussion of the improvements in analytical chemistry in recent decades, see Chemical Compounds in Food-Producing Animals: Criteria and Procedures for Evaluating Assays for Carcinogenic Residues, 44 Fed. Reg. 17,069, 17,075-77 (1979) [hereinafter cited as Assays for Carcinogenic Residues].

204. While the statutory definition of "food additive" does not on its face require evidence of actual migration, it might be difficult for the FDA to explain why a substance that had been detected in food, even though at very low levels, was not potentially a food additive. The FDA is reportedly exploring ways of limiting its obligation to search for minute migrants by establishing criteria for detection methods similar to those it promulgated for animal drugs. *See* notes 237-50 *infra* and accompanying text.

205. Acrylonitrile Copolymers Used to Fabricate Beverage Containers: Final Decision, 42 Fed. Reg. 48,528 (1977). Petitions for review of the Commissioner's decision were later filed in the Court of Appeals for the District of Columbia Circuit, where argument was heard earlier this year. Monsanto Co. v. Kennedy, No. 77-2023 and consolidated cases Nos. 77-2024, 77-2026, and 77-2032 (March 15, 1979).

206. Acrylonitrile copolymers had received informal FDA approval for use in some food contact applications as early as 1948. Acrylonitrile Copolymers Intended for Use in Contact with Food, 41 Fed. Reg. 23,940, 23,941 (1976).

In 1976, the agency amended the existing interim food additive regulation, 21 C.F.R. § 121.2010 (1976) (recodified at § 180.22 (1978)), to allow the use of acrylonitrile copolymers to fabricate containers for nonalcoholic beverages. 41 Fed. Reg. 23,940 (1976). The history of the FDA's handling of acrylonitrile is recounted in the agency's 1976 amendment and in the Commissioner's decision, *supra* note 205.

207. 42 Fed. Reg. 48,528 (1977).

sumed "to become a component of food," within the meaning of section 201(s), even though available methods of analysis cannot detect migration, if evidence demonstrates that the material can diffuse into packaged food.[208] This presumption may be defeated only if the petitioner can prove that diffusion does not occur when the packaging contains lower residual levels of the material.[209]

The Delaney Clause will increasingly be implicated in regulatory decisions involving indirect additives because many chemicals used in the manufacture of food contact materials are suspected or unequivocal carcinogens. Realization of this fact is partly a result of accumulating evidence of the effects of industrial exposure, as in the case of workers engaged in the manufacture of vinyl chloride and acrylonitrile.[210] It also results from demands stimulated by other regulatory agencies, notably the Occupational Safety and Health Administration[211] and the Environmental Protection Agency, for toxicological evaluation of industrial chemicals.[212]

Scientific developments on two fronts are therefore likely to precipitate application of the Delaney Clause to compounds whose presence in food could not have been predicted, much less detected, only a few years ago. Enforcement of the Food Additives Amendment in this context may produce unexpected results.

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208. The evidence that the Commissioner relied on consisted of tests conducted on older containers that had higher concentrations of acrylonitrile monomer, which was shown to migrate at low levels into beverages and food-simulating solvents. The Commissioner stated that, although the concentration of acrylonitrile monomer in the newer bottles had been reduced, the observation of migration in the older containers made it reasonable to expect some migration from the newer containers as well. *Id.* at 48,530.

209. *See id.* at 48,530-31. Some readers of the Commissioner's decision were initially skeptical that such a showing could ever be made. Reportedly, however, manufacturers of polyvinyl chloride another plastic packaging material of considerable commercial importance and a frank carcinogen in man as well as laboratory animals, have preliminarily persuaded the FDA's Bureau of Foods that they have devised a method of manufacture that prevents migration of residual vinyl chloride monomer. The method reduces the residual monomer to the lowest achievable levels during synthesis, and vacuum-strips the material to eliminate all remaining monomer to a level below the capability of chemical analysis. In addition, the manufacturers have proferred plausible support for a theory that, at very low levels, the residual monomer is bound within the plastic and unable to migrate. *See* 20 FOOD CHEMICAL NEWS, October 9, 1978, at 7.

210. *See* Occupational Exposure to Acrylonitrile, 43 Fed. Reg. 45,762 (1978); Standard for Exposure to Vinyl Chloride, 39 Fed. Reg. 35,890 (1974).

211. *See* Identification, Classification, and Regulation of Toxic Substances Posing a Potential Occupational Carcinogenic Risk, 42 Fed. Reg. 54,148 (1977).

212. *See* Health Risk and Economic Impact Assessments of Suspected Carcinogens: Interim Guidelines and Procedures, 41 Fed. Reg. 21,402 (1976); Pesticide Programs: Registration, Reregistration, and Classification Procedures, 40 Fed. Reg. 28,242 (1975). *See also* Toxic Substances Control Act, 15 U.S.C.A. § 2601 (Supp. 1979).

Unlike most intentional ingredients, these "new" food additives, such as acrylonitrile, are found (if at all) only at very low parts-per-billion in packaged food. But the Delaney Clause flatly forbids use of a carcinogenic material for food packaging if it is likely to migrate to food in any quantity,[213] and the clause could reach other, more remote, uses of the material, such as conveyor belts and water pipes made from vinyl chloride.[214] Furthermore, section 409 does not allow any showing of an additive's special utility to overcome a finding of carcinogenicity. The law appears to make no allowance for the fact that the risk posed by migrating quantities of food packaging material, while not negligible, is likely to be considerably less than that posed by most direct food additives, which are used at much higher levels.[215]

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213. The legislative history of the Food Additives Amendment does not reveal whether Congress fully appreciated the potential interaction between the expansive definition of "food additive" and the Delaney Clause. The House Report discusses both "intentional" and "incidental" additives together and lists examples considered illustrative of both categories. These include "substances intended for use in producing, manufacturing, packing, processing, preparing, treating, packaging, transporting, or holding food." H.R. REP. No. 2284, 85th Cong., 2d Sess. 3 (1958). Congressman Delaney explained that one event which had prompted him to introduce his amendment was the use of a pesticide chemical known to induce cancer, 104 CONG. REC. 17,420 (1958), but he failed to note that pesticide residues fall outside the coverage of § 409 and, thus, beyond the reach of the Clause that bears his name. While some members questioned the wisdom of Delaney's proposed definition, none cited cases in which its application would be unsound. 104 CONG. REC. at 17,421-22.

The Senate Report indicates that incidental food additives were to be subject to the Delaney Clause, just as direct additives, and went on to observe,

> [W]e want the record to show that in our opinion the bill is aimed at preventing the addition to the food our people eat of any substances the ingestion of which reasonable people would expect to produce not just cancer but any disease or disability. In short, we believe the bill reads and means the same with or without the inclusion of the [Delaney Clause]. This is also the view of the Food and Drug Administration.

S. REP. No. 2422, 85th Cong., 2d Sess. 11 (1958).

Although not technically a part of the formal legislative history of the Food Additives Amendment, the original report of the Delaney Committee provides examples of the type of compounds the proponents of the clause hoped to reach. The report alluded to the problem of indirect chemical additives, citing antibiotics which were used to treat dairy cattle and which subsequently appeared in milk products. The report also stated that the problem extended beyond pesticides and chemical additives, and included paper, fiber, and plastics used as food containers, wrappers, and handling equipment. H.R. REP. No. 2356, 82d Cong., 2d Sess. 4-5 (1952).

214. For a revealing discussion of the FDA's current position on polyvinyl chloride water pipes, see Vinyl Chloride Polymers In Contact with Food, 40 Fed. Reg. 40,529, 40,534-35 (1975). *See also* Doniger, *supra* note 130.

215. The FDA has banned the use of acrylonitrile bottles, which yield a concentration of acrylonitrile in the bottled beverage of less than 10 parts per billion (ppb). 42 Fed. Reg. 45,828, 45,829 (1977). In contrast, saccharin, a direct food additive, is used in concentra-

2. *Animal drug residues*

Compounds administered to food-producing animals as drugs or feed supplements compose a second category of indirect constituents of human food, for they may leave residues in meat, milk, or eggs. Animal drugs and animal feed additives are both subject to the Delaney Clause, but with an important qualification created by a special amendment to the clause passed by Congress in 1962. Before examining this qualification, a brief summary of the regulatory framework for animal drugs and feed additives is in order.

Compounds added to animal feed are subject to the Food Additives Amendment of 1958 on the same terms as intentional ingredients of human food; the Act's definition of "food" specifically embraces "articles used for food or drink for man or other animals."[216]

Accordingly, a substance added to animal feed must be generally recognized as safe, be used in accordance with a prior sanction issued by the FDA or the USDA, or be the subject of an approved food additive regulation. The procedures for approval of animal feed additives generally do not differ from those applicable to ingredients of human food.[217] The central inquiry is usually whether the ingredient will be safe for the animals to which it will be fed. However, the FDA has not undertaken a formal review of the safety of animal feed, nor has it established any system for affirming the general recognition of specific ingredients as safe.[218]

Prior to the passage of the Animal Drug Amendments of

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tions of approximately 400 parts per *million* (12 milligrams per fluid ounce). *See* 21 C.F.R. § 180.37(d)(1) (1978).

The FDA is currently considering ways of escaping from this dilemma. One possibility under discussion would be to establish a level of migration below which § 409 would not apply, a level so low that the risk posed by any migrating material could be ignored. As the next section explains, the FDA has devised a similar approach for dealing with residues of carcinogenic animal drugs. The distinctive feature of that approach is that the residue level which the agency would ignore, *i.e.*, allow to go uncontrolled, is keyed to the carcinogenic potency of the compound. This feature can more readily be reconciled with the text of the statute governing animal drugs. *See* notes 237-59 *infra*, and accompanying text. It remains to be seen whether under the present statute FDA could justify a similar approach to indirect food additives, which are regulated under a provision of the Act that appears to speak in terms of the occurrence, or likely occurrence, of physical migration. *See* § 201(s) of the Act, 21 U.S.C. § 321(s) (1976).

216. 21 U.S.C. § 321(f) (1976). The definition of food additive in § 201(s) does not differentiate between food for humans and food for animals. *See* 21 U.S.C. § 321(s) (1976).

217. *See* notes 132-39 *supra* and accompanying text.

218. *See* text at note 160 *supra*.

1968,[219] animal drugs were potentially subject to the general requirements of section 505, which was applicable to all new drugs, veterinary as well as human.[220] That section, from 1962 on, required that a new animal drug be proved effective as well as safe for the animals to which it would be administered.[221] Furthermore, a drug to be used in food-producing animals in a fashion that could leave residues in the edible tissues had to meet the food safety requirements of the Food Additives Amendment.[222] The 1968 amendments established a consolidated licensure procedure, but did not alter the substantive standards applicable to animal drugs that may contaminate human food.[223]

The standards applicable to drugs used in food-producing animals thus require the FDA to balance the risks and benefits of a drug for the animals and to verify the safety vel non of any residues that might occur in food. For an animal feed additive, the agency must evaluate the safety of the compound under the criteria of section 409, including the Delaney Clause. As they apply to animal drugs and feed additives, however, the criteria were significantly changed in 1962. Following the passage of the Food Additives Amendment in 1958, the FDA concluded that no compound found to induce cancer in laboratory animals could be approved for use as an additive to animal feed, on the unexceptionable ground that the Delaney Clause prohibited the approval of any carcinogenic "food additive." This interpretation precluded the marketing of a number of compounds that promised significant savings in the cost of producing livestock. Moreover, it preserved a monopoly for manufacturers of implantable dosage forms of such compounds, which could escape the food additives law if the FDA concluded that they could not "reasonably be expected to become a component of food."[224] The notable example

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219. Animal Drug Amendments of 1968, *supra* note 9.

220. *See* 21 U.S.C. § 355 (1976).

221. A "new animal drug" is one that is not generally recognized as safe and effective for its intended uses. 21 U.S.C. § 321(w) (1976). *See* U.S.C. § 321(p) (1976) (parallel definition of "new drug" for humans). Congress thus excluded from the requirement for premarket approval drugs—human as well as animal—that already enjoyed a reputation among scientific experts as safe and effective. As a practical matter, however, virtually all new chemical entities introduced since 1962 have been subjected to the premarket approval process.

222. This result followed from the Act's definition of food additive, which includes any substance whose intended use "results or may reasonably be expected to result, directly or indirectly, in its becoming a component . . . of any food." 21 U.S.C. § 321(s) (1976).

223. *See* S. REP. No. 1308, 90th Cong., 2d Sess. 1 (1968).

224. This interpretation, which could hardly be said to fly in the face of the statutory

was diethylstilbestrol (DES), a synthetic estrogen believed to be an animal carcinogen. As part of the Drug Amendments of 1962,[225] Congress addressed these problems by adding the following, qualifying language to the flat prohibition of the Delaney Clause:

> *[T]his proviso shall not apply* with respect to the use of a substance as an ingredient of feed for animals which are raised for food production, *if the Secretary finds* (i) that, under the conditions of use and feeding specified in proposed labeling and reasonably certain to be followed in practice, such additive will not adversely affect the animals for which such feed is intended, and (ii) *that no residue of the additive will be found (by methods of examination prescribed or approved* by the Secretary *by regulations . . .) in any edible portion of such animal after slaughter or in any food yielded by or derived from the living animal . . . .*[226]

Known as the "DES proviso," this language requires the FDA to prescribe analytical methods for measuring residues of a carcinogenic drug or feed additive in animal tissues (meat, milk, and eggs) used for human food. This amended version of the Delaney Clause is implemented through the procedures for licensing animal feed additives and new animal drugs.[227] Under current FDA practice, the manufacturer of a new animal drug or animal feed additive that might be a carcinogen must conduct chronic toxicity tests of the compound (and selected metabolites) to determine whether the Delaney Clause applies to the product. If the drug is found to induce cancer,[228] the manufacturer must submit chemical analytical and confirmatory methods adequate to detect unlawful residues.

The formal administrative process for the approval of new

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language, also aggravated other competitive inequities. Some producers of additives to animal feed had obtained informal FDA approval for their products in the mid-1950s. These approvals, in the agency's view, constituted "prior sanctions" within the meaning of § 201(s), 21 U.S.C. § 321(s) (1976). Thus, some manufacturers were able to market feed supplements that promoted growth while others were stifled by the FDA's interpretation of the new law. Address by Richard Kingham, Course on Food and Drug Law for FDA Scientists, at University of Virginia School of Law (August 18, 1978).

225. Drug Amendments of 1962, § 104(f)(1), Pub. L. No. 87-781, §104(f)(1), 76 Stat. 785 (1962) (codified at 21 U.S.C. § 348(c)(3)(A) (1976)) H.R. REP. No. 2464, 87th Cong., 2d Sess. 5 (1962); H.R. REP. No. 2526, 87th Cong., 2d Sess. 20 (1962) (Conference Report).

226. 21 U.S.C. § 348 (c)(3)(A) (1976) (emphasis added). Essentially identical language was incorporated in the Color Additive Amendments of 1960, *supra* note 9, and was later included in the provisions that Congress enacted in 1968 to govern approval of new animal drugs, 21 U.S.C. § 301b (d)(1)(H) (1976).

227. *See* 21 U.S.C. §§ 348, 360b (1976); Assays for Carcinogenic Residues, *supra* note 203, at 17,069.

228. Perez, *Human Safety Data Collection and Evaluation for the Approval of New Animal Drugs*, 3 J. TOXICOLOGY & ENVT. HEALTH, 837, 852-53 (1977).

animal drugs resembles that for human food and animal feed additives, with comparable opportunities for a formal evidentiary hearing on any denial of approval and for judicial review. Essentially the same procedures must be followed if the FDA wishes to withdraw approval of a compound on the ground that it fails to meet the requirements of the modified Delaney Clause or is otherwise unsafe for humans.[229]

Before approving a new animal drug, the FDA must determine that the drug is effective for its intended uses in target animals (including, if pertinent, growth promotion), that it will be safe for the animals, and, if the animals are sources of human food, that any residues will, with reasonable certainty, be safe for human consumption.[230] In applying the first two criteria, the agency makes a rough risk-benefit analysis of the kind it conducts in evaluating drugs for human use. The third criterion, however, embodies the basic safety standard of the Food Additives Amendment, which, in the agency's view, does not permit balancing any risk to human health against benefits to animal husbandry or food production.[231] In substance, the drug residue is treated sim-

229. There is a notable distinction between the statutory procedures applicable to new animal drugs and those applicable to animal feed additives. Under § 512, the FDA may not withdraw the approval of a drug without first according the manufacturer an opportunity for an evidentiary hearing unless the Secretary of HEW personally determines that the drug poses an "imminent hazard" to human health. *See* 21 U.S.C. § 360b(e) (1976). Until very recently, the FDA had construed "imminent hazard" to include only situations in which the risk of injury is both serious and *immediate*. Thus, the cancer hazard associated with smoking cigarettes would not constitute an "imminent hazard" because of the lengthy latency of the illness, coupled with its close association with prolonged exposure. The Subcommittee on Oversight and Investigations of the House Commerce Committee has severely criticized this narrow definition, contending that "imminent hazard" referred to the potential seriousness of injury and had little to do with the length of time necessary for its occurrence or its likelihood. SUBCOMM. ON OVERSIGHT AND INVESTIGATIONS OF THE HOUSE COMM. ON INTERSTATE AND FOREIGN COMMERCE, 94TH CONG., 2D SESS. FEDERAL REGULATION AND REGULATORY REFORM 293-95 (Comm. Print 1976).

The same imminent-hazard standard applies to human drugs. The Secretary of HEW has only invoked this standard once. *See* Phenformin: Public Hearing, 42 Fed. Reg. 21,845 (1977). This proposed ruling, involving a drug in wide use for the treatment of diabetes, may well liberalize the FDA's historical interpretation of the "imminent hazard" language. Without the involvement of the Secretary of Health, Education and Welfare the FDA could make the withdrawal of a food or feed additive regulation effective pending a hearing simply by refusing to stay its action, even if objections requiring a formal evidentiary hearing were submitted. *See* 21 U.S.C. § 348(e) (1976).

230. *See* 21 U.S.C. § 360b(d) (1976).

231. The decision in Hess & Clark, Div. of Rhodia Inc. v. FDA, 495 F.2d 975 (D.C. Cir. 1974), suggests a contrary conclusion. However, the court's dictum fails to distinguish between the criteria applicable to human drugs and those applicable to animal drugs, which in effect incorporate the "no benefit" formula of the Food Additives Amendment. *See* Freedman, *supra* note 114, at 268-70. Moreover, the court's implication would anoma-

ply as another type of indirect food additive. Accordingly, if an animal drug would leave unsafe residues in food, the FDA would not approve it even if its use might lower production costs, reduce meat prices, or control animal disease. The agency has never seriously considered requiring that meat derived from treated animals be labeled to alert consumers to the potential risks from drug residues.[232] Moreover, most meat and many poultry products are packaged at the point of sale, which would make it difficult to enforce such a labeling requirement comprehensively.

The Act does not accord special treatment based upon their prior use to residue-producing animal drugs, as it does for certain classes of intentional ingredients of human food or animal feed.[233] The law does not require premarketing approval of animal drugs that are generally recognized as safe and effective,[234] and it does "grandfather" certain products marketed prior to 1938 or 1962.[235] As a practical matter, however, neither escape route is available to most currently marketed animal drugs that are capable of leaving residues in human food, nor would either be open to any new product. Accordingly, the modified Delaney Clause can be

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lously permit the FDA to consider the benefits of human food "additives" administered to food-producing animals in the form of drugs but not the benefits of constituents resulting from the use of additives in the feed of such animals, which remain regulated under § 409.

232. The FDA probably could assert authority over the labeling of retail packages of meat and poultry products, although the agency has historically deferred to USDA regulation in this area. The practical difficulties posed by the jurisdictional overlap aside, the FDA has found in the Food, Drug, and Cosmetic Act authority for comparable labeling requirements for other products. For example, the FDA has required manufacturers of hair dyes containing coal-tar dyes to include a warning that the product contains an ingredient that can penetrate the skin and which causes cancer in laboratory animals. Coal Tar Hair Dyes Containing 4-Methoxyl-M-Phenylenediamine or 4-Methoxy-M-Phenylenediamine Sulfate, 43 Fed. Reg. 1101 (1978). The authority of the FDA to require warnings about ingredients has been upheld by the District Court for the District of Columbia. Cosmetic, Toiletry & Fragrance Assn. v. Schmidt, 409 F. Supp. 57 (D.D.C. 1976). Although in that case the agency relied on the "false or misleading" provison applicable to cosmetics, an identical provision applies to food. *Compare* 21 U.S.C. § 362(a) (1976) *with* 21 U.S.C. § 343(a)(1) (1976). For a discussion of the overlap between FDA and USDA jurisdiction over labeling of meat and poultry products, see 5 SEN. COMM. ON GOVERNMENTAL AFFAIRS, 95TH CONG., 1ST SESS., STUDY ON FEDERAL REGULATIONS 113 (Comm. Print 1977).

233. There are relatively few prior sanctioned additives to animal feed, although the FDA did countenance the marketing of DES as an animal feed additive by a few manufacturers prior to 1958. The agency has subsequently sought to limit these approvals and to extinguish them at any opportunity, *e.g.*, when a manufacturer's plant burned down. The few prior sanctioned feed additives are subject to the standards of 21 U.S.C. § 342(a)(1) (1976). *See* note 164 *supra* and accompanying text.

234. *See* 21 U.S.C. §§ 360b(a), 321(w) (1976).

235. 21 U.S.C. § 321(p)(1), (w)(1) (1976). The 1962 Drug Amendments Act contained additional transitional provisions, *see* Pub. L. No. 87-781, § 107, 76 Stat. 781 (1962).

considered potentially applicable to almost all drugs used in food-producing animals, a significant number of which are suspected laboratory animal carcinogens.[236]

Precisely for this reason Congress's 1962 modification of the Delaney Clause has long been controversial. The FDA has assumed that the amended clause does not automatically forbid approval of a carcinogenic drug or animal feed additive simply on a finding that its use may result in *some* residues, however small. Rather, the agency contends that the law permits approval if the sponsor submits analytical methods capable of measuring—and thereby of controlling—any residues that may be unsafe.[237] Until 1977, however, the FDA had not adopted formal criteria for evaluating analytical methods offered to control unsafe residues. It reviewed each new drug individually and, generally, required that no residues should be detectable by the best analytical method then available.[238] Because some animal drugs have been tested chronically and found carcinogenic only after they were initially marketed, however, a few drugs obtained approval on the basis of assay methods less sensitive than might now be prescribed.[239]

Improvements in analytical chemistry have affected the FDA's efforts to control animal drug residues almost as dramatically as its regulation of indirect food additives. The agency has initiated proceedings to withdraw approval of DES implants because the drug has been found to leave residues at levels that

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236. In 1972 Dr. Klemens Johnson, former Director of FDA Bureau of Veterinary Medicine's Division of Veterinary Medical Review, prepared a 36-page memorandum criticizing the agency's method for detecting drug residues in food animals. Dr. Johnson also assembled a list of 19 animal drugs which were potentially carcinogenic but for which no adequate method existed for detecting residues. This "Johnson Memorandum" was later the target of a congressional investigation that resulted from the Bureau Director's attempts to recall and suppress all copies of the memorandum. For a full discussion of the memorandum and subsequent investigation, see HEW Review Panel on New Drug Regulation, Report of the Special Counsel's Investigation of Allegations Relating to the Bureau of Veterinary Medicine Food and Drug Administration 34-82 (May 1977).

237. Assays for Carcinogenic Residues, *supra* note 203, at 17,086-87.

238. Chemical Compounds in Food-Producing Animals: Criteria and Procedures for Evaluating Assays for Carcinogenic Residues in Edible Products of Animals, 42 Fed. Reg. 10,412 (1977).

239. *See, e.g.*, SUBCOMM. OF OVERSIGHT AND INVESTIGATIONS OF THE HOUSE COMM. ON INTERSTATE AND FOREIGN COMMERCE, 94TH CONG., 2D SESS. FEDERAL REGULATION AND REGULATORY REFORM 288 (Comm. Print 1976) (nitrofurans); Diethylstilbestrol: Notice of Opportunity for Hearing on Proposal To Withdraw Approval of New Animal Drug Applications, 41 Fed. Reg. 1804 (1976) (DES); *Regulation of Diethylstilbestrol, 1975: Joint Hearings Before the Subcomm. on Health of the Senate Comm. on Labor and Public Welfare and the Subcomm. on Administrative Practice and Procedure of the Senate Comm. on the Judiciary*, 94th Cong., 1st Sess. 245 (1975) (Johnson Memorandum).

cannot be detected by the methods accepted a decade ago.[240] And, as in the case of indirect food additives, the capacity of analytical methods to measure even smaller residues will enlarge the class of animal drugs and feed additives that are subject to the strictures of the modified Delaney Clause.[241] By contrast with the Delaney Clause itself, the DES proviso makes the *detection* of residues in edible animal tissues, rather than the *addition* of the compound to animals or their feed, the critical inquiry. This focus of the proviso has enabled the FDA to regulate carcinogenic animal drugs and feed additives in a fashion that might logically be applied to other classes of indirect food constituents as well.[242] In a February, 1977 regulation, *Criteria and Procedures for Evaluating Assays for Carcinogenic Residues in Edible Products,*[243] the agency announced the standards it would apply in determining the level of residues an assay for a carcinogenic animal drug or feed additive must be capable of measuring if the compound is to be approved. As reproposed in 1979, the regulation describes the agency's current criteria for deciding what residues may safely be allowed to go undetected.[244]

The 1979 proposal embodies several basic requirements:

1. It mandates chronic testing of any compound that the FDA concludes may leave carcinogenic residues in human food.[245]

2. It dictates that the FDA, by extrapolating from the re-

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240. *See* Diethylstilbestrol: Notice of Opportunity for Hearing on Proposal To Withdraw Approval of New Animal Drug Applications, 41 Fed. Reg. 1804 (1976). An initial decision by the FDA Administrative Law Judge has upheld the withdrawal of approval of the use of DES. *See* Proposal To Withdraw Approval of the New Animal Drug Application for Diethylstilbestrol, [1978 Transfer Binder] FOOD DRUG COS. L. REP. (CCH) ¶ 88,198 (1978).

241. *See* Assays for Carcinogenic Residues, *supra* note 203, at 17,075-77.

242. *See* notes 213-15 *supra* and accompanying text.

243. The FDA's February 1977 regulation was set aside by the United States District Court for the District of Columbia on the ground that the agency had failed to afford manufacturers an adequate opportunity to comment on the scientific rationale for its final criteria. Animal Health Institute v. Califano, ___ F. Supp. ___ (D.D.C. 1978). The court's opinion, however, does not suggest that the agency's basic approach is suspect. In March 1979 the FDA republished its criteria as a proposal and invited further comment. Assays for Carcinogenic Residues, *supra* note 203. The reproposed criteria and the agency's discussion of them differ in only a few details from the version promulgated in ostensibly final form two years earlier. Because the 1979 proposal represents the FDA's latest statement of its policy respecting carcinogenic animal drugs, however, the balance of the discussion in text refers to that document.

244. While on its face the proposal merely prescribes the standard for detecting residues, it effectively sets the criteria for establishing a tolerance. If the FDA-approved test cannot detect a residue, that residue is legally not present even if a more sensitive analytical technique might detect it.

245. Assays for Carcinogenic Residues, *supra* note 203, at 17,078-81, 17,084-86.

sults of positive chronic tests, *e.g.*, tests that demonstrate carcinogenicity, shall project the level of potential residues in the average diet (of meat, milk, or eggs) that corresponds to a one in one million individual lifetime risk of cancer. The proposal terms this risk "acceptable," emphasizing that the risk is only one of many to which individuals are exposed and comparable to that posed by other materials that are considered safe.[246]

3. Finally, the 1979 proposal specifies that before a compound may be approved, the sponsor must provide the FDA with a practicable[247] assay method capable of measuring residues at a level that will assure that no individual is exposed to greater than the extrapolated "acceptable" risk.[248] To increase the probability that actual residues would not exceed the level prescribed, the drug's labeling will specify the scientifically determined period prior to slaughter during which the drug should not be administered or implanted.[249] In substance, the agency is saying that if the potential residues of a carcinogenic animal drug in food will not increase any individual's chance of getting cancer by more than one in one million, those residues may be ignored.

Like the February, 1977 regulation, the 1979 proposal does not contemplate that the FDA will balance the risks and benefits of animal drugs or feed additives. It simply specifies a maximum level of risk—expressed as a level of drug residues that the approved assay method might theoretically fail to detect—which the agency will consider "acceptable." For most carcinogenic animal drugs and feed additives, the sensitivity of an acceptable assay—and thus the level of "permissible" undetectable residues—will have to be in the very low parts-per-billion range. This

246. *Id.* at 17,087-93. The only statutory support for the FDA's designation of an "acceptable risk" of 1 in 1,000,000 is the obligation imposed by the DES proviso to develop *some* criteria for approving assay methods. The FDA stated that such a risk level could he considered of insignificant public health concern because it was the maximum, and therefore unlikely, human risk level. *Id.* at 17,092. The specified level of risk is the risk for an individual who consumes the maximum residue levels every day over a lifetime, and that level assumes that meat products constitute one-third of the total human diet. From these conservative assumptions, the FDA believes that the most likely human risk is several orders of magnitude less than the theoretical "acceptable risk." *Id.*

247. *Id.* at 17,098-101.

248. In some cases, the test sensitivity prescribed will be only indirectly related to the acceptable level of residue. Because many animal drug residues are metabolic by-products of the ingested drug, the presence of any residue is often calculated from measurements of these by-products.

249. *Id.* at 17,101-03. The proposal specifies, it should be noted, that the approved assay method must reveal *no* detectable residues when a drug is used as intended. Otherwise, the drug cannot be approved.

will strain, and perhaps exceed, the capability of most analytical methods currently approved for animal drugs.[250]

3. *Pesticide residues*

Residues of chemicals used to control animals and insects that threaten crops constitute a third class of undesired but not unexpected food constituents. Pesticide residues often remain on raw agricultural commodities after they have been harvested and prepared for consumer purchase without further processing. Residues also appear in processed foods made from raw commodities to which pesticides have been applied. As is outlined below, the present law treats these two situations differently.[251]

Federal regulation of pesticide residues differs from the pattern of the categories of food constituents previously discussed because the primary responsibility for determining permissible levels of human exposure rests with the Environmental Protection Agency, not with the FDA.[252] Most pesticides are subject to

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250. Relying on its understanding of Congress's objective in enacting the original Delaney Clause, the FDA's 1977 regulation specified that if a practicable assay were developed that was more sensitive than the agency's criteria demanded, it would require that the new method be used. 42 Fed. Reg. at 10,418-19. The FDA's preamble conceded that the legislative history of the DES proviso provides no clear indication of Congress's intent. One interpretation of the DES proviso is that it merely permits the use of drugs that have conclusively been shown to leave no residues. The agency rejected this interpretation on the ground that it would render the clause a "Catch-22" because modern methods of chemical analysis have confirmed that any drug will leave some residues, alheit perhaps below the level of detection.

The FDA's 1977 decision was controversial: One of the regulation's objectives was to provide some stability in the regulation of animal drugs, and to forestall continuous pressure to develop even more sensitive methods for detecting residues. The agency's decision would not have avoided the uncertainty posed by the possible development of new assays capable of detecting residues below the "acceptable risk" level. Without explanation, the 1979 proposal omits the qualification that the FDA may later demand use of a more sensitive assay than the one required by the agency's criteria.

251. Residues may also contaminate commodities other than those on which pesticides are used, through drift following initial application or persistence in the environment. When this occurs, the FDA currently regulates the residues as environmental contaminants under §§ 402(a) and 406, 21 U.S.C. §§ 342(a), 346 (1976). Thus, a single pesticide may be subject to regulation under both § 406 and § 408 of the Act, 21 U.S.C. §§ 346, 346a (1976). *But see* United States v. Ewig Bros. Co., 502 F.2d 715 (7th Cir. 1974). The discussion here exclusively concerns federal efforts to regulate residues on raw agricultural commodities for which a pesticide has been specifically approved and residues in processed foods derived from those commodities.

252. Responsibility for this function formerly rested with the FDA, and authority to register pesticides with the Department of Agriculture. *See* Reukauf, *Regulation of Agricultural Pesticides*, 62 IOWA L. REV. 909, 910-11 (1977). The reassignment in 1970 of authority for establishing tolerances under § 408 still left the FDA with primary responsibility for monitoring marketed foods to assure compliance within EPA tolerances. Reorg. Plan No. 3 of 1970, 84 Stat. 2086, *reprinted in* 5 U.S.C.A. app. II, at 60 (Supp. 1979).

regulation under two statutes. The Federal Insecticide, Fungicide, and Rodenticide Act (FIFRA)[253] requires licensure of any pesticide distributed for use in the United States. Sections 408 and 402(a)(2)(B) of the Food, Drug, and Cosmetic Act forbid the distribution of raw or processed foods bearing pesticide residues that have not been sanctioned by the EPA.[254] The safety of food for human consumption is the concern of the latter provisions.

Under FIFRA, every pesticide used in the United States must be "registered," *i.e.*, licensed, by the EPA.[255] A pesticide "shall" be registered if, in addition to meeting other requirements not pertinent here, "when used in accordance with widespread and commonly recognized practice it will not generally cause unreasonable adverse effects on the environment."[256] Congress has defined this standard to forbid "any unreasonable risk to man or the environment, taking into account the economic, social and environmental costs and benefits of the use of any pesticide."[257] Under this broad language, the EPA considers the full range of a pesticide's possible health effects, including its capacity to induce cancer,[258] and is empowered, indeed obligated, to weigh against these risks a pesticide's ability in eradicating pests and promoting food production.[259] FIFRA does not preclude registration of a pesticide that induces cancer in laboratory animals, although the EPA has relied on such evidence to terminate registration of several compounds and has established a presumption against initial or continuing registration of pesticides that are recognized or suspect animal carcinogens.[260] In the registration

253. 7 U.S.C. §§ 135-136 (1976). In 1972, Congress substantially revamped the existing statutory scheme for pesticide control when it passed the Federal Environmental Pesticide Control Act, Pub. L. No. 92-516, 86 Stat. 973 (1972) (codified in scattered sections of 7, 15, & 21 U.S.C.). That law provided a transitional period to permit reregistration, in accordance with new, more demanding standards of safety, of all pesticides previously registered under FIFRA. In 1978, Congress again amended the statutory scheme for pesticides control to permit the conditional registration of pesticides while the data necessary for complete registration is being generated. The amendments also seek to expedite the registration process by permitting the EPA to register pesticides on a generic basis. *See* Federal Pesticide Act of 1978, Pub. L. No. 95-396, 92 Stat. 819.

254. 21 U.S.C. §§ 342(a)(2), 346a(a) (1976).

255. 7 U.S.C. § 136a(a) (1976).

256. 7 U.S.C. § 136a(c)(5) (1976).

257. 7 U.S.C. § 136a(bb) (1976).

258. Health Risk and Economic Impact Assessments of Suspected Carcinogens, 41 Fed. Reg. 21,402 (1976).

259. *Id. See also* Regulations for the Enforcement of the Federal Insecticide, Fungicide, and Rodenticide Act, 40 C.F.R. § 162.11 (1978).

260. The EPA has established a set of rebuttable presumptions against registration to aid in determining whether a pesticide is likely to cause unreasonable adverse effects.

process, the EPA is concerned principally with the health of persons exposed to the pesticide during its application, while harvesting or transporting crops, or in the environment generally. The agency regulates the compound's risks as a potential contaminant of food under sections 408 and 409 of the Food, Drug, and Cosmetic Act.

A pesticide that is applied to a commodity consumed by humans might "reasonably be expected to become a component"[261] of food, whether the commodity is marketed in a raw state or after processing. To exclude pesticide residues from its compass, the statutory definition of food additive excepts pesticide chemicals "in or on a raw agricultural commodity," and thus exempts such constituents of food from the requirements of section 409.[262] At the same time, section 402(a)(2)(B) of the Act deems a food adulterated "if it is a raw agricultural commodity and it bears or contains a pesticide chemical which is unsafe within the meaning of section 408(a)."[263] This provision was added to the Act in 1954 as part of the legislation that authorized the FDA to establish tolerances for residues of registered pesticides on raw agricultural commodities.[264] Pursuant to this authority, which appears in section 408 of the Act, the EPA determines the quantity of a pesticide that may remain on a raw commodity when it enters interstate commerce. While FIFRA requires the registration of all pesticides, section 408(a) of the Food, Drug, and

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A rebuttable presumption arises if the pesticide exceeds specified criteria for any of three types of effects: (1) acute toxicity; (2) chronic toxicity; or (3) lack of emergency treatments for exposed humans. Chronic toxicity is defined in terms of oncogenic (carcinogenic) or mutagenic effects. These rebuttable presumptions shift to the applicant or registrant the burden of demonstrating for a pesticide initially found to be chronically toxic that (1) when considered with proposed restrictions on use and common practices of use, the pesticide will not concentrate, persist, or accrue to levels to have any significant chronic adverse effects; or (2) that the EPA's determination that it exceeds the criteria for risk was in error. In addition, the applicant may submit evidence to demonstrate that the economic, social, and environmental benefits of the use of the pesticide outweigh the risk of use. *See* 40 C.F.R. § 162.45 (1978).

While the EPA is particularly attentive to the carcinogenic potential of pesticides, *see* Health Risk and Economic Impact Assessments of Suspected Carcinogens, 41 Fed. Reg. 21,402 (1976), the agency may still permit registration of a carcinogenic pesticide if its economic benefits outweigh the health risk. *See* SUBCOMM. ON OVERSIGHT AND INVESTIGATONS OF THE HOUSE COMM. ON INTERSTATE AND FOREIGN COMMERCE, 94TH CONG., 2D SESS., FEDERAL REGULATION AND REGULATORY REFORM 198 (Comm. Print 1976) (letter of Russell Train, Director of EPA).

261. *See* 21 U.S.C. § 321(s) (1976).

262. 21 U.S.C. § 321(s)(1) (1976).

263. 21 U.S.C. § 342(a)(2)(B) (1976).

264. Act of July 22, 1954, Pub. L. No. 83-518, § 2, 68 Stat. 511 (1954)(current version at 21 U.S.C. § 342(a)(2)(B) (1976)).

Cosmetic Act requires a tolerance only for "[a]ny poisonous or deleterious pesticide chemical which is not generally recognized . . . as safe for use."[265] Accordingly, residues of a pesticide that are GRAS do not require formal government approval.[266]

Section 408(b) prescribes the criteria the EPA must use to establish tolerances:

> [T]he Secretary shall give appropriate consideration, among other relevant factors, (1) to the necessity for the production of an adequate, wholesome, and economical food supply; (2) to the other ways in which the consumer may be affected by the same pesticide chemical or by other substances that are poisonous or deleterious; and (3) to the opinion [of the Secretary of Agriculture as] submitted with a certification of usefulness [of the pesticide]. . . . In carrying out the provisions of this section relating to the establishment of tolerances, the Secretary may establish the tolerance applicable with respect to the use of any pesticide chemical in or on any raw agricultural commodity at zero level if the scientific data before the Secretary does not justify the establishment of a greater tolerance.[267]

Conspicuously, this language does not mention the risk of cancer, and since a pesticide residue on a raw commodity is excepted from the definition of a food additive,[268] the Delaney Clause does not apply. The EPA could, therefore, establish a finite tolerance for a pesticide that has been shown to induce cancer in experimental animals (indeed in man) but that, because of its utility, remains eligible for registration under FIFRA.[269] In short, the Act permits the approval of constituents of food—residues of pesticides on raw commodities—that could not lawfully be added as direct ingredients. This inconsistency is amplified by the Act's distinctive treatment of pesticide residues in processed foods.

While many types of processing substantially reduce the levels of pesticide residues on raw agricultural commodities, few

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265. 21 U.S.C. § 346a(a) (1976).

266. Few pesticides qualify for this exception because by design, they are biologically active substances capable of causing adverse effects in living organisms.

267. 21 U.S.C. § 346a(b) (1976).

268. *See* note 262 *supra* and accompanying text.

269. So far as I am aware, this has rarely occurred. One recent example occurred in the summer of 1977, when the EPA authorized the use of a carcinogenic pesticide, BAAM, on two critical crops in Oregon and Idaho. 42 Fed. Reg. 37,437 (1977). A similar exemption was granted in February 1978 for certain crops in California and Utah. 43 Fed. Reg. 5884 (1978). In both cases, the EPA determined that the economic consequences of failing to permit the pesticide's use outweighed the minimal health hazard of its limited use and occurrence as residues in foods.

processes eliminate all such residues.[270] Congress therefore recognized that some provision was needed to control pesticide residues that persist on raw commodities used to make finished foods, *e.g.*, canned vegetables. Accordingly, the exception for pesticide chemicals in the Act's definition of food additive extends only to residues "in or on a raw agricultural commodity."[271] A pesticide residue on a processed food, unless it is GRAS or prior sanctioned, is a food additive which therefore adulterates food if no regulation approves its presence.[272]

A processed food containing any residue of a pesticide for which the EPA has not established a tolerance on the raw commodity is adulterated under section 402(a)(2)(C) of the Act.[273] But if such a tolerance has been established, Congress dispenses with the requirement that the pesticide in the processed food also be approved under section 409—if certain conditions are met.[274] These conditions are set out in a proviso to section 402(a)(2)(C), which was added in 1958 and states:

> *Provided,* That where a pesticide chemical has been used in or on a raw agricultural commodity in conformity with an exemption granted or a tolerance prescribed under section 408 and such raw agricultural commodity has been subjected to processing such as canning, cooking, freezing, dehydrating, or milling, the residue of such pesticide chemical remaining in or on such processed food shall, notwithstanding the provisions of sections 406 and 409, not be deemed unsafe if such residue in or on the raw agricultural commodity has been removed to the extent possible in good manufacturing practice and the concentration of such residue in the processed food when ready to eat is not greater than the tolerance prescribed for the raw agricultural commodity . . . .[275]

The Act thus condones pesticide residues for which a tolerance has been established if that tolerance is not exceeded when the raw commodity is processed. This means that if the EPA estab-

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270. *See Cancer-Causing Chemicals—Part 2: Hearings Before the Subcomm. on Oversight and Investigation of the House Comm. on Interstate and Foreign Commerce*, 95th Cong., 2d Sess. 30-31 (1978).

271. *See* note 262 *supra* and accompanying text.

272. *See* text at notes 113-39 *supra.*

273. 21 U.S.C. § 342(a)(2)(C) (1976).

274. The legislative history of the 1958 Food Additive Amendments does not explain why Congress chose to exempt pesticide residues on processed foods. Presumably it concluded that the evaluation of safety performed under § 408 adequately protected consumers so long as the amount of residue did not exceed that authorized for the raw commodity. But no evidence suggests that Congress was sensitive to the fact that the applicable criteria for evaluation under §§ 408 and 409 are not the same.

275. 21 U.S.C. § 342(a)(2)(C) (1976).

lishes a finite tolerance for a carcinogenic pesticide on a raw commodity, that pesticide may lawfully appear in the processed food in a quantity that does not exceed the tolerance—"notwithstanding," as the proviso states, the Delaney Clause.

One further example illustrates the exquisite, if arcane, relationship between section 409 and the provisions of the Act applicable to pesticides. Although processing may reduce the residues of a pesticide on a raw commodity, it may sometimes concentrate the residues by shrinking the volume of solid material.[276] When this occurs, the proviso to section 402(a)(2)(C) is not satisfied and the quantity of the pesticide that exceeds the section 408 tolerance is considered a food additive.[277] In such a case, a distributor of the processed food needs a food additive regulation to prevent the food from being considered adulterated and, to obtain such a regulation, must demonstrate, with reasonable certainty, that the quantity of the pesticide is safe.[278] Many food additive regulations authorizing concentrated pesticide residues have been promulgated by the EPA, which is also responsible for implementing this facet of the Food Additives Amendment because it is familiar with the safety data submitted to support tolerances under section 408.[279]

Suppose that the EPA established a tolerance for a pesticide on raw cabbage at ten parts per million. Suppose further that the pesticide induces cancer in animals but, because of its importance in controlling crop pests, the EPA maintains its registration. Under the proviso to section 402(a)(2)(C), up to ten parts per million of this carcinogenic "additive" may lawfully appear in food. But if residues of the pesticide concentrated during processing, any quantity in excess of ten parts per million would constitute an "unsafe food additive" and, under the Delaney Clause, presumably could not be approved.[280] However, if the EPA were to raise the tolerance for raw cabbage to a level that the residues in the processed cabbage would not exceed,[281] in a legal sense the

276. *Cancer-Causing Chemicals—Part 2: Hearings Before the Subcomm. on Oversight and Investigations of the House Comm. on Interstate and Foreign Commerce*, 95th Cong., 2d Sess. 30 (1978).

277. *See* 21 U.S.C. § 342(a)(2)(C) (1976).

278. *See* text at notes 112-28 *supra*.

279. *See* 21 C.F.R. § 193 (1978).

280. In administering § 409 of the Food, Drug, and Cosmetic Act, the EPA is presumably bound by the Delaney Clause, as the FDA would be.

281. The EPA would of course have to determine that this higher level would meet the more general safety criteria of § 408 of the Act. *See* 21 U.S.C. § 346a (1976).

food additive would disappear—and the Delaney Clause would not preclude marketing the treated cabbage!

It should be noted that even a zero tolerance for a carcinogenic pesticide does not assure that no residues will appear on the raw commodity or in processed food. Effective enforcement of a zero tolerance depends on growers' and food producers' observance of meticulous processing standards and intensive FDA monitoring. The FDA simply lacks the inspectional capability to guarantee that no commodities containing measurable, and thus illegal, pesticide residues reach consumers. Moreover, even lot-by-lot monitoring would suffer from the limits of the analytical methods for measuring pesticide residues. In reality, therefore, a zero tolerance may be considered a finite tolerance, established at the level that available analytical methods can measure. This is true for any unintended constituent of food whose occurrence cannot be effectively controlled or whose benefits are thought to justify its continued use.

The procedure for obtaining a tolerance for pesticide residues on a raw commodity resembles the procedure for obtaining approval of a food additive, with one significant difference. The EPA on its own initiative may, or at the petitioner's request must, submit the petition to an advisory committee of experts appointed by the National Academy of Sciences for evaluation and recommendation.[282] The Act provides an opportunity for a formal evidentiary hearing before the EPA may refuse to establish a tolerance, although few petitioners have ever requested a hearing.[283] The EPA must follow the same procedures in revoking or modifying a tolerance once established. When petitioned to promulgate a food additive regulation authorizing a residue on a processed food in excess of that sanctioned for the raw commodity, the EPA must follow the same procedures as those that apply to the FDA.[284]

IV. Conclusion

This Article describes the ways in which current federal law attempts to assure that food is safe for human consumption. It should be obvious even to the casual reader that safety, in this case, is an objective, rather than a reality. The law's efforts to make food safe are inevitably tempered by competing considera-

282. 21 U.S.C. § 346a(d)(3)(5) (1976).
283. 21 U.S.C. § 346a(d)(5) (1976).
284. *See* text at notes 132-39 *supra*.

tions, such as a desire to retain traditional foods, the wish to produce food abundantly and cheaply, and practical limitations on our ability to detect or eliminate contaminants. As the preceding sections demonstrate, however, Congress has not simply instructed the FDA to attain the optimum mix of benefits and risks in controlling consumer exposure to possibly toxic food constituents. Rather, Congress has divided the universe of food constituents into several categories, and specified different, occasionally inconsistent, criteria for regulating each of them. In a few instances, these criteria reflect a definitive congressional assessment of the risks and benefits of a category of constituents as a class. More often, they specify the primary objective—safety—and leave other considerations unmentioned.

In general, the Act's food safety requirements are intended to minimize risk. Congress has usually instructed the FDA to restrict or ban any food or food constituent that might expose any significant number of consumers to a risk of harm—regardless, presumably, of any countervailing benefits. But the qualifier, "presumably," is important: Congress often appears to have ignored the question of competing benefits because it assumed that few constituents of food, natural or added, would pose significant risks. For example, in 1938 Congress probably believed that most agricultural commodities—if adequately protected from man-made filth—would be perfectly safe for virtually all consumers.[285]

The present law, however, is not naive. While the FDA has sometimes had to interpret the Act imaginatively,[286] its general structure reflects an awareness of the competing interests. The

285. Alternatively, Congress may simply have concluded that the interests involved in producing agricultural commodities were so substantial that only a showing of a serious risk could justify regulatory action against a staple of the American diet. Congress obviously intended to make it more difficult for the FDA to regulate naturally occurring constituents of familiar foods. *See* notes 59-63 *supra* and accompanying text. Indeed, it could be said that many of the categories recognized by the current law reflect implicit congressional risk-benefit judgments. For example, it is possible to interpret the statutory definition of food additive—including the exceptions for GRAS substances and prior sanctioned ingredients—with § 409's high standard for approval as representing a similar risk-benefit judgment, in this instance a judgment that no synthesized new ingredient was likely to prevent benefits that would justify any risk. To the extent that such policies must be inferred from the structure of the statute, rather than stated in its terms and legislative history, however, the present law can fairly be criticized for lack of candor.

286. The collection of provisions found in the original 1938 act—§§ 402(a)(1), 402(a)(2)(A), and 406—have posed the greatest challenge to the agency's ingenuity. No theory of statutory construction can satisfactorily reconcile these provisions. The difficulties the FDA has encountered are apparent from its analysis in Poisonous or Deleterious Substances in Food: Notice of Proposed Rulemaking, 39 Fed. Reg. 42,743 (1974). *See* notes 91-92 *supra* and accompanying text.

central distinction between "added" and other constituents, I suggest, recognizes both important differences in government's ability to control exposure to constituents and in the "benefits" that are popularly ascribed to various classes of foods. For example, I suspect that most consumers of potatoes would prefer them to almost any synthesized source of carbohydrates containing fewer potentially toxic constituents. Similarly, Congress's establishment of separate licensing systems for pesticide residues, food and color additives, and animal drugs is not only a logical response to concerns about the risks posed by different classes of "added" constituents, but might be adopted again if the law were rewritten today.[287]

That the Act permits the FDA to treat environmental contaminants as "added" to food may weaken the statute's candor, but this arrangement grew largely from the FDA's desire to establish an administrative mechanism for determining the level of exposure that is compatible with consumer health and technological reality, rather than to leave the issue to individual judges in suits to enforce the Act's general prohibition against adulterated food. Whatever one thinks of the agency's handling of specific contaminants, an approach to setting tolerances similar to the one it has devised under section 406 seems a logical way to cope with the problem.

But though the Act can be considered rational in its general structure, the current system for regulating food safety is under enormous strain. The causes of this, I believe, require that consideration be given to revising the current law. A subsequent article will describe the detailed features of a revised statute, but the reasons for considering revision may be suggested here.

First, the public is increasingly aware that large numbers of foods contain constituents that pose risks to health. This awareness comprehends that manufactured foods contain suspicious chemical preservatives and other synthesized ingredients, and that even natural constituents of home-grown fruits and vegetables may pose risks. And it recognizes the danger in the growing category of substances that become or, in the words of the Act,

287. While one might for administrative convenience retain separate statutory systems for regulating these constituents, there is little basis for the minor procedural differences that appear in the current provisions of the law. *See* notes 132-39, 229, 282-84 *supra* and accompanying text. More fundamentally, as suggested below, text at note 288 *infra*, there is no obvious reason why different substantive standards should apply to pesticide residues, animal drugs, and food contact materials—"indirect" constituents that present similar problems of control and provide comparable benefits.

"may reasonably be expected to become," components of food through their use in packaging, pest control, or livestock production. Second, although such generalizations are treacherous, there is a popular appreciation of the benefits associated with some of these risk-creating constituents. Certainly there is more emphasis on developing and using technologies that make food abundant, cheap, and easy to transport and prepare.

These developments complicate regulatory decisions, because they have not produced, nor been accompanied by, a national consensus about what kinds of benefits are important and what kinds of risk are acceptable. Regional and ethnic differences in diet have given way to strongly-held, widely dispersed preferences for special types of foods ranging from synthesized diet foods to organically grown vegetables. Increasing variations in dietary preferences have been accompanied by national production and marketing of food, which make it more difficult for individual consumers to control the source of their foods, and more difficult for government regulators to identify the mix of benefits and risks that will satisfy the majority of the population. Furthermore, regulation abhors diversity. It is difficult for an agency to develop, and more difficult for it to implement, a policy that permits regional or social disparities in levels of individual exposure to risk. And it would be virtually impossible to justify such a policy in the Washington environment, where the insistent demand is to protect the most vulnerable.

The strains on the present system stem also from basic flaws, both substantive and procedural, in the law itself. While the Act's dichotomy between added and naturally occurring constituents may make sense, within categories of constituents the statute recognizes distinctions that cannot be justified as sound policy, and that allow the threshold classification of a substance to dictate its regulatory fate. For example, the Act divides the broad category of intentional ingredients into those used to color foods and those used for other purposes. The Color Additive Amendments establish a "positive list" system for regulating food colors: no color may be used which the FDA has not approved, following testing by the users. The Food Additives Amendment, by contrast, exempts ingredients that are GRAS, makes no provision for transition to food additive status, and provides apparently indefinite protection for ingredients once approved, however, casually, by the FDA or the USDA.

The distinction among the three primary categories of indirect food constituents—pesticide residues, indirect food addi-

tives, and animal drugs—are perhaps even less justifiable. In establishing tolerances for pesticides on raw commodities, the EPA may, and does, consider economic benefits. No such inquiry is permitted in regulating an indirect food additive. And the FDA maintains, I believe correctly, that the benefits of an animal drug may not lawfully be considered in deciding how much, if any, of it may remain in human food.[288] The disparities are even more exquisite when one considers the Delaney Clause. The clause does not prevent the approval of a carcinogen in the form of a pesticide residue. Nor does it prohibit the approval of a carcinogenic animal drug, so long as any residue in food escapes detection. But the clause unequivocally forbids the approval of any carcinogenic packaging material that may conceivably migrate to food. All of these substances are used to enhance food production, handling, or storage. If a residue contaminates food, it makes no difference, in terms of human risk, where the residue came from. And no one of these sources is notably difficult to control or more costly to forgo.

The Delaney Clause produces strain of its own as the dispute over saccharin reveals. While one may argue the principle of Delaney—either as an operational statement of scientific knowledge or as a way of preventing the FDA from succumbing to the pressures of food producers—it causes problems because it applies unevenly. A prior sanction can reprieve a vulnerable, but important carcinogen, such as sodium nitrite. Similarly, calling an added substance "unavoidable" may qualify it for more flexible treatment under section 406. And I have already alluded to the different ways in which Delaney applies to indirect constituents of food. The exceptions to Delaney in, or read into, the Act exert enormous pressure to find an escape route when an important substance is discovered to be an animal carcinogen.

Another flaw in the present statute is its consistent failure to define the FDA's authority to consider criteria other than risk. Section 402(a) is a case in point. The Act does not indicate whether, in determining whether a food naturally containing a

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288. *See* Assays for Carcinogenic Residues, *supra* note 203, at 17,075 where the Commissioner observed that, aside from §§ 406 and 408, "the Federal Food, Drug, and Cosmetic Act contains no provision requiring the Commissioner to consider costs or technical feasibility in making any safety decision, including any decision involving cancer-causing chemicals. . . ." After analyzing the so-called DES proviso, the Commisioner concluded:

> From this statutory structure and language, it is evident that any consideration of feasibility and costs is subsidiary to the overriding congressional purpose to permit no additional human cancer risk from food additives, color additives, or animal drugs.

toxic substance is likely to be "ordinarily injurious," the FDA may consider the food's long use, its popularity, or its economic importance. Presumably not, but the statute does not say, and as more natural constituents are discovered to be toxic at some level, the pressure on the FDA to give weight to these statutorily extraneous, but obviously important, factors will increase. The same point can be made about section 409 of the Act, which specifies that the FDA must find a food additive safe and functional, but does not state whether other considerations may enter into its judgment. Here the agency has been explicit; it will not consider an additive's benefits in determining whether it satisfies the basic safety standard. The Act's failure to specify the criteria that the FDA may legitimately weigh invites ingenuity in statutory interpretation when a flat "no risk" standard seems likely to produce an unpopular result.

The Act contains significant procedural flaws as well. The variety of substantive standards governing food constituents is paralleled by an even more striking variation among the statutorily prescribed procedures for reaching regulatory decisions. To establish that a natural constituent renders a food "ordinarily injurious" under the second clause of section 402(a)(1), the FDA must marshal expert testimony in court to prove its contention by a preponderance of the evidence. This process theoretically must be repeated each time the agency seeks to enforce its view against another distributor or shipment of the food. The Act does not expressly authorize it to issue regulations defining the levels of a natural constituent that will adulterate a food.

In regulating contaminants, by contrast, section 406 empowers the FDA to establish tolerances that determine conclusively when a food is adulterated. Tolerances are set through formal rulemaking under section 701(e) of the Act, a complex and costly process which the United States Administrative Conference has sharply criticized.[289] This procedure requires a proposal, opportunity for comment, publication of "final" regulation, opportunity for objections, and, if justified, a formal evidentiary hearing, followed by an administrative law judge's initial decision and the opportunity for an appeal to the Commissioner. Variations of this process are prescribed for establishing pesticide tolerances and to approving food additives, color additives, and animal drugs.

The foregoing description of the formal process overstates the FDA's actual burden. A food distributor's inclination to assert its

289. *See generally* Hamilton, *supra* note 103.

statutory right to a formal hearing depends largely on the consequences of a delay in the agency's decision and the costs of participating in the proceeding. It is extremely rare for a petitioner for a food or color additive or a manufacturer of an animal drug to insist upon a hearing when the FDA appears disinclined to approve its product for initial marketing. Ordinarily it is faster and less expensive to conduct any additional tests the agency demands or to modify the use of the product to conform to the data already submitted. Since 1938, no manufacturer of an animal drug or petitioner for a new color additive has demanded a formal hearing at the initial approval stage. Only two such requests have been made for hearings on food additive petitions.[290] The EPA's experience under section 408 is similar.

By contrast, when the Act requires an opportunity for an evidentiary hearing before the FDA can limit exposure to a product, *e.g.*, before it may withdraw approval of an animal drug or establish a tolerance for a contaminant, the incentives for distributors to insist upon the full procedures mandated by statute are much greater. Hearings have been requested on the last two color additives for which the FDA withdrew approval.[291] The manufacturers of DES have engaged the agency in a hearing on the proposed withdrawal of that compound for more than three years.[292] A requested hearing on the FDA's proposed tolerance for PCBs in paper packaging has been pending for nearly five years while the agency has attempted to forge a settlement that will avert the formal statutory procedure.[293]

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290. The two instances involve cyclamate, for which a food additive petition was filed several years after FDA's initial determination that it was no longer GRAS, and aspartame, another artificial sweetener, which the FDA originally approved, then delayed, for marketing pending a hearing requested by two public opponents of its use, whose interest lay in prolonging the administrative process. *See* notes 135-36, 155 *supra* and accompanying text.

291. The hearings involved FDC Red No. 2 and FDC Red No. 4. Technically, the hearing in each instance was on the FDA's refusal to permanently list the color. *See* 41 Fed. Reg. 15,053 (1976); 41 Fed. Reg. 41,867 (1976). Both colors had previously been provisionally listed and in use since 1960. Thus, the practical effect of the agency's decision was to withdraw approval—and the predicted incentives to challenge the decisions were operative. Because of the peculiar procedures applicable to provisionally listed colors, however, the FDA's decision in both instances became effective before the hearing was held.

292. *See* note 240 *supra* and accompanying text. The proceeding commenced with the publication of a notice of opportunity for hearing in January 1976, 41 Fed. Reg. 1804 (1976), following a court decision ruling that the FDA's earlier attempt to withdraw approval of the drug without a hearing was invalid. *See* Hess & Clark, Div. of Rhodia, Inc. v. FDA, 495 F.2d 975 (D.C. Cir. 1974).

293. The proceeding is described in Polychlorinated Biphenyls (PCBs) in Paper

The FDA's realization that a hearing will usually be requested when it will delay and possibly avert regulation has led it to rely primarily on "action levels" to limit exposure to environmental contaminants. The agency asserts that a proposed tolerance may serve as an action level pending completion of formal rulemaking[294]—and thereby escapes any pressure to finish setting the tolerance. For many contaminants the FDA has relied exclusively on action levels, which are established simply by publication in the Federal Register.[295]

The FDA has thus minimized the costs of the Act's procedural requirements, but it has done so at a price. The agency makes most decisions to approve the use or occurrence of food constituents without hearing public comment and often without explaining the reasons for its judgments. It ordinarily approves food additives simply by publishing in the Federal Register a regulation specifying the terms of the approval and reciting that the additive has been found safe. The supporting safety data are evaluated privately, except on those rare occasions when a member of the public comes to the agency to evaluate the petition. The process for approving new animal drugs is likewise effectively closed to public review. When the FDA announces an action level for a contaminant, it makes available the data supporting its decision and permits access to its internal analysis of risk, avoidability, and detectability, but it accepts no responsibility to respond to any comments it might receive.[296]

Neither Congress nor the FDA has seriously explored regulatory options other than mandatory limitations on exposure to potentially toxic constituents of food. Notably, the Act in most instances does not contemplate the possibility that label warnings or another form of consumer information might be a more discriminating means of regulating consumer exposure.[297] For example, neither section 409's general safety clause nor the Delaney Clause appears to permit the FDA to allow the use of a possibly toxic but useful additive, accompanied by label warnings

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Food-Packaging Material; Order Ruling on Objections and Hearing Regarding Temporary Tolerance, 40 Fed. Reg. 11,563 (1975).

294. *See* 21 C.F.R. § 109.6(d) (1978).

295. *Id.* at § 109.4(b)(2); 42 Fed. Reg. 52,817 (1977).

296. *See* Poisonous or Deleterious Substances, 21 C.F.R. § 109.4(b)(2); 42 Fed. Reg. 52,814, 52,817 (1977).

297. For a more detailed, though ultimately unconvincing, discussion of the possible range of regulatory approaches, including labeling, see Institute of Medicine of the National Academy of Sciences, Food Safety Policy: Scientific and Societal Considerations 8-1 through 8-13 (1979).

on the product. The agency has proposed to do this in the case of hair dyes containing 4-methoxy-m-phenylenediamine, an animal carcinogen, but its proposal clearly indicates that this approach is a second best alternative to banning the substance altogether, which the Act does not allow.[298] The difficulty of devising a genuinely informative label for potentially hazardous constituents, such as saccharin, while protecting consumers who cannot or simply do not read labels, may ultimately force abandonment of this approach, but it is one that merits investigation.

This Article does not purport to solve the problems raised by the Act's treatment of toxic substances in food. I reserve specific recommendations for the Act's revision for a subsequent article. At this juncture I will simply conclude with suggested objectives for statutory reform. First, any new system for regulating food safety must explicitly recognize the special role that food plays in our society. Food provides the nutrients essential for health, but it also underpins many important traditions and accompanies many important ceremonies. Modest risks associated with foods that have little importance for most consumers ought to be considered more serious than greater hazards in foods that enjoy a long acceptance. A system of regulation that attempts to ration exposure to risks in food based solely on some mathematical formula will quickly encounter problems that it cannot resolve.

Second, any new system must explicitly recognize the government's inability to obtain complete information about risk or benefits before a regulatory choice must be made. Adequate data can be obtained about the safety of compounds that are not yet in use and which have commercial sponsors. But problems loom as soon as a compound is approved and become more serious as scientific advances erode the original grounds for approval. Shortage of data becomes most serious when the government attempts to control constituents whose presence in food is not desired or readily controllable, and for which, therefore, there are no petitioners. The FDA must often determine the marketability of contaminated food long before data are available to support definitive judgment. Yet its initial judgment *must* be definitive, at least for the moment, if the agency is to control human exposure effectively. And its decisions must be subject to revision without substantial cost and delay.

Third, any revised system should simplify the procedures for reaching regulatory decisions and force regulators to explain the

298. *See* 43 Fed. Reg. 1101 (1978) and note 232 *supra*.

scientific bases and policies that underlie their determinations.

Finally, Congress should exhaustively describe the criteria regulators may consult and should specify those that are to be ignored. No regulator should be left to determine without legislative guidance whether consumers want cheaper peanut butter and more aflatoxin, more expensive fish and a reduction in exposure to PCBs and mercury, or artificially sweetened soft drinks accompanied by a heightened risk of bladder cancer.