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Food Drug Cosmetic Law JOURNAL

Papers Presented at the 14th Annual Educational Conference of the Food and Drug Law Institute, Inc., and the Food and Drug Administration

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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.

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TO THE READER

1970 FDLI-FDA Conference.—The following articles were presented at the 14th Annual Joint Educational Conference of the Food and Drug Law Institute, Inc., and the Food and Drug Administration, held in Washington, D. C., on December 10 and 11, 1970. Additional articles from the Conference will be presented in the February issue of the FOOD DRUG COSMETIC LAW JOURNAL.

Charles C. Edwards, Commissioner of Food and Drugs, FDA, opened the Conference with "FDA—Today and Tomorrow." Dr. Edwards enumerates FDA's considerable activities to protect the consumer during the past year, and previews some of next year's activities. There will be more educational programs, greater emphasis on prevention, increased consumer protection, and an effort by FDA to see that it is the joint responsibility of consumers, industry and government to provide for nutrition, health and safety. The article begins on page 508.

"State Agencies Protect Consumers," by *John G. McClellan*, presents a brief examination of the problems, rivalries and overreactions associated with attempts to protect the consumers by the various federal and state agencies. The article begins on page 513. Mr. McClellan is Administrator of the General Laboratory Division of the Wisconsin Department of Agriculture.

Consumers, industry and government participate in a "partnership of necessity," with respect to health, nutrition and safety, according to *Frank E. McLaughlin*, a member of the President's Committee on Consumer Interests. The necessity to change the way this partnership does business is explored by Mr. McLaughlin in his paper, "The Consumer-Business Partnership." We must build a constructive bridge of understanding leading to a reconciliation among government, business and people in the communities served. The article begins on page 519.

"White House Recommendations: FDA's Goals and Progress," by *Virgil O. Wodicka*, begins on page 525. Mr. Wodicka explains FDA's position, which is to adhere to the spirit and objectives of the recommendations, and to deviate, when necessary, in the area of means. The primary areas in which FDA has taken action on the recommendations are safety of food components, quality of nutrition, value ("quality per unit price") and communication focused on labeling. Mr. Wodicka is Director of FDA's Bureau of Foods.

In "Consumer Expectations from the White House Nutrition Conference," *Robert J. McEwen* gives some insight into the progress made in consumer protection practices as a result of the Consumer Task Force of the White House Nutrition Conference. The topics explored are consumer expectations and the press-broadcasting media, labeling and consumer information and food dating. Mr. McEwen, whose paper begins on page 531, is a professor of Economics at Boston College.

Beginning on page 539, *William D'Aguanno* discusses "Preclinical Investigations." The aspects of drug testing in animals that Dr. D'Aguanno touches upon are pharmacologic screening, toxicity studies, drug metabolism, enzyme induction and drug interaction. Dr. D'Aguanno is Chief Pharmacologist of the Bureau of Drugs, Food and Drug Administration.

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Food·Drug·Cosmetic Law
Journal

FDA—
Today and Tomorrow

By CHARLES C. EDWARDS, M.D.

Dr. Edwards Is the Commissioner of Food and Drugs, Food and Drug Administration.

I RECOGNIZE that this conference is traditionally attended not only by many leaders from industry and outstanding members of the Food and Drug Bar, but also by regulatory officials from many States. We are, as the theme expresses, partners for better nutrition, health, and safety, which makes this annual meeting appropriate and constructive.

During this conference you will hear from several members of our team at the FDA. Both science and compliance are well represented, and I am certain you will find the remarks of the Directors of the Bureaus of Foods, Drugs, and Veterinary Medicine, to be most informative. Since their statements, and the accompanying panel discussions will consider in detail many of the critical items and programs with which the FDA has dealt over the past year, I have chosen a few key topics for my discussion.

FDA's Role in the Past Year

As the American consumer develops greater interest in and understanding of the difficult scientific decisions which FDA is required to make in the area of food, the need for better labeling disclosure and other consumer information aids become more apparent.

A great deal of attention has been given to the generally recognized as safe [GRAS] list. I submitted for publication in the *Federal Register*, a proposal which sets out in detail the scientific criteria by which the GRAS status of substances can be determined. Comments from the consumer, from industry, and, of course, the scientific community, will be extremely helpful to FDA as we move forward toward a final order.

In the food nutrition area, a considerable effort is under way at the FDA to prepare the first stages of nutritional guidelines for publication.

In the drug area, I believe most of you are familiar with the work this agency is doing on implementation of the drug efficacy study. And all of you are aware of the difficulties we had with the cyclamate problem, which has been resolved.

Digoxin has presented an interesting problem. Digoxin tablets, an important pharmaceutical, are manufactured by some 37 firms. For more than a year content uniformity difficulties resulted in many recalls. Nearly all the manufacturers of this product were having serious difficulty meeting product uniformity specifications. Our National Center for Drug Analysis at St. Louis, and our Washington laboratories led the investigation of this problem. It became evident that manufacturing problems resulted from the mixing of the ingredients, which contained only about one active part to 400 inactive parts. All the firms involved cooperated by voluntarily withholding distribution, and discontinuing the manufacture of Digoxin tablets, until the problem could be solved. FDA met with industry representatives to discuss both manufacturing and analytical techniques. Our people recommended a modification of the mixing techniques in the early stages of manufacture which provided the solution. In order to check the process, FDA, with the concurrence of industry, certified each batch before shipment. The Bureau of Drugs has reported that the problem has just about been eliminated.

The handling of this drug problem points out the benefits of good science, sound regulatory policy, and cooperation on the part of industry with the FDA, that I would like to see emulated in other areas.

This, in my judgment, is the kind of cooperative approach that must prevail, if the consumers' interests are to be truly protected.

Our educational programs continue to be effective in helping drug firms comply with the federal Food, Drug, and Cosmetic Act and regulations. More than 1,900 representatives from approximately 1,000 firms participated in drug manufacturing and control workshops presented by FDA district offices. Approximately 7,000 key drug personnel attended 212 showings of the FDA film, "Good Drug Manufacturing Practices: No Margin for Error." Five national conferences and training seminars were held on drug manufacturing and control. About 1,300 management and supervisory personnel, representing 955 drug manufacturers attended these seminars and conferences.

The government-industry voluntary compliance program has come to be regarded as one of the best methods of consumer protection. Voluntary recalls of defective food products increased from 137 in fiscal 1969 to 355 in 1970. But court actions also increased, from 282 cases filed in court in fiscal 1969, to 323 in 1970. Of the 1970 cases, 267 were seizures, 33 were criminal prosecutions, and 23 were injunction suits to restrain further violations.

The importance of the 1969 Good Manufacturing Practice [GMP] Regulations for food production was reflected in both educational and enforcement activities. Over 5,000 representatives of some 2,200 companies participated in 39 FDA district workshops, 5 in-plant seminars, and one national conference. The workshops and seminars explained the GMP requirements and spelled out the do's and don'ts of plant sanitation. Four national trade associations joined with FDA in plans for employee training materials.

FDA undertook production of fact sheets, films, and radio spots dealing with such varied subjects as correct use of pesticides, crab meat production, and sanitary warehouse management. Through convention exhibits, "FDA offices" were set up to answer compliance questions at numerous national and regional trade gatherings.

One item in product safety on which we have recently been active is liquid caustic drain cleaners. These products are regulated by the FDA under the Hazardous Substances Act. Because of their corro-

sive nature, these products have been responsible for a number of injuries. Most have involved children. In conferences between industry representatives and the FDA, a two-part approach has been developed. To make these products more difficult to ingest, industry is working on containers with safer closures. The other part of the approach is the development of an effective product with lower hydroxide levels. One company has been able to cut the sodium hydroxide content of their product, from 26% to less than 10%. Research which is able to give the consumer an effective product with far less risk, is certainly to be commended. Other manufacturers of liquid drain cleaners have also been cooperating with our Bureau of Product Safety.

These actions are consistent with a recent FDA proposal which would require liquid caustics containing 10% or more of sodium or potassium hydroxide to have an effective safety closure.

Also in the product safety area, a document on display today at Archives which is scheduled for publication in tomorrow's *Federal Register,* deals with the issue of "imminent hazard." In proposal form, we have come to grips with the matter of items so hazardous in nature that immediate action is required. Regulations of this kind are necessary to give us the flexibility for adequate consumer protection in critical situations.

During my past year as Commisssioner of the FDA, I have come to feel strongly about the need for this agency to treat like situations alike. Moreover, I strongly believe that industry and the consumer are entitled, whenever possible, to a unified government response to a problem. To that end, I have supported the establishment of FDA liaison committees with the Federal Trade Commission and the Department of Agriculture [USDA], and I look forward to the establishment of a similar committee with the Environmental Protection Agency. The Associate Commissioner for Compliance represents me in the monthly liaison meeting with the Federal Trade Commission. Either USDA or FDA may call a meeting of the liaison committee, which includes Assistance Secretary Lyng and other officials of USDA, as well as myself, my deputy and other top members of my staff.

We are currently reviewing all interagency agreements to which the FDA is a party, for the purpose of insuring the regulatory consistency which the state and federal government should strive to achieve.

Tomorrow's Role of FDA

I have said on many occasions that I strongly believe this country needs a well managed, scientifically sound FDA which administers regulatory policy firmly but fairly. While our present organization is by no means a management model, I believe we have made significant strides toward that end. With our house in good order, and our yesterdays well recalled, we have begun to plan our tomorrows. We have at the FDA Administration taken to heart the motto "The future is there for those who prepare for it." Educational programs for both industry and the consumer are being given renewed emphasis. Advisory groups in both the communications and consumer areas are at this moment being discussed. The most interested and knowledgable individuals representing consumer groups can be of great assistance to us in arriving at our message. Communications talent can help us convey that message clearly, directly, and reliably.

The FDA of tomorrow must begin having greater positive effect before the fact. No longer can our role be limited to a negative postmortem. A certain amount of pathology is inevitable, but I must say that preventive medicine, in my judgment, more effectively serves the best interests of all.

This agency will take the initative in science and regulatory policy with the foundations I have discussed. Insight and expertise can and must make the FDA a leader in consumer protection. As Commissioner I am committed to these principles.

In conclusion, let me wish you all a pleasant conference and extend to each of you my personal greetings. As partners for nutrition, health and safety—consumers, industry, and government are jointly responsible to assure a safe and nutritious food supply, an effective health care system, and the kind of environment in which we can all flourish. **[The End]**

State Agencies Protect Consumers

By JOHN G. McCLELLAN

Mr. McClellan Is Administrator of the General Laboratory Division of the Wisconsin Department of Agriculture, and Immediate Past President of the Association of Food and Drug Officials of the United States, Inc.

THE DEMOCRATIC FORM OF GOVERNMENT fundamentally recognizes the individual citizen as all important, the sovereign from whom all authority emanates. In such an idealistic social arrangement, the duly designated representatives of the general masses have been granted, by delegation, certain governing authority over the others, all for the obvious common good.

Conduct is thus controlled (governed if you please) by consent to relinquish certain rights or privileges in the interest of a common objective. That common objective is closely related to the guarantee of the remaining individual rights and privileges. I am sure there is no need with a group such as this to enumerate these rights or to emphasize their importance.

When one considers the social order and the hierarchy of authority evolving from a single individual, through a series of increasingly intricate units of society and the ever increasing demands for service, it becomes apparent that government is of necessity rather complicated. Human nature being what it is, laws, rules, and regulations are necessary whenever two or more people live in close proximity.

As we said before, the Constitution, as the basic law of a democracy, guarantees to each citizen the right to own property; to operate a private enterprise business; carry on a trade or profession; enjoy the fruits of one's labor, free of unnecessary governmental interference or restraint. It also places a protective shield of due process around suspected violators to prevent abuses of the power of government to regulate, punish, or control. It also, by agreed upon abate-

ment of certain sovereign authorities of lower units of government, imposes a federal consolidation of authority over and above the locally oriented, provincial governing units.

In actuality, we are and have been for some time observing the spectacle of ever increasing bureaucracy in the higher units of government, creating an evermore top-heavy structure with more and more centralization. The lower units have second (or third) shot at the tax money generated in their own jurisdictions.

Thus, with a trend toward centralization of governmental controls, in spite of its incumbent administrative inefficiencies, there is strong impulse to use the "centralized" tax money for all sorts of assistance programs sometimes called "shared responsibilities," "eliminations of duplication," "joint programming," or "in-service training." In the process of sharing all this information from the central fountain of knowledge, there, more often than not, is an usurping of authority, and even a coercion which some call "cooperation." Anyway you look at it, the lower unit of government is the one being "cooperated," and for the most part with money extracted from that very same lower unit. The reason for all this is proclaimed to be a "protection of consumers" in areas where the lower unit of government is unable or unwilling to provide "adequate" protection. You may say that centralization eliminates duplicated facilities. No doubt about it, the principles of efficiency dictate elimination of the duplication.

The popular thing to say these days, however, is that we are de-centralizing. What this really means is that "we are moving some of our paper shuffling activities from Washington to our regional offices," and some that previously was done in the region is moved into a "cooperated" state office.

Enforcement Philosophy

Most criminal laws prohibit some specific act and violations are matters of fact to be established by the courts.

When and how laws are enforced depends on many factors and their priorities assigned. Obviously, laws are enacted to be enforced. If they cannot be enforced, or if by choice or default they are not enforced, such laws on the books become "legal ghosts" and create a climate of disrespect for all laws. A democracy cannot exist without a high degree of voluntary compliance, which in turn, is based on respect for governmental authority.

Voluntary compliance implies knowledge of the law. Any person who engages in a business regulated by a specific set of laws has a

very compelling obligation to not only know and observe the law relating to his business, but also to exercise the necessary controls to minimize any possibility of involuntary violations. The cost of these control measures should be considered part of the legitimate operating expenses, the same as the cost of labor, machinery, utilities or rent. These control measures which guarantee operational compliance and product compliance are the responsibility of the operator of a food or drug plant and it should not be expected that government will provide this surveillance service by either intermittent inspection or by the highly acclaimed continuous inspection. Government has no responsibility to show that industry is not violating the law.

The philosophy of food law enforcement, which I firmly believe is sound, is based on the principle that all persons who produce, process, or deal in food must assume all responsibility for the wholesomeness of the foods they purvey and for their complete compliance with the law. In lieu of this and in case of any inadvertent violation, such person is in full jeopardy of the penalties imposed by the criminal law. An enforcement philosophy should; (1) put strong emphasis on voluntary compliance and preventive measures before the fact, (2) use all necessary legal sanctions to deal decisively with violations identified by effective surveillance, and (3) make full use of available incentives for in-house voluntary compliance measures.

The executive branch, as constituted in a democratic governmental scheme, is charged with enforcement responsibility. This responsibility may be shared by one or more overlapping jurisdictional authorities. Thus, within a single area, there may be a variety of enforcement philosophies as well as differences in priorities, and perhaps some actual conflict as to what constitutes a violation and what should be done about it. This situation is repugnant to any reasonable philosophy of food control, yet it persists. Philosophies depend on a number of factors, and priorities depend to a large extent on a thorough understanding of the law, its intended impact, the historical context in which it evolved, and the effect on society of a non-enforcement or of an unequal application policy.

At this point you may think that I am about to present a dissertation on states' rights, and the basic concepts of autonomy and sovereignty of local and state units of government. I have no such intention, but have merely presented this background as a launching point for a brief look at the various interfaces between federal and state responsibilities and capabilities and the intersection of authorities.

Consumerism

"State agencies protect consumers." Who are these people referred to as consumers? You and I are included, and also every other sovereign individual from whom governmental authority has derived. This is everybody who needs governmental assistance and some sort of safe-conduct visa through a forest of hazards to which there is no "other side" and no marked trail or guideposts. The word protect implies some insidious force from which all of us sovereign individuals are completely unable to defend ourselves; we rely on our government to ward off the hazards at every turn. The word also implies that if there are such hazards, they must be perpetrated, or at least not abated, by some person or persons.

The feeling of distrust and skepticism on the part of consumers engendered by continual hysterical outcries of publicity seeking or political advantage seeking individuals, creates doubt and even outrage. These emotions engendered with respect to the safety and efficacy of our food and drug supply, as is the case in so many other facets of our society today, have a strong tendency to polarize the population. There must be a target for vengeance. You know as well as I, what group is target for venting polarized emotions with respect to food and drug supply. I do not lay blame at anyone's doorstep for being emotional about the safety of his food, but, is it asking too much to consider facts before categorically condemning? Frankly, I do not understand the rallying cry for more consumer protection. I do not contend that consumer goods and services are perfect, there are bound to be slips and isolated instances and a lapse here and there. But in spite of these, our food supply is the best protected of any in the world today or previously in history.

How far should government be expected to go in regulating every spoonful of food consumed? Should not the consumer, this sovereign individual, assume some responsibility for protecting himself, at least in the twilight zones of obvious hazards. I do not buy the idea that the consumer is a babe-in-the-woods person, a red-riding hood in a dark forest of hazards, completely at the mercy of the wolves ready to price-gauge, deceive, and poison the food supply. If anything, this innocent consumer has the big stick and wields the weapon of controlling economics.

It is time that action be taken to combat the hysteria and take steps to restore confidence in the food supply, and see to it that consumers accept their fair share of responsibility for the safety of their own foods, at least from retail store to the home table.

Partnership Protection of the Food Supply

We in government are tending more and more to react to every whim and every twig in the breeze, resulting in ineffective all-directions policies of surveillance, applying our efforts and resources where there is the most public relations mileage to be achieved, and not necessarily where we believe the utmost in protection will derive. I frankly believe the time is now to reverse the trend, to re-evaluate priorities, abolish ineffective paper shuffling and numbers game type of activities, and to combine state, local, federal, and industry efforts in one direction. I know of no way to combine fifty state and uncounted local agencies under one administrative head, but there is a way to put an end to the incredible bureaucratic sprawl at the federal level and bring all food control, beyond raw commodities, together under one administrative head, completely divorced from sociological and agrarian problems. When one looks objectively at the overall picture, protection of consumers from any real food hazards spins off in a number of directions with the basic responsibility residing with the omnipotent consumer. (Whether he accepts it, is a matter for conjecture.)

Secondary responsibility originally resided with local and state government, with federal authority extending only to commerce involving two or more states. Upon casual observation, there appears to be a profusion of mandates or assumed mandates, from whatever may be the source, to various agencies of the federal executive, with a predictable resultant competition between agencies for tax dollars with which to lead, advise, subsidize, and even coerce state and local agencies. The regulated industry in many cases is left completely out of the partnership, and in fact, is confronted with a variety of philosophies of law compliance surveillance. The role of states in this partnership is not clear under the present system of splintered responsibilities and in many cases obsolete laws conflict with those of other states and the federal government. This situation makes only for hostility and rivalry among counterpart agencies in other states and even within the same state. It appears that the major difficulty of non-correspondence of agencies must first be attacked by the law-making bodies. The states must get their laws in order with high priority given to eliminating colloquial and provincial provisions which have no, or at best, only subjective bearing on true consumer protection, it is also time for congress to clearly delineate responsibility and designate the one federal agency to exercise authority.

In delineating the role of states, careful consideration must be given to a number of factors concerned with "consumer protection."

It is almost impossible to confine states to the concept of intrastate commerce, as a means of reducing overlapping authority or duplication of efforts. Any proper division of labor must recognize the potential for performance, the available resources, and the legal obligations of both federal and state government. It must also consider the scope and national impact of decisions on problems which arise. Problems presently confronting all states, the federal food control agency, and industry as well, are the following:

1. What kind of nutritional information is really needed on food labels?

2. What components of nutrition should be artificially adjusted and in what foods?

3. How does any individual food relate to the total diet of diversified segments of the population?

Policy on questions such as these, and many more, especially in the medical and scientific fields can be answered through utilization of resources and facilities only available at the national level. Obviously, the federal food control agency must tap all available valid technical advice, including industry sources. States should accept these findings and should operate as a co-operating, co-ordinated force for assisting in the implementation. States and local agencies are especially suited, when properly funded, staffed, and dedicated, to serve as experts in surveillance and are more adapted for fast action when problems arise. For these programs there is urgent need in all states for good sound management planning, free of any jealousies, rivalry, and especially free of any dictation or coercion on anyone's part.

Summary

In conclusion, let me summarize a few points. Responsiveness to the actual needs of consumers demands:

1. Elimination of rivalry and hostility between agencies and a team effort with federal, state, and local agencies working with industry to deter violations before the fact.

2. Modernizing antiquated laws and clarification of the enforcement mandate.

3. Application of modern business management techniques, program planning, and evaluation of compliance.

4. Zeroing in on health hazard areas.

5. Abolishing inspections and laboratory tests done simply for the sake of compiling figures which have little or no correlation with violations or potential hazards. **[The End]**

The Consumer-Business Partnership

By FRANK E. McLAUGHLIN

Mr. McLaughlin Is a Member of the President's Committee on Consumer Interests.

IF A "PARTNERSHIP" for nutrition, health and safety exists at all, I'm afraid it does not fit easily into any of the classifications or definitions of the standard law dictionary. In fact, there are many who believe that the only worthwhile objective of business is profit and that the businessman has no social responsibility in the fields of public health, nutrition and safety. That does not sound like the joint effort —joint benefit criteria of a partnership does it?

The point has been made, valid no doubt, that the concerns and orientation of industry are generally of a short-term nature. The Marketing Professors Buskirk and Rothe illustrate this point in the October, 1970, *Journal of Marketing* in their comment.

"Top management's insistence on quarterly and annual budgeting performance may force operational management to make short run decisions detrimental to the consumer because the impact of such decisions will not be reflected during operational management's tenure in that position. Consequently, when a product revision is needed, the response may be increased advertising and promotion expenditures rather than the more appropriate effort."

Standing in the way of a partnership relationship is the historical and still popularly advocated marketing theory that the "consumer is king," an adequate defender of his interests with a life and death power over the business enterprise represented by his dollar choice. At war with this concept and, therefore, at war with the partnership image is the belief that 20th century techniques of advertising and promotion create an irrational demand unrelated to more important needs of the individual; that business in a "Pavlovian" exercise is stimulating artificial demand rather than discovering real need.

As stated by Morton H. Broffman, President of Morrell & Company in an October, 1970, speech before the American Meat Institute:

"While the modern marketer may concede that some consumer behavior is irrational, he regards as legitimate any need that is not antisocial, whether the consumer already is aware of it, or if he responds to it only when it is called to his attention."

The other side of that coin is seen in Dorothy Sayers statement: "A society in which consumption has to be artificially stimulated in order to keep production going is a society founded on trash and waste. . ."

Working against the partnership relationship is the widely discussed consumer ignorance of economic and marketing factors. Professor James Carman speaking of widespread economic illiteracy asked: "How can one react logically to a radical, new idea for structuring our economic system and economic institutions when one does not have a basic understanding of the working of the present system?" Rephrasing the question one might ask, how can there be a partnership when one party doesn't understand the business?

The same lack of understanding is attributed to government. Writing in the November issue of *The Chief Executive* on this subject, Mr. J. V. Clyne of Canada wrote: "Tax reforms, changes in the unemployment insurance act, proposals for the control of foreign ownership, etc., often containing impractical and visionary ideas, can be put forward by men of good will but with little real understanding of the impact of their ideas on business." I recall reading something similar about certain proposed "cents off" and food standards regulations on this side of the border.

And then, of course, there is the argument that the consumer is not a full partner because someone inside or outside of government is always presuming to speak for him. Recently, I spoke at an industry meeting where a marketing professor singled out certain congressmen and senators for vigorous criticism as "consumer activists" representing only themselves and not consumers. It would seem that there is quite a distance between the schools of government and business on his campus.

Mr. Broffman of Morrell and Company argued that "Some spokesmen (for the consumer) tend to have no awareness of higher costs, and the possible unwillingness of consumers to pay more for the value received by a given protective measure."

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If there is a partnership, it is a partnership which has seen continuous polarization throughout the last decade over issues of proof of drug efficacy, the adequacy of the average American's diet, scope of color additive pre-clearance authority, the role of food standards in advancing the interest of the consumer—the list goes on and on. The list is likely to face expansionary pressures in the 70's on the questions of extrapolation of lower animal test results to man, pre-marketing standards for medical devices and cosmetics, "imitation" versus "traditional" foods and other issues which we can but dimly perceive at this time.

What kind of partnership are we talking about anyway?

Partnership of Necessity

In keeping with the "equal time" posture I have set above, I wou'd like to give you a few relevant comments on the subject of this "partnership" made last month by Mr. F. Ritter Shumway, President of the Chamber of Commerce of the United States.

"Our triumphs and accomplishments have helped make America what it is. And our mistakes and our shortcomings have also had other impacts. We can glory in the one, and try to remedy the other, but the goods as well as the bad are the unerasable evidence that business is embedded in the social as well as the economic fabric of our nation. Business can no more live apart from society than society can live apart from business. We interact constantly with other great American institutions. Education, government, the family and labor, among others, are as much a part of our social and economic environment as air, water, and land comprise our physical environment. Each of these institutions has responsibilities toward all the others and to the society we all belong to."

To paraphrase, consumers, industry and government participate in a partnership of necessity.

What does the consumer expect of this partnership? At a minimum he wants the rights that three successive presidents and the American marketing system have affirmed. I refer to the right to be informed and to be heard, i. e., the right of communication. One of the reasons that President Kennedy's 1962 consumer statement struck a responsive chord with the business community is that the basic premise of the American marketing system is discovering and responding to the consumer's needs. Of course, rights to choose and to safety go with the right of communication, but without communication, discussions of relative safety and relative degree of choice are academic.

Talk of credibility gaps, age gaps and information gaps is very fashionable these days. Recently, Mr. Herb Cleaves of the General

Foods Company gave a speech about the "consumer gap." The message of consumerism in the 70's is symbolized by a bridge recognized thus far by only a few. The fact that editors and publishers of newspapers in the early 60's began paying reporters to cover consumer-related topics on a full time basis has nothing to do with the desire of newspaper management to reduce the size of the unemployment rolls. Consumer columns in a paper sell newspapers. Consumer topics on TV and radio swell the size of the audience and bring in new sponsors. Inexpertly perhaps, but inexorably nevertheless, an increasingly better educated American consumer is bridging the interest gap. He has communicated that mood to the media and to others.

The old catch words like "nutrition won't sell" and "safety won't sell" are beginning to sour in the mouths of marketers. "Service won't sell" they said until words like "We service what we sell" and "the set with the works in a drawer" began to make the cash registers sing.

"Stressing warranties is negative selling" they said. The simplification and liberalization of warranties now underway are rapidly changing that statement.

"People don't care about environmental issues" they said, but womens' groups writing in to the government for lists of the phosphate content in detergents just keep writing and city councils keep placing environmental issues on their agenda.

Words like "extrapolation," "ecology," "persistent pesticides," "food additives," "functional bumpers," "unit pricing," and "code dating" are becoming a part of the everyday vernacular.

I expect that at least five more studies will be done showing that unit pricing and code dating are unusual, unneeded, costly and possibly fattening, but the handwriting on the wall was read clearly by Mr. Cleaves, when he said ". . . if Mrs. Jones wants to know the unit price of what she buys, and the nutritional content, and how long it has been on the shelf, it won't infringe our God-given right to do business to tell her, right on the label . . ."

The appeal to right of information will in short be so powerful that, wonder of wonders, the consumer will undoubtedly be told the price of what she is buying.

The interest in consumer issues and the growing sophistication of the consumer have not been lost on legislators either and the events

of this last session of Congress, where much was debated and little enacted, will no doubt become grist for the election mill of '72.

Even the dignified corridors of the National Archives building have been penetrated by the growing interest and awareness of the consumer. Perhaps you missed the notice, but the December 1, issue of the *Federal Register* carries a proposal that all documents be accompanied by key word identification and head note. The notice explained in part:

"Over the years many persons have pointed out the *Federal Register* is a difficult document for the average laymen to use. Comments and criticisms have increased in the recent past in direct proportion to the growing interest in consumer affairs." It just may be that the government will begin to take some pains to explain what it is about.

Generally, what does this partial bridging of the interest gap by consumers mean for government and business?

I think it means, among other things, that the combination of increased education, greater exposure to mass media and growing sophistication of consumers is forcing an alteration of the two-handed game of regulators versus the regulated. I think there is a growing and demonstrable disenchantment with the job that independent and old line agencies have done as stand-ins for and representatives of consumer voters.

I think it means that government and industry will be forced, for the first time, to turn briefly away from the substance of a particular key issue and do some agonizing over the procedure for bringing the issue to a public forum or public opinion registering mechanism for consideration. Opening up the decision making process may have either of two effects for the government administrator, namely, presenting him with evidence that his proposed decision does not have public support, or presenting him with insulation against pressure from private interest groups to change his proposed decisions.

By the above, I do not mean that issues of great economic, health, or safety import which have not been supported by public argument and subjected to public scrutiny should be dumped on the committee

system of Congress for resolution. There are limits on the ability of Congress to expose flaming issues to reasoned debate for the correct period of time.

It is now time to talk in specifics.

I think that this new partnership for nutrition, health and safety that is emerging means in part the following:

if the Delaney amendment has deficiencies, those deficiencies and any suggested remedies should be proposed and discussed openly.

if the concepts of imitation, traditional, and standard foods are to be replaced, then the public should be let in on the replacements which are contemplated as well as the potential health and actual economic effects of the replacements.

if the merits of pre-market standards for cosmetics and medical devices cannot, in the months to come, be discussed openly then the partnership must accept the inevitability of the winds of fate and the uncertainty of pressures acting upon Congress.

whether on the front pages of newspapers or through more protracted and orderly avenues the public will be educated to the limitations of lower animal chemical studies.

if we do not carefully use existing sources of information regarding public nutritional understanding, we may well be putting the cart before the horse in a horse race of nutritional labeling claims.

In short, I think this "partnership" of necessity will be changing the way it has done business.

Mr. Lelan F. Sillin, Jr., President of Northeast Utilities, made the same point a good deal better than I have in the November issue of *The Chief Executive* when he wrote: "People are telling us over and over again, in some cases violently, that they want and demand a participatory role in shaping the events that affect their lives."

All of us, in the utility business and in society at large, are in serious trouble unless we can build a constructive bridge of understanding leading to a reconciliation among government, business and people in the communities we serve. **[The End]**

White House Conference Recommendations FDA's Goals and Progress

By VIRGIL O. WODICKA

Dr. Wodicka Is Director of the Bureau of Foods, Food and Drug Administration.

THERE WERE MANY White House Conference recommendations directed specifically at the Food and Drug Administration [FDA] and many others offered on an open basis for anyone to accept. The recommendations were sometimes in conflict with each other, sometimes unclear, and sometimes unrealistic in terms of the proportion of our national effort that can reasonably be expected to be directed to food, nutrition and health. Nevertheless, the combined set of recommendations is at the very least thought provoking and challenging and there is enough community of thought represented among thoughtful and experienced people from a wide variety of backgrounds to require that the recommendations be taken seriously and to give some guidance to action on which there was a widespread feeling of need.

The FDA has tried to respond to the spirit of the recommendations rather than to adhere to them in every detail. We are aware of the fact that the participants in the conference had an extremely limited time to study the ideas discussed, and as a consequence, there was no opportunity to consider various alternative ways of reaching the objectives. Accordingly, we have tried to concentrate on the objectives, and our deviations from the recommendations have been more in the area of means.

In discussing the actions taken by the FDA, I shall try to cluster them into four areas: safety, quality, value and communication.

Safety of Food Components

As always, we should start with safety. The general thrust of the White House Conference recommendations was to emphasize the paramount position of safety in establishing the status of elements of the food supply and to bring our knowledge of safety up to date on food components that have not been looked at for a long time.

Under the Food, Drug, and Cosmetic Act, substances are permitted in the food supply either because they are food additives governed by specific regulations or because they are generally recognized as safe. Under the law, components of foods are permissible only if they are one or the other. This means that common foods such as meat and potatoes, when they are components of a formulated dish, must qualify on the basis that they are generally recognized as safe. On the other hand, when the Food Additives Amendment to the Act, which set up this dichotomy, became part of the law in 1958, it was recognized that there were many minor constituents of foods, not foods in the conventional sense, which would have to be tested for safety as food additives unless they could enjoy the same status of general recognition of safety as conventional foods. In order to generate some sort of order in this situation, the FDA created a list of such substances generally recognized as safe which has become known from its acronym as the GRAS list. At the time of the White House Conference, there was particular concern being expressed from various quarters about the safety of several materials in the food supply, and these all happened to be GRAS substances rather than regulated additives. Accordingly, the recommendations of the conference paid particular attention to GRAS items.

Since the conference, the FDA has taken a number of actions to carry out the recommendations. One of the items about which particular concern was then widespread was the group of cyclamates. These have now been banned from all use in foods and drugs on the basis of the Delaney Amendment forbidding use of food additives found to cause cancer when fed to man or animals. I might mention parenthetically that many foreign countries have taken a similar action because of the precedent we set. Others have only restricted the use of cyclamates, as has the World Health Organization.

The conference was also concerned about the safety of monosodium glutamate, particularly in baby foods, and over the safety of both salt and modified starches in baby foods. Concern was also expressed over the safety of saccharin. As a consequence, the FDA asked the Na-

tional Academy of Sciences [NAS] for special studies on all these substances. In view of the fact that in all instances definitive test information was lacking and a safety decision would have to be based on scientific judgment applied to all existing evidence, it seemed appropriate to go to the highest scientific body in the nation for a recommendation. Reports on all these substances have now been received. The committee named by the Academy for this study found no hazard associated with monosodium glutamate except to certain sensitive individuals but concluded that it conferred no positive benefit to babies and, therefore, recommended that it not be used in baby foods. Baby food manufacturers had already removed it from their formulations because of the earlier controversy and, accordingly, no regulatory action was necessary. The committee found no hazard associated with modified starch, and although it did not find existing levels of salt in baby food harmful, it recommended as a matter of prudence that added salt be limited to 0.25 percent. The baby food manufacturers have unanimously indicated that they will follow this recommendation. In all three of these instances, because there was no safety issue but only a matter of good practice, and the industry has indicated that it will comply with the recommendations, no regulatory action is considered necessary by the FDA.

In the case of saccharin, the committee directed attention to a number of unanswered questions relating to consumption at relatively high levels over long periods of time. At the same time, the committee concluded that saccharin appeared to be safe for all present and contemplated uses but indicated that its conclusions were based on feeding tests, which when adjusted with an appropriate factor of safety would come out to a maximum consumption of 15 milligrams per kilogram of body weight per day.

The FDA and other agencies are now conducting tests to develop firm evidence on the questions relating to long-term, high level intake. In the meantime, it is studying mechanisms for the most practical means of permitting the continued appropriate use of saccharin while yet giving assurance that intakes will not exceed those supported by existing evidence.

In continuing its review of the GRAS list, the FDA has established a contract with the NAS to develop and test a questionnaire that will ultimately be mailed to manufacturers, formulators and users of minor ingredients of food as represented by the GRAS list to elicit the kinds of information that would be necessary to make

an up-to-date review of safety status. This questionnaire has been developed and sent to a test list of 47 companies. Returns are now in the process of being analyzed.

The FDA has also searched its own files for all relevant information bearing on the safety of minor food components and is in the process of establishing a contract with the National Library of Medicine for a systematic literature review of published work to supplement information already in the files.

We expect to complete the review of all minor food components by the end of calendar year 1971 and to make a definitive decision, on all those, for which the evidence is considered sufficient, to determine whether these substances should be continued to be generally recognized as safe or should become regulated food additives or should be banned. Obviously, we cannot now identify any in this third category because if we could we would already be taking action on them. It is likely, however, that there will be some substances on which the existing evidence is insufficient for a final decision. It is our present thinking that these will probably be made food additives under an interim regulation to give time to gather the necessary evidence and, at the same time, to control the use of these substances while the evidence is being gathered.

Quality of Nutrition

In the area of quality, our emphasis has been on action in the area of nutrition. There were a number of recommendations from the White House Conference that standards of nutritional quality should be set. We have interpreted this to mean that the conference felt that the consumer should have a way of being assured of the nutritive value of foods. At least for the present, we have avoided setting formal standards. Instead, we propose to select classes of food which should have minima and maxima established for their nutritive value and to issue guidelines to the food industry conveying this information. We have established a contract with the NAS to recommend those classes of foods for which there would be guidelines and to recommend what the guidelines should be. The Food and Nutrition Board of the Academy has appointed a committee for this purpose and this committee has selected prepared dinners as its first target class. We are awaiting its recommendation on the guidelines for this class within the next few weeks. The contract, which was established in August, has a two-year term and we hope to have the job largely done within that period.

From conversations with leading elements of the food industry, we are confident that once the guidelines are issued, the major factors of the industry will follow them. If they do so, we would expect the pressures of the marketplace to cause adherence to spread. We hope thereby to get the effect of standards without incurring the delays inherent in the standardizing mechanisms.

Quality Standards

In considering the category of value, I shall define value as "quality per unit price." Our major activity in this area is on food standards. There were many recommendations of the White House Conference on the subject of standards, mostly in the direction of reducing the amount of restriction of a recipe type that they now afford in order to permit more development without impairment of basic quality or value. Accordingly, we have started a systematic review of all existing standards of identity, quality, and fill to try to remove needless restrictions without impairing the basic protective value of the standards. As these standards are reviewed, the revised drafts will be published for comment and thereby afford an opportunity for revision in any other respect for which there is a need. At the same time that we do this, we hope to incorporate provisions of appropriate standards in the Codex Alimentarius to facilitate international trade.

Labeling

The concerns of the FDA in the area of communication are predominantly focused on labeling. The White House Conference had two strong recommendations in this regard. The first of these was to communicate the nutritive value of food on the labels and the second was to declare the mandatory ingredients in standardized foods and thereby make the labels comparable in completeness with those of unstandardized foods.

We have an ongoing effort in the area of nutritional labeling. Obviously, on food classes for which there are guidelines, much of the value of the guidelines will be lost if the processors, who would adhere to them, do not declare the fact on the labels. On the other hand, this label declaration is also the key to enforcement. If the processor makes the label claim that the guidelines are being followed and the food does not then have the nutritive value claimed, the processor is guilty of misbranding and is punishable. From the action standpoint, therefore, there is no essential difference between

the guideline and the standard once the processor elects to offer his food in compliance with the guideline.

The fact that the food complies with the nutritional guideline could conceivably be considered adequate declaration of nutritional reliability except for the fact that it is not now contemplated that guidelines will be developed for all classes of foods. Emphasis is now being placed on formulated foods for which the consumer has no easy way to determine nutritive value. For commodity-type items that have long been in the food supply, the need for guidelines is less apparent. On the other hand, there is much to be said for having the key nutritive value of commodity items as well as formulated items presented on the label instead of requiring the consumer who cares to keep all the facts in mind or to look them up in tables. Accordingly, our nutritional labeling efforts are focused on an attempt to present the key nutritional facts about foods, whether or not guidelines have been established for them, in a way that will meet the most important needs of nutritionists, home economists, and physicians, and at the same time communicate effectively to ordinary consumers without specialized training. Several possible approaches have been developed toward this end, and arrangements are now being made for testing with consumers to select the best approach. We are trying to move as rapidly as possible in this program. At the same time we are trying to get enough input from a variety of quarters to have some feeling of confidence that we shall be reasonably close to right the first time, and thereby have to do it only once.

With respect to ingredient declaration, I would remind you that I mentioned earlier a review of all existing food standards to relax the rigor of some of the recipe type provisions and to reconcile them with the standards of the Codex Alimentarius. As we do this, we expect to modify the ingredient statement on important foods to show the mandatory ingredients as well as optional ones. With this and the nutritional labeling program, therefore, we expect to give effect to the major recommendations of the White House Conference with respect to labeling.

There are a number of other recommendations of the White House Conference on which we are also taking action but they represent scattered detailed items of substantially less magnitude than the ones I have touched upon. Let me say only that the actions we are taking in these respects are consistent with the philosophies and procedures already discussed. **[The End]**

Consumer Expectations from the White House Nutrition Conference

By ROBERT J. McEWEN

Mr. McEwen Is a Professor of Economics, Boston College.

ONE OF THE PRIORITIES suggested by the Consumer Task Force of the White House Conference, the very first one singled out for emphasis, was the lowering of food prices. The report of the consumer task force said "recent inflation has caused great injury to both low and moderate income families. In many inner city areas, the proportion of family income spent for food exceeds the proportions spent in undeveloped countries. The high cost of food, and the resulting malnutrition, is a burden on both the low income family and the taxpayer.... High costs and poor quality of foods have been an important factor in the riots and discontent of the past decade."

The goal of the consumer action in this connection was stated by the consumer task force as follows: "to lower food prices by reducing forms of promotion that have little to do with nutrition or other food values supplied to consumers." The report had singled out the reduction of expenditures for promotion as "one of the most significant ways by which food industry costs and retail food prices must be lowered." I see no significant progress on the achievement of this goal. I still urge the consideration of a complete ban on the use of chances, games and prizes in connection with the sale of food. The usual gimmicks, games and gadgets offered by supermarkets as prizes have an incongruity that is somewhat revolting. I was tempted in writing this section to say that it would almost be like inviting students to a college or university because of the promise of superior dancing girls at the institution. On reflection and after seeing a

couple of Saturday afternoon football games with their intermission "entertainment", I decided this was not a good parallel at all. Or perhaps it is such a good parallel that it shows the incongruity of such advertising on the part of both universities and supermarkets.

While on this subject of chances, games and trading stamps, I note with interest the emergence of consumer challenges to supermarkets who advertise "we have eliminated trading stamps and therefore our prices are lower." The present consumer challenge to such advertising is taking the form of a demand for proof that the saving of money formerly put into trading stamps has truly been passed on to the consumer and not diverted either to other forms of promotion or to the profit of the store.

Food Advertising

Since the conference (and I hope as a result of its recommendations), during the past year we have seen some improvement in advertising. A great deal more attention is now paid to nutrition, the nutrient value of food and nutrition education in some of the advertising by food sellers.

Many supermarket and food firms have established posts with titles like director of consumer relations or director of consumer affairs and in some cases have put knowledgable consumer people into those jobs. It remains to be seen how effective the consumer's voice will be through these people because it really depends on how sincere management is in wanting to change any of their practices or procedures in line with consumer wishes and desires. If management doesn't really want a "vice-president in charge of revolution" as a consumer spokesman really should be, and if, on the contrary, it really wants just window dressing to get respectability from the use of a famous name, or if businessmen and industrial groups see this as a way of heading off consumer complaint before it has a chance to crystalize, then I'm afraid these moves will turn out to be nothing more than show business with very little profit to the general consuming public.

The second priority of the consumer task force last year was an improvement of governmental structures and operation in the food field. This included:

(1) A demand for greatly strengthened and expanded representation of the consumer in all structures and levels of government dealing with food inspection or regulation. Not enough progress has been made on this matter during the past year and I think

that the willingness and eagerness of some agencies leaves much to be desired. The U. S. Department of Agriculture, for instance, has not yet established a special consumer advisory group in this operation and there seems to be quite a bit of hesitancy on the part of this agency and others to move in this direction. However, if the government and its bureaus are ever to convince the public that they really pay attention to consumer needs and consumer desires, a greatly expanded input from consumers is going to be required in policy making.

(2) Adequate budgets for federal agencies in the fields of food inspection, labeling and standards were recommended. I see no indication that this is taking place. On the contrary, the demands of the general budget and the demands of the war and defense have imposed at least a standstill in budgets for these programs and at times actual reductions in the amount of budgeted funds for efforts at food protection.

(3) The conference report suggested "the work of such agencies should be evaluated by an independent outside group with strong consumer orientation." There is very little evidence that this is being done with much aid or encouragement from the government itself. Some of Ralph Nader's groups are attempting to fill this vacuum but they are doing it entirely on their own or with some help from private foundations. I have said for some time that I considered foundations derelict in their duty for not having supported consumer activities on a much wider scale than they have in the past.

(4) The report made a recommendation that "a program of federal grants and technical aids to state and local authorities be inaugurated to implement nutrition policy, to improve food and health inspection, and to strengthen weights and measures enforcement on state and local levels." This highly recommended and necessary suggestion is still waiting for effective implementation.

As a matter of fact the Wholesome Meat Act is meeting its deadline this month and the federal government will have to decide whether state programs have been improved sufficiently to be certified by the federal government or whether the federal government itself will have to take over all the meat inspection activity for delinquent states. I gather the impression that the theoretical desirability of a joint federal-state program, which was a cornerstone of this administration's "federalist" approach to the problem of meat inspection and which was adopted by Congress as a premise of the Whole-

some Meat Act as passed may not be successfully vindicated by the course of events. I greatly fear that the U. S. Department of Agriculture is not going to be as insistent with the states on the upgrading of their meat inspection systems as it should be and the federalist concept will turn out to have been a snare and a delusion by which all segments of government shared joint irresponsibility in the field of food inspection.

Consumer Expectations and the Press-Broadcasting Media

I have distressing doubts about the way the press and the media in general operate to keep the public informed about the realities of governmental functioning in the food inspection and regulation area. The problem is that newspapers act like bees instead of tigers. Instead of focusing on an issue like the adequacy of the state's food inspection system and worrying it to death until the public has enough to understand both the problem and the possible solutions, the news media act like bees flitting from one sensational flower to another just skimming the top of the story and then dropping it perhaps for weeks or months.

This, I submit, does not fulfill the function of exposing problems to the reader. The very nature of this process involves the presentation of a few sensational changes, facts, or allegations with very little effort to put them in backward or forward context. The public is left thoroughly confused, without understanding the true problem or the possible solutions, and quite a bit frustrated. I wish there were some way for the media to meet their responsibilities as organs of public information in these matters.

In fairness I must say that, at least in several instances, I have noticed recently some newspapers assigning teams of reporters to do an in-depth study and survey of certain problems. Then they do attempt to put the whole immediate situation into some kind of focus. I only wish this practice were a little more widespread. If only commercial television would put its best talent and resources to work in this field in an effort to show the public what the situation actually is with respect to governmental activity in protection of its food supply.

I have often said that the worst of all possible worlds exists when the consumer mistakenly thinks that government is performing certain protective activities for him. He therefore relaxes his own guard and his own investigations because he relies on the supervision of the government. If the government isn't doing this, I say the consumer has the worst of all possible worlds because he ends up with

no protection. He doesn't take the precautions he should himself because he is relying on the promise of the government to do this. And the government is letting him down.

Labeling and Consumer Information

I would like to put special emphasis on informative labeling and an expanded consumer information program. These two topics are linked quite closely. Ideally, the label of a food package or can should, within the limits of its size, be as informative to the purchaser as it possibly can. In this whole area of labeling and consumer information and education there are two somewhat contradictory schools of thought. One approach suggests that the label should contain precise and rather technical descriptions and identifications of contents and nutritive value. The other approach says this would be unintelligible to the average consumer and, therefore, confusing. This second approach recommends some effort at popular labeling in nonscientific terms with whatever sacrifice of accuracy is required to achieve this goal.

This debate is not peculiar to the food field, but is one that arises whenever consumer information is at issue. Let me state my general philosophy on this, which I think agrees with neither of the two alternative schools of thought that I previously mentioned. I believe it is true that the average consumer will have neither the educational background nor maybe even the inclination to use full and detailed, precisely technical, information about food or any other product. (A long program of education of the consuming public would have to be undertaken to make them a little more able to profit from information furnished by sellers in pursuance of these campaigns for full disclosure of pertinent facts about products. But this is a long-range goal.)

My own conviction is that labeling and a consumer information program in whatever field you care to consider has really three objectives. Let me list them:

1. The objective of getting down in print on packages and labels, to the extent possible, all the precisely technical information about the product that is required or even useful to judge its suitability for consumer needs and its required conditions of care, storage, preparation and use. In the case of food, we need also whatever information is necessary to relate this particular food to the total diet and the total nutritional needs of a person.

In other words, objective one is to get the producer to put in print as much pertinent information about his product as a customer would ever need or use, even though the complete interpretation of this information requires the aid of an expert or a translator from among the consumer groups.

2. Recognizing the fact that the average consumer will not be presently either able or disposed to use or understand all this technical information, an effort should be made to get popular symbols, numbers, letters or other signs that can be used to identify for the purchaser those qualities of a product that are most critical for him to understand. Therefore, I am urging, as a second goal, some attempt at popular labeling, rating and classifying of products.

3. The last objective of a consumer information program, which is really independent, to some extent, of how much Mr. Average Consumer understands at this moment in history, has to do with the competitive effect on industry of the requirement of full disclosure of pertinent facts about products. The Department of Transportation has taken the lead with the ingenious theory that the publication of consumer information performance data about automobiles can be a backdoor approach to make the manufacturers produce a higher quality product. This will be achieved merely because of the fact that disclosure of characteristics will reveal one manufacturer's weakness with regard to his competitors.

I think this general principle can be applied throughout the whole field of consumer products. From producers who are forced to make complete disclosure of all pertinent information about their product, we can expect a gradual improvement in the product itself. The cruel light of full disclosure will reveal, to those who have eyes to see, the shoddy and inadequate character of many of the products that have enjoyed a highly advertised notoriety and "reputation" in the eyes of the general public. I don't think that I can adequately emphasize the potential that I see in this third objective of a program of informative labeling and full disclosure.

I may also hasten to say that this objective may be achieved completely independent of whether there is widespread understanding and use of the consumer information data made available. The mere

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fact of its being in print and in the public domain constitutes a risk that no manufacturer will want to voluntarily endure for very long if his product looks inadequate or much worse than his competitor's. Therefore, all those frantic surveys of what consumers presently understand or want or will use are irrelevant to the achievement of desirable goals from a consumer information program. This is particularly so with reference to this third aspect.

I emphasize this point very strongly because opponents of consumer information programs are constantly making what I consider to be two very unfair and illogical and impossible demands. They want we who are advocating consumer information to be able to show that the information we demand from sellers will be presently useful to the average consumer on a large scale—right now—before there has been any opportunity to educate even the experts among the consumer groups to the interpretation and understanding and meaning of information to be supplied. This is a tactic which I see as a deliberate attempt on the part of opponents of full disclosure of information to delay or prevent the imposition of legal requirements that producers have to tell the whole truth to the buyers.

I must admit that goal or objective numbers one and two are not mutually exclusive because I can easily foresee that consumer groups and agencies will have one or two knowledgeable specialists among their members who will make it a job, if not a hobby, to acquaint themselves very thoroughly with all the technicalities of at least certain groups of products. If they do this there will be a certain filtering down effect of this information through the consumer bodies and groups to their members and through them to an even wider circle of the general public.

In this connection also I should mention the very valuable and praiseworthy efforts of newspapers, radio stations, and television stations to handle programs of consumer problems and consumer information. This can be a very valuable method of spreading public awareness of the interpretation and meaning of the data furnished about products by their labels and packages.

Food Dating

One of the most important aspects of informative labeling now coming to the fore is the problem of open dating of packaged food. As the system of distribution of food becomes more and more remote and complicated from the point of view of producer and consumer

alike, it becomes almost impossible for the average consumer to be a reliable guide for himself on questions involved in the freshness of foods.

In this connection, if you stop to think about it, there are about three problems associated solely with age and dating of food. A consumer needs to know when a thing was canned or packaged, and when it should no longer be used or eaten. In between these two points, of course, sellers have to have information about how long they should leave a product on their shelves. This, of course, implies some judgment of how soon after purchase a consumer is assumed to eat or use the product.

I think the present shameful and disgraceful confusion in the marketplace on this subject of codes and dates and dating is a real blot on the reputation of the food industry and must be changed immediately. As a matter of fact the situation, instead of getting better, may be getting worse. Some companies that previously practiced open and intelligible dating of their products have suddenly abandoned that now in favor of secret codes.

I have been looking at this problem of dating and coding of food for many months now and I confess to utter frustration. No sooner does a consumer group or individual understand how to read and interpret a certain code than he finds that after a few weeks it has been changed. It almost has the appearance of a deliberate conspiracy on the part of sellers to keep the consumer off balance and to prevent him from ever penetrating the secret of how old the food product is when he buys it. Therefore, the Consumer Task Force's recommendation 3B asked for the 1) labeling of packages with the date of packing, 2) storage recommendations, and 3) the expiration date.

We should also ask supermarkets and other sellers to upgrade the information in the possession of their employees. I have had classes of students investigating this subject for some months now and the answers they get from store personnel to their questions about age dating and storage of food betray abysmal ignorance. Frequently the store personnel either denies there is any age code or in answer to a question about how long a consumer can keep a product, they'll tell them "forever." **[The End]**

Preclinical Investigations

By WILLIAM D'AGUANNO

Dr. D'Aguanno Is the Chief Pharmacologist in FDA's Bureau of Drugs.

THE JOINT EDUCATIONAL CONFERENCE of the Food and Drug Law Institute and the Food and Drug Administration has long been considered the major forum for free and open discussions between leaders of the regulated industries and Food and Drug Administration (FDA) officials. These meetings provide a means of communication between the lawyer and the scientist. The difficulties encountered have been capsuled by two friendly adversaries and staunch supporters of these conferences. Mr. Vincent Kleinfeld has one view: "As soon as any physician enters the confines of the Food and Drug Administration he becomes overnight a legal expert as well as an expert in semantics." Dr. Arnold Lehman's view was in the form of a succinct statement conspicuously posted in the pharmacology division office: "You too can learn pharmacology in two easy lessons, each ten years long."

The significance of this latter statement will be appreciated more readily as we focus our attention on some of the considerations involved in the preclinical investigations in drug safety evaluation.

Studies on the safety of new drugs in laboratory animals are intended to provide some prediction of effects which might be expected when the drug is administered to man. In the initial stages of safety evaluation there is usually an interdigitation of studies in man and experimental animals. Then, as clinical investigations progress, additional animal data are developed to support broader clinical trials and, ultimately, to support the general availability of the drug to the medical community. It is the combined judgment of the pharmacologist, toxicologist, and clinician that should determine the orderly progression of animal studies in relation to initiation or continuation of investigations in man.

Pharmacologic Screening

Pharmacologic screening is usually an early step in the development of a new drug entity. Provided appropriate parameters are monitored, a general pharmacologic profile of the test material can usually be developed. The outcome of these preliminary tests often forms the basic rationale for clinical testing. Pharmacologic studies of the primary biological action of therapeutic interest should be intensive enough to delineate dose-response relationship, duration of action, residual effects, interactions with other drugs, and if possible, mechanism of action. Information derived from these studies may also alert the clinical investigator to potential side effects. One type of adverse effect would be the exaggeration of the primary pharmacological effect. For instance, an overdose of digitalis may lead to an alarming bradycardia; signs of excitation or hallucinations may occur after the ingestion of excessive quantities of amphetamine.

Since the effects of drugs are multiple, the secondary effects or reactions unrelated to the desired therapeutic effects should also be explored. Many of the cardiovascular side effects of the tricyclic antidepressants noted clinically have been demonstrated in animal experiments.

Pharmacologic studies should include broad exploration of the effects of the drug on major physiological systems such as the central and autonomic nervous systems, musculoskeletal system, urinary system, respiratory system and the endocrine system. The importance of these studies becomes apparent when we consider, as examples, such hypothalamically mediated endocrine effects as dioestrus, amenorrhea, galactorrhea, gynecomastia and altered glucose metabolism produced by psychotropic agents.

Toxicity Studies

Toxicity studies are performed to determine the effects which cannot be evaluated in standard pharmacological profile workups or occur gradually after repeated administration of a drug. In the selection of species for these studies, consideration should be given to the capability of those species to absorb the drug by the route of administration employed. The eliciting of a systemic pharmacologic effect would suffice in most cases. Other acceptable evidence of absorption might be the production of some systemic effect, measurements of blood or tissue levels or of excretion of the drug or its metabolites.

We have been recommending that comparative drug metabolism data be developed in the early stages of human investigations and that the choice of species for prolonged or chronic toxicity studies be made from among those that handle the drug most like man.

The duration of studies in animals depends on the proposed treatment regimen in humans. For drugs that are to be given only once or twice, two weeks to a month may be sufficient. The Expert Committee of Drug Toxicity of the British Pharmaceutical Industry has recommended that even when only a single dose of a drug is intended in humans, toxicity studies should be of three weeks duration. The rationale behind their recommendation is that it may take that long for changes in nervous tissues to reach pathological state comparable to changes in liver cells easily recognized some hours after insult.

FDA recommendations for chronic toxicity studies of 18 months treatment in the rat and 12 months in a non-rodent species to support clinical use of unlimited duration have met with objections in some quarters. There are toxicologists who maintain that all adverse effects of a drug, except for carcinogenesis, can be elicited in animals within three to six months provided the study is properly designed. Information in our files dictates against a reduction in the recommended duration.

A summary of ocular toxicity in the dog on tricyclic psychotropic compounds indicates that four of the nine compounds tested in one laboratory produced retinopathy or lenticular changes. The onset of these lesions was noted between the sixth and twelfth months of treatment. Also we have reports of similarly late appearance of toxicity evoked by various other compounds including anticonvulsants, analgesics and hypocholesteremic agents. Moreover, longer studies may, in some cases, compensate for unforeseen shortcomings in experimental design.

While preclinical testing in animals has the obvious advantage of allowing exaggeration of drug insult, the usefulness of these studies is only as great as their predictive value. As experimental toxicology developed as a discipline, the rat and the dog became the most frequently used animals for predicting what might happen in man. This choice has been more or less an arbitrary one in most cases and has reflected to a great extent the ready availability of both the animals themselves and the considerable amount of baseline data on these species.

A retrospective study by Litchfield of six drugs of different types showed that observations in dogs were more closely related to those

in man than were the findings in rats. On the other hand, an analysis of data from studies of cancer chemotherapeutic agents showed that mice, rats and dogs all had predictive value for toxic effects on bone marrow, gastrointestinal tract, liver and kidneys.

Subhuman primates have received attention in drug safety evaluation studies in recent years. However, the primate may sometimes fail to provide any greater assurance of safety for man than do lower species. The suitability of an animal model cannot always be assured solely by its place on the taxonomic scale.

The toxicologist has long realized that logical prediction involves more than the addition of new species to his experimental procedures. Conversely, attempts to discover a single species which predicts perfectly for man offer little hope for success.

Drug Metabolism

The emergence of drug metabolism as a subspecialty and the application of newer physical techniques to identification of small amounts of drugs and their metabolities in blood, urine and tissues can be viewed as a major step in the transition from an empirical to a more precise scientific approach to safety evaluation.

From a toxicologic standpoint, the disposition of the drug following administration by any proposed clinical route becomes an important consideration. Absorption, distribution, metabolism and excretion are major factors in determining the effect of the drug on the organism.

In the body most drugs are metabolized by non-specific enzymes in two phases. In the first phase occur the reactions which are classified as oxidations, reductions and hydrolyses.

The products of the first phase may then proceed to a second phase to form conjugation products. There may be considerable interspecies variation in these metabolic pathways.

The magnitude of an administered dose may not be correlated with the human dose but the effect may depend on the difference in rate and pattern of drug metabolism. The onset of toxicity of lithium carbonte correlated well with serum lithium levels of similar magnitude (2.0 mEq/L) in the several species in which this drug was studied, despite the fact that the actual dosages varied widely. To achieve a serum lithium level of about 1.25 mEq/L the dosage on a mg/Kg basis is 20 for man, 25 for dog, 100 for rat and 400 for mouse.

Marked differences in metabolism in various species are not necessarily associated with differences in sensitivity of the target

organ. The concentration of a drug at the receptor site is usually a reflection of the concentration of drug in the plasma. The measurement of plasma levels at the time of disappearance of pharmacological effect could therefore provide a measure of sensitivity of the receptor site. The plasma concentration may be in the same range for all mammals, while the dose required to produce the effective concentration may vary widely among species. The duration of action of carisoprodol varies in four species from 0.2 hr. in the mouse to 10 hr. in the cat, but the plasma levels are essentially the same on recovery of the righting reflex. In the rat the duration of action is three times longer in the female than in the male, but again, on recovery the plasma levels are in the same range.

Some scientists have advanced the opinion that the finding of direct dependence on plasma level for a pharmacologic effect in animals and the probable occurrence of this effect in man at a similar plasma level should be utilized in the design of studies to evaluate safety. That is, the toxicological studies should be carried out on dose schedules which maintain a plasma concentration of the drug at least as high as those obtained in man at therapeutic doses. However, since the duration of action of some drugs cannot be related to plasma levels, assignment of meaningful dosage levels for these compounds may have to be based on time-response studies.

An important consideration in relating differences in actions of drugs to differences in metabolism should be whether the activity is ascribable to the parent compound or to its metabolites. In the absence of active metabolites, variations in the rate of metabolism and elimination must be considered. Conversely, if an effect is mediated by a metabolite rather than the parent compound, the differences in activity may be related to differences in the relative importance of the metabolic pathways as well as by the rate metabolism.

Enzyme Induction

Adaptation, or decrease in sensitivity to a drug upon repeated administration has long been a perplexing problem for both the pharmacologist and the toxicologist. In some cases, diminishing responsiveness can be attributed to "enzyme induction;" that is, the systemic administration of drug results in stimpulation of synthesis of hepatic microsomal enzymes which are involved with its metabolism.

The list of compounds for which enzyme induction has been demonstrated exceeds 100 in number. Most often the end result is

enhancement of detoxification to an inactive metabolite, which is more readily excreted.

The stimulatory effect may be relatively long-lasting. Dogs which were treated with a 100 mg/kg dose of phenylbutazone for 14 days showed a reduction in plasma levels and decreased side effects. A subsequent dose of 100 mg/kg after 50 days without treatment still gave low plasma levels in some of the dogs. Similarly, a long-lasting stimulatory effect of barbiturates on drug metabolism has been reported to exist for one to three months.

The stimulatory effect of drugs may also influence the activity of other drugs. For example, pretreatment of rats with the potent inducer, 3-methylcholanthrene has been shown to markedly decrease the acute toxicity of zoxazolamine. While dose of 150 mg/kg of zoxazolamine killed all the control rats, there were no deaths in a second group of rats given a single injection of the inducer 24 hours before zoxazolamine administration.

As with other types of tolerance development, the propensity for this type of activity must be considered in the design and evaluation of subacute and chronic animal studies. Evidence of enzyme induction in humans has been reported, but the question of its significance remains unresolved.

As an approach to evaluation of a drug's enzyme induction potential, certain tests should be conducted early in the safety evaluation program. These could include: (1) duration of action of hexobarbital and zoxasolamine; (2) metabolism *in vivo* of drugs such as phenylbutazone and antipyrine; (3) ascorbic acid or hydroxycortisone excretion; (4) activity of drug metabolizing enzymes in liver microsomes *in vitro;* and (5) changes in hepatic endoplasmic reticulum (by election microscopy).

Drug Interaction

Multiple drug therapeutic regimens and fixed combination dosage forms add to the complexity of drug safety evaluation. During a period of hospitalization, 10 to 15 different drugs may be given to the patient. The problem of drug interaction becomes extremely important if there is an inhibition or intensification of either desired or undesired effects in the therapy of the patient. One problem has

been alluded to in the foregoing discussion of enzyme induction; that is, enhanced metabolism of one drug subsequent to administration of another drug. The potential for other types of pharmacological interaction should be explored also. We have recommended that acute studies comparing individual agents with combinations of co-administered drugs in at least one species be performed. Additionally, subacute studies are usually recommended with fixed combinations and with other combinations representative of the probable therapeutic regimen.

A partial list of mechanisms for drug interactions would include, in addition to enzyme induction:

(1) *Interference with intestinal absorption*

Magnesium and aluminum interfere with the absorption of tetracycline (among other drugs) from the intestinal tract.

The ion exchange resin, cholestyramine, will bind with drugs with an appropriate pH at which the two coexist in the gastrointestinal tract. The absorption of phenylbutazone and thyroxine, among others, may be impaired by the administration of cholestyramine.

(2) *Alterations in drug excretion*

The inhibition of penicillin excretion by the potent inhibitor or renal tubular transport, probenecid, is probably the best known illustration of this mechanism. Toxicity in this case would not appear to be a problem unless massive doses of penicillin are used.

(3) *Blockage of the transport of a drug to its site of action*

The tricyclic antidepressants such as imipramine inhibit the action of guanethidine and related antihypertensive drugs. These adrenergic neuron-blocking drugs are actively transported into the adrenergic neurons by the same membrane transport system responsible for norepinephrine re-uptake into the neuron.

The antidepressants inhibit this concentrating mechanism, thus preventing the blocking action on the sympathetic postganglionic neurons.

The pressor action of tyramine depends on its transport into the neuron by the same mechanism as that of guanethidine. By

testing the pressor response to tyramine it should be possible to predict which drugs will inhibit the antihypertensive action of guanethidine.

(4) *Alteraction of the mediator of a drug's action by another drug*

The intraneuronal breakdown of norepinephrine is diminished by monamine oxidase (MAO) inhibitors within the adrenergic neurons. This renders more transmitter available for release by the indirectly acting amines such as tyramine and amphetamine, resulting in a potentiation of pharmacologic activity of these amines. The hypertensive crises involving ingestion of tyramine-containing foods by patients on MAO inhibitors have received wide publicity.

(5) *Interaction of drugs that bind to plasma proteins*

Some drugs when bound to plasma proteins are pharmacologically inactive. A number of drugs are known to compete with one another for protein binding and this is the basis for a type of drug interaction. When a drug is displaced from the binding site by another drug, there may be an intensification of pharmacological effect by the unbound active form of the first drug.

Tolbutamide can be displaced from its binding sites by bishydroxycoumarin. The presence of more tolbutamide in the free form may produce a dangerous reduction in blood sugar of the diabetic patient who is also taking the bishydroxycoumarin.

In today's discussion, I have attempted to touch briefly on a number of aspects of drug testing in animals. By no means should this be considered an overall survey of preclinical safety evaluation.

Evaluation

It is generally recognized that experiments in laboratory animals can be valuable in assessing the effects of drugs in terms of both safety and potential therapeutic usefulness. The development of newer experimental methods and adaption of these methods to drug safety evaluation presage improvement in predictive value. The avenues of communication between scientists in industry and FDA should be kept open with the hope that an orderly development of data can be achieved. **[The End]**

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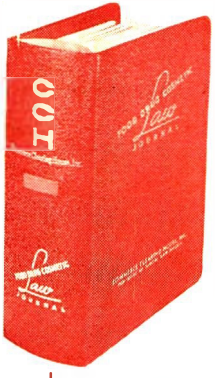

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