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Food Drug Cosmetic Law JOURNAL

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

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

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

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FOOD DRUG COSMETIC LAW JOURNAL

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REPORTS

TO THE READER

Seventeenth Annual Educational Conference of the FDLI and FDA. The following papers were presented at the 17th Annual Educational Conference of the Food and Drug Law Institute, Inc., and the Food and Drug Administration, which was held in Washington, D. C. on December 11th and 12th, 1973.

Daniel F. O'Keefe, in his article, "A Fine New Twist—A Brief Commentary on the Commissioner of Food and Drugs' First Oral Hearing," briefly describes the OTC Review, a procedure which determines the safety and effectiveness of over-the-counter medicines. Mr. O'Keefe is the President of the FDLI. This article begins on page 116.

In the article beginning on page 119, *Harvey L. Hensel,* Assistant General Counsel for Swift and Company, advocates the advancement of uniform federal and state regulation of food labeling. His article is entitled "Federal-State Concurrent Regulations—What Can We Do to Help Make the System Work?"

Dr. William J. Minor, in his article, "USDA—Meat and Poultry Inspection Program," discusses the Department of Agriculture's inspection programs. Dr. Minor is Chief of Products Standards Staff, Animal and Plant Health Inspection Services, USDA. This article begins on page 124.

In his article, "Communicating Facts to the Consumer," *Arthur T. Schramm* stresses the necessity for effective communication to the public by scientists in government, industry and academia. Mr. Schramm is President, Food Materials Corporation and Chairman, Committee on Public Information, IFT. This article begins on page 131.

In an article beginning on page 139, *J. Richard Crout* espouses the use of package inserts and encourages the development of a national drug compendium. His article is entitled, "In Praise of the Lowly Package Insert." Dr. Crout is Director, Bureau of Drugs, Food and Drug Administration.

"Communication of Drug Information to the Physician," an article by *Frank N. Allan,* discusses three principle media used to convey information concerning prescription drugs to physicians. Dr. Allan is Chairman Emeritus, Medical Department, Lahey Clinic. The article begins on page 146.

Hugh A. D'Andrade discusses the regulation of the prescription drug "package insert" and "direct mail advertisement," in his article "Communicating with Physicians: A Regulatory Overview." Mr. D'Andrade is the Counsel, Pharmaceutical Division, Ciba-Geigy Corporation. The article begins on page 154.

Irwin C. Gerson, Vice President of William Douglas McAdams, Inc., discusses the methods of improving communication to physicians in his article, "Developed and Developing Equations in Pharmaceutical Communications," which begins on page 159.

"Drug Monographs," an article by *Mary A. McEniry,* discusses the validity, contents, and advantages of the monograph approach to regulating drugs. Ms. McEniry is Assistant to the Director for Regulatory Affairs, Bureau of Drugs, FDA. This article begins on page 166.

"An Overview of Medical Device Legislation," by *Edgar Vanneman, Jr.,* enumerates the regulatory provisions concerning medical devices that are contained in the Kennedy-Rogers Bill. Mr. Vanneman is the Counsel for Sherwood Medical Industries Inc. The article begins on page 171.

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A Fine New Twist— A Brief Commentary on the Commissioner of Food and Drugs' First Oral Hearing

By DANIEL F. O'KEEFE, JR.*

Mr. O'Keefe Is President of the Food and Drug Law Institute.

JANUARY 21, 1974, was an historic day. It marked the first time a Commissioner of Food and Drugs has personally participated in a formal oral hearing on an issue before the Agency. And it went well! The subject happened to be the "antacid monograph"—the first proposed monograph emanating from the so-called "OTC Review."[1]

By way of brief background, in May of 1972 the Commissioner issued a final order establishing procedures for the classification and review of all over-the-counter (OTC) medicines from the standpoint of safety and effectiveness.[2] Under the procedures, the Food and Drug Administration (FDA) would determine, on a category-by-category

* The views expressed by Mr. O'Keefe do not necessarily represent those of The Food and Drug Law Institute.

[1] For a full explanation of the "OTC Review," see O'Keefe, "The Over-the-Counter Drug Review—Helping the Client Make Decisions," 29 *The Business Lawyer* 649 (January 1974).

[2] 21 C. F. R. § 130.301 (1973). The lengthy and informative preamble to those regulations is set forth at 37 Fed. Reg. 9464 et seq. (1972).

basis, which drugs are "generally recognized as safe and effective" (GRAS/GRAE) and are "not misbranded." Those which do not fall within these categories and do not have an approved New Drug Application (NDA) are illegally on the market.

The OTC Review Process

The OTC Review process starts with appointment by FDA of a panel of "qualified experts" to evaluate the safety and effectiveness of a given category of OTC drugs. Industry and consumer groups each have a nonvoting "liaison" member of the panel. Extensive data is solicited from industry and the public. After review of material available to it, the panel issues a report and "monograph" defining, in essence, its view of the parameters of GRAS/GRAE for the category of OTC drugs under review. FDA then publishes a proposed monograph (which may or may not be the same as that recommended by the Panel), provides opportunity for written comment, publishes a "tentative final monograph" and provides opportunity for written objections to it as well as requests for a non-delegable oral hearing before the Commissioner. After the hearing, a final monograph is issued from which appeal lies to the courts. The Review is being conducted by FDA with unprecedented openness, and industry and others have extensive opportunity to present their data and views to the panel and the Agency.

The Antacid Products

Antacid products are the first category to go through the process. At the various stages of the Review of antacid products, issues were identified, clarified, and narrowed. By the time the "tentative final monograph" was issued, only ten requests for oral hearing were filed and only fourteen issues were raised for argument. The preamble and tentative final monograph for antacids encompassed ten pages in the *Federal Register*.[3]

A notice of oral hearing was published in the *Federal Register*.[4] That notice set forth the "agenda" for the hearing, and allocated time among those requesting to be heard on the various issues. No less than five minutes and no more than twenty minutes were allocated for any given issue. A brief opportunity for "rebuttal" comments

[3] 38 Fed. Reg. 31260-69 (1973).

[4] 39 Fed. Reg. 1359 (1973).

was also afforded. Commissioner Schmidt was accompanied by Peter Barton Hutt, his General Counsel, and by Dr. Richard Crout, his Director of the Bureau of Drugs. The three comprised a panel and freely asked questions as the day proceeded. The hearing lasted about four hours. In view of the precedent-making nature of this "hearing," a few comments and observations would seem timely.

The Oral Hearing

The hearing certainly is no substitute for an evidentiary hearing, nor was it designed to be. There was, of course, no cross-examination and witnesses presented, on the whole, more argument than evidence. Much of the presentations—and this was no surprise—constituted "rehashes" of points previously made in written comments.

On the other hand, the hearing tended to focus the attention of the Commissioner and his principal decision-makers on the major remaining issues in the monograph. One left the hearing with some confidence that the Commissioner and his deputies had the opportunity to grasp these issues as presented firsthand, and concisely, by those most affected by them. The panel listened intently, questioned witnesses frequently and in depth, and, in my judgment, were better able to understand and resolve the issues than they otherwise would have been.

While the time permitted to present a given issue was limited, as Commissioner Schmidt stated at the outset, "An awful lot can be done in a carefully constructed ten minutes." I agree, and I felt that in most instances, the witnesses successfully did so. Indeed, in many cases, one sensed that the discipline of the time constraint forced the witnesses to sharpen their points so that they were exceedingly clear and well-presented. Undoubtedly, the "oral hearing" would not have gone as well if the various issues had not been clarified and narrowed throughout the review process. As this monograph turned out, the oral hearing was the capstone on a review well-implemented throughout.

The oral hearing by the Commissioner is, indeed, a fine new twist which can be useful in many rule-making proceedings. I hope we see more of them in other areas, particularly where the issues are narrowed prior to the hearing. **[The End]**

Federal-State Concurrent Regulations— What Can We Do to Help Make the System Work?

By HARVEY L. HENSEL

Mr. Hensel Is Assistant General Counsel, Swift and Company.

WHETHER THE SUBJECT is called the "concurrent regulations," "conflicting regulations," "lack of uniformity in regulations," or "federal preemption," it is clear that the general subject area has been the topic of many speeches and much discussion during the last ten years. One might presume that there has been so much discussion that the problem has now been solved. On the contrary it appears that we have complied with a recommendation George Burditt gave me years ago. It was his sound advice that it was proper for lawyers to discuss problems but not solve them.

Nonuniformity in Regulations

We not only have *not* solved the problem, but the amount of nonuniformity has increased rapidly during the last three years. With the advent of consumerism, there has been greatly increased pressure on all legislative bodies to pass new laws and regulations which presumably will benefit the consumer. Food labeling has become a natural favorite target of this consumer pressure. With federal agencies, state legislatures, counties and cities, all being requested to pass laws and regulations concerning open dating, nutritional labeling, full disclosure of ingredients, etc., and with no real effort being made by the consumer advocates to have the same uniform law or

regulation on the subject passed by each of the regulatory bodies involved, the result is increased nonuniformity. Furthermore, there is every reason to believe that the situation will get worse rather than better, unless representatives of industry and government take appropriate action to reverse the trend.

The importance of today's uniformity problem is its relationship to productivity in the food industry. We need all the food we can produce. Having several production lines to produce the same food in order to meet local nonuniform ordinances reduces productivity and increases the cost of food.

Steps to Increase Uniformity

There are some positive things that can be done. Let me mention just four possibilities.

First, steps must be taken to increase the input of state and local officials into proposals being made by the Food and Drug Administration (FDA) and the United States Department of Agriculture (USDA). If state and local officials really felt that their views are being given thorough consideration, both from the standpoint of additional legislation that they felt was needed, or from the wording of a proposed federal regulation, it would reduce the amount of nonuniform state and local food labeling regulations. I realize that FDA and USDA are each working with a committee of state officials. This is apparently not sufficient communication to make most state and local officials feel that they are "part of the action" in Washington.

Second, there should be an improvement in communication to all interested industry representatives regarding proposed action at state and local levels on food labeling. The problem is a difficult one because we are dealing with, not only 50 states, but potentially every city and county in the United States. Recent history shows, however, that where this information is made available at an early point in time —before people's minds are completely made up regarding the wording of a regulation—it is often possible to get a proposal amended so that it is uniform with other laws or regulations on the same subject. I suggest a meeting of trade associations and the interested portion of the press to see if better communications could be developed.

Third, Industry needs to cooperate in the adoption of a model regulation on subjects such as open dating so that states and local governments will have a model to follow. The failure of this to happen in the case of open dating is at least partially responsible for the great variety of laws and regulations we now have. We now have a model open dating ordinance coming from an unusual source —The National Conference on Weights and Measures.

Fourth, the subject of uniform food laws needs national guidance from an organization that is interested in all food laws as they apply to the entire food industry. I strongly recommend that the Food Law Institute consider taking on this subject as a special project.

Despite cooperation between state and federal authorities, and despite efforts by Industry to work with local and state officials to prevent the enactment of nonuniform laws and regulations, states, counties and cities will continue to yield to the political and consumer pressures and pass nonuniform legislation. The problem the meat industry has had in Michigan, and the problem the entire food industry is having in Massachusetts at the present time, are two current examples of this.

At this point a question may be asked—what can the lawyers do to help the food industry in this situation? To answer the question I would like to devote the remaining portion of the paper to a very basic analysis of the legal aspects of this problem. I ask the lawyer's indulgence for the oversimplification of the problem. To the scientist, I can only say that many times I wish they had been speaking to me in much simpler terms.

Legal Aspects of Achieving Uniform Regulations

For the purpose of this analysis, I would like you to consider four categories. Each category describes a different factual and legal situation. The category which your problem falls into will determine your chance of success on achieving uniformity by way of the legal process. Furthermore, and this is very important, your chance of being successful rapidly decreases as you move from category one down the list to category four.

The first category includes situations where state or local authorities attempt to impose additional labeling requirements on products

covered by the Wholesome Meat Act or the Poultry Products Inspection Act. These two federal acts have strong, clear federal preemption clauses. A court action to enjoin local or state authorities from enforcing regulations different than the federal regulations clearly should be successful. It is interesting to note, however, that quite often court action is still necessary.

The second category includes attempts by state or local authorities to impose regulations on products covered by the Federal Food and Drug Act where the Act, or a regulation under the Act, expressly regulates, on a compulsory basis, the same subject. Here, too, your chances of being successful in court are reasonably good. This is also a form of federal preemption.

The third category includes the regulation by state or local authorities of products covered by the Federal Food and Drug Act where the federal regulation is on a voluntary basis. An example is the voluntary nutritional labeling regulations of the Food and Drug Administration and the problem that now exists in Massachusetts where that State is considering making the same regulations compulsory. The chances of being successful in court here are only fair. The legal argument still would be that the voluntary regulations are a form of federal preemption.

The final category includes situations where various state or local governments have imposed a type of regulation on food products covered for other purposes by the Federal Food and Drug Act, but where the Food and Drug Administration has taken no action on the subject. The obvious example that fits this category is open dating. Here, the legal argument is that the local regulation is an undue burden on interstate commerce. The chances of winning this type of case are poor.

Success in the Courts

The question might be asked—what can be done to improve our chances of being successful in the courts? The answer, in terms of my analysis, is to move from one of the lower categories to a higher category. For example, a bill has been introduced in Congress (H. R. 11448), which, if it becomes law, would add a federal preemption clause to the Food and Drug Act in regard to certain specific subjects, i.e., open dating, nutritional labeling, and federal ingredient labeling for standardized foods and require federal regulation

on these subjects. If this bill is passed, open dating, which is in category four in my analogy, would move to category one. We would then have regulation of open dating by the Food and Drug Administration and all state and local authorities would be prevented from enacting any nonuniform regulations on this subject.

Because it is neither clear that such a bill will be passed, nor how long passage would take, consideration might also be given to a less dramatic way to increase uniformity on open dating. If the Food and Drug Administration would issue regulations on this subject, this type of problem would be moved from category four to category two and we probably would be successful in defeating conflicting state or local regulations on the subject. At this point in time the Food and Drug Administration has indicated that they do not intend to issue such a type of regulation on their own, but if a petition was filed with the Administration requesting such a regulation they would publish the petition and probably issue a regulation. Even though it is very difficult to get industry representatives to agree on this subject, it is possible that one company or association might petition the FDA for such a regulation.

Although the legal problems involved in achieving uniformity are complicated, thinking about which of the four categories a problem belongs in may help simplify this subject.

A final optimistic note—ten years of talking and working on these problems of uniformity has shown that there has eventually been a solution for each type of nonuniformity. We solicit the assistance of everyone in the audience to help fight today's nonuniformity problems. **[The End]**

USDA—Meat and Poultry Inspection Program

By WILLIAM J. MINOR

Dr. Minor Is Chief of the Products Standards Staff, Animal and Plant Health Inspection Services, U. S. Department of Agriculture.

TODAY, WE SEE MOUNTING EVIDENCE that consumers are looking far beyond the price tag and the attractive package enclosing the products they purchase. It is evident that more and more they are reading product labels and depending on precise labeling information to assist them in selecting the product that meets their particular needs or preferences.

Retail outlets generally have responded to the demands of consumers for information on the displayed products through the use of unit pricing systems, explanations on the meaning of date codes for perishable products, accurate and descriptive names for meat cuts and the employment of consumer advisers to work with consumers and their organizations toward understandings that might lead to improved marketing conditions for both the buyer and seller.

The Department's program for the approval of meat and poultry products, their packaging and labeling is a primary consumer protection service since it provides consumers with products that meet minimum composition standards and which are identified with labeling information sufficient to permit knowledgeable selections of products that are wholesome, unadulterated, and properly packaged.

The Federal Meat and Poultry Inspection Acts contain unique requirements to control the identification of consumer products. The laws provide the Secretary of Agriculture with a mandate for approving formulas, methods of preparation, containers, and labels, prior to distribution of meat and poultry products. The Secretary is

also required to station inspectors in the processing plants to give direct supervision to the preparation of the products, their packaging, and the application of labels.

Product and label approvals are also required for imported meat and poultry articles. U. S. Department of Agriculture (USDA) inspectors are in a continuous travel status reviewing the operations of the overseas plants that are approved to prepare products for shipment to this country. They review the production techniques, the equipment, the facilities and the inspection procedures. These must be at least equal to the construction hygiene standards applied in this country to packing plants.

The products must meet all of the requirements that apply to the preparation and labeling of similar items made in the United States. When the products are presented at ports of entry, USDA inspectors review each shipment to assure that the items represented are proper in all respects, including their composition and labeling. Laboratory facilities are maintained to provide information on any points that cannot be otherwise ascertained by the inspectors.

Informative Composition of Meat Labels

People, when purchasing packaged meat and poultry products have little information about such foods other than that which appears on the labels. In order for a label to be informative it must, at least, display the true name of the product, an ingredients statement if the product is made from two or more ingredients, a statement of quantity of contents, the name and address of the packer, manufacturer, or distributor, and an inspection legend with the identifying establishment number. Labels must also display a warning statement when special handling, such as refrigeration, is needed to maintain the products in a wholesome condition until consumed. The regulations require additional labeling information when necessary to insure products are descriptively identified to consumers.

USDA has not as yet announced proposed nutritional labeling requirements but has distributed guidelines for use by processors electing to voluntarily utilize such labeling. These requirements conform generally to the Food and Drug Administration regulations on this subject published earlier this year, but include two additional

important requirements. These are: (1) Meat and poultry products that require cooking before consumption must present nutritional information on an "as purchased" as well "as prepared" basis. With this type of product, cooking instructions will be required on the label adjacent to the nutritional information. (2) Plant-operated quality control programs will be the fundamental tool by which USDA will judge compliance.

Guidelines for Ingredient Labeling

Guidelines have also been recently announced to provide for the percentage labeling of product ingredients. The guidelines emphasize that percentage labeling is voluntary and concern the declaration of quantities of significant or characterizing ingredients or components declared as a percentage of total net weight. The statement on percentage declarations must be placed on the principal display panel adjacent to the product name and is permitted when the firm conducts a control program on processing and labeling that insures accuracy of the stated percentages.

Proposed regulations to provide for code dating of meat and poultry products were recently announced in the *Federal Register*. The comments received on the proposal are now being evaluated to decide if such regulations are needed and if so, the provisions that they should include.

The approval of labels, along with proposed formulas, processing methods, and packaging, before their use on inspected products is clearly delegated to USDA by the Federal Meat Inspection and Poultry Products Inspection Acts. The prior approval provisions in the laws provide the Department's label approval reviewers with the opportunity to ascertain if the planned formula and characteristics of proposed products are correctly represented by the names on labels. For each meat or poultry food item prepared under federal inspection (for which there does not exist a standard of composition or identity), the application, through label approval, of requirements on product characteristics and ingredients assures that the consumer is provided with a product that contains ingredients and exhibits properties that have been traditionally associated with the name used for its identification.

Compositional requirements for most of the well-known meat and poultry food products are specified in the federal meat or poultry products inspection regulations, or other official printed publications. The products not publicly identified in these publications are reviewed for approval purposes on the basis of information in the Department's records from prior approvals of comparable products. Such information provides a basis for determining the ingredients and processing that have been common or usual to products with distinctive properties and which have been identified with specific names.

Recent Proposals on Product Standards

Within the past year, several proposals by the Department on product standards have attracted widespread public interest. The first of these is a revised standard for cooked sausages such as frankfurters and bologna. Two *Federal Register* announcements with proposed standards drew nearly five thousand comments. Based on these comments, revised standards for the sausages were announced and will be implemented on January 1. The standards have explicit ingredient requirements which will, we anticipate, dispel opportunities for the products to be dealt with derogatorily in news accounts as has been the case far too frequently heretofore.

Other proposals with wide impact on the composition and labeling of meat products were announced by the Department last May 4. One would authorize alternative labeling to the term "imitation" for products that resemble standard articles but which fail to comply with the standards. The proposal would permit fanciful or descriptive names, in conjunction with ingredient statements declaring the main ingredients by percentage amounts. Such products would be required to meet a nutritional equivalency in comparison to the products they resemble.

The second proposal would provide labeling rules for meat products containing textured vegetable base products in quantities sufficient to influence their appearance and texture. If the vegetable ingredient resulted in the meat product appearing to contain more meat than actually present, then labeling would be required to offset the misconceptions on this point. An example of such labeling would be "Chili with Textured Vegetable Product."

The third proposal involves meat products commonly referred to as "patties." It would provide for the preparation and labeling of

such items that look alike yet consist of meat only or are made from meat combined with a variety of other substances such as water, meat by-products, vegetables, poultry, and milk foods of various types. The proposal would reserve the name "meat patty" for products containing meat alone or meat with seasonings. The second category, meat combined with other food materials, would be labeled "Patties with Meat" and would be required to contain not less than 70 percent meat.

These proposals generated a great many recommendations for changes. These are now being considered so that either final regulations or revised proposals can be published in the near future.

Guidelines Concerning Control of Federal Meat Inspection Act

A proposal was announced on October 2 that probably has special interest for many present here today. It would establish regulations setting forth the conditions determining when a product that contains meat is amenable to the Federal Meat Inspection Act. Since it would incorporate the policies that have been followed for many years in deciding on matters of amenability, it was felt the proposal would be generally acceptable. The comments to date indicate that this will be the case. When implemented, the regulations will provide guidelines for use by interested parties in deciding if their products with meat ingredients need to be federally inspected.

Proposed standards have been announced by the Department on products labeled meatballs, bockwurst, lard, beef sausage, and Italian style sausage, and to provide for xanthan gum in meat and poultry products. These proposals are presently at various stages in the administrative rule-making process.

Code of Hygienic Practices for Packing Operations

Meat and Poultry Inspection Program staff members participate directly as delegates from this country in meetings of the Codex Alimentarius Committees for Meat Hygiene and Processed Meat Products. The committee concerned principally with meat hygiene is presently developing minimum requirements for the hygienic production of meat extending from the slaughter of animals to meat transportation. The Committee is deliberating currently on minimal requirements for the ante-mortem and post-mortem inspection and handling of food animals. One of the codes being considered at present

is to assure that the slaughter of food animals and the preparation and transport of the meat will be conducted in a sanitary environment. The second code being formulated is to assure that the food animals will be adequately inspected for wholesomeness so that only healthy animals will be used for food production.

The Committee on Processed Meat Products is now developing a code of hygienic practices for use in commercial meat packing operations. Also, the Committee is considering comprehensive standards of composition and processing for meat products that are prominent in international trade such as canned hams, canned corned beef, canned chopped meats, and luncheon meat.

In addition to the standards or codes of these two committees, our staff members are also contributing indirectly as advisors to the U. S. delegates on several other committees of Codex Alimentarius which deal with the production and identification of products that are subject to the Federal Meat and Poultry Inspection Laws. A foremost example in this regard is the Committee on Food Hygiene which establishes both hygienic practices and wholesomeness standards for application to poultry and poultry products. Other committees with which we collaborate are concerned with food additives, pesticide residues, fats and oils, food labeling and methods of analysis and sampling, since these committees deal with areas of importance to the inspection of meat and poultry products.

In consideration of the growing importance of world trade in foods, we are expanding our Codex staff to assist in efforts that assure this country's views are effectively communicated on international codes involving meat and poultry products. Our objective is to provide expertise to the U. S. delegations for which we have principal or advisory responsibilities.

A Listing of Approved Additives to Meat and Poultry

The Department's regulations presently provide for the use of certain food substances as ingredients for meat and poultry products. The regulations specify the substances or additives by name, the products in which they can be used, the purposes for their use, and the amounts authorized in formulas. Petitions to include additional substances in the charts should clearly indicate they have been cleared for safety by the Food and Drug Administration, the benefits they will add to the specified products or their processing, data showing

maximum amounts required to provide the benefits, practical plant controls to limit the quantity of use, reasonable tests for detection and quantitation and labeling that will assure informative identification for the individual materials. With this kind of information, the Department can decide if proposals to amend the chart of approved substances can be announced and supported. Any such additions to the list of approved additives would have to take place, of course, through the regular rule-making process.

The USDA meat and poultry inspection regulations both contain charts which identify food substances by names that are sanctioned as ingredients of specific products, along with permitted levels of use and their intended functions. These substances for the most part are listed on the basis of "prior sanction" authority, with the remainder classed either as "GRAS" or subject to food additive regulations. Insofar as the current review on the status of "prior sanction" substances by the Food and Drug Administration is concerned, USDA does not intend to take any action, other than to make available upon request any background material in our records that might be useful, except in the cases of nitrates and nitrites. These substances as components of certain meat products, we believe, deserve thorough consideration for several important reasons. First, investigations indicate nitrites can constitute health hazards by combining, during digestion, with secondary amines to form nitrosamines which are carcinogenic. Unfortunately, at this time details on the reactions are so sketchy as to prohibit valid conclusions. On the other hand, nitrites are recognized as effectively inhibiting the growth and development of the microorganism Clostridium botulinum in a wide variety of products that when combined comprise a significant part of the country's meat supply. Cooperative studies between USDA, FDA, and meat industry members have not as yet produced sufficient information for decisions to be made on the future status of the cure substances in meat and poultry products.

The Food and Drug Administration has announced the intention, in the *Federal Register*, of temporarily permitting substances to be used in foods that are named on a recognized industry list such as compiled by the expert technical panel of the Flavor and Extract Manufacturer's Association (FEMA). Upon inquiry, USDA has indicated the status of substances of this nature involved with meat and poultry products will be regarded on the same basis as announced by the Food and Drug Administration. **[The End]**

Communicating Facts to the Consumer

By ARTHUR T. SCHRAMM

Mr. Schramm Is President of the Food Materials Corporation and Chairman, Committee on Public Information, Institute of Food Technologists.

DURING FOOD UPDATE '73 in New Orleans, Louisiana in March, I presented a paper entitled "Science and the Consumer." My main purpose at that time was to put into perspective the complexity of the problems encountered in attempting to communicate objective scientific facts to the public. My conclusion was that ultimate success in communicating with the consumer will require incorporation of science into our basic educational process and that, pending the necessary educational changes, scientists interested in the public welfare will be faced with an uphill endeavor requiring the utmost in understanding, patience, objectivity, tolerance and persistence. Today, I shall describe what certain professional societies, particularly The Institute of Food Technologists (IFT), have been doing and plan to do in this frustrating area, and mention some of the major hurdles involved.

The Institute of Food Technologists

As many of you know, The Institute of Food Technologists is a professional scientific society, founded in 1939. Its members are concerned with the advancement and application of new and existing knowledge to the improvement of the food supply for the benefit of mankind. This involves the coordination of the basic and applied disciplines of many sciences and engineering, including chemistry, biology, genetics, biochemistry, microbiology, nutrition and toxicology. IFT members are drawn from these and related fields, and

increasingly from courses of study specifically designated as food science and food technology.

As IFT defines these areas, *food science* involves the understanding of the scientific basis underlying the efficient provision of a nutritious, safe and acceptable diet. *Food technology* includes the application of this basic knowledge to the practical development of new and improved food sources, products and processes, their more effective utilization by industry and the public, and their effective regulation by government agencies. While these areas of interest clearly reach both into agriculture at the production end, and nutrition at the consumption end, they are principally occupied with the use of food materials between harvest or slaughter and consumption.

To implement the professional and scientific interests of its members, IFT has a broad program of publications, scientific meetings, educational activities for both its members and the public, and liaison with related societies. IFT's members are active in industrial, academic, and governmental institutions. The costs of most Institute activities are supported by the general funds of the Institute, derived from individual members' dues, supplemented by exhibitors' fees and registration fees from the Annual Meeting and Exposition, and other sources. The journals of the Institute are primarily supported by advertising revenues, subscriptions and page charges to authors.

IFT Information Programs

The Institute of Food Technologists has developed an information program designed to provide members of the communications media and the public with reliable background information on food related topics of concern. For some time, IFT members have been aware of the increasing interest of the public in scientific matters, particularly those relating to health and safety. When the safety and nutritional value of our food supply is questioned, and this occurs in the media with startling frequency, we must be sensitive to the needs of the public for correct information. Unfortunately, considerable publicity has been given to experimental data that actually have little or no bearing on safety for human consumption but are presented in such manner as to dispose a large majority of the lay public to draw ominous conclusions. Careless reporting of such data, together with politically oriented Congressional hearings and er-

roneous statements by apparently qualified scientists, have contributed strongly to the atmosphere of distrust that exists in the minds of the majority of the public.

The amount of misinformation concerning food safety and nutrition has been a growing cause of concern to responsible scientists specializing in the scientific disciplines involved. Thus far, professional societies have failed to deal effectively with such problems. Over two years ago, the Institute responded to the need for getting the "whole story" before the media and the public by establishing three groups: An Expert Panel on Food Safety and Nutrition, a Committee on Public Information and a group of Regional Representatives of the Expert Panel. The Expert Panel is composed of distinguished scientists, recognized authorities in food science and technology, drawn largely from the nation's major universities. The principal function of the Expert Panel is to define areas of significance and potential public interest related to food safety and nutrition, and to prepare summaries and interpretations of existing knowledge and scientific judgment in these areas.

Scientific Status Summaries

These papers are called Scientific Status Summaries. Each summary is critically reviewed by the entire Expert Panel and by other experts in the field prior to release for publication in IFT's *Journal of Food Science*. Preparation of these alone would be a major contribution, even if they were made available only to the scientific community, but this would be far from adequate for our purposes. Furthermore, such a panel, no matter how qualified, would have neither the expertise nor the time to present this information in the form required and disseminate it in the manner desired. The next step is taken by the Committee on Public Information (CPI) whose function is to work with and support the activity of the Panel in defining areas of interest. The CPI receives a Scientific Status Summary from the Expert Panel and through its own efforts (or those of professional assistants) converts it to a form suitable for general consumption. Then, the popularized version is carefully rechecked and approved by the Expert Panel for scientific accuracy and balance prior to release. The popular version is then published in *Food Technology*, another IFT publication, and a news release is prepared.

The CPI also has the responsibility for effective distribution of the reports and news releases to the communications media and other appropriate groups.

This, however, is still far from sufficient. News is made and read or heard largely at the local level. IFT's program involves the use of regional scientifically oriented spokesmen for the work of the Expert Panel, and in general as a source of reliable scientific information for the media. Like members of the Expert Panel, Regional Representatives—IFT members—are drawn largely from universities and are well qualified authorities in food science and technology. Their identity has been made known to local media representatives such as science editors, food page editors, and television commentators. Regional Representatives pass on to the media, information on matters of current interest and are prepared to receive and answer questions from the media. We are aware that no local spokesman's expertise can be expected to be the source of all the answers. He will inevitably receive questions that he cannot answer authoritatively and promptly. In such instances, he will place the questioner in touch with an appropriate Expert Panel member, or other appropriate expert. Local spokesmen also report back to the Expert Panel the questions, attitudes and problems they encounter, as these may well be subjects for further Panel consideration.

In 1973, the IFT membership provided a budget to hire a full-time director of public information to expedite the efforts of the CPI in producing the popularized versions of the summaries, and more importantly to work with the Regional Representatives to help them become more effective in their contacts with the media. His duties also include producing a variety of materials to extend the program and make it more broadly useful to the intended audience, and general press relations work in IFT matters.

Four Scientific Status Summaries and their popular versions have been prepared and distributed:

(1) Botulism.

(2) Nitrites, Nitrates, and Nitrosamines in Food—a Dilemma.

(3) Mercury in Food.

(4) Carrageenan.

A Status Summary has recently been prepared on "Organic Foods," which will be published in *Food Technology*. Other Summaries nearing

completion are on Nutritional Labeling, Phthalates, and Shelf Life of Foods.

Conference—September 1973—Alta, Utah

Other professional societies have taken cognizance of their growing responsibilities in the public interest. I attended a conference in September, 1973 in Alta, Utah on "Scientists in the Public Interest—The Role of Professional Societies." This conference was sponsored by the American Academy of Arts and Sciences, Western Center, in cooperation with various departments of the University of Utah. The goals of the meeting were:

(1) To acquaint a group of active leaders of a number of different scientific societies with each other, and activities in their respective organizations.

(2) To discuss and possibly launch joint ventures.

(3) To explore the developing structure and plans for technology management in the Executive Branch and in Congress.

Among the attendees were representatives of The American Society of Mechanical Engineers (ASME), The American Chemical Society, The Biophysics Society, The Institute of Electrical and Electronics Engineers, The American Association for the Advancement of Science (AAAS), The American Physical Society (APS), The Federation of American Societies for Experimental Biology, and the Society for Industrial and Applied Mathematics, each of whom described activities of his society in the public interest. None described a program like IFT's with respect to informing the public, but all expressed interest in that objective. The greater emphasis appeared to be in the direction of improved professional status of members, publicity programs for establishing identity, and public relations activities directly related to providing the various branches of government with objective scientific information.

Other attendees were from federal and state governmental agencies, universities and consumer oriented groups. A large portion of the program dealt with needs for technical advice in various branches of government and the problems involved in making such advice available in an effective manner. As a matter of interest in this connection, three of the Societies, the ASME, AAAS, and APS, have instituted congressional science fellowships. At the present time

there are only one or two scientists in Congress and only a few scientist staff members. A number of members of Congress have indicated that they felt that it would be highly desirable to have technical experts on their staff as a way of obtaining solid technical input for new legislation. The first of these fellows was placed by The American Society of Mechanical Engineers with a Senate Committee in January, 1973. His salary is being paid half by ASME and half by the University from which he is taking leave. Five or six additional fellows were expected to be placed by the other Societies before the end of the year.

Another significant part of the program dealt with public interest research, including such subjects as cleaning the environment, safety of nuclear reactors, and herbicide assessment. The portion of the program directly related to the public interest activities of the IFT, was called "Educating the Public," and included excellent commentaries on how to deal effectively with representatives of the communications media. In IFT, we feel that the real difference between our plan and those which simply supply technical pamphlets, is that through the Regional Representatives we hope to establish personal relationships with members of the communications media and convince them of our sincerity and objectivity. Two of the speakers at the Alta conference, who have had experience both as scientists and journalists, indicated that for effective communication, scientists must speak "English—not scientific jargon," cultivate personal relationships with media people, convince them of their credibility, be informed of the views of qualified opponents to their position, and above all, avoid arrogance.

Effective Scientific Communication to Public

This points up one of the major difficulties in trying to communicate scientific information to the general public. The scientist, by the very nature of his education, has been set apart from the layman. He must now make every effort to eliminate the image of elitism thus generated, develop a sense of social awareness and communicate honestly and clearly with the public if he hopes to overcome the resentment the public feels. That resentment developed because the lay public has been excluded from information or judgments concerning science and technology, which have had a profound effect on their lives in a manner over which they have had

no control. In other words, what is required is a scientist not merely with expertise in a given discipline or disciplines, but also with the capacity to develop his expertise in the context of social significance. I am pleased to say that I have observed quite a number of outstanding scientists who have developed the capacity for effective communication with the public but are now groping for a suitable medium of expression. Frequently, however, the unfortunate fact is that a scientist, in his very efforts to present the objective facts in a balanced manner, gives the impression that he is uncertain and as a result he is no match for the scientist, qualified or not, who makes unequivocal statements regardless of conflicting information on the subject.

A scientist creates serious problems when either for publicity or out of enthusiasm concerning a recent discovery or observation, he exposes himself to exploitation by making remarks that are unsupported or only partially supported by facts. Generalization of such observations have led to sensational claims before the real significance to food safety or nutrition has been evaluated by qualified colleagues in the appropriate perspective. Subsequent exploitation fails to mention that the newsworthy conclusion reached has not been supported by proper scientific procedures and puts into the hands of the media and the public a responsibility for making judgments far beyond their capabilities. This frequently creates unwarranted alarm among consumers and tends to undermine their confidence in the quality and safety of the food supply and in the credibility of government regulatory agencies and industry.

In my opinion, the entire scientific community has a responsibility to safeguard the public from the effects of misinformation particularly in such vital areas as food safety and nutrition. There is a great need, in the public interest, for a code of ethics, or a set of guidelines, delineating clearly the responsibility of scientists involved in research in food safety and quality when they communicate technical information to the media and the public. Such guidelines would assist the sincere and honest scientist who, in the excitement of the moment, may respond in a misleading manner to questions posed by media people eager to present sensational information to the public, and would improve the opportunity for prompt correction of misinformation carelessly or deliberately transmitted to the public.

Public Misinformation Must Be Avoided

There should be a general effort by scientists in government, industry and academia to communicate effectively with consumers. Long-range success depends on basic changes in our educational system, but intermediate success will require that all segments of the scientific community adopt that common objective. This includes government regulatory agencies, some of whose scientists have been panicked into making or permitting premature decisions unwarranted by the experimental data and unnecessarily alarming and costly to the consumer; industry, some of whose scientists have permitted advertising and marketing practices that appear to support unfounded claims concerning toxicity of various food additives and Generally Recognized As Safe (GRAS) substances; and academia, some of whose scientists have yielded to the temptation to make misleading public announcements outside of the area of their expertise or with insufficient supporting scientific data.

Furthermore, government regulatory agencies should attempt to avoid meaningless and superflous requirements, written in ambiguous language, lest in their very efforts to protect the consumer, they mislead and misinform him. In this sense, these agencies must assume a degree of responsibility for educating the consumer. Industry should share such responsibility, but it must be discharged in a common effort. When experts in a regulated industry find the language and intent confusing, how can we expect the consumer to understand?

[The End]

DRAFT PROPOSAL ON DRUG LABELING AVAILABLE FOR COMMENT

Various professional, scientific, trade, and consumer organizations are invited to comment on a draft proposal prepared by the Food and Drug Administration in order to develop and implement more definitive and comprehensive standards regarding the kinds of information that must appear on labeling for prescription drugs for use in man. The draft proposal is available for inspection at the office of the Hearing Clerk, Food and Drug Administration, Rm. 6-86, 5600 Fishers Lane, Rockville, Md. Copies of the draft are available upon request from the Hearing Clerk. Comments on the draft proposal may be submitted until April 25, 1974.

CCH Food Drug Cosmetic Law Reporter

In Praise of the Lowly Package Insert

By J. RICHARD CROUT

Dr. Crout Is Director, Bureau of Drugs, Food and Drug Administration.

OUR TIMES are fraught with many anomalies. However, to the dispassionate observer of our drug labeling system, the package insert must surely appear as one of today's larger peculiarities.

We labor long to bring a good package insert into being with each newly approved drug, agonizing over detailed phraseology, but in full knowledge that the therapeutic usage of drugs is hardly influenced by nuances of language in these documents. We invest enormous effort under the Investigational New Drugs (IND) procedures to develop the data needed for "adequate directions for use," but once a drug is approved we permit the medical quality of the package insert to deteriorate through the years from neglect and obsolescence. We insist that the drug industry spend several million dollars a year putting an insert in every package, knowing full well that at least 99% of these pieces of paper end up in the waste basket.

Yet, in spite of these anomalies, the package insert is becoming increasingly recognized by physicians as a document of significance. Not too long ago, package inserts were wholly ignored by the medical profession, and of course until the New Drug Amendments of 1962 they deserved to be ignored, since most were simply promotional brochures. In the past decade, however, the scientific quality of package inserts has improved remarkably. Today, many package inserts are excellent resource documents for information not summarized elsewhere, and some are even readable! Even the old complaint that physicians never see package inserts is no longer correct. It is now common practice for drug firms to distribute package inserts directly to physicians through mailings and personal contacts by

detailmen. Since 1968 the *Physicians' Desk Reference* has also been officially recognized by the courts as a compendium for drug labeling, and as a result this volume has become essentially a compilation of package inserts.

Due to the great importance of the package insert in our drug regulatory system and its growing value as an informational resource to physicians, it is essential that we reexamine the package insert in light of today's problems. It is time to ask again: What are the important functions of the package insert? What can we do, and what should we do, to improve package inserts? What is the role of the package insert in medical practice? And finally, how can the package insert best be used as an educational resource to physicians?

In addressing each of these questions, I must emphasize that these thoughts are my own. I am in no way announcing new Food and Drug Administration (FDA) policy on these matters or representing Agency views. However, you are entitled to know what my opinions are, and I in turn want your thoughts on these matters. Public policy in regard to drug labeling is important; it is essential that we think together constructively.

What Are the Functions of the Package Insert?

As I see it, the package insert has three basic functions: **Function 1:** The package insert is a summary of the essential scientific and medical information about a drug which the physician should know in order to use the drug safely and effectively for the listed indications. The Food, Drug and Cosmetic Act is quite clear in requiring that these indications be supported by "substantial evidence" consisting of "adequate and well-controlled trials." This means that such evidence must be obtained through systematic clinical research, and it must be presented to the FDA and be acted upon, before new information can be added to the labeling. Given this system, it is evident that a time lag will occur between the publication of studies providing substantial evidence for a claim and the actual appearance of that claim in the package insert. In other instances, a claim made in a published paper may fall by the wayside after additional studies. Poorly documented therapeutic claims are widespread in the medical literature, and it would be folly to catalogue all such "information" in the package insert. For these several reasons—both legal and

scientific—there is little alternative to the proposition that package inserts must be solid, authoritative documents based on substantial evidence.

Function 2: The package insert has a well-established legal function as a written standard for the regulation of prescription drug advertising. There is a clear need for a document stating those claims which can legitimately be promoted, and I am convinced that the package insert can serve this purpose well, but only if the claims are limited to those supported by substantial evidence. I cannot overemphasize to writers of package inserts that Function #1—namely, the communication of essential information to physicians—is primary, while Function #2—the regulation of advertising—is secondary.

Almost every package insert submitted to the FDA for approval is initially burdened with fiction, ranging from vague soft-sell language to outright false claims. When faced repeatedly with such nonsense, it is relatively easy for those of us in the FDA to become cynical and, in counterattack, to find promotional connotations everywhere, even in innocent sentences describing the positive actions or benefits of a drug. Nothing is more frustratingly prolonged and tortured than controversy over labeling between two antagonists who have both forgotten that the true purpose of the package insert is to inform physicians honestly. I do not have a ready solution for the seemingly endless bargaining between the FDA and drug firms over phraseology in package inserts. Perhaps there is no "solution," and bargaining is simply in the nature of the work. But I really do suspect that package inserts would be better if all of us looked in the mirror three times a day and said: "The purpose of a package insert is to tell physicians the truth!"

If I were in the privacy of my own home, I might also confess to believing that package inserts would be improved if lawyers were kept away from them, especially the Adverse Reactions section. However, since I am your guest at this distinguished meeting of the Food and Drug Law Institute, I will not make such an inhospitable remark.

Function 3: The package insert can serve an important role in guiding the development of a new drug. Most Phase III research is done not to support safety and efficacy in general but to support specific labeling claims in the intended package insert. In recognition of this, we are increasingly urging drug firms to write a proposed

package insert at the end of Phase II. Those portions of the insert which cannot be written thus serve to identify the need for studies during Phase III. It is a great mistake to write a package insert for the first time when the New Drug Application (NDA) is being prepared for submission. This is an invitation to prolonging the work-up of a new drug through neglect of important studies which should have been foreseen.

What Should We Do to Improve Package Inserts?

As I have noted previously, today's package inserts on newly approved drugs are really quite good. If an improvement is needed, it is to bring all package inserts up to the standards of the best. To accomplish this, the FDA will soon have available for circulation to all interested parties a draft of a proposed *Federal Register* statement outlining new guidelines for package inserts. These guidelines will define the purpose of each section and identify precisely the information needed in each section. They will basically assert that a good package insert should describe for the physician the fundamental actions of the drug, its clinical pharmacology, its correct indications, the limitations of use; those contraindications, warnings, precautions, and adverse effects the physician should know to use the drug properly; and the correct way to administer the drug. The indications for use should all be supported by substantial evidence derived from controlled trials, but statements based on uncontrolled data may be used under certain circumstances in outlining the limitations of use and in describing adverse effects, warnings, precautions, dosage and administration. Package inserts are also to be short, clear, and readable. The purpose of these guidelines is not to carve out new regulatory ground but to build on past experience and codify that which has worked best. We will want broad input to these guidelines from this point on, both before they are published for comment in the *Federal Register* and during the comment period. We welcome your participation in the further process of improving these guidelines and bringing them to fruition.

What Is the Role of the Package Insert in Medical Practice?

If information in the package insert is based on substantial evidence, it follows that the physician can use the insert as an

authoritative reference source for drug usage in the care of patients. However, as mentioned previously, it also follows that the package insert may not contain the most up-to-date information about the drug. Thus, the physician must be free to use the drug for an indication not in the package insert when such usage is part of the practice of medicine and for the benefit of the patient. When such usage is done as part of a research project on a marketed drug, however, it is still permissible but should be done under an IND.

The above paragraph is completely in line with announced FDA policy on this matter. Nevertheless, there continues to be enormous concern among physicians that mere usage of a drug for an indication not in the package insert is in some way illegal and that, by itself, may open the physician to some form of legal jeopardy. This is not true, but we in government have not yet been able to impart this message credibly to physicians. We clearly must do a better job of articulating public policy on this matter in the future.

The world we want is one in which the physician welcomes a well-documented package insert because he finds it useful, and he finds it useful because the information in it is supported by substantial evidence. Such a package insert would be unique among medical documents. The physician can already ascertain from the medical literature new and interesting proposed uses for marketed drugs, and he can discover at any medical meeting the many innovative ways in which experts use drugs in patient care, some of which are not in the package insert. The physician does not need yet another document which enumerates these newer uses. The package insert's most important educational value derives from the fact that it is a well-reviewed, authoritative document.

Drug Usage Beyond Package Insert Directives

However, to achieve this world we want, it is essential that those of us in regulatory agencies and in the legal profession not take offense at drug usage outside the package insert merely because it is occurring. We must understand how our drug labeling system works and recognize that such usage will occur as a necessary part of the practice of good medicine; and the more current the physician is in his practice, the more often it will occur. Understanding this, we in government and in law cannot threaten to use the package insert as a tight regulatory standard for the practice of medicine.

Such a threat would do nothing beneficial for patient care and would serve only to antagonize the medical profession for no good purpose. Any attempt to compel a physician not to use a drug for the good of his patient merely because the drug firm was slow in presenting the evidence in an approvable form to the FDA or because of the normal lag time required for processing the application should properly be resisted by physicians and patients alike.

In presenting these views, I am not endorsing the notion that a physician can, with impunity, use a drug simply as he pleases. The physician has a responsibility always to be well informed about the drugs he prescribes. Use of a drug for a purpose not in the package insert, when done, should be based on a firm scientific rationale and on medical evidence. Also, the physician should be aware of the information in the package insert, including appropriate warnings, precautions, and dosage. Congress intended that the courts, not the FDA, judge whether a physician has met his obligations in the event of patient harm from a marketed drug. In making this determination, the courts have found that the package insert, along with medical literature and expert opinion, may constitute evidence of the proper practice of medicine, but it alone is not controlling on this issue.

Neither am I defending the notion that the practice of medicine should not be monitored or regulated. I would only suggest that there are more effective and palatable means of regulation than through the package insert. Such means include the use of computerized drug-ordering systems which alert the physician to potentially dangerous drug interactions, the monitoring of selected drugs for review by peer committees, direct education of the public so that patients place fewer improper demands on physicians for drug therapy, and perhaps most importantly, the review procedures currently being established under the Professional Standards Review Organization (PSRO) mechanism.

Where Should We Go in the Future?

First, let me say we cannot go anywhere in this area until our older package inserts are revised and upgraded, and until we gain a national consensus on the role of the package insert in medicine. Once current controversy dies down, however, I believe physicians will want a collection of up-to-date package inserts as resource docu-

ments, and then we will be ready for another important step—the creation of a national drug compendium.

In my judgment, the ideal compendium would contain a package insert for every marketed prescription drug, but duplication would be avoided by the use of class labeling for related drugs, followed by a listing of all manufacturers of each product in the class. Depending upon how much one grouped drugs together into classes, the size of such a volume could be kept at the same or twice the size of the current *Physicians' Desk Reference*. Creation of this volume is, of course, the easy step. The difficult job is to get excellent package inserts and to keep them current.

I might add that such a compendium need not be produced by the FDA, although the labeling in it would have to meet the requirements of the Food, Drug and Cosmetic Act and be reviewed by the FDA. Regardless of who the sponsoring organization might be, substantial input from physicians, pharmacists, and basic scientists would be necessary, so that an advisory committee mechanism of some type would seem essential.

At that point in time the package insert would complete its life cycle, having served a useful purpose honorably. For, once compendia were in the hands of physicians and pharmacists, and a mechanism were assured for updating them annually, then the requirement for inserts in each package could be waived. Finally, the money now spent on sending package inserts to the wastebasket might, if properly redirected, go a long way toward providing a free compendium for every physician and pharmacist.

At that point, the world of drug labeling might not be perfect, but it would be far more sensible, more cost-effective, and more educational than it is now. I believe that is a world worth working for.

[The End]

Communication of Drug Information to the Physician

By FRANK N. ALLAN

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IN RECENT DECADES, tremendous changes have occurred, as we all know, in the treatment of human ills by drug products. The early years of this century were characterized by therapeutic nihilism which extended well into the twenties, gradually replacing the abuses of polypharmacy and empiricism. Pharmacology appeared to be a barren field. As a medical student, I had the good fortune to be an eyewitness of the turning of the tide and later as a practicing physician to enjoy the benefits of almost miraculous progress in drug therapy.

I recall a statement made by one of my medical teachers who declared in a pessimistic mood, "There are only two drugs in the whole pharmacopeia that can cure anything." He had in mind quinine for malaria and salvarsan for syphilis. He deplored the widespread use of traditional concoctions, and the general idea that there must be a medicinal remedy for every complaint.

Among the most commonly prescribed drugs at that time was nux vomica (the source of strychnine), thought to be effective as a nerve tonic, but now long forgotten. Another widely used drug was acclaimed in the then current jingle. "When in doubt and can't decide, use potassium iodide." KI was used for almost every chronic condition from syphilis to arteriosclerosis, asthma, and arthritis.

The pessimistic attitude of this professor at the Toronto General Hospital was voiced at the very time that the work leading to the discovery of insulin had begun in the Physiology Department of the University of Toronto across Queen's Park. He did not live to witness the succession of triumphs that followed the introduction of other new drugs since then, but the era of scientific drug investigation was now under way. Consider just a few of the other landmark events: the introduction of sulfonamides, antibiotics, adrenal steroids, chemical agents for treatment of malignancy, psychopharmaceuticals, contraceptives, prostaglandins, and many other drugs.

The benefits are beyond calculation. Yet the use of almost every potent effective drug may be accompanied by undesirable side effects or even harmful results. In rare cases, the harmful results may be life-threatening. The physician must know both good effects and bad effects. He must take into account the ratio of benefit to risk. He must also be aware of interactions. In other words, the doctor must be fully informed to use medication wisely, effectively, and safely. Furthermore, his knowledge must be continually refreshed. Drugs most commonly used today were unknown before World War II. The doctor who finished his training even ten years ago must constantly strive to keep up to date.

Sources of Drug Information

All of this is well-known. But where does the practicing physician get the information he needs in today's world? What are the sources available to him? How well does he use these sources? And how reliable are they? How much influence do they have on his prescribing?

Sources of information may be classified under three headings: first, those promoted by drug manufacturers; second, those controlled by the government; and third, independent sources. Surveys have been made to determine the scope and influence of such sources. One of these surveys of particular interest was reported by the American Medical Association in the June 25, 1973, issue of *American Medical News*. A questionnaire submitted to a representative sample of physicians dealt with prescribing in addition to other matters.

Commercial Promotion

Drug companies utilize three principal media to convey to physicians information concerning their prescription drugs; namely, direct mail,

advertisements in medical journals, and detailmen. (Table 1.) Direct mail was reported to have a major influence on their prescribing by 17 percent of physicians, advertisements in medical journals by 25 percent. Of these a marked influence was indicated by 1 or 2 in 100. Among the remainder, the effects of these media were rated minimal or nil or yielded "no opinion." Detailmen were credited with a marked influence by 11 percent and a major influence in a total of 52 percent. Thus, nearly half the physicians considered information supplied by manufacturers of little or no use to them, whether delivered indirectly or in person. A two-fold explanation appears to be the feeling of doctors that they are snowed under with promotional material and also that many are skeptical of enthusiastic claims.

Table 1

DRUG INFORMATION PROMOTED BY MANUFACTURERS*

Medium of Communication	*Influence on Prescribing*		
	Marked	*Moderate*	*Total*
Direct mail	1%	16%	17%
Journal ads	2%	23%	25%
Detailmen	11%	41%	52%

* *American Medical News*, June 25, 1973.

Personally, I find information provided by drug companies useful, accurate, and usually presented with fair balance as required. I have found most detailmen reasonable and sincere, although I have not depended on drug companies as a major source of information.

To the onlooker, the returns to the manufacturer from costly promotion seem small; yet one can assume that the expense must be justified from the viewpoint of business.

Journal advertisers contribute substantial revenue to medical periodicals. For this, editors and subscribers should feel grateful, but certainly not obligated in any manner.

Government-Controlled Information

Sources controlled by the government include direct mailing of notices and publications by the Food and Drug Administration, package labeling, and the *Physician's Desk Reference* (PDR). (Table 2.) It is not generally appreciated that the content of PDR is based on labeling approved by the government.

Table 2

DRUG INFORMATION CONTROLLED BY GOVERNMENT*

Medium of Communication	*Influence on Prescribing*		
	Marked	*Moderate*	*Total*
FDA publications	18%	44%	62%
Package labeling	17%	40%	57%
Physician's Desk Reference	37%	47%	84%

* *American Medical News,* June 25, 1973.

Currently, the *FDA Drug Bulletin* represents a major effort of government to promote communication. Six hundred thousand copies are distributed periodically to physicians and other health professionals to disseminate drug information and to explain the Agency's actions and policies.

The Food and Drug Administration (FDA) this year undertook evaluation of its program by means of a questionnaire submitted to representative physicians in all geographical areas and in all types of practice. Analysis of the results has not been completed, but according to a preliminary report (from Dr. Arthur Ruskin), 85 percent of physicians read the *FDA Drug Bulletin*, and 43 percent of those responding have stated that it has resulted in modification of their prescribing habits. The latter figures seems to indicate a distinctly favorable response to the efforts of the FDA; the hope of supporting rational prescribing seems to be achieved in some measure. (There are, however, critics who charge that the FDA's influence on prescribing is too often negative—that physicians are deterred from using drugs that would benefit their patients.)

The American Medical Association (AMA) study indicated a high degree of importance of the annual *Physician's Desk Reference;* 37 percent of physicians considered its influence marked, 47 percent moderate, thus of major importance by a total of 84 percent. It may seem surprising that package labeling was considered to have a marked influence by 17 percent, a moderate influence by 40 percent, a total of 57 percent. In addition to the direct impact of package inserts, it should be remembered that they provide the basis for the statements not only in PDR but also in all advertisements and other promotional material. Those who minimize the significance of labeling and who speak of it as a package stuffer, who say that doctors never see it, fail to recognize fully these indirect effects. In summary, the overall effect of government-controlled information is substantial and its authenticity is recognized.

Criticism of FDA

Conflicting opinions exist regarding the FDA's control of drug information. The Agency is accused of excessive caution in the approval of new drugs, and in recognition of new indications for drugs on the market. It has been charged with interfering with the practice of medicine, and with depriving citizens of this country of remedies that might relieve illness, ease suffering, and even prevent death.

In my opinion, such charges are based on misunderstanding of the responsibilities given the FDA by law. It must determine the facts in regard to the effects of drugs, make judgments regarding benefits and risks, approve the drugs for marketing when justified by the facts, and finally provide information regarding safe and effective uses. The physician can then use his judgment taking such information into account, and his own experience, along with other sources of information.

Independent Sources of Information

Independent means of securing drug information cited by the AMA included direct contact with other physicians, with marked influence in the opinion of 30 percent of doctors, with moderate influence by 50 percent, and thus of major importance by a total of 80 percent. (Table 3.) *AMA Drug Evaluations,* the book published by the Association, was considered to have marked influence by 20 percent, and moderate influence by 31 percent—a total of 51 percent. This book, in my opinion, deserves even wider usage. It is comprehensive, factual, and authoritative.

Table 3

DRUG INFORMATION FROM INDEPENDENT SOURCES*

Medium of Communication	*Influence on Prescribing*		
	Marked	*Moderate*	*Total*
Other physicians	30%	50%	80%
AMA Drug Evaluations	20%	31%	51%
Journal articles	No Information		
Medical meetings	"	"	
Books	"	"	
Pharmacists	"	"	

* *American Medical News,* June 25, 1973.

Surprisingly, no information was secured by the AMA in regard to the influence of other highly important sources of information; namely, other books, medical journals, medical meetings, and also personal

contact with pharmacists. Incidentally, the editor of the *New England Journal of Medicine* wrote to the AMA to ask why medical journals had not been included in the questionnaire. In reply, he was told that it was simply an oversight.

However, articles in medical journals provide early information that is usually authentic, but not always so. Published articles do not always give complete information. Editors and editorial reviewers do not always have sufficient data to enable them to make sound final judgments. Journals, to some extent, function as a forum for presentation of different points of view.

Papers dealing with the incidence and severity of adverse reactions to drugs in recent years illustrate the diversity of observations and contradiction of conclusions accepted for publication.

One report[1] stated that (according to nurse monitors), 830 hospitalized patients had 405 drug reactions; 35 percent had at least one. Even more startling was the fact that 26 percent of the reactions were said to be life-threatening. However, investigation of 70 percent of the reactions by a clinical pharmacologist confirmed the diagnosis of a drug reaction in only 69 percent.

A paper entitled "Fatal Drug Reactions Among Medical Inpatients"[2] stated in the summary that 27 fatalities ("deaths due to drugs") were recorded in a series of 6,199 patients (between four and five per thousand). In the text, it was revealed that the deaths also involved serious diseases on the one hand and injudicious treatment on the other hand—for example, fluid overloading (in patients with heart failure given intravenous infusions) and heavy potassium dosage given to patients with uremia. "Five of the patients were considered terminally ill immediately prior to the onset of their reactions and though drug therapy was judged responsible for their death, life was probably not appreciably shortened as a result."

Alarming statements are balanced by a report of a Drug Reaction Registry[3] that the overall incidence of adverse drug reactions in five teaching hospitals during a two-year period was less than one-half of one percent.

These low figures may be explained partly by under-reporting and also by exclusion of minor, trivial side effects, temporary deviations

[1] I. T. Borda; D. Slone; and H. Jick, "Assessment of Adverse Reactions Within a Drug Surveillance Program," *JAMA*, 205:645-647 (August 26, 1968).

[2] S. Shapiro, et al., "Fatal Drug Reactions Among Medical Inpatients," *JAMA*, 216:467-472 (April 19, 1971).

[3] M. M. Reidenberg, "Registry of Adverse Drug Reactions" (Philadelphia), *JAMA*, 203:85-88 (January 1, 1968).

expected in the course of adjustment of therapy, and other manifestations not considered important enough to warrant description in the hospital records.

In my opinion, there has been strong exaggeration of the problem of adverse drug reactions. The often-quoted statement[4] that 5 percent of all hospital admissions result from drug reactions and that 15 percent of all hospitalized patients suffer from drug reactions is not in accord with my experience. The statement was based only on limited observations on some wards of some hospitals in which certain drugs were frequently prescribed. Nevertheless, some people tend to accept as truth anything that appears in print and is processed by computer.

Needless to say, the critical medical reader will take note of the warning published each week in fine print under the masthead of the *New England Journal of Medicine*, "The Journal does not hold itself responsible for statements made by any contributor." The *Journal of the American Medical Association* makes a similar disclaimer, "The author is responsible for all statements made in his work."

The AMA found that next to PDR, physicians are most influenced by drug information from the other physicians. Presumably, this includes reporting of drug experience at hospital staff meetings and also casual informal conversations in the hospital coatroom and corridors. Such information may be highly important. However, it is not unusual for a doctor to pick up scraps of information and proceed to prescribe a new or unfamiliar drug without full knowledge.

Pharmacists can often give a ready answer to questions about drugs that the doctor is about to prescribe. I have found that a brief telephone call or visit to a pharmacist is the quickest way to learn about costs, to check on dosages, and to obtain other prescribing information, perhaps by referring to his file of package inserts. Cooperation of physicians and pharmacists can be mutually beneficial in these areas, but the physician cannot delegate to a pharmacist the responsibility he carries for clinical decisions affecting diagnosis and therapy.

Survey of Physician's Attitudes in 1959

Brief mention may be made of an opinion study conducted by the American Medical Association in 1959. Data were collected in a different fashion. Physicians were asked to name two or three sources of

[4] L. G. Seidl; G. F. Thornton and L. E. Cluff, "Epidemiological Studies of Adverse Drug Reactions," *Amer. J. Public Health*, 55:1, 172-1, 173 (August, 1965).

drug information they considered most important. Of all media, detailmen were listed at the top by 68 percent. Journal articles and journal advertisements were both rated important by 32 percent. It is noteworthy that at that time, no mention was made of government-controlled information.

Exchange of Information

Communications should be a two-way system. It is hoped that the *FDA Drug Bulletin* will stimulate exchange of ideas and observations so that the government can achieve maximal effectiveness in providing service to the people who need it.

Physicians are urged to report to the FDA and/or to the manufacturer any unusual observation concerning the action or effects of medication. The manufacturer is required by law to transmit to the FDA all such information received. The accumulated data can then be analyzed and evaluated. It may lead to a report in the *FDA Drug Bulletin*, to a change in labeling, or perhaps some appropriate regulatory action.

Conclusions

(1) The physician has access to many sources of information regarding drugs but too often acts without being fully informed.

(2) Casual bits of information passed on by word-of-mouth from other physicians may be inadequate and misleading.

(3) Although he may feel overwhelmed by drug promotion, by the mass of factual data presented in fine print in advertisements and brochures, and by conflicting reports in the literature, the prudent physician will check one source of information against another.

(4) Independent sources are not always reliable and free from bias. Physicians should be as critical in evaluation of medical publications as of commercial advertising.

(5) Even the printed word in prestigious medical journals may be challenged, as indicated by editorial disclaimers.

(6) The physician should be familiar with the content of package labeling, even though deviation from its recommendations may be considered necessary and desirable in individual cases.

(7) The reliability of information supplied by the government or controlled by the government is accepted by a substantial majority of physicians. **[The End]**

Communicating with Physicians: A Regulatory Overview

By HUGH A. D'ANDRADE

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BY WHAT METHODS DO MANUFACTURERS of prescription drugs communicate with physicians; and what regulatory conditions are imposed on these communications?

An answer to this question is vital to a discussion of how communications with physicians can be improved.

The package insert is the basis of all manufacturers' product-oriented communications with physicians. Surprisingly, however, the package insert is not the creature of the Food, Drug and Cosmetic Act, at least not directly.

It is of course true that the Act requires that the labeling of every drug, over-the-counter or prescription, contain "adequate directions for use."[1] But you should not suppose that the package insert is designed to satisfy this requirement, quite the contrary.

It would make eminent sense to construe the statutory term "adequate directions for use," in the case of prescription drugs, to mean adequate directions under which a physician could safely and effectively prescribe the drug (something Bruce Brennan argued for before this same group in 1972[2]); however, the Food and Drug Administration (FDA) does not see it that way.

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[1] 21 USC 352 (f) (1).

[2] Brennan, "Achieving Rational Use of Safe and Effective Drugs" Fifteenth Annual Joint Educational Conference, FDLI/FDA, 12/7/71.

FDA's Definition of "Adequate Directions for Use"

FDA defines "adequate directions for use" to mean "adequate directions under which the *layman* can use a drug . . . safely and for the purposes for which it is intended."[3] Since by definition prescription drugs are just those drugs which cannot be safely used by laymen, they would, were it not for some regulatory slight of hand, be impossible to properly label.

Rather than adopt the approach suggested by Brennan, FDA has chosen to exempt prescription drugs from the "adequate directions for use" requirement.[4] To earn this exemption, labeling, on or in the package from which the drug is to be dispensed, must bear adequate information for physicians to be able to administer the drug safely and for the correctly intended purposes.[5] If the drug is a new drug or a certifiable antibiotic, the provided information must be the same as that furnished in the approved new drug application.[6] Thus, the package insert earns the drug its exemption from the statutory requirement and might well be called the bastard child of "adequate directions for use."

Before continuing, we should note one more of the package insert's oddities. As befits a bastard child, the insert is hidden away and the physician for whom it is written rarely sees it. Because the regulations require the package insert to be contained in the package from which the drug is dispensed, it ends up not in the hands of the prescriber but on the floor of the dispenser.

Not so odd, in my view, is the fact that the remedy for this regulatory misfire was devised within the industry. It is the Physician's Desk Reference (PDR) which provides physicians with the current package insert, prescribing information for most commonly prescribed drugs, in a readily usable form.

If the package insert is the foundation for all of a manufacturer's product-related communications with physicians, then journal ads are surely a major part of the structure which is built upon it.

Composition Requirements for Advertisements

With the passage of the 1962 amendments to the Food, Drug and Cosmetic Act, each advertisement for prescription drugs was required to contain a brief summary of information relating to effectiveness,

[3] 21 CFR 1.106 (a).
[4] 21 USC 352 (f).
[5] 21 CFR 1.106 (b) (3) (i).
[6] 21 CFR 1.106 (b) (3) (ii).

side effects and contraindications of these prescription drugs.[7] Despite what seemed to many to be a clear indication in the legislative history that the statute meant just what it said, a "brief summary," the FDA proceeded to promulgate a growing body of regulations governing compliance with this new section of the Act. This action culminated in 1969 with the current regulations which created such nonlegislative standards as "fair balance"[8] and a listing of 20 "taboos" which applied not to the "brief summary" but to the advertisement itself.[9]

Again, it is not surprising to me that, despite some initial legal scrimmaging and some loud voice insisting that FDA's regulations be held to the letter of the statute, the industry, recognizing the vital importance of maintaining the credibility of its message, accepted the Agency's broad view of its mandate. Therefore, the industry, since 1969, has prepared advertisements with the genuine intention of meeting the demands of the new regulations.

In addition to journal advertisements, the industry carries its drug message to physicians through other media such as direct mail advertisements. To understand the rules which apply to this form of communication one has to understand that such advertisements are not, in the regulatory scheme of things, considered to be advertisements, but are regarded as labeling.[10] A brief summary therefore is not required, but since all prescription drug labeling must contain the prescribing information which earns the drug its exemption from the "adequate directions for use" requirement, a duplication of the package insert information is required to be made part of or to accompany all such promotional labeling.[11]

I do not wish to pass over another of the Act's oddities with that simple explanation of promotional labeling.

Direct Mail Advertisements

The Act's definition of labeling is "all labels and other written, printed or graphic matter upon or accompanying an article."[12] Clearly, a direct mail advertisement sent to a physician does not, in a physical sense, accompany the drug, which is sent not to the physician but to the wholesaler or pharmacist. Why, then, is such a mail piece considered labeling? The U. S. Supreme Court holdings clearly establish that "accompany" must be understood not in a physical but in a

[7] USC 352 (n) (3).
[8] 21 CFR 1.105 (e) (5).
[9] 21 CFR 1.105 (e) (6).
[10] 21 CFR 1.105 (1) (2).
[11] 21 CFR 1.106 (b) (4).
[12] 21 USC 321 (m).

metaphysical sense.[13] If written material is intended to promote the sale of a drug or to encourage or explain its use, it is therefore considered to accompany the drug for purposes of satisfying the statutory definition of labeling.

Under this concept, then, and under FDA's regulations, such labeling includes: brochures, booklets, mailing pieces, detailing pieces, file cards, bulletins, calendars, price lists, catalogs, house organs, letters, exhibits, literature and reprints containing drug information, when such materials are supplied by or on behalf of the manufacturer.[14]

Thus, when a physician requests a reprint, from a manufacturer, which contains references to one of that manufacturer's drugs the reprint will be accompanied by a package insert for that drug. Therefore, when a physician requests information about an unapproved use for a manufacturer's drug he may get little to no assistance, for the manufacturer's response would constitute labeling and the discussion of an unapproved use could cause the manufacturer to be cited by FDA for a violation of the Act.[15]

In May of 1967 the FDA proposed a set of comprehensive regulations governing promotional labeling which would have incorporated the detailed concepts of the advertising regulations, including "fair balance."[16] There is, I think, substantial doubt as to the legality of this type of regulation of prescription drug labeling, especially if the legality of the regulation is based on the exemption from the "adequate directions for use" rationale described earlier. In my mind, however, FDA should feel no need to take on this battle because in fact the industry's promotional labeling is adequate, accurate and informative.

So much for the regulatory overview. What proposals do I have for improving industry's communications with physicians? I apologize that my expertise does not lie in this area; however, I would put the following questions to those who would seek to achieve such improvement by greater regulation.

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[13] *Kordel v. U. S.*, 335 US 345 (1948); *U. S. v. Urbuteit*, 335 US 355 (1948).

[14] 21 CFR 1.105 (1) (2).

[15] The following statement appears in the preamble to a recent proposed regulation concerning the legal status of approved labeling (37 F. R. 16503, 16504, August 15, 1972): "Thus, where a manufacturer or his representative, or any person in the chain of distribution, does anything that directly or indirectly suggests to the physician or to the patient that an approved drug may properly be used for unapproved uses for which it is neither labeled nor advertised, that action constitutes a direct violation of the Act and is punishable accordingly."

[16] 32 FR 7533, May 23, 1967.

Why does not the Agency find the concept of "adequate directions for use" acceptable for application to prescription drugs?

Why must package inserts, and every minor change in them, continue to be printed and reprinted by the millions and stuffed into packages never to be seen by physicians?

Why isn't the industry given more credit for providing the physician with the prescribing information he needs through PDR?

Why is it not more often acknowledged that the industry's advertisements are probably the most truthful advertisements appearing in America today?

And finally, how can the FDA and the industry work together to insure that physicians get the information they need to make clinical judgments about the use of drugs, rather than merely providing them with information about clinical judgments which have already been made for them? **[The End]**

LABELING FOR OTC ANTHELMINTICS REVISED

A new regulation has been issued by the Food and Drug Administration specifying that anthelmintic drugs not carrying a prescription statement should be labeled to include the statement "For a satisfactory diagnosis, a microscopic fecal examination should be performed by a veterinarian or diagnostic laboratory prior to worming." The FDA maintains that this regulation is necessary because the lay person generally does not have the experience or the equipment necessary to isolate and differentiate between the many kinds of parasites found in animals.

Various comments received on the proposed regulation sought clarification of whether diagnostic procedures would be mandatory in all cases of treatment for worms. The FDA revised its original proposed labeling to delete specific references to diagnostic procedures, since they might not always be appropriate. Another comment requested that the required labeling not apply to medicated feeds, but the FDA stated that labeling feed would be helpful to livestock and poultry producers, since they may not be familiar with all parasites.

CCH Food Drug Cosmetic Law Reporter

Developed and Developing Equations in Pharmaceutical Communications

By IRWIN C. GERSON

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IT SEEMS A BIT IRONIC to travel 225 miles from home to discuss improving communications to the physician, because if I had spent the day back at the office, I probably would be doing the same thing—trying to improve communications with physicians. Communicating with the physician is, of course, the basis of pharmaceutical promotion, and my fifteen years of involvement in the field has given me ample opportunity to observe, and participate in, both the revolutionary and evolutionary improvements in our ability to communicate effectively. It has also given me the opportunity to note some unfortunate communication excesses to which physicians occasionally have been subjected. Such promotions have usually floundered because of foolish bombastics, irrelevance, tasteless flippancy, sheer technical incompetence, and occasionally because of downright untruthfulness.

In these types of messages, the sender places his own interests above the needs of the receiver. Invariably, they result in negative communication, or, at best, in no communication at all. Unfortunately, it is this type of communication that is most often held up to public and governmental scrutiny as the indicia of pharmaceutical promotion. In truth, it is the exception, not the rule, and under present stringent controls, is much less evident today than ten years ago.

The Philosophy of the Communication Process

In discussing good and bad communication, let me review the philosophical underpinnings of the communication process. Commu-

nication, by its very nature, involves two groups: the senders and the receivers. In the situation which is most familiar to me, the senders are the pharmaceutical manufacturers and other related companies in the health care field. The receivers are the physicians and other professional and para-professional people who are potential users of the goods and services the senders offer, and who need to assimilate a great deal of information about these goods in a short period of time.

Pharmaceutical promotion today is engaged in providing information. Unlike consumer advertising, pharmaceutical advertising does not have to create the need. The need exists because of the burden of illness, particularly attending an expanding and longer-living population. We, as pharmaceutical promoters, can only win the allegiance of physicians by providing more useful information than our competitors and other "attention-getters" that vie for the doctors' time.

When I first began my career, one commonly used technique was to inundate physicians with a deluge of postcards containing a brand name and possibly an indication but nothing more. This form of communication was limited; it was clearly one-sided, and overwhelmingly oriented to the needs of the sender, not to the needs of the receiver.

The "Receiver-Oriented" Approach

Today, both the industry and its audience have become much more knowledgeable and sophisticated, and a significant part of the flow of company communication to the physician is now strongly "receiver-oriented." Its aim is not merely to gain attention, but also to reward it, often by bridging the time lapse between the completion of scientific research and the availability of the results of that research to physicians. Its content is frequently informational or educational material of significant intrinsic worth to the audience. Product promotion, if it is included at all, is a far cry from the blatant "hard sell" that predominated a decade or more ago.

This receiver-oriented promotion has been and continues to be far more effective, because it serves both sides of the *communication equation*. The approach is not only compatible with good medical practice, but in many ways enhances it, by utilizing the skills of expert communicators to provide the physician with swift and accurate information (pertaining to drugs, disease, medical practice, and, most important, how patients can best be treated and served) in a form that he can easily remember.

I mentioned earlier that my daily work is concerned with improving communication to the physician. In judging materials we prepare on behalf of our clients, I have a "rule-of-thumb" I always try to apply. I ask myself, "Will this be accepted by the receiver because it is telling him something he *needs* to know?" Also, as a corollary, "Would other senders feel that the presentation is accurate and transmitted fairly?" In short, "Does the presentation reflect a basic respect for and understanding of the audience and the problems that the audience confronts?" If these questions can be answered affirmatively, the presentation will serve the co-interests of both sender and receiver, and in virtually all cases, assure effective communication.

Criteria in Pharmaceutical Communications

It would, of course, be naive to suggest that all pharmaceutical promotion today has become solely receiver-oriented, or even that all that is receiver-oriented is automatically valid, effective, and worthwhile. The senders are not immune to special interests and objectives, not the least of which is to make a sale, that color the form and content of the communication equation. Nevertheless, most of the senders in the health care field today—and this includes medical publishers, professional organizations and government agencies as well as pharmaceutical companies and their advertising agencies—*are* motivated by a common desire to communicate accurate, understandable information in the area of drugs, disease, and patient needs which the physician can put to use in his professional practice.

The important criteria such communications should meet are:

(1) That physicians get the necessary information

(2) That they achieve new skills

(3) That they develop expertise in the use of drugs

(4) That they modify their professional practices to the ultimate benefit of their patients.

Recognizing that drug manufacturers communicate with physicians primarily because they are trying to sell products, can we regard them as a reliable source of information? With rare exceptions, I believe we can! There are two very good reasons why it would be all but suicidal for a pharmaceutical company to practice anything short of *truth in medical communication*. One is legal correctness, the other, medical goodwill. The Food and Drug Administration (FDA) regu-

lations leave very little room for spurious promotion, and no reputable company wants to jeopardize its good name, not to mention its sales, by risking a federal demand for "corrective" advertising, much less a seizure for misbranding. A similar, if less drastic, safeguard of truthful promotion is that our industry must preserve and increase the respect and trust of the profession and maintain the rapport with the medical audience that we have spent years cultivating. For these reasons, there is no doubt in my mind that of all advertising, ethical pharmaceutical promotion must be and is the most dependable and accurate. This reliability extends just as much to informational and educational materials supplied by pharmaceutical companies to physicians as it does to direct product promotion.

Consider the *communication equation* strictly from the receiver's point of view. What are the needs of the physician audience that a communicator must meet? And what specifically qualifies pharmaceutical manufacturers to meet these needs? The primary need that physicians expect the pharmaceutical industry to fill is the need for new and better drugs, accompanied by concise, accurate, easily digestible information on how to utilize them in their respective practices. The accuracy requirement is well served by the FDA-approved package insert. The insert succeeds in making very specific information about a particular drug available to the physician.

Revision of Package Inserts

Let me digress briefly to make a plea, in the interest of effective communication, that the format of these inserts be revised by both industry and government. This revision should readily distinguish information directly needed for prescribing, and present less prominently, supportive information in the body of the insert for referral. In their present form, the inserts do not make the information they contain quickly assimilable by the busy doctor.

Pharmaceutical promotion, within the boundaries set by FDA, frequently helps crystallize the potential and active role of a product in the physician's practice—it communicates. If it did not do so effectively, and if it did not meet a real need, pharmaceutical promotion would not enjoy the acceptance it does. The weight of professional opinion favors it. Few of the profession are willing to forego it when offered such an opportunity. For some time now, several companies have invited physicians to have their names removed from promo-

tional mailing lists simply by returning a preaddressed business reply card. Not surprisingly, the number of cards returned has been infinitesimal.

What about the "educational" promotional programs? Is the need for such materials genuine? If so, should the pharmaceutical industry continue to play so large a part in attempting to meet it? To both questions, the answer is "YES."

The informational needs of physicians and the related health care audience are expanding exponentially. New drugs, new techniques of patient care, and new methods of diagnosis are continuously being added to the body of knowledge that requires assimilation. Add to this the on-going need for information about Professional Standards Review Organizations (PSRO), the changing medical education requirements, the increased emphasis on postgraduate educational programs such as those demanded by the American Association of Family Practice (AAFP), the American Medical Association (AMA) and various specialty groups, together with providing current information on relicensure and on Board Recertification Programs. If that is not enough, consider the heavy daily patient load of the average physician and his need to keep abreast of constantly changing norms of "good medical practice" in caring for them.

The physician's need is not merely for more information, but for information conveyed as skillfully and memorably as human communication talent and technology can manage. The volume of crucial information is so large I do not see how government alone could adequately meet the demand. I also firmly believe that the government would be foolhardy to try to meet such needs alone.

We in the industry are constantly honing our skills, testing and reevaluating our messages. We hold workshops, seminars, group discussions and motivational meetings. We employ consultants from both clinical and academic medicine and do extensive market research, all aimed at improving our communication effectiveness. Yet, we find ourselves continuously confronted with criticism, regulation and reevaluation.

However, in spite of criticism, we have continued to develop skills in direct product promotion. In this era of receiver-oriented communication we have readily adapted these skills to help meet

the informational and educational needs of our audiences. I do hope we will recognize our joint interest, that we will stop judging the past and concentrate on improving the future by working together to help the physician cope with the expanding universe of medical knowledge. After all, there are very few improvements in medical treatment that do not involve new drugs or new demands in the legitimate use of established ones. It seems to be the best and most logical commitment that we can make together.

Increased Technology of Communication

Finally, I would like to briefly consider the technology of communication. We have concentrated, so far, on the message rather than the medium, but without some pretty spectacular advances in the media of communication, I doubt if it would be possible to cope with the sheer volume of messages we must deliver.

Traditionally, the printed word has been the chief vehicle of communication between the senders and the receivers of pharmaceutical promotion. However, we have already entered a new period. Television has become the major source of news input for the American people. Our children are the intellectual products of the television age, and many a young physician learned his ABC's in Romper Room.

Today's physician is awash in the mainstream of programmed instruction techniques, closed-circuit television conferences, and also, Muzak. He has demonstrated his receptivity to the burgeoning world of electronic media by his rapid acceptance of programmed audio cassettes, among other things. Multi-media learning systems for teaching hospitals and all types of postgraduate educational programs are changing the educational scene and undoubtedly will become as commonplace as textbooks in the medical milieu of the coming decade. This does *not* mean that the printed word will be eclipsed nor that the anchorman of medical communication, the professional service representative, will go out of style. What it does mean is that tomorrow's communication to the physician will lean heavily on the technological advances of our time, because they are effective. Since they expand our ability to communicate and the physician's ability to absorb the message, they will play an increasing role in every area of medical communication.

It is significant, and by no means coincidental, that the pharmaceutical industry has been the major innovator in improving communication to physicians. From the beginning, the industry has been in the forefront of the movement to harness the developing electronic media to solve the informational and educational deficiencies of today. Closed-circuit television programs are one significant example.

At this point I think it would be appropriate to summarize by quoting from the special issue of *Advertising Age*, November 21, 1973: *The New World of Advertising*. The entire issue reviews changing trends and speculates on the future. The section on pharmaceutical advertising is titled, "Medical advertising keeps doctors informed on burgeoning new drugs" and concludes with this paragraph:

"The key word in the expanding market activities of the nation's pharmaceutical companies is education; less product orientation, more physician/patient service orientation. Demands made on today's physician are unrelenting; his continued professional existence increasingly depends on "up-to-the-minute" knowledgeability. He is increasingly subject to review by his peers in the form of increased testing of his medical know-how. American drug companies contribute to the advancing professional qualifications of the nation's doctors by spending $725,000,000 a year on research, an expenditure matched by few industries, and by spending large sums on advertising—revenue which gives medical media the wherewithal to produce high-quality informational products."

Regardless of the media employed, the goal remains the same, as do the fundamental rules for communicating to physicians. Whatever that peculiar synthesis of disciplines may be that allows one to compound science, semantics, selling and the law to produce good, helpful pharmaceutical promotion, we will always find the same underlying principle: an ability to match sender interests with receiver needs, an ability to find and utilize co-interests. By identifying our co-interests, we hook up. We connect. We make contact. We participate in a reciprocal equation. We improve communication to physicians. **[The End]**

Drug Monographs

By MARY A. McENIRY

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THE FOOD AND DRUG ADMINISTRATION (FDA) has stated, on several occasions during the last two years, that the monograph approach to the regulation of prescription drugs will be used. This policy, thus accepted, is seen by many as the establishment of a major new approach by the Agency in the area of drug regulation.

We are all familiar with the old approach to the control of prescription drugs as exemplified by the utilization of the Abbreviated New Drug Application (ANDA) in implementing the findings of the Drug Efficacy Study. We are all familiar with the refrain that when the National Academy of Sciences-National Research Council (NAS-NRC) review panel concluded that a drug was safe and effective for specified uses, the drug was generally recognized as safe and effective (GRAS/GRAE) and not a new drug. In effect, a *Federal Register* notice, describing the conditions whereby a drug may be marketed under an approved ANDA, is an old drug monograph. If one analyzes the notice, it implies that the generic drug is generally recognized as safe and effective, and hence is not a new drug because no additional safety and effectiveness data need be submitted in the ANDA. The purpose of the ANDA is to demonstrate, *first* that the specific drug product the manufacturer proposes to market is the same as the generic drug, and *second* that the manufacturer has the capacity to make it. Once he has done this, the specific drug product is generally recognized as safe and effective. When a drug is so recognized, it may be marketed without the necessity of premarket clearance, provided there is assurance that the drug can be manufactured to meet adequate standards, is properly labeled, and has the same therapeutic effectiveness in humans as

other identical drugs in the marketplace. Whether the procedures, used by FDA to assure that these marketing conditions are met, involve the approval of an ANDA or the promulgation of a drug monograph, should be of little consequence to the manufacturer. The Food and Drug Administration is ready to begin establishing these marketing conditions for the more than 500 prescription drugs which are covered by the Drug Efficacy Study and for which a *Federal Register* notice has been published stating that marketing of these drugs shall be provided for by an ANDA.

The Validity of the Drug Monograph

The Supreme Court has applauded across-the-board rule making by the Food and Drug Administration, upheld its authority under section 701(a) to issue regulations for the efficient and effective enforcement of the Federal Food, Drug and Cosmetic Act, and held that these regulations do have substantive effect.

The monograph approach to regulating prescription "old drugs" was the subject of an aborted effort in 1968. A new effort in this direction had been held in abeyance awaiting the outcome of recent Supreme Court cases to determine if this approach is legally viable.

For the monograph approach to be of value, either to the Food and Drug Administration or the regulated industry, it must be widely used. Ideally, a large number of monographs should be published as rapidly as possible. This will depend, to a great extent, on the Agency's resources as well as on the cooperation and, perhaps, the active participation by or on behalf of the industry. The regulation will provide a mechanism for all interested persons, including manufacturers and drug trade or manufacturers' associations, to petition the Agency for the establishment of drug monographs. This procedure will afford these interested persons the opportunity to define the conditions for marketing the drug and to write the labeling to be included in the monograph for the drug. Each monograph will be tailored for the specific drug which is the subject of the monograph. This is an area where the United States Pharmacopeia and The National Formulary could serve a very useful role. The Bureau of Drugs will, of course, assign a unit the responsibility for developing and promulgating these monographs. Obviously, this will be an extensive and massive undertaking.

Content of the Monograph

As for content, the monographs will specify the conditions under which the drug may be marketed without the manufacturer first obtaining premarket approval from the FDA. The monographs will include complete labeling, including indications that there is substantial evidence supporting a general recognition of safety and effectiveness, all adverse effect information, dosage information, and a description of the dosage form, specifications and methods of analysis (or references for such methods), requirements for expiration dates and bioavailability data (as determined to be needed and appropriate), and a reporting requirement. Other information considered necessary to assure the safety and effectiveness of the drug will be included, dependent upon the peculiarities of the specific drug. For example, for some drugs it may be considered necessary to specify the method of manufacture or a list of the inactive ingredients which are suitable for use in formulating the finished dosage form.

The selection of drugs suitable for monographs must be made on the basis of their generally recognized safety and effectiveness, experience in the use of the drug, extent of use, and the adequacy and availability of specifications and methods of analysis to assure their integrity and safety. Drugs which have been evaluated in the NAS-NRC Drug Efficacy Study and found to be effective, and for which a notice has been published in the *Federal Register* requiring ANDA's as a condition for marketing the drugs, will be the source of most of the early monographs. The labeling for these drugs is already available, for all practical purposes. Other early monographs will be developed for classical drugs marketed prior to 1938 and not covered by New Drug Applications (NDA's). Drugs which are covered by NDA's, approved since 1962, will also be candidates for monographs.

Issues Involved in the Monograph

By adopting the monograph approach the FDA will be covering at one time all of the issues regarding a drug whether the drug is a "new drug" or an "old drug," and it will include issues of adulteration and misbranding. Manufacturers will have the option of either complying with the monograph or obtaining new drug approval if they are to market a drug which does not meet the monograph. Once a monograph is finalized and in effect, regulatory action against

drugs which are not in compliance with the monograph and not the subject of an approved NDA will be based on an illustration that the drug fails to meet the monograph. The questions of whether a drug is safe and effective, or whether or not it is a new drug, will not be the issue. Based on the recent Supreme Court decisions, the FDA will view a monograph that is in effect as a binding substantive rule for a drug which is generally recognized as safe and effective and not misbranded.

The "old drug" status of a drug product may change as new information is gained concerning the effects of the drug, or the treatment methods for the disease or condition for which the drug is intended. As progress is made in the medical sciences, a drug may become obsolete, particularly if a more effective or less hazardous drug is developed. We anticipate that when it has been determined, on the basis of present knowledge, that a drug is neither safe nor effective, then it will be declared a "banned drug" and made the subject of a *Federal Register* announcement.

It is essential for the Food and Drug Administration to monitor experiences with drug usage in order to assure that their GRAS/GRAE status has not been altered, that the labeling is current and clearly reflects up-to-date information, and that the benefit-to-risk ratio has *not* been significantly altered. Thus, it is essential that a requirement for marketing a drug under a monograph, is the maintenance of records and submission of reports on drug experiences.

The Monograph's Benefits

In summary, the new approach to the regulation of prescription drugs by the establishment of drug monographs is not, after close examination, a significant departure from the old approach. By whatever name we assign the approach, once it is determined that a drug is safe and effective, either procedure allows the marketing of a drug without unduly burdensome requirements. The procedure whether it involves approval of an ANDA or the establishment of a monograph, sets conditions to assure that the drug is properly manufactured and labeled and has the same therapeutic effectiveness in humans as identical marketed drugs.

You might ask, "What is the advantage of the monograph approach over the ANDA procedure?" The major advantage to the FDA is anticipated to be the freeing of limited resources occupied

in reviewing multiple ANDA's for identical products which have been extensively used for many years, to concentrate on the more imperative needs of reviewing and monitoring investigational drugs and more recently, approved new drugs. Surveillance over the monographed drugs will be maintained through the field inspectional forces, review of required reports and laboratory analyses through drug sampling programs. It is also anticipated that periodic label updating will be undertaken.

For the industry, advantages will be many, including the removal of burdensome paper work and the elimination of the waiting period for Agency approval to introduce a drug on the market.

Once the monograph system is implemented for prescription drugs as well as over-the-counter drugs, there will be a new era in which every drug fits into a category, and the requisite marketing conditions will be known to all. The "old drug-new drug" doubts, controversies, and distinctions should gradually fade away.

The procedures for establishing prescription drug monographs are under preparation and should be published early in 1974, but this will be only a beginning. The publication of numerous new monographs and continuous updatings is an enormous undertaking. It will require persistence and dedication. **[The End]**

FDA REQUESTS DATA ON SKIN TEST ANTIGENS

Skin test antigens will be studied next by the Food and Drug Administration as part of its review of biological products. Interested persons are invited to nominate qualified experts to serve on an advisory panel and to submit published and unpublished data and other information pertinent to all active ingredients used in the products. The products to be studied include coccidioidin, diphtheria toxin for Schick test, histoplasmin, lymphogranuloma venereum antigen, mumps skin test antigen, Schick test control, trichinella extract, tuberculin, old, and tuberculin, purified protein derivative. Data concerning propagation techniques and manufacturing processes are also required for the review. To be considered, twelve copies of submissions must be filed with the FDA in the prescribed format by May 28, 1974.

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An Overview of Medical Device Legislation

By EDGAR VANNEMAN, JR.

Mr. Vanneman Is the Counsel, Sherwood Medical Industries Incorporated.

THE PROSPECTS OF MEDICAL DEVICE LEGISLATION took a giant leap forward this fall with the introduction of bills[1] by Senator Edward M. Kennedy and Congressman Paul Rogers, the respective subcommittee heads in the Senate and House. It was obvious that these bills had been prepared after consultation with many interested persons, including the Government, and that it was a joint effort to move medical device legislation forward. The nature of the hearings also indicated a desire for quick action. Hearings both before Senator Kennedy and later before Congressman Rogers included approximately the same testimony by the Administration, interested congressmen, consumers, professional medical associations and industry associations. The hearings in each case lasted less than two days. There is no question but that the climate is excellent for passage early in 1974 of medical device legislation.

Although the Administration had previously introduced its own bills, and although other congressmen had introduced bills from time to time on the subject, it was apparent at the hearings that there was little interest in the other bills. The issue is what amendments will be made to the Kennedy-Rogers bills and there is no need to compare these with other proposed legislation. Indeed, as Mr. Pilot has stated, the Senate Labor and Public Welfare Committee last week approved a modified version of the bill.

[1] S. 2368 and H. R. 9984.

Regulatory History of Medical Devices

I am certain that those of you who are interested enough in the subject to be here today are well aware of the steps which led to this climate. The present regulatory scheme in the Food, Drug and Cosmetic Act[2] provides for considerable controls for drugs but has little to say about devices, except for labeling. The courts, however, in the *AMP* and *Difco* cases[3] greatly expanded the definition of the word "drugs" to where it seemed to include what everyone had always supposed were devices. The Food and Drug Administration (FDA) announced that it intended to treat devices as drugs under these cases in any situation where they thought there was an unreasonable danger to the consumer and they promulgated extremely broad regulations concerning *in vitro* diagnostic products.[4] These activities left all those concerned in a state of confusion. Doctors developing new devices did not know whether they were dealing with a drug or a device from a regulatory standpoint and were uncertain as to whether the economic impact of construing it as a drug would make it worthwhile to continue working on such devices.

The report of the 1969 Conference on Medical Devices sponsored by the Association for the Advancement of Medical Instrumentation contained recommendations from the consumers, physicians, hospitals and industry group representatives strongly urging medical device legislation and the Cooper study group was formed by the Department of Health, Education and Welfare (HEW) to implement these recommendations. The Administration and others subsequently introduced bills in an effort to supplement the Cooper study group and the Association for the Advancement of Medical Instrumentation (AAMI) conference recommendations.[5]

Device or Drug?

It was recognized by all who had any knowledge of the subject that medical devices are a completely different proposition than drugs. The medical device industry is primarily composed of very

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[2] 21 U. S. C. A. Sec. 301-392.

[3] *AMP v. Gardner,* 389 F. 2d 825 (CA 2d., 1968), cert. den. 393 U. S. 825 (1968); *U. S. v. An Article of Drug . . . Bacto-Unidisk,* 394 U. S. 784 (1969).

[4] 37 Fed. Reg. 16613 (Aug. 17, 1972).

[5] See Miller, "Device Legislation," 47 *JAHA* 81 (1973).

small manufacturers. Typically, new devices are developed by individual physicians and surgeons rather than corporations and the devices are subject to rapid changes as the state of the art advances. Unlike drugs, most devices are merely an extension of the surgeon's arm rather than something that is of itself effective. Finally, any workable law must recognize that a device is "safe" when the risk of its use is less than the risk of the diseased state that it treats and that it is the best device available. Tremendous benefits have accrued to thousands of persons because of the discovery and development of many devices which would not be on the market had a rigid premarketing clearance system, requiring absolute safety, been in effect. Put in this perspective, the restriction of "quack" devices is only a minor element in the development of a regulatory scheme which will also allow the continuation of these dramatic and exciting developments in new medical devices.

What do the Kennedy-Rogers bills provide? Do they help the situation or not? In my opinion, these bills, while they still have certain deficiencies, go a long way toward meeting the goal of controlling medical devices where necessary without discouraging new innovations and advances which will help the patient.

Scope of Introduced Regulatory Information

In the first place, the bills define what a medical device is. It seems that everyone interested in the problem has helped to define "medical devices," yet there is general satisfaction with the definition. Indeed, I cannot recall anyone at the hearing who said he could improve on the definition. The definition refers to articles "which do not achieve any of their principal intended purposes through chemical action within or on the body of man or other animals and which are not dependent upon being metabolized for the achievement of any of their principal intended purposes."[6]

The Kennedy-Rogers bills first set up a classification system.[7] This requires that classification panels be established within sixty days and that all devices be classified within one year into three categories: (1) Those where there is insufficient information available

[6] Sec. 706 of S. 2368 (Kennedy Bill). [7] *Id.*, Sec. 511.

as to their effectiveness or which may cause unreasonable risk of illness and for which standards or other means are not appropriate. This is the Scientific Review category. It is my understanding that the revised Senate bill has put any life threatening or life sustaining device in this category. Of course, these words are very difficult to define. (2) Those for which standards are appropriate and for which there is no other more practical means to reduce risk of illness. (3) Those devices which are safe and effective when used in conjunction with instructions.

One of the primary problems with this portion of the bills is that FDA can use existing classification panels for this purpose despite the fact that these panels have not had the same guidelines and that they have been meeting in secret without adequate representation. The existing panels, in my view, are clearly operating contrary to the purposes of the Federal Advisory Committee Act.[8]

Another deficiency appears to be that the existing bills do not provide any feasible method for new devices, not classified during this first year of regulatory activity, to be utilized by persons who would otherwise suffer or die without them. Obviously, it would destroy the whole concept of the bill if every new unclassified device had to wait for what would amount to years of preclearance. I understand that the revised Senate bill, which I have not yet seen, remedies this deficiency.

Performance Standards for Devices Advanced

The bills next consider the area of performance standards.[9] The Secretary is authorized to publish notice that it desires to consider standards regarding a certain type of class of device. Those interested in the subject may offer to develop such standards and the Secretary may utilize existing standards or refer the matter to an independent advisory committee. An opportunity is given for input by all concerned and review of the proposed standards and court appeal is permitted. The Act authorizes the establishment of current good manufacturing practices to insure compliance with standards, including the method of testing for compliance.

[8] 5 U. S. C. A. App. I.

[9] Sec. 513, S. 2368.

Veterinary devices are excluded. Temporary permits, pending amendment of standards, are permitted. Custom devices ordered by the licensed practitioner apart from applicable standards are also permitted, although the definition of custom devices is too narrow.

Unlike the drug regulations, the new Act would not permit deviation from a standard even if the label clearly indicated the deviation and even if there is no danger to the public. I suspect the bills may be amended in this regard, however.

As to scientific review,[10] the type of premarketing clearance required under the Act, provisions are again made for the Secretary to consult with appropriate outside review panels. An exemption is provided for investigational use.

The bills contain premarketing validation standards which will allow a manufacturer of a device that is subject to frequent modification or rapid obsolescence an opportunity to market his product under closely regulated conditions as an alternative. I understand that this was included to permit the continued improvement of these products and still provide maximum safety for the patient.

Finally, the Kennedy-Rogers bills, among other things, contain provisions concerning devices which fail to comply with standards or contain defects.[11] These devices require the registration with the FDA of device establishments and the maintenance of certain records.

As products, devices are quite different than drugs. The industries which supply them are different and the economics of devices, particularly in terms of unit product volume and rapid advances in the state of the art, are different. It is these significant differences which require that the regulation of devices be different from the regulation of drugs. In general, the approach of the Kennedy-Rogers legislation recognizes this. With some amendments, I believe the bills are a responsible solution. **[The End]**

[10] Sec. 514 of S. 2368.

[11] Sec. 516 of S. 2368.

"HYPOALLERGENIC" DEFINITION PROPOSED BY FDA

Cosmetics designated on labeling as "hypoallergenic" would have to have met certain standardized requirements or they would be considered misbranded, according to a regulation proposed by the Food and Drug Administration. The term is subject to various interpretations and different manufacturers mean different things by it, according to the FDA, rendering such label statements as appear on many cosmetics misleading to consumers.

The agency said that some manufacturers label their products as hypoallergenic simply because they do not contain known sensitizers or perfumes which have a history of causing adverse reactions. Others perform tests with groups of varying sizes and designate as hypoallergenic any cosmetic with causes less than a specified number of reactions. There is no agreement as to a minimum percentage of adverse reaction permitted before a product may be labeled as hypoallergenic.

Consumers generally lack sufficient medical knowledge to distinguish between adverse reactions resulting from allergy and those caused by irritation. The FDA has requested the submission of data showing consumers' interpretation of the term hypoallergenic.

The FDA's proposal would permit the use of the term or other words to the same effect only when the product has been shown by scientific tests to result in a relative frequency of adverse reactions which is less than the relative frequency of such reactions from a "reference product." The reference product or products are similar-use competitive products ranking high in sales volume for the product category. Reports of such tests would have to be filed with the FDA before marketing of a new product or as soon as completed for a product already in distribution at the time the regulation is promulgated.

Views and comments on the proposal may be filed with the FDA until April 26, 1974.

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