VOL. 29, NO. 4 APRIL 1974

Food Drug Cosmetic Law JOURNAL

Concluding Papers Presented at the 17th Annual Educational Conference of the Food and Drug Law Institute, Inc., and the Food and Drug Administration

A COMMERCE CLEARING HOUSE PUBLICATION
PUBLISHED IN ASSOCIATION WITH THE FOOD AND DRUG LAW INSTITUTE, INC.

THE EDITORIAL POLICY of this JOURNAL is to record the progress of the law in the field of food, drugs and cosmetics, and to provide a constructive discussion of it, according to the highest professional standards. The FOOD DRUG COSMETIC LAW JOURNAL is the only forum for current discussion of such law and it renders an important public service, for it is an invaluable means (1) to create a better knowledge and understanding of food, drug and cosmetic law, (2) to promote its due operation and development and thus (3) to effectuate its great remedial purposes. In short: While this law receives normal legal, administrative and judicial consideration, there remains a basic need for its appropriate study as a fundamental law of the land; the JOURNAL is designed to satisfy that need. The editorial policy also is to allow frank discussion of food-drug-cosmetic issues. The views stated are those of the contributors and not necessarily those of the publishers. On this basis contributions and comments are invited.

The FOOD DRUG COSMETIC LAW JOURNAL is published monthly by Commerce Clearing House, Inc. Subscription price: 1 year, $20; single copies, $2. Editorial and business offices, 4025 W. Peterson Ave., Chicago, Il. 60646. Printed in United States of America.

April, 1974
Volume 29 • Number 4

Second-class postage paid at Chicago, Illinois and at additional mailing offices.

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Legislative Overview of Medical Devices—Statement

By MICHAEL J. MILLER

Dr. Miller Is Executive Director of the Association for the Advancement of Medical Instrumentation.

THE ASSOCIATION FOR THE ADVANCEMENT OF MEDICAL INSTRUMENTATION (AAMI) is a professional association of users and manufacturers of medical devices. Our objective is to improve patient care by furthering the application of technology to medicine. We serve our professional and industry membership through programs that ultimately benefit the patient: publications, education, standards, and professional certification.

AAMI supports reasonable and responsive medical device legislation and feels that the Kennedy/Rogers legislation, with amendments we have proposed, can be reasonable and responsive to the needs of the patient. Our philosophy on legislation is that it must establish a system of regulation by industry, consumers, and the professions *with* administration and enforcement by government. Government should not "regulate": it does not have the technical expertise. This is the philosophy behind all of the amendments we have suggested to Congress.

I will now briefly express my opinions—not AAMI's—on the challenges medical device legislation presents to government, consumers, industry, and the professions. AAMI also assumes the responsibility for these challenges.

Government

Legislation and regulation *will* impede technological advances in the medical instrumentation field. This impediment will be mitigated by the government's utilization of the industry's and the profession's experience and knowledge. If government takes actions that make it a regulatory island unto itself the adverse impact will be felt by the patient.

"Safety overkill" legislation and regulation would be based on fear, irrational and misinformed judgments, and would serve no interest. Government must not attempt to overprotect itself because it lacks technical or scientific expertise. Seeking absolute protection by attempting to achieve a shield of absolute objectivity and independence in its regulatory decision-making process may serve only to further lack of knowledgeability to the detriment of the patient.

Consumers

Consumer advocates must weigh relevant information that provides a total picture and not utilize bits of information that present one point of view. Their constituency is not the press nor their own nonconsumer followers; their constituency is the patient and his interest. Consumer advocates can play a valuable role in providing information to government that might not otherwise be obtained. This is a heavy responsibility that must be assumed with care. For the most part, industry and the professions have conducted themselves responsibly in bringing medical devices to patients. The development of a data base by the Food and Drug Administration (FDA) under proposed medical device legislation, in my opinion, will bear out this statement.

Industry

The device industry must attempt to posture its reactions to government actions in a manner that will lead to a consensual, conciliatory process of regulation. Device regulation need not be a

defensive, polarizing, adversary process. Many device manufacturers must struggle to adopt a new frame of reference for medical device regulation. If the device industry reacts to government within the frame of reference of past forms of regulation, government officials will polarize their viewpoint and react accordingly. Industry and its trade organizations must anticipate and *act*; they must not hold back until threatened with regulatory action and then *react* defensively.

Industry must make its experience and knowledge accessible to government. Otherwise, regulation, administration, and enforcement may be unilateral, unnecessarily stringent, and arbitrary. Hopefully, government will be receptive and responsive to this experience and knowledge. Trade associations must further industry and government cooperation; they must not strive to increase their own internal power base by a negative, adversary relationship with government.

The Professions

The professions must assume the heavy responsibilities of the regulatory process. The resources of the professions will be thinly spread if they are to perform as envisioned under proposed medical device legislation. The conscientious work of a few professionals will not get the job done. Professional societies must assume a stronger role in assisting the federal government in carrying out its responsibilities. These roles cannot be ignored nor placed on the shoulders of a few professionals and a few professional organizations.

Conclusion

Regulation can be effective only if interest groups and government work together from some basis of trust. Fear, self-interest, and mistrust must be transcended by cooperation in the interest of the patient. **[The End]**

A Device Amendment

By VINCENT A. KLEINFELD

Mr. Kleinfeld Is a Partner of Kleinfeld, Kaplan and Becker, a Washington, D. C. Law Firm.

THERE IS NO QUESTION but that problems have arisen in the past in the therapeutic device field. Difficulties have been encountered regarding various electronic devices, nonelectronic medical devices and equipment, artificial heart valves manufactured with defects (leading to excessive clot production and propagation), malfunctions of artificial kidney machines, hip prostheses having mechanical disruption, metal implants of various kinds that break or become corroded, and others.

Even those who may still be opposed, for philosophical or other reasons, to the preclearance of devices, must realize that in the near future an amendment to the Act will be enacted by Congress, providing for some type of preclearance and standardization of devices.

Preclearance of Medical Devices

There are two problems. One, of course, is "What kind of legislation?" Do the consumer and Congress wish complete preclearance by the Food and Drug Administration (FDA) of the safety and efficacy of all devices, past and future, and without grandfather clause protection? Will the criterion of substantial evidence be the same as that provided by the Drug Amendments of 1962 as construed by the FDA and the courts? Will long-term clinical use, often derided as "testimonial evidence," be disregarded? A former Assistant Secretary of Health, Education, and Welfare said, a few years ago:

"Our objective has to be twofold: We have to make certain that the public is given every reasonable assurance that medical devices are safe and effective before they enter the marketplace, and we have to assure a climate in which device development is encouraged and abetted, not hampered by federal regulation.

"This is, of course, the same purpose behind the regulation of drugs. We recognize that drug clearance is less than perfect, and we are looking hard for ways to improve this process. Certainly, in developing a regulatory scheme for medical devices, we are going to seek to avoid some of the problems that have arisen in the drug field, while at the same time making every effort to achieve the highest possible level of consumer protection."

This is a laudable objective—but indeed a difficult one to achieve. Whether the difficulties which have arisen in the new drug field can be avoided or surmounted is somewhat doubtful. What evidence is there that the government has learned the "facts of life" in its handling of the drug area since the enactment of the Drug Amendments of 1962?

Effectiveness of a Device Amendment

Will Congress, prodded by zealous but sometimes not well-informed persons, overlegislate and impose onerous requirements which may be almost impossible to overcome and which will lead to lengthy delays and tremendous increases in cost to the consumer? Further, everyone who has spent time in or who has dealt with any government agency, knows that the manner in which a law is administered and construed is often more important than the contents of the law itself. The effectiveness of any new amendment, no matter how it is drawn, will depend on the manner in which it will be interpreted and on the reasonableness, ability and expertise of those administering it. Will the administrative body be composed of men who will adhere to the law and not be "pushed around" by industry, overzealous consumer groups, or even by a Congressman or Senator? In this connection, will any device amendment, no matter what language is employed, inevitably end in total preclearance of all devices both as to safety and effectiveness as a result of consumer group pressures, administrative aggressiveness, and the overwhelming desire of practically every agency to extend its authority?

The *Bacto-Unidisk* Case

Is a device amendment really required as a matter of law? In the *Bacto-Unidisk* case, the Supreme Court stated that the legislative history directs us to read the classification "drug" broadly, and to confine the device exception as nearly as possible to the types of items Congress suggested in the debates, such as electric belts, quack diagnostic sales, and therapeutic lamps, as well as bathroom weight scales, shoulder braces, air conditioning units, and crutches. The device ex-

ception was created primarily for the purpose of avoiding the semantic incongruity of classifying as drugs certain quack contraptions and basic aids used in the routine operation of a hospital.

The Power of the FDA

The tremendous scope of the authority granted to the FDA by this and other examples of judicial legislation raises the query whether, as a matter of law, legislation is really needed. Thus, a report in the *Washington Post* a few years ago after the *AMP* case stated that:

"The position taken by the FDA, on the advice of its counsel . . . was that the products were legally 'new drugs' and therefore could not be sold until their safety and efficacy had been demonstrated to the Agency.

"It argues that any products used to diagnose, prevent or treat disease legally fell under the more stringent procedures governing 'new drugs' rather than the weaker controls regulating 'devices.'

. . . "Now, [FDA] counsel . . . said, the Agency has power to require that, like drugs, they be cleared for safety and efficacy before being sold.

"In addition, he said, the FDA now will have the same powers for articles that affect any of the bodily functions. Thus, . . . the FDA will be able to regulate, before sale, intrauterine birth control devices, which are used by possibly 1 million women in this country and by 6 to 8 million in others."

Further, if the Food and Drug Administration was legally authorized to enact its somewhat startling regulation covering "In Vitro Diagnostic Products For Human Use," it may be logically assumed that it is authorized to enact further and similar regulations covering all devices. In addition, there is always the innovative administrative approach, apparently accepted by the Supreme Court, that the end justifies the means, that the Food and Drug Administration may legislate to fill gaps in the Federal Food, Drug and Cosmetic Act.

It is understandable, however, that the Food and Drug Administration prefers a lengthy, detailed and ambiguous amendment to the Act, in this instance enacted by the Congress. In any event, as I have indicated, as a fact of life, legislation will be enacted. Our problem is, "What kind of legislation?" **[The End]**

Remarks on Legislative Overview of Medical Devices

By LARRY R. PILOT

Mr. Pilot Is Director, Division of Compliance, Office of Medical Devices, Food and Drug Administration.

ALMOST THREE YEARS AGO in a speech to the Medical-Surgical Manufacturers Association, Commissioner Edwards made the following statement:

"Let me first make it abundantly clear that the philosophy of the Food and Drug Administration with regard to medical devices, as with other products we regulate, is directed toward giving the consumer adequate protection, and at the same time providing encouragement for the development of new products. The consumer, the medical profession and the industry are best served only if these objectives are kept in delicate balance and constantly in the forefront.

"I would also like to make it clear that the stance of the Administration of FDA with regard to industry is not punitive. Rather, FDA is more concerned with encouraging responsible industrial and medical experts to develop the products which are needed to achieve the highest quality health care."

Dr. Edwards further stated that we were at a crossroads with several avenues open to us and he admonished that "if we proceed in the role of regulator vs. regulated or antagonist vs. protagonist, we will all suffer and the ultimate beneficiary, the patient, will be robbed of the best possible health care—the goal we all seek."

New Medical Device Legislation

As we move closer to the passage and enactment of new device legislation, I believe these remarks continue to reflect the attitude of the Agency toward the regulation of medical devices. Certainly tremendous progress has been made toward the achievement of a goal that many have anticipated for well over a decade. The legislation has been slow in developing, but the length of the process has so far resulted in an effort which is truly innovative in its approach and sufficiently broad so as to provide the FDA with appropriate regulatory tools.

In view of the fact that the subcommittees on health in both the Senate and the House have held hearings and received testimony from all interested parties, and the Senate Committee on Labor and Public Welfare recently reported out of committee Senator Kennedy's bill, it would be absurd to suggest that new device legislation is not imminent. As a matter of fact, I believe it is reasonable to suggest that at this time next year we will be talking about the scope and application of GMP (Good Manufacturing Practices), procedures for registering manufacturers and devices, implementing a system for reporting adverse incidents associated with devices, mechanics for reviewing new device applications with the aid and assistance of advisory committees, and other activities over which FDA will have primary jurisdiction.

The Effectiveness of Device Legislation

I know that most of you agree with the concept of new device legislation and that it is necessary and imminent. By the same token, I know that a number of you are concerned that this legislation will have a negative effect and that development of new devices and introduction of these devices into the marketplace will be severely hampered. We disagree and we further believe that the possibility of such an outcome will not materialize if we accept the fact that our mutual concern is for the patient that any one of us might become if illness or injury should strike. If we can imagine ourselves as being potential consumers, we will expect that the devices we are to use or which are to be used on us will be safe, effective and reliable and we would not settle for anything less.

We can make the legislation work to this effect if we will recognize that each of us—consumer, health professional, industry and government—has an opportunity to make a major contribution. New device legislation will not work very well if it is undertaken with an arrogant attitude by the FDA which will only serve to draw fire from consumer and professional groups, industry and Congress. In order for this legislation to work effectively, FDA must receive and be willing to receive maximum input from each of the groups mentioned previously.

A careful review of the legislation, the Congressional hearings and FDA's activities over the last few years will reveal that the FDA is completely serious about hearing from and listening to anyone having something to offer. I believe our efforts to inventory devices, develop a new definition for the term "device" and undertake a process where-

by devices could be classified into appropriate regulatory categories represent significant examples of accomplishments which have been achieved through mutual and open cooperation.

Premarket Scientific Review

The new device legislation focuses on this in a number of different ways but most notably in the area of premarket scientific review. The Cooper Committee placed heavy emphasis on the need to rely on experts outside of the Agency for scientific advice. This concept has been retained in the Administration Bill as well as the Kennedy-Rogers Proposal and it has been expanded to include representation from consumer groups as well as industry. This approach would represent a significant departure from the procedure which now applies to new drugs, and we believe it represents an approach which can properly utilize the talents of those individuals who are outside of the FDA. If this approach is not satisfactory to the interests of all concerned, then we are perplexed and not at all sure what would represent an acceptable approach. Further, if this approach does not work, then both government and industry have failed to accept their responsibilities and contribute their share.

The medical device legislation we will discuss is good legislation and it will be effective legislation if each of us recognizes the importance of dialogue and each of us does his share to keep that dialogue open and honest.

Devices Differ from Drugs

Finally, as we talk about legislation, we must recognize that devices by their very nature are different from drugs. In the case of devices which are used by licensed practitioners, the skill and knowledge of the practitioner can make the difference between the successful or unsuccessful application of a device. In addition, we must recognize that many of the great innovations in the device area have come about through the efforts of individual practitioners and that a device manufacturer serves as the vehicle for bringing a new device to all practitioners so that the patient can be served better.

However, regardless of who develops a device, we must recognize that as manufacturers it will be your responsibility to manufacture a safe, effective and reliable device which conforms to the requirements of the law. It will be our responsibility to assure that every device is manufactured, labeled and distributed in accordance with the law and that each manufacturer is complying with the law at all times.

[The End]

Medical Device Legislation

By RODNEY R. MUNSEY

Mr. Munsey Is Associate General Counsel, Staff Liaison to Medical Devices and Diagnostic Products Section, Pharmaceutical Manufacturers Association.

AS INDICATED PREVIOUSLY, it is expected that device legislation will be enacted next year. It has also been noted that currently pending are Senator Kennedy's bill (S. 2368), Congressman Rogers' bill (H. R. 9984), the Administration bills (H. R. 6073, S. 1446) and Senator Nelson's bill (S. 1337). The Kennedy and Rogers bills are very similar and are amended versions of the Administration bills. It is likely that final legislation will be a modified version of Kennedy and Rogers. The Food and Drug Administration (FDA) and Health, Education and Welfare (HEW) officials have indicated general approval of those bills. The Nelson bill is not likely to receive much attention because it is based on drug regulatory concepts long discarded by those familiar with the peculiar characteristics of devices.

Many of the amendments to the Administration bill contained in Kennedy/Rogers are the direct result of much effort by representatives of industry, the professions, and government to devise legislation suitable for medical devices. Starting over four years ago (after court decisions held that many products previously considered to be devices could also be considered new drugs and, therefore, subject to premarketing clearance requirements), the Pharmaceutical Manufacturers Association (PMA) began meeting with about 15 other trade and professional associations interested in the field in an effort to devise legislation appropriate for medical devices. As experienced as some of you are in the difficulty of getting agreement within your own company and the even greater difficulty in obtaining agreement within the companies of one trade association, you can well imagine the somewhat limited degree of optimism with which some of us approached the task. Nevertheless, agreement on an industry bill was finally reached and after much discussion and exchanges of

correspondence with appropriate persons, some of the concepts of that bill were included in the Kennedy and Rogers bills as introduced.

Meanwhile, in 1971, after considering the recommendations of the Cooper Committee referred to by Messrs. Pilot and Vanneman, the Administration bill was introduced. It is clear from a reading of the bill that it was contemplated that standard setting would apply far more often than would premarketing clearance. I mentioned a moment ago that the Kennedy and Rogers bills were amended versions of the Administration bill and that some interassociation generated amendments were included in those bills originally introduced. Examples of some of these are: a medical device definition which would include *in vitro* diagnostic products, an exemption of custom devices from premarketing clearance and standard-setting requirements, a provision to the effect that performance standards are preferable to material or identity standards, and a product development protocol mechanism for use in lieu of premarketing clearance in some circumstances.

In September, Senator Kennedy's Subcommittee on Health held hearings on his bill. Changes requested by industry included changes in the premarketing clearance criteria, the type of tests to be required on effectiveness in new device applications, the type of regulations that could be promulgated for manufacturing practices, the provision authorizing FDA to require lot testing for some products subject to standards, and in the provisions mandating manufacturers to notify purchasers of defects and to provide remedies for such defects.

Among the changes included in the Kennedy bill as reported since testimony in September are changes in the premarketing clearance criteria, changes in hearing rights, changes in defect notification and remedying provisions, changes in the regulation of prescription device advertising, and changes in FDA control over exports. Additional changes include a modification in the custom device exemption, the inclusion of a provision banning fraudulent devices, the inclusion of a provision banning the stockpiling of devices between the time a standard was promulgated and the time it was made effective, and a proviso calling for an expedited amendment to standards in some circumstances.

In October, industry and other groups testified before the House Subcommittee on Public Health and Environment on the Rogers bill. As would be expected, the statement was basically the same as that made before the Senate Committee. We are hopeful that the legislation that passes the House will incorporate some of the changes proposed in our testimony, especially in the areas of premarketing clearance criteria and the type of studies required to support claims of effectiveness. **[The End]**

Science and the Consumer

By ARTHUR T. SCHRAMM

Mr. Schramm Is President of Food Materials Corporation. His Paper Was Presented at the Food Update '73 Conference Held in New Orleans, Louisiana on March 25—29, 1973.

DURING RECENT YEARS, questions concerning the safety of certain food additives and Generally Recognized as Safe (GRAS) substances have kept the entire food processing industry in an embarrassingly defensive position; one that is not warranted by the objective scientific facts.

The communications media have given considerable publicity to animal experimental data, actually having little or no real bearing on safety for human consumption, but presented in such manner as to dispose a large majority of the lay public to draw ominous conclusions. Such reporting, together with politically-oriented congressional hearings, and careless statements by apparently qualified scientists have contributed strongly to the atmosphere of distrust of industry that exists in the minds of the majority of the public. This, in turn, has created psychological pressure on legislators and regulatory administrators with the resulting enactment of superfluous and unnecessarily restrictive laws and regulations without valid supporting data.

Corporate Abuse of Consumers

Adverse allegations concerning the food industry are symptomatic of the overall picture of corporate abuse of consumers. The result has been, as we well know, the movement known as "consumerism." The magnetism of this movement is obvious: for the media, it provides audiences; for the politicians, it wins votes; and for publishers, it creates sales. Thus was spawned the consumer advocate, the self-designated protector of the consumer, who has undertaken not merely to expose his concept of corporate unworthiness, but who has actively tried to influence legislative, regulatory and judicial action to support *his* view of consumer interest. Furthermore, since everyone is

a consumer such defense is inherently attractive, particularly in our increasingly complex society which reflects the influence of science and technology. Increased industrialization and specialization have confused the consumer to the point where he is no longer able, on the basis of his own personal knowledge, to make meaningful judgments concerning advertised utility and safety of the products that he buys. Loud claims questioning safety and quality have been leveled against not only food, but automobiles, drugs, fabrics, repairs, services and warranties to the extent that consumer advocates have convinced many consumers that most corporations are willing to sacrifice the welfare of the consumer for profit.

Since federal, state and local regulatory agencies have been instituted to protect the consumer from abuses by uninformed or unscrupulous manufacturers, the consumer activists have taken steps to discredit those agencies. This has been manifest in attacks, for example, on the Food and Drug Administration (FDA) for favoring the industries it has been assigned to regulate. What makes it so difficult to deal with the "logic" of the consumer activist is that he fails to admit the realities of the risk-benefit and the cost-benefit concepts, and the fact that *absolute* safety cannot be proved for anything, whether it be a food additive or a natural food product. Having described his view of the sad posture of the American consumer, the activist offers familiar remedies. Included are a requirement for absolute safety regardless of potential benefits, establishment of standards, licensing of products, total regulation of advertising and creation of a watchdog federal agency to represent the interests of the consumer in all other federal agency activities.

Validity of Claims of Consumer Activists

How true are the claims of the consumer activists? There is a degree of truth in much of what they say and there is a place for the sincere, informed ones in our society, but is it worth the abandonment of the free enterprise system? Shall the consumer be totally without judgment and responsibility concerning his own well-being? Should Big Brother take over? It seems to me that any system involving humans will experience a slight degree of abuse or error. Just as there are individuals unmindful of the rights of others, so there are corporations that neglect the safety and quality of their products and ignore the rights of the consumers. Just as individuals have human frailties, so do corporations, and there are bound to be accidents, poor communications concerning product performance and misleading advertising,

especially in a free enterprise economy as complex as ours. But, let's not abandon the entire system! Let's not penalize all corporations to reach the few culprits! Let's enforce existing laws. Zero defect is a laudable goal but an unrealistic one. We must always strive for it but with a view to cost-benefit and risk-benefit.

What Is a Reasonable Risk?

The questions to be answered are—what is a reasonable risk? What responsibility must the consumer himself take to learn the safe handling of potentially hazardous products and processes? Certainly manufacturers must be increasingly diligent in producing good products and in accurately describing their proper use, but shouldn't the consumer be expected to read the instructions on the label? The automobile is often cited as an example of risk-benefit. It costs thousands of lives annually. Fortunately, we are not talking about risks of this nature in the case of food additives and pesticide residuals—but slight as the risks are they must be compared with the potential benefits before being permitted. With proof of absolute safety as a requirement we could not use pesticides, nor food additives, nor even food, for that matter. Further, with the absolute concept, the wonder drugs of the 20th century would not have been approved—and this would have cost uncounted thousands of lives.

Danger of "Out of Context" Information

The activist, particularly in the food field, has frequently used information out of context such as isolated scientific observations, to prove abuse of the consumer by the manufacturer, with the claim that invariably the risk is to the consumer and the benefit to the corporation. Such scientifically unqualified statements have been accepted at congressional hearings without demand for scientific validity, thus putting the legitimate manufacturer on the defensive, obliged to prove safety under rules that do not apply to his accuser.

A further complication is that decisions concerning safety of a substance to be used in foods require scientific judgments in toxicology, a science requiring considerable acquired expertise and one where the layman would be confused and frightened by the intricacies involved. This adds to the suspicion. What is overlooked is the fact that the pretesting of food additives is so extensive that many natural food products, safety of which is unquestioned for mystical reasons, would fail to meet the requirements.

I could go on and on, but at this point, I want to make it clear that I freely admit that all consumer activists are not bad, nor are all corporations good. There are abuses by both. There is a need for consumerism but not for the type that disdains the scientific method and does not face up to the realities mentioned above.

Extensive Public Information Necessary

Now, let us talk about the vast majority of processed food manufacturers. Why can't they get their message across to the consumer? Why can't they present the scientific facts, the full truth, and expect understanding? In general, the complexity of issues requires a scientific background that today's average consumer does not possess. He must trust the opinions of qualified experts until such time as our educational system is suitably modified to add practical science to the three "R's" very early in the educational scene. Hopefully, at some time in the future, we should be able to explain the following to the consumer. (Just imagine trying to do it now!):

(1) All decisions in life involve a risk-benefit concept.

(2) It is impossible to prove the absolute safety of a food additive or of a natural food for that matter.

(3) Many natural foods contain toxicants which would eliminate them from the food supply were their safety judged by the same criteria as now apply to synthetics.

(4) There are systems in our society designed to protect the consumer; for example, that involving the Food and Drug Administration, the U. S. Department of Agriculture and the National Academy of Science working in cooperative effort.

(5) Most scientific decisions will have to be made by experts until radical changes in our educational system are in operation long enough to permit reliable judgments to be made by consumers.

(6) Experts in the same scientific discipline sometimes disagree because this is the way scientific knowledge is developed.

(7) Television cannot portray new scientific facts in a news program because television is suitable for portraying events, whereas scientific matters are so complicated that a documentary type of programming would be required.

(8) A scientist who is a recognized expert in a given discipline is probably a layman in many other scientific disciplines and

should be considered as such when he cannot resist the limelight when asked to respond to questions outside of his expertise.

(9) Despite the fact that practically instant communication exists, we do not have instant solutions to real problems in science and probably never will have.

(10) Not all consumer activists are representing the consumer out of humanistic motives. Some, unfortunately, are motivated by greed and desire for power and position. How will the consumer recognize the difference?

(11) Most news media commentators are probably sincere, but their failure to understand the scientific method leads to inaccurate reporting.

(12) Some politicians are seeking votes but not necessarily the truth.

(13) Sensational opinions, though not true, get more attention than the truth, which is frequently very difficult to dramatize.

(14) In handling the problems of society, priorities must apply; everything cannot be taken care of simultaneously.

(15) Opinions must be distinguished from facts. Scientists sometimes exaggerate the amount of applicable knowledge that they possess and offer confident solutions to social problems which, when tried, fail.

(16) Many consumers accept the judgment of activists. Why don't they trust that of qualified scientific experts?

(17) Marketing practices of some companies make them appear to concur in the unfounded claims of certain activists.

Effective Communication

I have mentioned the foregoing difficulties not to discourage attempts to communicate but to put the complexity of the problem into perspective. Effective communication in science will not be achieved in a year or in five years, and perhaps not in a generation. We must continue to try to overcome bias and present the facts and hope that some day we will find a receptive climate created by a suitable educational system. I repeat, we must continue in our efforts to present the facts but we will have to call upon the utmost in patience to do so. As further evidence of the problems in communication with which we are faced, I would like to relay to you thoughts that were expressed during a recent meeting of the American Association for the Advancement of Science on the subject of communicating science to the public.

Communicating Science to the Public

In the course of the talks and ensuing panel discussion it was pointed out that approximately 60 per cent of the United States public regards television as a primary source of news and information, frequently placing more confidence in what is seen over the television than in the newspapers and magazines. There is significant evidence that the impact of television news and analysis on the viewer is more intense than that of the print media by several orders of magnitude. Frequently, when we look at the world as it appears on the television during 60 to 90 minutes of the late afternoon and early evening, we see a world in which science has almost no useful role, either as an intellectual pursuit or as a significant influence on the human condition. We see certain aspects of medical science if it touches human tissue. We see certain aspects of technology, especially if it moves, and most of what we see stimulates vague apprehension rather than hope for improving the state of mankind. For the most part, what science has presented to the public either mystifies or terrifies. For the really tough questions in science, there is almost no input in television. Press releases are religiously prepared for newspaper reporters, but none for television. The progress of science lends itself better to the nonvisual type of reporting. In television, we meet people who are introduced as scientists, and we are impressed by the confidence with which they reveal truth, until they begin quarreling among themselves. It is important to consider how much the present manner of television interpretation of science derives from the ways in which scientists present themselves to the medium, and how the medium presents them to the public.

The Impatient Public

The public has become accustomed in recent decades to expecting instant solutions to the very complex problems which arise. This in turn evokes rapid responses from the experts without the opportunity for time to study the fragmented data that is usually available and the many inferences that may be drawn. Such responses from the scientists, symbols of certitude, make them vulnerable to attack by consumer activists and news-making reporters. In other words, television as presently used is a poor medium for science.

One of the participants indicated that television needs much, much more help in correcting the situation described above. He likened television to illustrated headlines, where brevity is essential, and with a long story being only three minutes in duration. In most cases, this

is far from sufficient time to detail the complex issues involved, particularly for a public which is relatively poorly-informed in scientific matters. He found that the scientific sources for information are particularly limited, and ascribes this to a sort of fear of castration by the scientists themselves, who are accustomed to precision which is defied by demand for brevity. This is complicated by the fact that the timing of television presentations, during the dinner hour and/or late at night, finds the audience distracted and not desirous of the indepth treatment of science that is required. He urged changes in the scientific community, an awakening to the 20th century. Thought should be given to effective use of slides and dramatic visual presentations. He urged scientific organizations to develop technical information specialists, and underlined the importance of the use of documentaries.

Another participant stated that we cannot afford the scientifically illiterate citizenry that we now have and that science educators owe it to the public to share the sense of adventure, beauty, and aesthetics that scientists experience. The scientist must overcome the appearance of arrogance and must learn to express what he is doing in broad, understandable layman's terms. He advised that scientists should not take issues, but simply provide facts on issues, together with options, costs, risks, and benefits.

The Uninterested Consumer

Despite our increasingly scientific and technological society, the nonscientific ordinary citizen's knowledge of and interest in scientific and technological matters appears to be declining, and at times he actually becomes hostile in his attitude. Scientists must learn not only to communicate among themselves but also with the consumer. The consumer must be informed so that he understands how scientific knowledge is gained and how scientists and technicians think and work. Only then will he be in a position to understand that disagreement among scientists may be a good sign and not necessarily a bad one.

Basically man is instinctively curious. As a child he asks questions about everything and usually is given the impression that there are simple, unambiguous answers to all queries. At some point in life he is thrown on his own resources to obtain answers about the universe around him. Then, he has to draw upon his experience and use either intellectual effort or mystical sources for additional knowledge. The most effective system developed by man to add to his body of knowledge is the scientific method. Whether man likes it or not, the scientific method impinges with increasing impact upon daily life, concerning not only university professors and industry and government scientists.

Definition of Science

First, let me define science as a body of organized knowledge which has been obtained, and is constantly being added to, by means of the scientific method. Pure science is a quest for knowledge for its own sake, whereas applied science is the use of such knowledge for practical purposes.

Some scientists are motivated by a desire to search for truth simply as an end in itself, regardless of whether the ultimate result is beneficial or harmful to mankind. Some scientists are motivated by a desire for unlimited extension of knowledge but all are interested in interrelating information obtained from diverse sources and then attempting to explain a complexity of facts by a simplicity of causes. New observations, experiments and theories must logically fit the established pattern of a relatively few basic principles accepted as true mainly because no one has yet been able to disprove them. These are the facts accumulated through centuries of scientific investigation.

Reevaluation of Scientific Principles

Science is dynamic— self-analytical and self-correcting. All new theories and observations must meet the test of existing principles, but the principles themselves are subject to constant examination. This process of reevaluation is used in all fields of research, but it is most clearly evident in the exact or measuring sciences where conditions can be precisely controlled, varied with confidence, and the effect of changes recorded numerically.

With each new principle, other possibilities and combinations become evident and applications of the new knowledge overcome previously existing barriers to shed light on problems that had previously defied explanation.

The Scientific Method

Thus, the scientific method is really a set of rules for thinking and a way for examining the world. It starts with a question which leads to collection of data by observation and by experiment. The method of observation appears simple—watch carefully and record the data. Unfortunately, many people look but do not see, and emotions and bias interfere. Accurate observation requires considerable training and discipline and comparatively few people are competent to do it. Hence, insofar as possible, the human observer is replaced by measuring instruments, and his observations checked by another worker. Untrained observers are responsible for much of the misinformation on scientific matters that the media publicize today.

Obtaining data by experiment requires controlled, repeatable conditions. The goal of a properly conducted experiment is to establish an artificial, reproducible situation in which the factor to be studied can be isolated and observed. This is not a simple matter because, if the results are to be valid, they must be capable of being reproduced by other experimenters using the same procedure. Furthermore, controls must be established where possible as a check on the experiment. If there are several factors that can be altered, observations and measurements on one of them must be completed while the others are held constant; then another variable may be selected for alteration, the same precautions being observed. There are also advanced techniques whereby several variables may be observed simultaneously with valid results.

The next step is systematization of data by tabulation or mathematical manipulation. Then an effort is made to show how the new data fits into the accepted body of knowledge. This is now frequently done by scientists other than those who had performed the experiments and observations. At one time it was not unusual for the same scientist to make observations, conduct experiments, systematize his results, draw conclusions and publish his work in the scientific literature. The explanation of the facts is called an hypothesis and it must fit all the previously existing facts. If so, it can be tested by verifying a prediction based on the assumption. If the new experiment does not confirm the prediction, the hypothesis is invalid. If repeated experiments show that the prediction is verified consistently, the assumption becomes a part of the body of knowledge.

The scientific method is demanding and time-consuming. Now, with the demand for instant truth, impatience sets in, and we are asked to lay bare this whole procedure with its complexities and seeming contradictions before an uninformed and suspicious public. Impossible!

What the consumer activists and news-hungry commentators are doing in certain instances is short-circuiting the scientific method by isolating unproved observations and using them to support a preconceived conclusion.

Scientific Status Summaries

In an effort to present the facts without bias, the Institute of Food Technologists (IFT) has organized an Expert Panel on Food Safety and Nutrition and a Committee on Public Information. The principal task of the Expert Panel is to define areas of significant current and potential public and regulatory interest in food safety and nutrition and to prepare scientific papers summarizing the state of the

knowledge on such topics. These papers, called scientific status summaries, will be updated as additional knowledge is obtained, and are designed to present the facts objectively. The Committee on Public Information is responsible for converting the scientific status summary into a popular version for general consumption. The popular version is then checked and approved by the expert panel for scientific accuracy; at that point a news release is prepared and a popular version is distributed among more than two thousand members of the communications media.

The unusual part of the program is the use of local scientific spokesmen for the work of the expert panel. These spokesmen are actually an extension of the panel and their identity has been made known to media representatives such as television and radio commentators, and the press. The local representatives will supply information to the media on matters of current interest and will be prepared to receive and answer questions from the media. We are aware that no local representative's expertise will be sufficiently broad to handle all questions and he will inevitably receive questions he cannot answer immediately or authoritatively. At that point, he will put the questioner in touch with an appropriate expert on the subject. Local representatives will also feed back to the expert panel questions, attitudes, and problems that he encounters for further consideration.

Science in Educational Process

During the pilot stage of this program we have been exposed in depth to problems involving objectivity, bias, communications, interpretations, and all the pitfalls that tempt us to say "to hell with it," but intellectually we feel strongly that this is the right way to go. We are now planning to implement the program on a basis that will have all of the resources of the IFT behind it. We hope that other organizations will take the same approach. We recognize that this will be an uphill endeavor that will require considerable understanding, patience, tolerance, and persistence; and the real "payoff" may lie down the road 10 or 20 years. Ultimate success in communicating with the consumer will depend on the effectiveness of educators to incorporate practical science, not as a separate elective, but as an essential part of our educational process beginning with the earliest years.

My purpose is not to alarm but to present our problems in perspective so that we will have the patience to pursue diligently and aggressively a program for presenting the whole unglamorous truth.

[The End]

An Assessment of the Delaney Clause After 15 Years

By B. L. OSER

Dr. Oser Is Scientific Editor of the Food Drug Cosmetic Law Journal. His Paper Was Presented at the Society of Toxicology's Annual Meeting, New York, March 21, 1973.

IT IS SMALL WONDER that the Delaney Clause, inserted into the U. S. food additives legislation as a bulwark against the addition of potential carcinogens to foods, has come to be regarded by many toxicologists as scientifically unsound. During the gestation period of the Food Additives Amendment, nearly 20 years ago, there were even administrators in the regulatory agency who regarded this provision of the law as redundant and it was prophesied that, in time, experience would show it to be impractical. In the past few years, various prestigious groups of scientists have recommended modification of the Delaney Clause to permit some latitude for the exercise of scientific judgment in the implementation of its intent. Now, 15 years since enactment of the Clause, it is revealing to take a retrospective look at how the "concept" has been applied in the regulation of pesticide residues and color and food additives.

Carcinogenics Outlawed

Acute and chronic toxicity studies on Aramite®, a highly effective acaricide, were undertaken in 1949, long before the passage of the Pesticides and Food Additives Amendments. The dosage range was

®Registered trade mark of Uniroyal, Inc.

set before any information was available on residue levels on fruits and vegetables, and the upper limit of 5000 ppm was believed to be reasonable in view of the low acute oral toxicity (LD_{50} 3.9 g/kg). At the maximum and intermediate doses, hepatic tumors were observed. The study was questioned by the Food and Drug Administration (FDA) mainly on the ground that it failed to demonstrate a no-effect level. The issue hinged on whether the liver lesion found in only one rat in the group given the lowest dietary level (500 ppm) was carcinomatous or simply hyperplastic. An *ad hoc* advisory committee appointed by the FDA under the terms of the newly enacted Miller Amendment confirmed the opinion of the petitioner's pathologists, and the tolerance (1 ppm) remained in effect. Subsequently, much more extensive carcinogenic studies corroborated the earlier findings in rats (Oser & Oser, Toxic. appl. Pharmac. 1962, *4*, 70; Popper *et al.* Cancer, N. Y. 1960, *13*, 1035). However, dogs dosed at 1580 ppm showed marked evidence of hepatic carcinoma (Sternberg *et al. ibid* 1960, *13*, 780) and Aramite was dropped from use on food crops.

The herbicide, 3-amino-1,2,4-triazole, a thyrocarcinogen, was permitted for post-harvest use on cranberry bogs provided it left no residue on the next crop. As a result of misuse, residues were found in two lots of cranberries just prior to Thanksgiving Day, 1959. Although more than 95% of all the lots tested were negative, the sale of cranberries came to a virtual halt since it was not possible to trace the distribution of the contaminated cranberries throughout the country.

More recently several of the chlorinated organic pesticides have been banned or threatened on the ground of alleged carcinogenicity. The question concerning dieldrin and aldrin has not been finally resolved despite exhaustive study by NAS-NRC Advisory Committees, while DDT, one of the most effective and economically important pesticides, is to be prohibited by the Environmental Protection Agency, the Administrator having reversed a decision reached by an Examiner after 7 months of hearings that the evidence had not established DDT as carcinogenic.

Among the food additives that have been outlawed under the Delaney concept are natural oil of sassafras and its component, safrole, and oil of calamus, characteristic flavoring components of root beer and vermouth, respectively. Coumarin and its natural source, the tonka bean, were withdrawn from use (principally in artificial vanilla flavorings) when a routine feeding test of a commercial flavor mixture revealed it to be the component responsible for hepatomas in rats.

Approval for the oil-soluble food colorings, FD&C Yellow Nos. 3 and 4, was withdrawn in 1959 following toxicity tests in rats and the demonstration of traces of the bladder carcinogen, 2-naphthylamine. Currently tests are under way on several other certifiable colorings whose noncarcinogenicity has not been "proven" to the satisfaction of certain critics here and abroad.

Cyclamates

Perhaps the most notorious application of the Delaney Clause in terms of its effect on the food industry was the summary prohibition of the use of cyclamates in 1969. This followed rather abruptly upon the demonstration of bladder carcinoma in a small proportion of a group of 70 rats fed a diet containing 5% of a 10:1 sodium cyclamate/sodium saccharin mixture (equivalent to 2500 mg/kg). Most of these lesions were evident only microscopically after the animals were sacrificed at 2 years (Price *et al.* Science, N. Y. 1970, *167,* 1131). The study was originally designed to determine whether the effect of this mixture of non-nutritive sweeteners was toxicologically synergistic, the dosage range having been determined on the basis of earlier studies on the individual substances. Nevertheless, the cyclamate alone, rather than the mixture, was assumed by the Department of Health, Education and Welfare to be the carcinogen, a conclusion that may prove to have been unwarranted in the light of recent findings. At the time, however, it seemed justified on the grounds that saccharin had been in use much longer than cyclamate without apparent adverse effects, and some humans were known to convert a small proportion of cyclamate to cyclohexylamine, a compound whose chronic oral toxicity had not been investigated.

That the almost worldwide banning of cyclamates may have been premature is now suggested both by failure to induce bladder cancer in rats given cyclohexylamine at an assumed 10% conversion rate (Morgareidege *et al.* Toxic, appl. Pharmac. 1972, *21,* 330) and by the rumored finding of bladder tumors in rats fed diets containing 7.5% saccharin. Moreover, studies of cyclamate, saccharin and mixtures of the two in several other laboratories appear not to have confirmed the earlier findings with the mixture.

Fault of the Delaney Clause

The basic fault of the Delaney Clause lies in the assumption that the ingestion of any substance by animals, irrespective of the magnitude,

frequency or duration of dosage, is an appropriate method for determining its carcinogenic potential for man. This concept flies in the face of fundamental pharmacological principles, not to mention common experience.

There are several separate and distinct parts to the Delaney Clause, which states (Code of Federal Regulations, Sec. 409c, 3, A) that a substance is deemed unsafe and hence is proscribed as a direct or indirect component of food . . . .

". . . . 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 in man or animal. . . . ."

Under the first phrase, any substance that is found to induce cancer when fed in any dose to any animal daily for its entire lifetime must be banned from use in food. As administratively construed, this is a legal mandate which leaves no room for scientific judgment as to whether the oral dose is a reasonable one. The phrase following the conjunction "or" made provision for the later adoption of acceptable procedures employing non-oral routes of administration.

The Delaney Clause violates the fundamental principle enunciated by Paracelsus in the maxim "Poison is in everything and no thing is without poison. The dosage makes it either a poison or a remedy." The cardinal significance of the dose was recognized by Congress when it substituted the Food Additives Amendment of 1958 for the "poison *per se* doctrine" implicit in Section 406(a) of the Food, Drug and Cosmetic Act, and thus provided for the safe use of substances which in higher doses could be toxic.

Dose-Response Relationship

Pharmacologists and toxicologists have long considered the dose-response relationship to be applicable generally to all chemicals and drugs. Numerous carcinogenesis studies, employing as criteria either the duration of the induction period or the incidence, size and severity of experimentally induced tumors, have demonstrated threshold doses below which no evidence of tumors is found and above which the indicia increase. Oncologists, however, deny the existence of threshold levels of carcinogens. For example, Druckrey (in "Carcinogenesis—Mechanisms of Action," edited by G. E. W. Wolstenholme and Maeve O'Connor, p. 110, Little, Brown & Co., Boston, 1958) has explained that "The reason why extremely small doses produce no cancer is not that there is a threshold dose, but because the necessary induction

time becomes longer than the total life span." Similarly, Weisburger & Weisburger (*Fd Cosmet. Toxicol.* 1968, *6,* 235) have stated that "there are doses for which no tumors are seen over the average life span. Were the animals to live longer, tumors could be *predicted* to occur" (emphasis supplied). This very criterion, however, could be regarded as defining the conditions for establishing a "safe" dose of a potential carcinogen.

It has been postulated that a single molecule of a chemical may cause a mutation in a single cell sufficient to initiate a malignant process. The hypothesis that subthreshold doses of a substance may induce unrecognized (and possibly unrecognizable) cellular alterations of a precancerous nature does not justify a conclusion that the substance has been "found . . . . . to induce cancer" as specified in the Delaney Clause. To deny this and contend that "no one knows how to establish a safe dose for a carcinogen" is scientific agnosticism of the first order.

Carcinogens in Natural Food

From time immemorial, animal species have throughout life been exposed to low levels of carcinogenic substances introduced into their food or environment either by nature or by man. The variety and multiplicity of these substances would seem to suggest that man, as a species, is capable of surviving such exposures. Some substances known to be carcinogenic when administered orally occur ubiquitously in natural or conventionally prepared foods. Among them are polycyclic aromatic hydrocarbons in smoked or roasted meats, fish and nuts, mycotoxins in grains, seeds and nuts, estrogens in soya beans, grains and certain fruits, nitrosamines in cured meats, safrole, asarone and related substances in spices and flavorings, selenium in grains grown on seleniferous soil and ergot in rye flour (Miller, in "Toxicants Occurring Naturally in Foods," Food Protection Committee, 2nd ed., NAS-NRC, Washington, in preparation 1973). In addition, many subsubtances are known to induce tumors when inhaled or injected subcutaneously, but these routes are not considered appropriate for carcinogenicity testing of food components. The fact that potential carcinogens in common foods are not etiologically correlated with the incidence of human cancer, supports the probability that trace amounts can be safely tolerated or that the risk, if any, is extremely remote.

Apart from cases of cancer induced by occupational exposure to certain chemicals, evidence correlating the incidence of human cancer with the ingestion of substances demonstrated to be carcinogenic in

animals is sparse indeed. It is misleading and fallacious to categorize as a "carcinogen" for man any substance that, under exaggerated conditions, can cause cancer in some species of test animal. In view of the many variables, including species, dosage and route, associated with the experimental induction of carcinogenicity, the term should be explicitly defined in the context in which it is used.

For carcinogenesis studies designed to investigate the etiology or mechanism of the cancer process, the approach is quite different from that appropriate for evaluating the safety of trace substances in the human diet. In the former type of study, highly exaggerated conditions and a variety of dosage routes may be used to shorten the induction time or increase the incidence of neoplasms.

Toxicological Tests of Food

Toxicological tests of food components are based on the premise that for every substance there are toxic and "no-adverse-effect" dose levels, the goal being to determine these levels and evaluate responses in relation to intended or potential uses. A considerable volume of evidence has accumulated to show that carcinogens are no exception to the dose-response relationship. In long-term toxicity studies of food additives, the usual dosage range encompasses a reasonable multiple of the potential human intake and extends high enough to elicit a toxic response. In carcinogenicity testing, however, the highest dose is set at the maximum tolerable level, one that will not materially reduce longevity (Food Protection Committee, "Evaluating the Safety of Food Chemicals," NAS-NRC, Washington, 1970; Joint FAO/WHO Expert Committee on Food Additives—Fifth Report, Tech. Rep. Ser. Wld Hlth Org. 1961, *220;* Ministry of Health, "Carcinogenic Risks in Food Additives and Pesticides," Mon. Bull. Minist. Hlth 1960, *19*, 108; Zwickey & Davis, in "Appraisal of the Safety of Chemicals in Foods, Drugs and Cosmetics," The Association of Food and Drug Officials of the United States, Austin, Texas, 1959). It is interesting that when the total "lifetime" (2 year) intake of an additive by a 400g rat is compared with the equivalent intake by a 50kg man given the same dietary level over a 50 year period, the man : rat ratio is approximately 650.

It may be useful at this point to review briefly the toxicological basis for estimating safe or acceptable levels of food additives and to show that they are not absolute or unequivocal determinations but are subject to many arbitrary experimental and judicious decisions. Some of the pitfalls, which in carcinogenicity testing may lead to false-posi-

tive or false-negative results have been summarized by Druckrey (in "Potential Carcinogenic Hazards from Drugs. Evaluation of Risks," edited by R. Truhaut, p. 60, Springer Verlag, Berlin, 1967). Among the former are spontaneous tumors, contamination of the test substance, food or environment, dietary deficiencies, infection with tumor-producing parasites, and various unspecific factors such as the presence of cocarcinogens, hormonal disturbances and the prolongation of life under the test conditions. False-negative results, on the other hand, may result from inadequate actual or effective dosage, insufficient length of study, insensibility of target tissues or the use of a resistant species. Furthermore, chemical and enzymic modifications within the gut may in a given species modify, reduce or enhance the biological effect of a test substance. It has even been shown that responses to intragastric intubation may differ from those produced when the test material is incorporated into the diet (Weil *et al.* Toxic. appl. Pharmac. 1972, *21*, 390).

No-Adverse-Effect Dose

Toxicologists generally have adopted the position that the no-adverse-effect dose should be based on the observed negative response of a test group, not on extrapolation from the response of higher dosage groups. The uncertainties involved in arriving at a truly maximum no-adverse-effect dose have been discussed previously (Oser, *Fd Cosmet. Toxicol.* 1969, *7*, 415). Particularly at low levels of dosage, the crucial evidence of "adverse effect" is often left to discovery by pathologists. (One could hope for better agreement as to the significance of borderline histopathological aberrations.)

The no-adverse-effect dose, expressed in relation to body weight, is converted to an acceptable daily intake for man by applying a safety factor to compensate for uncertainty in the interspecies transition from test animals to man, for differences in intraspecies susceptibility or resistance and for variations in human dietary patterns. It is interesting to note, however, that in the case of certain essential nutrients, safety factors vary over a wide range (Ostwald & Briggs, in "Toxicants Occurring Naturally in Foods," Food Protection Committee, NAS-NRC Publ. no. 1354, Washington, 1966). The chronic toxic dose of vitamin A, for example, is only 20-30 times as great as the currently accepted daily allowance, while in the case of sodium chloride the safety factor is only 2. Nevertheless, the factor of 100 has been hal-

lowed by usage and is, in fact, specified by regulations—except when evidence warrants some deviation. A decrease in the safety margin may be justified, for example, if the first effects observed could not occur with lower levels of intake (e.g. osmotic effects) or if they are compensatory rather than pathological (e.g. renal enlargement), if the additive is already present in the diet or body tissues in considerable amount, if the treated food is only rarely consumed or if favorable evidence is available from very long-term human experience. On the other hand, an increase in the safety margin might be indicated for additives proposed for use in staple foods, in foods likely to be eaten in large amounts by children or in foods subject to wide seasonal or other variations in consumption, as well as for additives on which the experimental evidence is incomplete and for those to be used in situations where controls might be inadequate. Moreover, if the effect is transitory or unaccompanied by structural or functional defects, a lower safety factor may be justified than when the effect is severe or irreversible. The slope of the dose-response curve must also be taken into account (Oser, *loc. cit.*).

These, then, are the steps toward estimating acceptable intake levels of substances in food for man. Legal tolerance limits for additives or pesticide residues are set no higher than necessary to achieve their intended functions and must, of course, fall within acceptable dietary ranges.

Zero Tolerance

One of the main difficulties with the Delaney Clause, as with other statutory provisions for "no residue" or "zero tolerance," has been the continuing improvement, without apparent limit, in the sensitivity of analytical instrumentation and techniques, as a result of which substances prohibited on a "no residue" basis have later been detected in traces so small as to be beyond the range of any conceivable toxicological significance (Zweig, in "Essays in Toxicology" edited by F. R. Blood, Vol. 2, p. 155, Academic Press, New York, 1970). Unless one accepts the dictum of *de minimis non curat toxicologiae*, it becomes necessary in the case of "carcinogens" to invoke the Delaney Clause.

The appraisal of the safety of food additives is a value judgment in which scientific evidence plays only a part, albeit a major one. Not only must the more or less arbitrary nature of the experimental conditions and the subjective aspects of the interpretation of the results be taken into

account, but the risks, however remote, must be assessed against the real or potential benefits. In this regard, considerations beyond the scope of toxicology must be weighed: risk and benefit can be balanced only in terms of socially acceptable judgments.

Because absolute safety is philosophically unattainable, some statisticians insist first on defining some level of permissible risk, say 1:100,000,000 (Mantel & Bryan, J. natn. Cancer Inst. 1961, *27*, 455; Weil, Toxic appl. Pharmac. 1972, *21*, 454). But in assessing risk, the toxicologist attaches significance not only to the incidence but to the nature of the observed effect of the substance. Was it transitory or cumulative, functional or organic, mild or severe, and to what extent was it referable to human populations under conditions of use? When the effect was irreversible, as in the case of cancer, was it induced only under extreme experimental conditions, by a dose, for example, exceeding the normal capacity of the animal to excrete or detoxify the substance, and how did this situation compare with the metabolic disposition of the substance when present in the diet of man?

Safety Evaluation—A Multidiscipline

In short, safety evaluation is a multidisciplinary activity—not the prerogative of any particular phase of toxicology, be it biochemistry, pathology, oncology or biometrics. It involves not only the judgment of qualified experts, with due recognition of the imprecisions and uncertainties inherent in the evidence, but a realization that the inevitable risk must be sufficiently remote to be socially acceptable.

In conclusion, and for the consideration of those who favor the amendment of the Delaney Clause to permit the exercise of scientific judgment in determining the appropriateness of safety evaluation procedures, I would propose the following version (bracketed words omitted, italicized words added):

". . . . 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 *deemed* appropriate *by scientists qualified by training and experience* for the evaluation of the safety of food additives, to induce cancer in man or animal, ..." **[The End]**

Speak Now— For the Worst May Be Yet to Come

By MERRILL S. THOMPSON

Mr. Thompson Is a Partner With the Chicago, Illinois Law Firm of Chadwell, Kayser, Ruggles, McGee, Hastings and McKinney. His Paper Was Presented at the 77th Annual Conference of the Association of Food and Drug Officials of the United States Held in Rapid City, South Dakota on June 20, 1973.

I FEAR THAT THE FOOD AND DRUG ADMINISTRATION (FDA) is establishing itself as an executive agency which believes that it has broad authority to act outside the law. Restricted only by good intentions, that Agency is routinely engaging in the processes of deciding what is good for us and implementing their decisions, almost as though there were no separation between executive and legislative powers. They are pursuing their objectives with too little regard for the means, and in the process doing serious damage to principles which are far more important than any goal they may have in mind. We have fought wars to preserve those principles.

There are many who would say that if the tragedy of our involvement in Viet Nam can be justified, that justification must be expressed as the protection of the *way* we govern ourselves under our Constitution. Our system of government—our government of laws, is a precious institution which requires vigilance and warrants protection. Today—right now—our system of government requires protection from the good intentions of the FDA.

FDA's "Good Intentions"

Don't misunderstand me when I suggest that the FDA leadership has "good intentions." By that I mean only that they believe

they are acting in the best interests of the public. It should not be inferred that they are unaware of the questionable nature of the power they are asserting. On the contrary, they are quite aware of their regulatory arrogance and the dangers that lie therein. They have openly warned you and me that if we dare to protect our constitutional system by calling their hand, they will then see to it that we suffer at the hands of Congress.

This morning I am expressing my personal views as an attorney and teacher with an intense interest in food and drug law. It troubles me greatly that FDA leaders, whom I respect, suggest that the Commissioner of Food and Drugs should be allowed to legislate where Congress has not, because his legislation will be more reasonable than would be the legislation of Congress.

Ladies and gentlemen, to me the signs are clear. If we who are interested in the process of regulating our foods and drugs do not speak out promptly, clearly and effectively, we will be accepting by our silence this extreme authority of the Commissioner, and we will be joining in the FDA's distrust of the Congress of the United States.

Commissioner's Extensive Authority

Consider these recent events which have not been effectively challenged as of this date:

(1) Last year the FDA adopted across-the-board cents-off regulations despite the clear language of the Fair Packaging and Labeling Act (FPLA) requiring commodity by commodity proceedings.[1]

(2) The Commissioner has now so commingled Food, Drug and Cosmetic Act and FPLA requirements that you cannot tell them apart even though the violation of the first is a crime and the violation of the second is not. As a recent example, the Commissioner now purports to regulate "servings representations" within his information panel regulation despite the fact that servings representations are regulated only by the FPLA.[2]

(3) The Commissioner is consistently denying hearings concerning patently valid objections to his orders despite the clearly

[1] 21 C. F. R. § 1.1d and 15 U. S. C. § 1454(c).

[2] 21 C. F. R. §§ 1.1(c) and 1.8d.

contrary congressional mandate within Section 701 of the Federal Food, Drug and Cosmetic Act.[3]

(4) Within recent months the Commissioner has adopted procedural rules which make it clear that you will never be granted a hearing in the future unless you are able to obtain from Washington, D. C. a copy of the Commissioner's order, identify the issues concerning your interests, review the available evidence, and formally prepare and present your case in full to the Commissioner in writing, all within thirty days.[4] Of course, if he disagrees with your evidence you won't get a hearing anyway. If this rule goes unchallenged, you will rarely, if ever, have the opportunity to test the reliability of the evidence upon which the Commissioner relies unless you appeal his decision in a court of law.

(5) This year the Commissioner seems to have adopted the practice of publishing final regulations specifically incorporating other regulations which are not even in existence yet, presumably because he is so confident they will exist sooner or later.[5]

(6) During the last twelve months final FDA orders and statements of policy have been published and even republished without inviting or allowing any time for public comment despite Mr. Hutt's assurance to this very audience one year ago that this would not happen again.[6]

(7) Thirty-five years after the fact the Commissioner of Food and Drugs is telling us that according to the Act of 1938, there is only one way you can talk about nutrition in labeling and there is only one way you can organize the mandatory information on your labels without making your labeling *per se* false or misleading.[7]

(8) Having adopted his "one way" interpretation, the Commissioner has ever since been telling us in great detail exactly how and when we have to do it his way, without following procedures which provide for hearings. His counsel, Mr. Hutt, is

[3] *See, e.g.*, 37 Fed. Reg. 13976 (July 15, 1972); 21 U. S. C. § 371(e).

[4] 38 Fed. Reg. 6968 (March 14, 1973).

[5] *See, e.g.*, 21 C. F. R. § 19.765(g), referring to 21 C. F. R. § 1.12 (proposed) and 21 C. F. R. § 1.17(a)(2) referring to 21 C. F. R. § 80.1 (tentative).

[6] For example, 21 C. F. R. § 3.88 (37 Fed. Reg. 5120 (March 10, 1972) and 38 Fed. Reg. 2137 (Jan. 19, 1973)); 21 C. F. R. § 102.9 (38 Fed. Reg. 6969 (March 14, 1973)); and 21 C. F. R. § 3.89 (37 Fed. Reg. 16174 (Aug. 11, 1972)).

[7] 21 C. F. R. §§ 1.8d and 1.17.

quoted as saying that it is enough that we had thirty days within which to react and to express our opinions concerning the nutrition labeling regulation.[8]

(9) In February, Mr. Hutt told us that this "one way only" interpretation is going to be enforced as though it has the force and effect of law *and* he says this interpretation is equally binding upon every state and local government, or as one state official has already described it to me, the FDA is now asserting an inherent preemption by executive fiat.[9]

(10) The same Mr. Hutt has, during the last six months, astounded many of his professional brethren by suggesting that the Food and Drug Administration has the implied power to implement the general philosophy underlying the Food, Drug and Cosmetic Act by doing anything within reason which is not specifically prohibited by that Act.[10] He states this theory despite the fact that within the Act virtually every affirmative designation of authority to impose substantive restrictions is carefully combined with procedural limitations to protect the individual citizen from abuses of discretion.

(11) And finally, in the March 14, 1973 *Federal Register* (page 6956), the Commissioner tells us that despite his knowledge that many will find it impossible to comply with his nutrition labeling law, he will not postpone that law. Instead, he will simply exercise broad and substantial enforcement discretion during the next few years. Apparently our obligations to comply with these new regulations will be measured not so much by what the regulation says, but rather by our talents, or by our resources, or by our education. The Commissioner has placed us on notice that even though his law is not a fair law, we should trust him to treat us fairly when we start our compliance negotiations with his representatives.

Case of Dilute Juice Beverages

There are numerous less notable actions which almost daily confirm the impression that the FDA leaders believe their mission entitles them to wink at the provisions of the same law they are com-

[8] Food Chemical News 9 (March 19, 1973).

[9] Food Drug Cosmetic Law Journal 160-161 (Feb. 1973).

[10] Food Drug Cosmetic Law Journal 179 (March 1973).

missioned to enforce. Little would be served by trying to list them all. But perhaps a recent episode from just one case history will help illustrate the practical nature of my concern. It is the case of dilute orange juice beverages. For all of the sixteen years during which I have been practicing food and drug law this Association and the Food and Drug Administration have been struggling with the need for standards for juce beverages. As a matter of fact, a Gene Holeman-chaired "juice" meeting in the basement of the Diplomat Hotel is the event I remember most vividly about by first AFDOUS meeting in 1958.

Standards for orange juice beverages, you may recall, were published by the FDA in May of 1968.[11] Objections were filed. The order was stayed pending a public hearing.[12] Meanwhile, political pressures were being brought to bear on the FDA to do something about the proliferation of dilute juice beverages.

Commissioner Action

After a few unsuccessful attempts to reconcile differences, the Commissioner decided that instead of holding a hearing he would publish a second set of standards in March of 1972.[13] This order included notice that the standards were to become effective in September of that year. The predictable objections were filed relating to virtually every provision of that 1972 order and a hearing was again demanded.

Under these circumstances the FDA faced a dilemma. The economic stakes were so high that they could not arbitrarily deny the requests for a hearing. A denial would almost certainly be appealed in a court of law. On the other hand, they had no wish to participate in a hotly contested hearing. For a while they simply did nothing. The September effective date of their order arrived and passed without further public notice or response from the FDA. So far as the public was concerned, the March 1972 standards became effective last September.

It is hard to tell when the solution to their problem occurred to the FDA leadership. It is clear that the unusual dilemma required unusual measures. As the very first official reaction to the year-old objections, they included in one of the many notices in the January

[11] 33 Fed. Reg. 6865 (May 16, 1968).
[12] 33 Fed. Reg. 10713 (July 27, 1968).
[13] 37 Fed. Reg. 5227 (March 11, 1972).

19, 1973 *Federal Register* an inconspicuous reference describing the 1972 order as a curious "Final Order Not Yet Confirmed."[14] I suppose a "Final Order Not Yet Confirmed" is something like the "Tentative Final Order" the FDA unveiled late last year. Perhaps some day they will tell us about the legal effect of a Final Order Not Yet Confirmed.

FDA's Solution

It was not long after that, however, before the FDA finally disclosed what they had decided to do. In the March 14 *Federal Register* they announced their two-phased plan.[15] First, in response to the objections which had been filed they stayed the effective date of the entire 1972 order and said that some day they would call a hearing. Next, in response to the outside pressures to do something for someone, they published for the first time a Part 102 standard prescribing 5% increment labeling for all diluted orange juice beverages. There it stands, a pseudo standard not quite like anything we have seen during the last nine years of publications, presumably representing the FDA's simplified solution to all problems. It was published for the very first time as an irrevocably final order with absolutely no opportunity for comment. And the FDA staff very frankly admits that they have no plans for a hearing concerning orange juice beverages. In this fashion the world has been told that as far as the Commissioner is concerned, he has heard all he wants to hear about orange juice beverages.

Objections to the 5% Increment Decree

This official dismissal of a problem crying for FDA leadership must have represented not-too-subtle notice to some that the FDA is willing to adopt novel measures never envisioned by Congress to frustrate protective measures which the Congress did contemplate. I say this because in that public file of objections which the FDA received in April of 1972 you will find at least one serious objection to the Commissioner's 1972 order requiring the declaration of 5% increments. The objector told the Commissioner that he could prove that 5% increments (a) are too small to represent material differences in nutrition, (b) are too small to contribute significant differences in cost or other value characteristics, (c) are so small that they will result in a confusing proliferation of meaningless and varying product

[14] 38 Fed. Reg. 2152 (Jan. 19, 1973).

[15] 38 Fed. Reg. 6969 (March 14, 1973).

names, (d) are so small that no one, including the FDA, could test or enforce the accuracy of such labeling, and (e) are so misleading that consumers would be deceived and unfair competiton would result if such 5% increments were used.

Having promised the hearing on that issue required by law, how could the Commissioner in good faith proceed to immediately enact a Part 102 standard requiring the use of 5% increment labeling? Shouldn't we all decry this action which borders on an outright evasion of the law?

Government of Laws

Today, whether it be in connection with nutrition labeling, special dietary uses, imitations, Part 102 names, or juice standards, when you point out such instances of misguided action the response seems to be—"so sue us!" But in the next breath the FDA will tell you that you really should not get too excited. After all, they have the power to exercise substantial discretion while enforcing their new laws. If you have a problem, just go in and discuss it with them.

This attitude reminds me of an aphorism I heard last month while attending a meeting in London, England. It goes something like this. In Germany everything is forbidden which is not expressly permitted. In England, everything is permitted which is not expressly forbidden. In France, everything is forbidden but nearly anything can be arranged.

Speaking for myself, ladies and gentlemen, I sincerely believe that we need to express ourselves now, forcefully and clearly, long before everything is forbidden but nearly anything can be arranged.

I am speaking in favor of our government of laws. I am speaking against being governed by men. **[The End]**

FOOD DRUG COSMETIC LAW JOURNAL

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