

FOOD SAFETY REGULATION: Reforming the Delaney Clause

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ABSTRACT

The safety of food has been an age-old concern. Early civilizations adopted laws that punished sellers of tainted food. In this country, before food safety became a responsibility of the federal government every state had enacted laws prohibiting the sale of food that contained poisonous substances. The modern scientific and legal instruments available to the US Food and Drug Administration and allied agencies have improved regulation and advances in food preparation, preservation, and storage have contributed to a safer food supply. Even so, some observers believe that contemporary threats to food safety have grown more serious, and they surely excite intense public concern. For nearly two decades Congress has been debating the adequacy of current laws governing food safety. In the closing months of the 104th Congress, both parties finally agreed on the first significant legislative change in over a generation. This chapter examines the origins of the issues that were the focus of this extended debate and analyzes the implications of their resolution.

POTENTIAL THREATS TO FOOD SAFETY

This review focuses chiefly on governmental regulation of chemicals used in food production, but it is appropriate, first, to place this activity in broader context. Current law reflects a crude distinction between dangers posed by substances that occur in food through purposeful human activity (such as the application of pesticides) and substances, including potentially pathogenic organisms, that “contaminate” human food despite efforts to control or eliminate them. Regulatory scientists draw another distinction: between acute hazards (which include most pathogenic organisms) and hazards associated with long-term exposure to toxic substances. The universes bounded by these distinctions

are not congruent, but there is substantial overlap. Many food constituents that could present chronic health hazards are purposefully used in food production, while organisms and substances capable of producing acute adverse effects are generally unintended contaminants.

Until recently, the popular press has mainly focused on potential chronic hazards associated with pesticides and food additives, but increasingly frequent outbreaks of foodborne disease have begun to attract attention. The Centers for Disease Control and Prevention each year receive reports of approximately 500 outbreaks of foodborne disease (3). The Food and Drug Administration (FDA) estimates that microorganisms and other toxins in food cause as many as 33 million cases of illness, and up to 9000 deaths each year, with an annual cost of between \$7.7 billion and \$23 billion (10).

A major cause of these episodes is *Salmonella*, a potential contaminant of poultry, beef, and eggs. Another possibly more serious threat has recently emerged, *E. coli* 0157:H7, the microorganism that in 1994 was implicated in three deaths and illness of 500 persons who had been exposed to tainted hamburger (40a). However, known sources of foodborne disease are only part of the challenge facing regulators: they regularly encounter new pathogens. It was only in the 1980s that *E. coli* 0157:H7 and *Vibrio vulnificus*, both potent pathogens, were recognized as contaminants of food (28). Changing demographics of the consumer population, e.g. the growing number of elderly, and alterations in lifestyle, e.g. fewer families cook meals at home, can affect disease risk. So, too, can changes in the origins and preparation of food (28).

The use in food of synthetic chemicals as ingredients, production aids, and packaging materials has increased dramatically since World War II (10). Industrial chemicals may also contaminate food as the result of persistent environmental release or sudden accident (47). Some of these materials when administered to test animals cause adverse effects, including cancer and birth defects. Despite serious public concern about the potential health effects of such materials, we have only the crudest estimates of the numbers of cases of chronic illness that may be associated with these technological changes. In 1979, the Office of Technology Assessment (OTA) reported that the long-term health risks associated with industrial contaminants of food were unknown (41). Two years later, in a study prepared for the OTA, Doll & Peto attributed no more than 1% –and perhaps less–of all cancer deaths in the United States to food additives, including pesticides (11, 42). No epidemiological study has convincingly linked consumption of particular processed food constituents with chronic human disease, but the limited power of such studies allows room for a substantial number of cases that will never be detected—and thus nourishes continuing debate over government efforts to control the use of man-made chemicals in food.

A recent Institute of Medicine Report suggests that preoccupation with artificial “additives” may be wrong-headed, declaring that “*natural components* of the diet may prove to be of greater concern . . . with respect to cancer” (emphasis added) (5). Among the many “natural” substances the IOM committee identified as potential sources of chronic disease are mycotoxins, including a contaminant of grain and nut termed aflatoxin, “the most powerful liver carcinogen known for some animal species” (5). The committee also identified dozens of inherent constituents of vegetables and fruits that appear to be mutagens or carcinogens when tested independently. No data exist from which to estimate the prevalence of disease associated with consumption of specific natural toxins or particular foods.

If we shift focus to diet generally, we find greater consensus supporting concern about the relationship between food and disease. The Surgeon General has reported (45) that five of the leading ten causes of death among Americans are diet related. Several accounts attribute 50% or more of the cancers among Americans to dietary factors, which include both the amount and type of constituents consumed (e.g. high in fat, low in fresh vegetables and fruit) (42). These findings, first widely publicized in the late 1980s, have significantly influenced both governmental and private behavior. FDA and the United States Department of Agriculture (USDA) were directed (27, 30, 66) to mandate changes in food labels to convey much more information about the macronutrient composition of foods and allow manufacturers greater freedom to make disease-related claims about their products and diets that featured more or less of desired or undesirable constituents. Food sellers have risen to the challenge, not only through the provision of label information but through reformulation of their products to reduce fat, cholesterol, calories, and sodium, and increase levels of desirable components. The role of government in influencing what foods people choose, i.e. what diets they consume, is still evolving. Historically, the regulation of food safety has focused on reducing or eliminating the dangers associated with individual foods or specific food constituents. This traditional regulatory responsibility is the subject of this chapter. I emphasize authorities and actions aimed at purposeful “additives” to the food supply, and, correspondingly, focus on efforts to identify and control potential chronic hazards to human health.

HISTORY OF FEDERAL LEGISLATION REGULATING FOOD SAFETY

The modern federal law governing food safety is a product of incremental legislative action and administrative adaptation. Its conceptual origins are found in legislation enacted nearly a century ago.

1906 Food and Drugs Act

The Progressive movement pioneered federal regulation of food safety with the Meat Inspection Act and the Food and Drugs Act of 1906. The latter law forbade the marketing of foods (and drugs) that were “misbranded” or “adulterated”, two concepts that still underpin regulation. The 1906 Act defined as “adulterated” any food that “contain[ed] any added poisonous or other added deleterious ingredient which may render [the food] injurious to health” (60). A food was also adulterated “if it consists in whole or in part of a filthy, decomposed, or putrid animal or vegetable substance, or any portion of an animal unfit for food . . . or, if it is the product of a diseased animal, or one that has died otherwise than by slaughter” (60). Congress was thus concerned about both potentially dangerous materials “added” to food and food that became unpalatable through improper processing. The latter definition of adulteration did not require proof of any hazard to consumers; it prohibited what is known as aesthetic adulteration even if it posed no risk to health whatever.

The most important feature of the 1906 Act was reflected in the means FDA was given to enforce its prohibitions. FDA could punish or interdict adulteration after the fact; it had no affirmative authority to restrict practices that could result in adulteration. FDA’s subsequent transformation from a policing agency to one empowered to evaluate the safety of substances and processes before they are introduced represents the most significant change in food safety regulation. This transformation, however, was not complete. Congress could assure premarket review of all purposefully used materials by flatly prohibiting any material that FDA had not approved, but the same legal mechanism does not fit naturally occurring “contaminants” or foodborne pathogens whose presence in food is neither planned nor desired.

The Federal Food, Drug, and Cosmetic Act of 1938

Revision of the 1906 Food and Drugs Act was one of the first initiatives of the Roosevelt New Deal. The 1938 Act, passed after the marketing of a therapeutic potion containing an untested ingredient, sulfanilamide, resulted in more than 100 deaths (34), broadened the 1906 Act’s food safety provisions. The new provisions aimed at insanitary processing forbade the sale of food consisting “in whole or in part of any filthy, putrid, or decomposed substance,” of food that was “unfit,” or of food that “has been prepared, packed or held under insanitary conditions whereby it may have become contaminated with filth, or whereby it may have been rendered injurious to health . . .” (62). The new law also recognized that harmful materials might occur naturally in food. A food containing an “added” poisonous substance was adulterated if it *might* be dangerous to health, whereas a food that naturally contained such a substance would not be adulterated “if the quantity of such substance in such food does

not ordinarily render it injurious to health" (62). In this fashion Congress acknowledged the value of, or consumer attachment to, long-used foodstuffs.

Except for the new authority given to FDA over therapeutic drugs, the 1938 Act was, like its predecessor, a policing statute. With two exceptions, the agency had no general authority to require advance proof of the safety of substances added to food or used in food production. The 1938 Act empowered FDA to prescribe so-called standards of identity for staple foods, such as "cheddar cheese," "mayonnaise," or "tomato catsup" (61). Under this authority, the agency could specify what ingredients could be in the official recipe, and it sometimes used this power to forbid ingredients about whose safety it had doubts (33).

Section 406, a provision permitting FDA to set tolerances for pesticides used in producing agricultural products, reflected Congress' awareness that use of chemical pesticides was becoming increasingly important in American agriculture, as well as its belief that FDA should be able to enforce fixed limits, rather than prove that a particular residue-bearing food could be harmful. FDA was allowed to specify the amount of residue that could, consistent with the public health, remain on food, taking into account the need for use of the pesticide (33). Section 406 never became an effective instrument for controlling pesticide residues, however, because FDA had the burden of assembling information about a pesticide's toxicity and of determining, after long and often costly evidentiary hearings, what residues would be safe on particular foods. Rather than set formal tolerances for pesticides, therefore, FDA came to rely on "action levels," which represented the agency's informal judgment of the maximum amount of pesticide that could be present without triggering a charge of adulteration.

Major Food Safety Amendments: 1954–1968

World War II spurred advances in American food processing, preservation, and packaging, and sparked wide interest in new ingredients and processing agents (8, p. 28). Since the law did not require advance approval for any of these technologies, a large number soon came into use. In 1952, Congress established a select committee, chaired by Representative James Delaney of New York, to examine the growing use of chemicals in food. The work of Delaney's committee laid the basis for a series of amendments to the 1938 Act, each intended to enhance the government's ability to assure that new materials added to or used to produce food did not endanger consumer health.

MILLER PESTICIDE AMENDMENTS In 1954, FDA (since 1970 it has been EPA) was authorized to prescribe permitted levels of pesticides on food. The amended FD&C Act made any food bearing a pesticide residue adulterated unless the

residue was within a “tolerance” previously established by the agency (8, p. 28; 63). The burden of seeking a tolerance rested on the marketer of food or, more realistically, on the maker of the pesticide who wanted to sell it to growers. In determining whether, or at what level, to establish a tolerance, FDA was instructed to “protect the public health” but at the same time consider “the necessity for the production of an adequate, wholesome, and economical food supply” (63).¹

FOOD ADDITIVES AMENDMENT In 1958, Congress required FDA approval for new ingredients in processed foods and so-called food-contact chemicals, such as packaging materials and equipment liners (64). The new scheme for “food additives” was in many respects similar to that for pesticide residues: Any food containing a food additive was automatically adulterated unless the additive had FDA approval, and the burden of gaining and conducting the studies necessary to support approval rested with the industry. But the 1958 law also reflected important differences. The sole criterion for approval was safety; FDA was not permitted to take into account any “benefits” associated with an additive’s use, not even the capacity to reduce other dietary risks (64).

And, in the Food Additives Amendment, Congress addressed a specific type of risk by including a clause inspired by Chairman Delaney himself. The famous Delaney Clause added to FDA’s mandate the following restriction:

Provided, That no additive shall be deemed to be safe if it is found to induce cancer when ingested by man or animal, or if it is found, after tests which are appropriate for the evaluation of the safety of food additives, to induce cancer or man or animal . . . (53)

The significance of this controversial provision is explored below.

Of more immediate practical importance, the 1958 Amendment did not apply to all food ingredients or food-contact substances. The definition of a “food additive” excluded substances “generally recognized by qualified experts” as safe for use in food (48). This so-called GRAS exception was meant to recognize ingredients that had a history of safe use or whose safety would seem obvious to most scientists. The exception remains in the law, and hundreds of GRAS substances are widely used in US food production. Indeed, a supplier or producer may independently conclude that an ingredient is GRAS and proceed to use it without notice to, much less formal approval by, FDA. This apparent safe harbor can be lost, however, if new information suggests that a once-GRAS ingredient

¹Several years earlier, Congress had amended the federal pesticide statute, the Federal Insecticide, Fungicide, and Rodenticide Act (FIFRA), to require federal registration of any pesticide sold in the United States. FIFRA was the mechanism by which the government—originally FDA and now EPA—assessed the general safety and utility of a pesticide. The Miller Amendments to the FD&C Act provided the mechanism by which an approved pesticide could lawfully be applied to, and remain on, food sold in interstate commerce.

may not be safe after all. This is what occurred in 1968, when the results of long-term feeding studies suggested that the sweetener cyclamate might be an animal carcinogen (15, 32). The mere possibility, according to FDA, nullified any claim that cyclamate was “generally recognized as safe”; this meant it was an unapproved “food additive,” whose use had to be terminated forthwith.

The Food Additives Amendment contained another permanent exception from premarket approval, for substances whose use in food had previously been “sanctioned” by FDA or by USDA (49). In effect, Congress determined that if the government has already approved an ingredient, reapproval as a food additive was not necessary. If FDA wishes to challenge the continued use of a once-sanctioned ingredient whose safety it has come to doubt, it must charge that it adulterates food under the 1938 Act’s “may render injurious to health” standard. Furthermore, because prior sanctioned ingredients are excluded from the definition of “food additive,” they are not subject to the Delaney Clause.

This is only one illustration of the falsity of the claim that the Delaney Clause prohibits cancer-causing chemicals in food (40). Indeed, the Clause does not even prohibit the *addition* to food of all proven animal carcinogens, a proposition dramatized by the relationship between the system Congress established for pesticide residues and the scheme it later fashioned for food additives.

The 1958 Amendment’s definition of “food additive” was broad enough to embrace any chemical added to food, including residues of pesticides (48). Since it had already established a mechanism for reviewing the safety of pesticides, Congress excluded pesticides on raw commodities from the food additive scheme. There remained, however, the issue of how to regulate pesticide residues in processed foods. Here Congress made two choices, one explicit, the other implicit. First, it provided, in what became known as the “flow through” provision, that a processed food bearing a pesticide residue would not be considered adulterated if the pesticide were approved (had a tolerance) for application to the raw commodity and the level of the pesticide did not exceed the tolerance (51).² In effect, Congress decided that FDA’s approval of the pesticide on the raw commodity signified that no greater amount of the pesticide would also be safe in processed food.³

But what if the level of a pesticide in the processed version of a raw commodity exceeded the level allowed by the raw commodity tolerance? Such “concentration” is not uncommon; for example, when fruits and vegetables with a high water content are processed, the ratio of pesticide residue to plant material

²A further condition was that the pesticide must have been removed to the extent possible through good processing practices.

³Congress apparently did not consider the possibility that consumers might ingest larger amounts of some commodities in processed form, which could render any judgment about a pesticide’s safety on the raw commodity an unreliable guide to its safety in processed versions.

rises. Congress's instructions about what FDA should do in such circumstances are not explicit. Congress clearly expected that some further review would be required, but what the legal basis for approval would be is a matter of dispute. FDA, however, proceeded to require so-called "food additive tolerances"—promulgated under section 409 of the Act—for pesticide residues in processed foods that exceeded the levels allowed on the raw commodities (8, 12).

This practice, later embraced by EPA, has had profound consequences. In granting a section 408 tolerance for a pesticide on a raw commodity, EPA may consider its importance to agricultural production as well as its safety; but in deciding whether a higher level of the pesticide may remain in processed food under section 409, it may not take "benefits" into account. Furthermore, the Delaney Clause, which applies only to food additives, precludes a finding of safety for any residue of a carcinogenic pesticide that requires food additive approval. Thus, until Congress's recent amendment, the law could bar from *processed* food a pesticide that was perfectly lawful on a raw agricultural commodity. The implications of this statutory paradox, and of Congress' attempt to resolve it, are explored below.

COLOR ADDITIVE AMENDMENTS Two years after passage of the Food Additives Amendment, Congress in 1960 created a new system for premarket review of substances used to color foods, as well as drugs and cosmetics. The color additive scheme generally paralleled the food additive regime, but it incorporated no exceptions for colors already in use or otherwise considered safe; all colors ultimately required approval, or "listing" (58).⁴ To list a color for use in food, FDA had to find that the use would be "safe" (58). Congress also included, this time at FDA's urging, a near duplicate of the 1958 Delaney Clause, which forbids the listing, for ingested (including any food) use, of any color additive "found by the Secretary to induce cancer when ingested by man or animal. . . ." (59).

ANIMAL DRUG AMENDMENTS The final piece of the current statutory framework was added in 1968. The primary purpose of the Animal Drug Amendments was to create a single integrated process for approving drugs and feed additives used in livestock production (6). The public health goals of regulation were to assure that such agents were safe and effective in animals and that any residues in food derived from such animals could be safely consumed by humans. Congress' regime treated animal drug residues as food additives (6).⁵ This meant that any residue in human food had to be shown to be safe. It also, in

⁴The 1960 Amendments did include a transitional provision, which allowed the continued use of colors approved under a provision of the original 1938 Act until their safety could be confirmed and "permanent listing" conferred.

⁵The Act's definition of "food additive" was amended to exclude animal drugs that had been reviewed and approved in accordance with Section 512 of the Act, the Animal Drug Amendments.

principle, meant that any carcinogenic animal drug could not be approved, because Congress in 1968 reenacted the Delaney Clause for such compounds (24).

As it applied to animal drugs and feed additives, however, the Delaney Clause included an important modification made in 1962 to address an anomaly in the law. Several years before passage of the 1958 Food Additives Amendment, two or three firms had obtained FDA approval to market diethylstilbestrol (DES), a growth promotant for livestock. Other companies later sought to enter the business but the agency turned them down on the ground that the intervening Delaney Clause forbade approval of any carcinogenic substance that was likely to become a component of human or animal food.⁶ However, it said it could not act against the brands already approved because they were “prior sanctioned” and, thus, not “food additives” (H&M; Kingham R. 1977. *Statutory and Administrative Theories by Which FDA Avoids Applying the Delaney Clause*, unpublished manuscript).

In 1962, Congress sought to rectify what it considered to be unfair discrimination between marketers of the same compound by adding language to the 1958 and 1960 versions of the Delaney Clause. It did not dictate approval or disapproval of DES; it simply placed all carcinogenic animal drugs on the same statutory footing. The so-called “DES proviso”, as it appears in section 409 of the Act, reads:

... [T]his proviso [the prohibition against approval of any additive found to induce cancer] 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 ... such additive will not adversely affect the animals ... and (ii) that *no residue of the additive will be found (by methods of examination prescribed or approved by the Secretary ...) in any edible portion of such animal after slaughter or in any food yielded by or derived from the living animal* ... (53)

(Emphasis supplied.)

This amendment was represented as entirely consistent with the policy of the original Delaney Clause, i.e. that no carcinogenic substances should be approved *for addition to human food* (46). It merely clarified that policy so that, if FDA were assured that no carcinogenic material would enter human food, the law would not automatically bar its use in animals.

SUMMARY OF THE STATUTORY FRAMEWORK PRIOR TO CONGRESS' 1996 REFORMS The enactment of the Animal Drug Amendments completed the current statutory framework for regulation of food safety. For man-made additives, the legal scheme had been transformed from one in which the agency had the burden of showing that a substance was (a) poisonous and (b) present

⁶Convincing evidence that DES was also a human carcinogen had not yet materialized.

at a level that could endanger health, to one under which the sponsor of a substance had the burden of supplying evidence sufficient to convince FDA that its addition to food would be safe. Furthermore, for three categories—food additives, color additives, and animal drugs—the amended law forbade approval of any compound “found to induce cancer when ingested by man or animal.”⁷ In aggregate, these changes meant that most new food ingredients or production agents required FDA approval and ostensibly equipped FDA to “prevent the addition of carcinogens to the food supply.”

Both generalizations were in fact overstatements. The requirements for food additives did not apply to many substances, either because they had previously been sanctioned or because they were generally recognized as safe. Carcinogenic animal production drugs could be present in food at levels below detection. Moreover, none of the post-1938 amendments purported to cover toxic materials that are not purposefully used in producing food but that find their way into food anyway.

REGULATING “ADDED” CARCINOGENS IN FOOD

The Delaney Clause’s Premises

Proponents of the Delaney Clause argued that no dose of a carcinogenic chemical could be shown to be safe, and that any dose posed *some* risk of cancer (47). The only prudent policy was, therefore, to forbid approval of any food additive shown to cause cancer.⁸ This was the policy that Representative Delaney sought, and Congress agreed, to codify. In 1958, neither advocates nor opponents of the policy, including FDA officials, believed it would have broad application, for only a handful of chemicals had then been shown to be animal carcinogens (37).

Members of the House committee responsible for including the Delaney Clause undoubtedly realized that it deviated from the premises underlying safety assessments of other food chemicals. For a generation, FDA scientists, led by Arnold Lehman, had used a simple, and still widely accepted, formula to decide whether a chemical could be safely used in food (36). This formula entailed determining the “no observed effect level” (NOEL or NOEAL) from animal experiments, adjusting for species size, and applying a standard safety factor, usually 100, to arrive at the “acceptable daily intake” (ADI) for the substance. If estimated human consumption of the food in which the substance was used

⁷Subject, of course, to the exception for animal feed additives and animal drugs that could satisfy the requirements of the DES proviso.

⁸Delaney proponents also accepted, of course, the premise that any substance found to induce cancer in animals had the potential to cause cancer in humans, and the law embodied this animal-to-man extrapolation.

would not cause consumers to exceed the ADI, that use could be considered “safe”—both legally and literally. If consumers might exceed the ADI, the usual response was to reduce the amount of the substance that could be used. This safety assessment regime assumed, of course, that the toxic effects of chemicals are threshold limited. Since, however, this assumption did not hold for chemicals found to induce cancer, Delaney supporters believed that such a finding should preclude approval altogether.

Another complication, some have suggested, was that the food additive law did not permit FDA to consider an additive’s benefits.⁹ While accurate, this criticism has been of little significance. Use, and thus consumption of most noncarcinogenic additives can usually be limited to levels below, often well below, the computed ADI without jeopardizing their functional value. It has been possible to “have one’s safety and eat it too.” For any carcinogenic additive, however, this result was foreclosed by science, and thus, Delaney defenders argued, should be foreclosed by the law as well.

FDA’s Efforts to Elude the Delaney Clause

The Delaney Clause recognizes no distinctions based on carcinogenic potency and, at least in theory, it applies equally to additives used in large amounts and to those present at barely detectable levels. It thus takes no account of the actual risk a carcinogenic additive might pose. As the number of chemicals shown to be animal carcinogens has risen, and analytical chemistry has enlarged the universe of previously unsuspected contaminants in food, FDA found the statute increasingly difficult to administer. The agency’s reluctance to invoke the Delaney Clause and its ability to avoid doing so are both products of one methodology: quantitative risk assessment.

The emergence of cancer risk assessment as a legitimate, increasingly sophisticated instrument of policy analysis is a theme that has pervaded the debate over food safety regulation for over twenty years. FDA was the first federal health regulatory agency to embrace this methodology, which it found appealing for two related reasons. First, at a time when one assumption underlying the Delaney Clause—that few substances in food would be found carcinogenic in animals—was being eroded, quantitative risk assessment offered a means of illuminating, indeed escaping, a second assumption—that all carcinogens were equally dangerous. Second, for substances to which consumers were exposed at low levels, quantitative risk assessment offered a way of determining that the

⁹The Act does not expressly forbid consideration of “benefits,” but the conspicuous omission of any reference to criteria other than safety—particularly since sections 406 and 408 both direct FDA to take additional factors into account—is strong evidence that section 409 does not permit FDA to consider benefits. Furthermore, the 1958 legislative history suggests that this was a deliberate choice.

associated risk, even if not zero, was small enough to accept or even ignore. The following paragraphs recount FDA's and, later, EPA's attempts to put this methodology to use in making regulatory decisions.

ANIMAL DRUG RESIDUES By 1970, DES had become widely used in beef and pork production, even though its carcinogenicity for humans, as well as in experimental animals, was well-established.¹⁰ USDA radiotracer studies of the carcasses of treated livestock soon confirmed what many scientists had long assumed: If an animal were given DES (or any drug), residues would remain in tissue derived from the animal no matter how long before slaughter the drug was withdrawn (16). Currently available analytical methods might not be capable of detecting residues, but eventually a method could be found that was sensitive enough to confirm their presence, regardless of whether they had any public health significance.

The realization that any animal drug would leave residues presented FDA with a conundrum. The DES proviso permitted the agency to approve of a carcinogenic animal drug if, but only if, no residues would be "found" in human food derived by the treated animal. If "found" meant "present," the proviso was an empty promise. FDA found a way to solve the puzzle. Focusing on the statutory language, the agency concluded that the important question was what criteria it should use in approving a method for monitoring residues (20). How aggressively should it search for residues? The agency's answer, in essence, was "hard enough to be sure that any residues that escape detection would not pose a significant risk to consumers." This answer required the agency to confront a second question: How to define "significant risk"?

FDA's answer to this question combined quantitative risk assessment and bare assertion. It first asserted that by using the Mantel-Bryan risk estimation procedure (20),¹¹ it could reliably estimate the maximum dietary risk posed by the residues of a carcinogenic drug. It then declared that if the lifetime cancer risk posed by consumption of food containing undetectable residues did not exceed 1 in 100,000,000, it was not significant (20).¹² This analysis was translated into a requirement that the sponsor of a carcinogenic drug provide a workable analytical method capable of detecting residues corresponding to a dietary risk of greater than 1 in 1,000,000 (43). Stripped of the agency's verbal and numerical gymnastics, the message of FDA's "sensitivity of method"

¹⁰DES was not the only livestock growth promotant believed to be carcinogenic. It was merely the drug that first confronted FDA with the challenge of interpreting the proviso Congress enacted in 1962.

¹¹FDA has since embraced the more "conservative" linearized multi-stage model (23).

¹²FDA later adjusted its numerical criterion downward to 1 in 1,000,000, a benchmark other federal agencies, including EPA, have come generally to treat as "insignificant" or "negligible," the equivalent of "safe."

solution to the animal drug residue problem was its willingness to allow the addition to human food of trace amounts of carcinogenic animal drugs that, in its judgment, presented no risk to public health.

“CONSTITUENTS” OF ADDITIVES A few years later, FDA discovered that several approved color additives contained impurities, some carcinogenic in animal experiments. The parent colors, however, displayed no carcinogenic activity. They were, however, vehicles for the “addition” of carcinogens—the impurities—to the food supply. This, it was claimed, the Delaney Clause prohibited.

The first time it confronted this puzzle FDA concluded that banning the “innocent” color additive, Green No. 6, would be pointless (25). The agency estimated that the risk posed by human consumption, in colored food, of trace levels of the “guilty” impurity was considerably below 1 in 1,000,000—the risk level it had previously found insignificant for carcinogenic animal drugs. FDA again called attention to the statutory text, pointing out that the Delaney Clause only forbids approval of a “color additive” only if *it*—the additive—is found to induce cancer (26). Since Green No. 6 did not cause cancer, the clause did not apply. The law did, however, require that the color (including its “constituent,” p-toluidine) be shown to be “safe.” FDA concluded that a risk as small as that estimated for Green No. 6 colored food was the equivalent of “safe.” With court approval, the agency listed the color for use in foods and ingested drugs (69).

DIRECT ADDITIVES POSING “DE MINIMIS” RISKS A pattern was beginning to emerge in FDA decisions. If the statute did not expressly forbid continued approval of a substance, even though it was or contained a carcinogen, the agency would not invoke the Delaney Clause if the estimated risk fell below its benchmark of 1×10^{-6} .¹³ This pattern was repeated the next time FDA grappled with the clause.

¹³In its regulation governing carcinogenic animal drugs, FDA offered the following explanation for its choice of this risk level as the functional equivalent of insignificant—or “negligible” or “de minimis”:

“The selection of an insignificant level of risk is a choice, which . . . cannot be answered solely by science or currently available information. It is instead a policy question that must be answered by weighing a number of subjective considerations. . . . FDA cannot, with assurance, state that the 1 in 100,000 level would pose an insignificant level of risk of cancer to most people. FDA can state, and comments agree, that the 1 in 1 million level presents an insignificant level of risk of cancer to most people. Furthermore, FDA has developed confidence in the merit of the 1 in 1 million level because in recent years the agency has considered that level as its benchmark in evaluating the safety of carcinogenic compounds administered to food-producing animals. Under these circumstances, the agency believes that the most reasonable level of risk to apply in these regulations is the 1 in 1 million level”

(Food and Drug Administration. 1985. Sponsored Compounds in Food Producing Animals: Criteria and Procedures for Evaluating the Safety of Carcinogenic Residues. *Fed. Regist.* 50:45530.)

Contemporary testing of the provisionally listed colors revealed that some were themselves animal carcinogens. Two in particular, Orange No. 17 and Red No. 19, used in lipsticks and other ingested cosmetics, “failed” such tests, and FDA was petitioned to ban their use. The petitioners’ theory was straightforward: These were color additives, subject to the Delaney Clause, which the agency had found were carcinogenic in appropriate animal studies; the law required them to be banned. FDA rejected the demand on the ground that the estimated risks, even assuming regular use of the cosmetics to which they were added, were orders of magnitude below the cut-off it considered *de minimis*. The agency claimed that it had inherent authority to ignore the language of the statute when literal application would be pointless.

This time, however, FDA failed in its effort to avoid the Delaney Clause. A reviewing court held that Congress had deprived the agency of discretion to find that a concededly carcinogenic direct additive was nonetheless “safe” (68). The court accepted FDA’s characterization that the risk posed by the two colors was indeed trivial, but concluded that the agency’s hands were tied by the unequivocal language Congress had employed. The court was impressed that FDA itself had urged incorporation of the Delaney Clause in the 1960 Color Additive Amendments and promised at the time that it would ask Congress to change the law if scientists ever agreed on how to estimate the risks posed by low-level exposure to carcinogenic chemicals.

PESTICIDE RESIDUES IN PROCESSED FOOD EPA confronted by far the most difficult challenge posed by the Delaney Clause, which grew out of the intersection between the food additives law and the 1954 pesticide amendments. I have described above the complex framework Congress originally established for setting tolerances for pesticide residues in food: Any residue on a raw commodity had to comply with a tolerance approved under section 408 (which contains no Delaney Clause); any residue in processed food that did not exceed the raw commodity tolerance needed no separate approval; but any residue in processed food that did exceed the 408 tolerance required approval as a food additive.

For two decades, this three-tier scheme was administered without major controversy, first, by FDA and, then, by EPA. By the early 1980s, however, two discoveries threatened disruption. Mandated chronic testing of many approved pesticides revealed that as many as five dozen widely used agents were, or might be, animal carcinogens. And recent studies demonstrated that many raw commodities lost moisture during processing, with the result that pesticide residues often could “concentrate” at levels above the raw commodity tolerance (8). The second discovery convinced EPA that many more pesticides required section 409 (or food additive) tolerances, while the first suggested that approval of many tolerances would be barred by the Delaney Clause. This result appeared to follow no matter how small the risk posed by residues in processed food and

regardless of the benefits of pesticide use that the agency might have weighed in granting the raw commodity tolerance.

A National Academy of Sciences report concluded that this state of affairs made little sense, and recommended that Congress should legislate, or EPA should adopt, a uniform legal standard for pesticide residues in both raw and processed food (8). The NAS report suggested that a standard barring any residues posing a significant risk, but allowing residues posing only a de minimis risk, would reduce aggregate dietary risk while permitting continued use of agriculturally important pesticides.

Accepting this recommendation, EPA announced that it would grant processed food tolerances for carcinogenic pesticides when it found that the risk did not exceed 1×10^{-6} —the same de minimis standard that FDA had unsuccessfully defended in the color additive case (13).¹⁴ EPA's refusal to revoke tolerances for four pesticides that met this standard was immediately challenged in court and eventually overturned in *Les v. Reilly* (67). The court accepted EPA's premise that residues in processed food above the raw commodity tolerance are to be regulated as "food additives." It did not question EPA's conclusion that the risks posed by the four pesticides were of no public health significance. But it concluded that the Delaney Clause allowed no exceptions.

Soon after this defeat, EPA agreed to a court-ordered schedule for implementing this rigid view of the law for some four dozen pesticides it suspected are carcinogenic and believed may concentrate in processed food. Congress' recent amendments have rendered this schedule obsolete. But an appreciation for what EPA (and pesticide makers and food producers) faced is essential to understand why Congress, after two decades of debating over "reform" of the Delaney Clause, was inspired to act.

The process to which EPA was committed would have involved lengthy administrative hearings to resolve contested factual issues relating to carcinogenicity and concentration because the stakes are high. EPA's plan represented the first broad-based and, thus, the most significant effort to enforce the Delaney Clause. By one estimate, at least 121 pesticide/crop combinations were in jeopardy.¹⁵ EPA officials felt obliged to adhere to the court-mandated schedule even though they perceived no public health emergency; in almost every case

¹⁴FDA had, however, prevailed when it applied this standard to carcinogenic contaminants of color additives, see *Scott v. FDA*, and had not been challenged when it made it the criterion for evaluating analytical methods for carcinogenic animal drugs.

¹⁵This universe was described in a draft settlement agreement submitted in *California v. Browner* (No. CIVS 89-0752 (WBS-GGH), U.S. District Court for the Eastern District of California, 1995) by EPA. The draft agreement listed all currently registered pesticides that it believed might be animal carcinogens and for which processed food, i.e., food additive, tolerances either had been approved or would be required. It is possible that universe of pesticide-crop combinations actually threatened by implementation of the Delaney Clause, before Congress's recent amendments, would have been

they had concluded that the dietary risk associated with the residues in dispute were indeed de minimis.

The stakes involved in EPA's proceedings against putatively carcinogenic pesticides were inflated by two arcane but important agency policies. The EPA's "concentration policy" embodies the criteria by which it determines whether a pesticide residue will exceed the raw commodity tolerance in processed food, and thus require a second approval (12). Until recently EPA employed worst-case assumptions, one of which was that raw commodities would contain residues at the maximum level allowed by the 408 tolerance. Since pesticide residues are usually far below the permitted level, this assumption exaggerated the frequency with which concentration was likely to occur.

EPA had agreed to modify its criteria for predicting concentration, but it refused to alter another policy implicated by its obligation to implement the Delaney Clause (29). This so-called "coordination" policy provided that if a pesticide concentrates in processed food, and required a food additive tolerance that the Delaney Clause would forbid, the agency would deny or revoke the tolerance that permits residues on the raw commodity (13, p. 41108). For example, if the Delaney Clause precluded approval of a food additive tolerance for a pesticide in tomato paste, EPA would deny or revoke the tolerance that permits use of the pesticide on raw tomatoes. Revocation of the tolerance for raw tomatoes in turn would require cancellation of the pesticide for use on tomatoes. EPA's rationale for this policy, which is not mandated by statute, is that only by this means could federal enforcement officials be sure that no illegal tomato paste will be marketed. Thus, EPA's "coordination policy" put in jeopardy not just the processed food tolerances to which the Delaney Clause applied, but all uses of a pesticide that *could* concentrate in processed food.

AGENCY DISCRETION TO INTERPRET "INDUCE CANCER" The Delaney Clause was written in simple language: "Provided, That no additive shall be deemed to be safe if it is found to *induce cancer when ingested by man or animal . . .*" The statute does not define either "cancer" or "induce." The legislative history does indicate that FDA was to be the ultimate judge of whether an additive "induce[d] cancer," and that the agency was to be guided by evolving scientific standards governing the design, conduct, and interpretation of animal studies (38). FDA has been unusually cautious about attaching this label to compounds alleged to be carcinogens.¹⁶ FDA scientists have rejected findings

smaller because some pesticides might not, on review, be found carcinogenic and/or residues on some raw crops would be found not to concentrate during processing.

¹⁶EPA historically has not been as cautious about labeling a chemical carcinogenic. Except in the context of approving processed food tolerances for pesticide residues—to which the Delaney

from studies they considered inadequate and distinguished experimental effects that had no human relevance (38). However, neither the statute itself nor any court opinion provides authoritative guidance regarding the scope of FDA's scientific discretion.

This issue takes on increasing importance as research findings expose the complexity of the processes of carcinogenesis. The paradigm that inspired Representative Delaney was monolithic: Chemicals that caused cancer did so by damaging cellular DNA, setting in motion self-replicating genetic mistakes. The process could be triggered by minuscule quantities of a carcinogen, perhaps by as little as a single molecule. No threshold could be assumed, much less demonstrated (44). More recent research has revealed that this view is much too simple. A key question confronting FDA is whether, or to what extent, the law permits officials to take new theories or compound-specific information into account.

A pressing issue is whether evidence of carcinogenic mechanism can be considered in applying the Delaney Clause. In 1973, the agency took the position that mechanistic evidence could be decisive. That year it approved selenium as a supplement for livestock feed in regions of the country where natural levels of the nutrient are low (17). With evidence that administration of high doses of selenium increased the occurrence of liver tumors in rodents, the Delaney Clause seemed to bar approval. FDA, however, concluded that selenium did not act directly. Tumors occurred only following severe, dose-related liver toxicity; cancer was, in the agency's terminology, a "secondary" (threshold-limited) product of acute toxicity.¹⁷ Accordingly, selenium did not "induce cancer" within the meaning of the Delaney Clause. FDA's approval of selenium was not challenged before the agency or in court. Indeed, the Health Research Group submitted comments essentially endorsing the decision.¹⁸

FDA's approval of selenium remains a precedent for the proposition that evidence of an "indirect mechanism" of tumor production may avoid a finding that an additive "induce[s] cancer." It should be stressed that FDA has not relied upon this precedent since, though neither has it formally rejected it. The agency is currently evaluating the carcinogenicity of at least two widely used food additives, for which some observers believe there is convincing evidence of a "secondary" mechanism. Reportedly, there is disagreement between the FDA scientists responsible for a final ruling and agency attorneys, who question

Clause applied—none of the other laws for which EPA is responsible make a finding that a chemical is "carcinogenic" determinative of how it is to be regulated.

¹⁷FDA drew an analogy to beverage alcohol, a cause of liver cancer among heavy consumers, which it similarly termed a "secondary carcinogen."

¹⁸HRG stressed, as FDA had done, that there was no evidence that supplementation of livestock feed would increase human exposure to the nutrient.

whether mechanistic evidence may, under the law, support a finding that an additive does not “induce cancer.”

Legislative Reform of the Delaney Clause

Despite the challenges it has posed for FDA and EPA, the Delaney Clause for almost forty years remained nearly impervious to legislative revision.¹⁹ This was true even though the clause’s defenders could not ascribe many victories to its presence in the law. Indeed, since 1970, FDA has invoked the Delaney Clause only twice—in its ultimately unsuccessful proposal to ban saccharin (22) and in terminating use of DES in livestock (24, 37).²⁰ In each instance the agency stated that it would have reached the same decision under the law’s general safety standard.²¹ EPA had never ended the use of a pesticide solely because of the Delaney Clause.

For the same reasons, critics of the Delaney Clause had difficulty generating serious interest in reform. In recent years, however, the clause has come under increasingly critical scrutiny. In 1979, a NAS committee concluded that the same safety standard should apply to all constituents of food and implied that the clause should be replaced (4). The Carter and Reagan Administrations both developed proposals to modify the clause, but political interest in the project eventually flagged, in part because saccharin was rescued and no other valued food constituents seemed to be threatened. The role of the Delaney Clause and pressures for its reform resurfaced as important issues after EPA’s failed effort to interpret the law as permitting carcinogenic residues in processed food that posed no more than a *de minimis* risk. The election of Republican majorities in Congress in 1994 appeared to create a receptive environment. However, as the 1996 presidential election neared, most observers accepted the conventional wisdom that the opportunity for legislative change had closed, at least until 1997. Then, rather abruptly, intense negotiations among congressional leaders of both parties, and including representatives of EPA, FDA, pesticide makers, food producers, and the organizations responsible for EPA’s defeat in *Les v. Reilly*, produced a bill, entitled “The Food Quality Protection Act of 1996,” that passed the House and Senate without dissenting votes and was signed by the President on August 3, 1996.

The debate over Delaney reform, leading up to this legislation, revolved around four main issues.

¹⁹The only change that Congress has made in the provision is the DES proviso enacted in 1962.

²⁰FDA had previously cited the Delaney Clause in banning two little used and quickly forgotten food additives.

²¹Saccharin remains available because Congress forestalled FDA’s ban by repeatedly reenacting a specific statutory exemption. Several recent studies of saccharin in animals, and more than one epidemiological study undertaken following FDA’s attempted ban, have cast doubt on the agency’s original conclusion that it poses a significant cancer risk for humans.

Relaxation of Delaney's flat ban This was the central issue. Advocates of reform contended that improved scientific understanding has exposed fundamental flaws in the premises of the Delaney Clause. Animal carcinogens are ubiquitous, and many find their way into food. At the same time, they are not all present in significant quantities and they differ widely in potency. Advances in quantitative assessment permit reliable estimation of cancer risks and allow regulators to differentiate between substances that pose serious risks and those that present only trivial risks. The reformers also cited the "costs" of Delaney, calling attention to the important pest control agents (and crop uses) that were jeopardized by EPA's plan to implement the court orders.

The latter argument for the first time dramatized the potential costs of literal enforcement of the Delaney Clause. Nonetheless, the clause's defenders opposed any weakening of the law's putative ban on carcinogens and questioned the reliability of the risk assessment tools FDA has relied on and that EPA would employ to estimate the risks of carcinogens.

Scope of reform Two types of reform proposals were introduced. One would have addressed the Delaney Clause directly and modified its terms to permit FDA (or, since under this variant pesticides would still be subject to the standards for food additives, EPA) to "exempt" from banning any carcinogenic additive whose use would pose at most negligible or trivial risk. Few members of Congress seemed comfortable advocating outright repeal of the clause, so the proposed statutory change was billed as "modification" or, even more appealingly, "modernization" of the Delaney Clause, and took the form of yet another statutory proviso. Among advocates of broad reform, revision of Delaney was (and is) simply one of several recommended changes in the law governing food additives.²²

A narrower reform proposal focused solely on the statutory provisions applicable to pesticide residues in food. This approach treated the Delaney Clause "problem" as largely a product of pesticide residues that concentrate in processed food. Advocates emphasized that the law applicable to residues in raw commodities contained no bar to EPA's approval of carcinogens that it believes are safe, and that the law also allowed carcinogenic residues in processed food that did not exceed the raw commodity tolerance. In this view, Delaney's application to residues that concentrate was an anomaly. Their proposal was to subject all pesticide residues, in raw or processed food, to the criteria of section 408 of the Act, which permitted EPA to establish a tolerance if it concluded

²²Other amendments would create a new, ostensibly faster process for the introduction of new food-contact materials and authorize sponsors of new direct additives to contract with FDA-sanctioned private organizations to conduct the initial review of safety, which the agency would be required to endorse or reject within 60 days.

that the residues allowed in food would be compatible with protection of the public health. Section 408 also allowed the agency to consider a pesticide's contribution to the maintenance of a plentiful and economical food supply.

Enactment of this proposal would solve the Delaney "problem" for pesticide residues by excluding all such residues from the operation of the Food Additives Amendment. But it would leave unchanged the Delaney Clause's application to food additives, and leave unresolved the question of FDA's authority to consider mechanistic evidence in deciding whether an additive "induce[s] cancer".

Consideration of "benefits" Proponents of narrow Delaney reform argued that EPA should be permitted to consider the benefits that use of a pesticide provides, as well as the health risks that it poses. This, they pointed out, EPA could do in setting raw commodity tolerances for any noncarcinogenic pesticide. Opponents strenuously resisted the idea that EPA should be permitted to allow consumers to be exposed to even small cancer risks upon a finding that farmers can grow more or consumers can pay less for treated food.

Special consideration of risks to infants and children Initially, the debate over the application of the Delaney Clause to pesticide residues proceeded on the assumption that EPA's criteria for setting safe tolerances were sound. In 1994, however, another NAS report challenged this assumption, questioning whether infants and children were adequately protected from dangerous residues (7). The report emphasized that children may potentially be especially vulnerable to toxic materials in food because of their small size and rapid physiological development. It also pointed out that many pesticide-treated foods are consumed by children in amounts much greater than assumed for adults. EPA acknowledged that its customary formula for establishing tolerances assumed that the "average" consumer weighed 150 pounds and ingested treated food at levels derived from surveys of adult consumption. Although the EPA immediately promised to adjust its formula to incorporate consideration of the special circumstances of children, once legislative change seemed possible, advocates of more rigorous regulation sought the addition of language that would make EPA's commitment binding.

The "Food Quality Protection Act of 1996" In 1996, Congress passed and the President signed a "narrow" version of Delaney reform, which overhauls the federal law governing pesticide residues in food.

The amended law excludes pesticide residues in processed as well as raw food from regulation as food additives (and, thus, from the Delaney Clause). It directs EPA to approve residues of a pesticide only if it finds them to be "safe," a finding that requires the agency to conclude that there is "a reasonable certainty of no harm would result from aggregate exposure to the pesticide

chemical”. This standard permits EPA to approve a tolerance for residues of a carcinogenic pesticide if it concludes that consumers would face no more than a negligible risk—described in the legislative history as 1 in 1 million lifetime risk. For pesticides causing threshold-limited effects, EPA is expected to apply a 100-fold margin of safety.

The amended law allows EPA to *retain* (but not initially approve) a tolerance for a carcinogenic pesticide residue that poses a greater than negligible risk if it concludes that use of the pesticide protects consumers from a greater health risk or “is necessary to avoid significant disruption in domestic product of an adequate, wholesome and economical food supply.” Even if either finding could be made, EPA may not approve the tolerance if the annual risk exceeds 1 in 100,000 or the lifetime risk exceeds 2 in 1 million.

EPA is directed to consider the consumption patterns and special susceptibilities of infants and children in setting any tolerance and must be able to affirm that any tolerance approved was safe for children. For nonthreshold effects, if EPA finds that infants or children will be significantly exposed to a pesticide, it is directed to apply an additional safety factor of 10 (thus a factor of 1000) in establishing the ADI.²³

The official history of this new law does not reveal why its passage suddenly was possible, after years of controversy over the Delaney Clause and the approach of the national party conventions. Clearly, one reason was that “reform” was confined to the pesticide provisions of the FD&C Act. Another was the willingness of pesticide makers and food producers to agree, first, to legislative language obligating EPA to take special measures to protect infants and children (which will result in a lowering of allowable residues for many pesticides) and to a revision of section 408 of the Act that limits EPA’s consideration of benefits to existing tolerances. But why did opponents of any relaxation of the Delaney Clause surrender on this key issue? One possible explanation is that they recognized that EPA would confront major impediments in its effort to implement the Delaney Clause as litigation over whether specific pesticides are carcinogenic or do concentrate in processed food extended into the next century (35).

Passage of the “Food Quality Protection Act of 1996” leaves the language of the Delaney Clause unchanged—but limits its coverage. The clause has ceased

²³ Assuming that ordinarily consideration of such consumption patterns and special vulnerabilities will often result in lower allowable residues, this mandate would pressure EPA to lower many existing, as well as proposed new, tolerances. This may not prove significant for growers and processors, however, because the bill would also permit the agency to rely on estimates or measurements of actual residues—and to end its practice of assuming that residues will be present at the tolerance level. EPA would also be permitted to take account of the percentage of food actually treated with a pesticide, rather than assume (as it historically has done) that all planted acres will be treated. In short, these divergent instructions may offset one another in EPA’s final calculations.

to be an issue for EPA, but it remains a constraint for FDA. Food additives, direct and indirect, color additives, and animal drugs all remain subject to its provisions. And thus debate over the meaning of the clause, and particularly over the scope of FDA's discretion to consider new theories—and supporting evidence—relating to chemical carcinogenesis will continue.

Unintended Carcinogens

The discussion so far has focused on FDA and EPA efforts to regulate chemicals purposely used in ways that result in their presence in food. For this universe of chemicals Congress has prescribed a consistent approach. The law generally treats an additive's presence as rendering food adulterated (and thus its use unlawful) in the absence of government approval. To gain approval, the sponsor must submit the results of laboratory (and occasionally human) studies. The government thus is given an opportunity to decide, in advance, whether the specific use of the additive will be safe (or safe enough).

Although this is a workable approach for regulating the safety of substances whose presence in food is advertent, it does not fit chemicals that may occur in food but are not purposefully "added" by anyone.

ENVIRONMENTAL CONTAMINANTS It is not uncommon to read that some food has been contaminated with an industrial chemical, such as PCBs or mercury (19). Contamination can be the result of a recent accident, the manifestation of long-term industrial discharges, environmental transport to fields or waters where foods are harvested, or even "natural" processes that bear no obvious human imprint. Improvements in chemical analysis have permitted more reliable detection of suspected contaminants; they have also exposed latent contaminants whose presence in food had not previously been appreciated. Such "discoveries" present several problems for regulators.

One is a classic, but challenging, risk assessment problem. Because additives have sponsors, FDA has no difficulty assigning responsibility for the studies necessary to assess what sort of hazard an additive might pose. The sponsor can also be required to supply information about the ways in which the additive will be used. For most contaminants, by contrast, the burden of acquiring information—about toxicity, potency, and exposure—rests with the government.²⁴

²⁴For some contaminants there may be copious information in the scientific literature. For those that are regulated for some other purposes, e.g., under the Toxic Substances Control Act or the pesticide law, the government may have elicited critical toxicological data. However, it will be rare that FDA can turn to any other agency—or even to the manufacturer of a material that has found its way into the environment—for information about the levels present in food or the amount of the food that is consumed, both critical in conducting any assessment of the risk.

A second problem in dealing with environmental contamination of food arises once FDA has concluded that consumers confront a genuine risk. With an additive or a pesticide, it is usually possible to curtail the risk promptly—by restricting or banning further use of the additive. The agency may confront the issue of recalling foods already distributed, but this is usually a short-term problem. Many contamination episodes, by contrast, are persistent. It is not practical to wait for the Great Lakes to cleanse themselves of PCBs. Indeed, it may not be practical, in the short term, to order industrial dischargers—if they can be identified—to cease dumping PCBs into the lakes. Other remedial strategies must be found.

FDA must first decide whether the risk to consumers warrants intervention. Initially, this is a matter of what legal standard the agency should apply. The FD&C Act does not provide a clear answer, perhaps because the risk of unintentional contamination was not grasped in 1938. FDA began to appreciate the potential dimensions of the problem in the early 1970s, when reports of mercury contamination of swordfish, PCB contamination of freshwater marine life, and aflatoxin contamination of corn and other grains gained wide attention. Searching the Act for guidance, the agency seized upon section 406 of the Act (19, 21). In combination with section 402(a), section 406 treats as adulterated any food that contains any added poisonous substance, but allows FDA to establish permissible limits—tolerances—for such a substance if it “cannot be avoided by good manufacturing practice. . . .” One advantage of this provision was that it empowered FDA to specify the level of contamination that rendered food unmarketable, and thereby avoid case-by-case inquiry into the risk confronting consumers.

Section 406 offered another advantage, illustrated by the following example. Aflatoxin is an unequivocal rodent and probable human carcinogen. It is also a common contaminant of grains and nuts grown or stored in many areas of the United States, a problem that worsens during years of persistent high humidity (18). Reduction of contamination levels is an important public health goal, but elimination of the contaminant—an “added” poison in food—is not achievable short of forbidding sale of contaminated food. It was therefore important for FDA to avoid regulating aflatoxin under any provision that contained a Delaney Clause. It was also important to find a legal framework that permitted consideration of the difficulty of avoiding or reducing contamination. Section 406’s criteria for setting tolerances suited the practical problem FDA confronted.

Section 406 directs FDA, in setting a tolerance for an unavoidable contaminant, to “limit[] the quantity. . . to such extent as [it] finds necessary for the protection of public health,” and to “take into account the extent to which the substance. . . cannot be avoided in the production of such [food]. . . .” The agency construes this language as authorizing a constrained form of risk-benefit

analysis. It attempts to estimate the dietary risk posed by different levels of contamination and then to compute the costs, in terms of processing measures and destruction of above-tolerance food, of achieving them, ultimately choosing a tolerance level that reflects what the agency considers a prudent balancing of risks and costs. FDA has acknowledged that this approach means it may allow the sale of foods that contain an “added” carcinogenic substance, pointing out that the Delaney Clause only applies to purposeful additives (18, 21, 139).²⁵

INHERENT CONSTITUENTS OF FOOD A recent NAS report concluded that “*natural components of the diet may prove to be of greater concern than synthetic components with respect to cancer . . .*” (5). (Emphasis supplied.) The NAS study was commissioned in response to work by Ames and colleagues, who have argued that many foods, including fruits and vegetables, include natural constituents that, when tested independently, are mutagenic in screening assays or, in some instances, are carcinogens in rodents. Ames and colleagues have claimed that modern regulation has been preoccupied with man-made chemicals and largely ignored what may be greater risks to public health (1, 2). The NAS report calls for more intensive research into the potential hazards of environmental contaminants, such as mycotoxins, long-accepted methods of processing (such as pickling and charcoal broiling), and natural, or inherent, constituents of agricultural products. It accepts Ames’ premise that some “natural” dietary components are potent animal carcinogens.

Such a finding has never yet caused FDA to address whether or by what authority it could act to limit consumption of a “naturally” hazardous food. We can only speculate how the agency might respond to this challenge. It would surely be slow to curb the sale of long-accepted foods. It would have no interest in contending that the inherent constituents of any agricultural product required approval. Presumably, FDA would be content to assume the burden of demonstrating that their presence rendered food hazardous for consumers.

It is easier to guess what statutory provision FDA would claim governed such an inquiry. The 1938 FD&C Act contained two tests of adulteration: A

²⁵FDA quickly discovered one disadvantage in its reliance on Section 406’s authority to establish tolerances; the statute prescribed a complex and potentially expensive hearing process for doing so. The agency therefore declared that it would only adopt formal tolerances if the available toxicological data were complete enough to support confident judgments about safe exposure and contamination levels were not fluctuating. For other—most—contaminants, it would instead announce so-called “action levels,” representing the level of contamination at which the agency would consider seizing food as adulterated. A citizen group unsuccessfully contested FDA’s refusal to establish tolerances, but later won a victory when a court held that FDA could not adopt action levels without first affording the public an opportunity to comment on its assessment of risk and balancing of the costs of reducing contamination levels. *Young v. Community Nutrition Institute*, 476 U.S. 974 (1986); *Community Nutrition Institute v. Young*, 818 F.2d 943 (D.C. Cir. 1987).

food is adulterated if it contains any “added” poisonous substance that “may render it injurious to health” (50). However, if a food contains a poisonous substance that is not “added,” the agency must establish that it will “ordinarily be injurious” (50). This would be a difficult standard for FDA to satisfy (50, 70), but this presumably would not trouble the agency if, as seems likely, it would be reluctant to restrict the sale of familiar agricultural commodities in the absence of convincing evidence of harm—perhaps epidemiological evidence.

The more intriguing question is whether FDA could remain passive in the face of convincing evidence that a natural food constituent was, under appropriate test conditions, a potent carcinogen. An example will illustrate the agency’s potential legal dilemma: Potatoes naturally contain the neurotoxin solanine. Assume that several rodent bioassays strongly suggest that solanine induces cancer in rodents. Potatoes sold as such presumably would be subject to the “ordinarily injurious” standard, but what about potatoes used in making vegetable soup. Arguably, they are an “added” substance in vegetable soup. Are they “generally recognized as safe”—and thus excluded from the definition of “food additive”? Or might the evidence of solanine’s carcinogenicity undermine such a conclusion? This line of speculation would be beside the point if there were evidence that FDA had “sanctioned” potatoes for use in making vegetable soup prior to 1958. There is a good chance, however, that there would be no such evidence precisely because, given potatoes’ long acceptance as an ingredient of vegetable soup, no producer would have thought to ask for FDA’s blessing.

This line of speculation is not wholly fanciful. If my example were peanuts, we would have no difficulty imagining that FDA would seek to minimize the level of aflatoxin contamination. Indeed, we would discover that the agency has adopted a section 406 tolerance limiting the allowable level of aflatoxin on peanuts. FDA has taken pains, however, to avoid forbidding the sale of all aflatoxin-contaminated peanuts, as it would be required to do if aflatoxin were considered a food additive. Peanuts are the major ingredient of peanut butter. It could be said that they are “added” to peanut butter. Why are not such peanuts—which surely cannot be said to be GRAS given FDA’s concern about aflatoxin—food additives? FDA has never offered an explanation.²⁶

²⁶A conclusion that peanut added to peanut butter are food additives would not automatically preclude FDA approval, though approval would be required. The agency could argue that the aflatoxin in or on the peanuts was a “constituent” of the peanuts—as p-toluidine is a constituent of Green No. 6. Assuming that, fed to test animals, peanuts themselves did not “induce cancer,” the Delaney Clause would not automatically bar approval—so long as FDA could responsibly conclude that the peanuts were safe. It is also just possible that peanuts have a prior sanction in peanut butter.

CONCLUSION

This survey of food safety regulation is a peculiarly American story. It reflects both the cautious, incremental approach to problems that characterizes much US legislation and—increasingly—a distrust of administration. Through its sedimentary addition and modification of statutory responsibilities, the US Congress has retained for itself primary authority to decide not only how “safety” should be pursued, but what “safety” means. Passage of the Food Quality Protection Act, which permits EPA to establish tolerances for pesticide residues on food unconstrained by the Delaney Clause, is in fact entirely consistent with this theme. While Congress has embraced quantitative risk assessment as a tool for estimating the potential health effects of agricultural chemicals—a gesture toward administrative flexibility—it has simultaneously restricted EPA’s approach, by instructing it to consider the risks faced by infants and children.

No one can doubt that this is, in principle, good public health policy. Decision makers should take into account the added risks faced by the heavily exposed or the specially vulnerable, as EPA had already resolved to do. It is a more difficult question whether instructions of such detail should be embodied in statute, rather than left to prudent administrative choice. There seems little doubt, however, that Congress’ reinforcement of EPA’s inclination will force reductions in the allowable use and permitted residues of some, perhaps many, agricultural pesticides. At the same time—for this important segment of “added” toxicants to food—decision making can escape the shadow of the Delaney Clause, which obscured the effort to make foods safe by diverting attention to the narrow, and sometimes unrelated, issue of whether a chemical should be labeled a carcinogen. But since Congress left the clause in place for conventional food additives, this issue is likely to continue to preoccupy, and frustrate, FDA.

ACKNOWLEDGMENTS

I thank Dominic Madigan, University of Virginia Law School Class of 1998, for assistance with research for this chapter.

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