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Food Drug Cosmetic Law JOURNAL

Additional Papers Presented at the 1970 Annual Meeting of the New York State Bar Association Section on Food, Drug and Cosmetic Law

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

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How the Chemical-Pharmaceutical Industry Views the Government's Patent Policy.—*Howard I. Forman* believes that a more precise government patent policy is needed. He points out the favorable response by industry to a 1965 Senate bill concerning patents that was never considered by the entire Senate. Mr. Forman, whose article begins on page 204, is a corporate patent lawyer who has written many articles concerning patent law.

Reasonable Grounds, Substantial Evidence, and Law and Order.—In this article, *Vincent A. Kleinfeld* claims that the FDA is not following orderly procedures and due process in its removal of certain drugs from the market without a hearing. The approach of the Government, he states, is to refuse to grant hearings after adverse NAS-NRC panel reports by the means of equating the concepts of "reasonable grounds" for holding a hearing with "substantial evidence" of the effectiveness of the drug. Mr. Kleinfeld is a member of the District of Columbia Bar. His article begins on page 210.

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Journal

New FTC Approaches to Food, Drug and Cosmetic Problems

By ALBERT G. SEIDMAN

Mr. Seidman Is the Attorney in Charge of the New York Office of The Federal Trade Commission. His Article and the Four Following Were Presented at the Annual Meeting of the Food, Drug and Cosmetic Law Section of the New York State Bar Association.

"NEW FEDERAL TRADE COMMISSION (FTC) APPROACHES . . ." is the announced subject of my talk. If you have been led to believe that I am about to forecast with accuracy the directions in which the Commission will move in the year ahead, I am afraid you are doomed to disappointment. I do not speak officially for the Commission, nor does it necessarily endorse the opinions I express. This traditional disclaimer is emphatic in this year of change in the Commission's Leadership.

Next to the Commission's headquarters building in Washington, D. C., stands the classic structure housing the National Archives. It carries the inscription "What is past is prologue."

So, too, the pilots on the old Mississippi sternwheelers, in negotiating a difficult bend in the river, would take a position at the rear of the vessel, and by taking sightings of landmarks on the shores already past, safely chart their course. If you will, therefore, join with me in a brief review of the Commission's most recent actions with regard to foods, drugs and cosmetics, we may gain some clues as to what lies ahead in the immediate future.

The past year saw a maximization of effort by the Commission to employ an industry-wide approach to many of the problems that have repeatedly plagued the industries which you represent. On May 29, 1969, it finally promulgated "Guides for Advertising Allowances and Other Merchandising Payments and Services" revised in the light of the Supreme Court's decision in *FTC v. Fred Meyer, Inc., et al.*, 390 U. S. 341 (1968). The revision further elaborates on the requirements of Sections 2(d) and 2(e) of the Robinson-Patman Amendment to the Clayton Act by spelling out in greater detail what constitutes "services and facilities," "proportionality" and "availability;" and includes within the definition of "customer," pursuant to the *Fred Meyer* decision, "any buyer of the seller's product for resale who purchases from or through a wholesaler or other intermediate reseller."

Games of Chance Regulation

The Commission promulgated a Trade Regulation Rule effective October 17, 1969, with respect to "Games of Chance in the Food Retailing and Gasoline Industries." In substance, it finds any of the following practices to be an unfair and deceptive act in violation of the Federal Trade Commission Act:

1) Misrepresenting participants' chances of winning any prize.

2) Engaging in any advertising or promotion which fails to disclose clearly and conspicuously:

a) The exact number of prizes in each category and the odds of winning each—where the game extends beyond thirty days, this disclosure must be revised weekly for all prizes valued at $25 or more.

b) The geographic area covered by the game.

c) The total number of retail outlets participating.

d) The scheduled termination date.

3) Failing to mix, distribute and disburse all game pieces totally and solely on a random basis throughout the game program and throughout the geographic area covered, and failing to maintain adequate records to demonstrate that fact.

4) Promoting, selling or using any game which is capable of or susceptible to being solved or "broken" so that winning game pieces or prizes are predetermined or preidentified by such methods.

The Commission has already announced it has drafted a complaint charging Shell Oil Co. and Glendinning Companies, Inc. with violation of the rules in that: (1) the television advertisements didn't provide sufficient time and exposure to permit the required disclosures to be read and comprehended by the viewing public; (2) greater prominence in point of sale promotional materials was given to the dollar amount of the largest prizes while subordinating the required disclosures; and (3) winning pieces were improperly seeded into boxes, rather than employing the required total random dispersal of all game pieces.

OTC Drug Guides

The Commission has also held hearings on proposed guides for the advertising of over-the-counter (OTC) drugs. These guides relate to the marketing and advertising of those drugs which, under the Federal Food, Drug and Cosmetic Act, may be dispensed without prescription. Among the more important inhibitions are those which prohibit dissemination of advertising which:

1. Represents the product to be a treatment *and* cure, remedy, or preventive measure for a stated condition or disease when, in fact, it only provides palliative relief from some of the symptoms commonly associated with the condition.

2. Represents the product unqualifiedly as providing relief from a symptom, condition or disease when, in fact, it provides no relief, or only temporary or partial relief, or does not provide relief for certain persons under certain conditions.

3. Represents the product as a remedy, relief or preventing a symptom, condition or disease when, in fact, it can be safely used for such purpose only under the supervision of a medical practitioner.

4. Employs a fanciful proprietary name for a drug or any ingredient in such a manner as to imply that the drug or ingredient has some novel or unique effectiveness when, in fact, the drug or ingredient is a common substance which would be readily recognized by the public if designated by its common or usual name.

5. Where a representation is made that a benefit will be derived from the action of any specified ingredient or combination of ingredients, such representation should be accompanied

by a clear and conspicuous disclosure of the common or usual name of such ingredient or combination of ingredients if such names are likely to be meaningful to the general public.

6. Advertisements should not feature ingredients in a manner that creates an impression of value different from or greater than their true functional role. The order of listing should be the same as the order in which they are listed on the label of the product, and the information in the advertisement concerning the quantity of each such ingredient should be the same as the corresponding information in the labeling of the products.

7. An advertisement should not represent that any benefit will be derived from the action of a specific ingredient or combination thereof unless the advertiser has established and can demonstrate that such ingredients or combination are as efficacious as represented for the purposes for which they are offered.

8. Representations that over-the-counter drugs will produce specified therapeutic benefits should be accompanied by clear and conspicuous disclosures of:

(a) the dosage to be used;

(b) any side effects or contraindications which may be anticipated;

(c) the course of treatment which should be used if it differs from that prescribed on the label;

(d) any other material limitations concerning the effectiveness of the drug;

(e) representations that the drug is safe should be accompanied by appropriate qualifications such as "if taken as directed on the label," or by a disclosure of any side effects, contraindications, cautions, warnings and similar information;

(f) the product should not be unqualifiedly represented as a remedy for symptoms or conditions which may be common manifestations of various diseases or disorders unless the drug will be effective in remedying the symptoms or conditions, regardless of complaint; and

(g) advertisements should not represent that consumers suffering from particular symptoms can themselves diagnose the complaint unless an accurate self-diagnosis can be made

by laymen; and medical or laboratory tests, or examinations conducted by or under the supervision of a doctor or competent technician are ordinarily unnecessary to permit an accurate diagnosis.

The guides also inhibit advertising which is not consistent with the required labeling; and it is not a defense that the statements contained on the label explain or modify the advertising claims. In the absence of clinical proof, advertisers may not represent that the drugs are more effective or superior or preferable to other products, or are more powerful, faster acting or produce longer lasting effects. After six months from the time a product has been placed on the market, the product may not be represented as being "new." The guides contain additional inhibitions with respect to guarantees and warranties consistent with the general rulings of the Commission, as well as those which make reference to the character, size of business, extent of testing or the use of deceptive or imitative trade or corporate names or trademarks.

Additional Pending Regulations

Also pending before the Commission is a proposed trade regulation rule dealing with the advertising of non-prescription systemic analgesic drugs. The proposed trade regulation rule would inhibit representations with respect to efficacy or safety which contradict or exceed the statements or directions for use appearing on the label of such products, or which represent any analgesic effects which are faster, stronger or longer lasting than those achieved by the use of competitive products unless the advertiser has established and can demonstrate that a significant difference in such effects exists. The trade regulation rule would require the advertiser to disclose the identity of the ingredients and to demonstrate that each such ingredient or combination thereof is as efficacious as represented for the purpose for which it is offered when the product is taken in accordance with the directions for use.

Recently the Commission has announced that it has initiated a trade regulation rule relating to retail food store advertising and marketing. The proposed rules are based upon the Commission's study in three large metropolitan areas of food chain selling practices. The proposed rules would declare it an unfair method of competition or an unfair or deceptive act or practice to offer a product

for sale at a stated price in areas served by stores that do not have the products in stock and readily available to consumers. In self-service stores it is required that clear and adequate notice shall be provided at the point of sale where customers would normally expect the products to be offered for sale, that the item or items are in stock and may be obtained on request. While the proposed rule does provide for defenses where the advertisement notes exceptions with respect to specific stores, general disclaimers such as "not all items available at all stores" will not constitute a defense. Even a "rain-check policy" is not deemed to be a defense where the products are unavailable during the effective period of the advertisement.

Despite the Commission's emphasis on industry-wide proceedings, it has not neglected to bring adversary proceedings where demanded by the public interest. Thus, the provisional consent order to cease and desist, which relates to the television advertising of Campbell soups, is now pending before the FTC. In this advertisement, marbles were employed so as to hold vegetables at the top of the bowl of soup televised, thus creating in the viewer's mind the impression that the soup contained vegetables in greater abundance than were, in fact, present.

I also call your attention to the recent decision of the Commission in the *Beatrice Foods Co., Kroger Co., Inc.*, case. In that proceeding, the complaint charged Beatrice Foods Co. with violation of Section 2(a) of the Robinson-Patman Act in granting preferential prices in the sale of fluid milk and other dairy products to the Kroger Co., Inc. The complaint likewise charged the Kroger Co., Inc. with violation of Section 2(f) of the Robinson-Patman Act in having knowingly induced and received discriminatory prices illegal under Section 2(a). The decision of the Commission dismissed the complaint against Beatrice Foods Co., finding that it had granted lower prices to the Kroger Co., Inc. in good faith, relying upon evidence furnished by the Kroger Co., Inc. that it was merely meeting the lower price of a competitor. The Commission found, however, that the Kroger Co., Inc. had misrepresented the prices offered by competition and had in fact induced and received from Beatrice Foods Co. a price below that quoted by competitors. The Commission, therefore, did issue an order to cease and desist against the Kroger Co., Inc. inhibiting it from knowingly inducing or receiving discriminatory prices.

Buyer's Rights

I have cited some of the highlights of the Commission's activities relating to food and drugs during the past year. Whether or not they constitute a prologue significantly relevant to Commission actions to follow remains to be seen. I suggest, however, that the interests of the consumer are likely to be paramount in the minds of decision-makers in the years which lie ahead. On October 30, 1969, President Nixon addressed a message to Congress in which he stated:

> Consumerism—Upton Sinclair and Rachel Carson would be glad to know—is a healthy development that is here to stay.
>
> That does not mean that *caveat emptor*—let the buyer beware—has been replaced by an equally harsh *caveat venditor*—let the seller beware. Nor does it mean that government should guide or dominate individual purchasing decisions.
>
> Consumerism in the America of the 70's means that we have adopted the concept of 'buyer's rights.'
>
> I believe that the buyer in America today has the right to make an intelligent choice among products and services.
>
> The buyer has the right to accurate information on which to make his free choice.
>
> The buyer has the right to expect that his health and safety is taken into account by those who seek his patronage.
>
> The buyer has the right to register his dissatisfaction and have his complaint heard and weighed, where his interests are better served.

There are no products more important to the consumer than food and drugs. They represent a significant part of the budget of both the underprivileged and the senior citizens, two classes of consumers meriting the special attentions of government agencies.

In January, Caspar W. Weinberger became a member of the FTC and was designated by President Nixon to serve as its Chairman. Before assuming office, he expressed agreement with the President's desire to increase consumer protection. He was quoted in Women's Wear Daily of December 18, 1969, as having stated: "There is a real need in the disadvantaged areas for more protection and for more emphasis on removing whatever consumer dissatisfaction or frauds might be detected."

Recently, he presided at the hearings on proposed trade regulation rules with respect to mandatory disclosure of washing and cleaning instructions for textiles. In his opening remarks, Chairman Weinberger stated:

> There is a rising demand for greater consumer protection from all segments of the community. I want to assure you it is the intention of this agency to respond rapidly to this demand.

[The End]

The Legal Status of Devices

By GERALD E. GILBERT

Mr. Gilbert Is a Member of the Law Firm of Hogan & Hartson.

THE MOST IMPORTANT ISSUE in discussing this subject is determining the legal definition of a device. Until two recent cases the need for a precise definition did not appear to be the subject of great debate. However, the *AMP*[1] and the *Bacto-Unidisk*[2] (also known as *DIFCO*) decisions have caused most attorneys who have any interest in devices under the Food, Drug and Cosmetic Act to take a close look at the definitions of both a device and a drug.

AMP and DIFCO Cases

Though most of you are familiar with the *AMP* and *DIFCO* cases, let's review the facts and decisions briefly. The *AMP* case involved two products used in tying off, or ligating, blood vessels severed during surgery. Both products consisted of a nylon thread applied by a disposable plastic instrument. The effect of the products is to tie a loop around the severed vessel, tighten it and lock it in place by a nylon button. The button functions as a knot does in conventional ligating methods. The excess part of the thread is cut off; the button and the rest of the thread remain in the patient's body.

The Food and Drug Administration (FDA) took the position that the product in question was a "drug"[3] and also a "new drug"

[1] *AMP Incorporated v. John W. Gardner, Secretary of HEW*, CCH Food Drug Cosmetic Law Reports ¶ 80, 192, 389 F. 2d 825 (CA-2, 1968), aff'g 275 F. Supp. 410 (D. C. N. Y., 1967), *cert.* denied, U. S. Sup. Ct., 1968.

[2] *U. S. v. Article of Drug * * * Bacto-Unidisk * * ** CCH Food Drug Cosmetic Law Reports ¶ 80, 231, 394 U. S. 784 (1969).

[3] 21 U. S. C. 201(g)(1): The term "drug" means (A) articles recognized in the official United States Pharmacopeia, official Homeopathic Pharmacopeia of the United States, or official National Formulary, or any supplement to any of them; and (B) articles intended for use in the diagnosis, cure, mitigation, treatment, or prevention of disease in man or other animals; and (C) articles (other than food) intended to affect the structure or any function of the body of man or other animals; and (D) articles intended for use as a component of any articles specified in clause (A), (B), or (C); but does not include devices or their components, parts, or accessories.

and therefore subject to pre-clearance requirements.[4] FDA's opinion was that the essential component of the product, a nylon suture, was listed in the United States Pharmacopeia (USP) and that the suture remained in the body in the same manner as the drugs contained in a disposable syringe, like any chemical pharmaceutical preparation. *AMP* argued that its product was a device[5] and specifically excluded from the classification "drug" according to the drug definition in the Food, Drug and Cosmetic Act which "does not include devices."

The District Court concluded that the product was a drug and therefore required pre-market clearance by the FDA. Though the court was not convinced that the mere fact that an item is listed in the USP makes it a drug for purposes of the Act, the judge stated that "the listing of an item in an official compendium should be some evidence that such item is a drug."[6] The District Court was affirmed by the Second Circuit.

The Court of Appeals similarly did not rely on the listing of sutures in the Pharmacopeia. After stating that the case would be an easy one if the definition of drugs did not exclude devices, the court went on to say that it did not find anything in the legislative history of the Act "indicating that the congressional purpose providing a separate definition of 'devices' was anything other than to avoid the incongruity of classifying such things as electric belts as 'drugs.' "

[4] 21 U. S. C. 201(p): The term "new drug" means—

(1) Any drug (except a new animal drug or an animal feed bearing or containing a new animal drug) the composition of which is such that such drug is not generally recognized, among experts qualified by scientific training and experience to evaluate the safety and effectiveness of drugs, as safe and effective for use under the conditions prescribed, recommended, or suggested in the labeling thereof, except that such drug not so recognized shall not be deemed to be a "new drug" if at any time prior to the enactment of this Act it was subject to the Food and Drugs Act of June 30, 1906, as amended, and if at such time its labeling contained the same representations concerning the conditions of its use; or

(2) Any drug (except a new animal drug or an animal feed bearing or containing a new animal drug) the composition of which is such that such drug, as a result of investigations to determine its safety and effectiveness for use under such conditions, has become so recognized, but which has not, otherwise than in such investigations, been used to a material extent or for a material time under such conditions.

[5] 21 U. S. C. 201(h): The term "device" (except when used in paragraph (n) of this section and in sections 301(i), 403(f), 502(c), and 602(c)) means instruments, apparatus, and contrivances, including their components, parts, and accessories, intended (1) for use in the diagnosis, cure, mitigation, treatment, or prevention of disease in man or other animals; or (2) to affect the structure or any function of the body of man or other animals.

[6] 275 F. Supp. at 414.

The court further stated that the "exclusionary classification 'devices' should, we think, be limited to such things as Congress expressly intended it to cover. The language of Section 201(g) plainly permits calling AMP's nylon thread and disc, in their intended use, 'drugs,' and we hold that that is their appropriate classification."[7] Certiorari was denied by the Supreme Court.

The *DIFCO* case involved a diffusion test using eight sensitivity discs. Seven are impregnated with antibiotics and one with sulfadiazene. A specimen from the infected patient is placed on each disc, and by observing these after incubation, the lab technician or M. D. can tell which drug is most effective in inhibiting bacterial growth and would be best to treat the patient. No part of the disc is administered to man or other animals, internally or externally.

FDA seized the product and argued that the product was a drug. The District Court and the Sixth Circuit held that the product was not a drug. Both courts held that the product was not recognized in the USP or the National Formulary and did not fall within the rest of the definition of "drugs" in the Food, Drug and Cosmetic Act. The Supreme Court reversed, holding that the discs were drugs.

While conceding that the law's language "is of little assistance in determining precisely what differentiates a 'drug' from a 'device' . . . ." the Court went on to say that "the legislative history, read in light of the statute's remedial purpose, directs us to read the classification 'drug' broadly, and to confine the device exception as nearly as possible to the types of items Congress suggested in the debates, such as electric belts, quack diagnostic scales, and therapeutic lamps, as well as bathroom weight scales, shoulder braces, air conditioning units, and crutches. In upholding the Secretary's determination here, without deciding the precise contours of the 'device' classification, we need only point out that the exception was created primarily for the purpose of avoiding the semantic incongruity of classifying as drugs (1) certain quack contraptions and (2) basic aids used in the routine operation of a hospital—items characterized more by their purely mechanical nature than by the fact that they are composed of complex chemical compounds or biological substances."[8]

It is certainly a matter of opinion and speculation whether these decisions will or should be construed narrowly in the future and also as to what extent FDA will or should apply these decisions to other products. A major concern of industry, of course, is whether products which have been considered to be devices in the past will now be

[7] 380 F. 2d at 830.

[8] 394 U. S. at 799-800.

deemed to be drugs and subject to costly and time-consuming pre-clearance.

While these decisions do not clearly define the difference between a "drug" and a "device," and though they have created a legal status of uncertainty, there are some things that can be concluded from them. The legal determination of a drug or device cannot be made by looking solely at the language of the statute. Courts recognize that the Food, Drug and Cosmetic Act is a public health statute and will give it liberal construction, so as to give the public maximum protection. FDA has some authority to treat as drugs, products that before these decisions may have been treated as devices.

In considering the impact of these decisions, it should be noted that the *DIFCO* decision was handed down on April 28, 1969. There has not been a wholesale attempt by FDA to reclassify devices as drugs since that decision. Nevertheless, the legal status of devices is, truly, unclear. This is not in the best interest of anyone, most of all the public. One obvious alternative to this uncertain status is legislation.

The Need for Professional Training

Before getting into a discussion of legislative proposals it should be noted that though legislation may help clarify the status of devices, it will not cure all of the legal problems in this area, many of which involve human error. In this regard, there appears to be a definite need for industry and the medical profession to focus on the training of the people who are using many of today's complex devices. I understand from representatives of FDA that a common problem with technical devices is that they are often developed by engineers and scientists who have little, if any, knowledge of the human body. The devices are then used by M. D.'s who often have little, if any, knowledge of electronics or other technical aspects necessary to use the devices safely. Clearly, there is a need in such situations for people who are trained in all areas essential to the safe and effective use of devices. Perhaps the progress of modern science in medical devices has created the need for an entirely new profession.

Legislative Proposals

There have been over 15 bills introduced in this Congress on devices. Most of the proposals, labeled medical device safety bills, are patterned after HR-10726, which was introduced in the 90th Congress by Chairman Staggers of the House Interstate Committee.

These bills, generally, call for FDA controls over certain devices similar to the FDA controls over drugs. We can anticipate additional bills on this subject. Among others, Congressman Rogers, the Acting Chairman of the House Interstate Health Subcommittee, has indicated that he will introduce a device bill this session.

There have been many recommendations from other sources as to what legislation in this area should encompass. The subject was discussed at length at "a national conference on medical devices" held at Bethesda, Maryland last September.[9] Many recommendations were made at that conference. Some of those recommendations, I understand, formed the basis for a general agreement on legislative proposals among the major trade associations concerned with devices.

In my preparation for this presentation, I had the privilege of discussing device legislation with several involved people, including Congressman Rogers, a representative of Mrs. Virginia Knauer—the President's consumer aide—as well as attorneys in the industry. It appears to me that, though there will be a push by some to accomplish legislation this session, it is unlikely that a comprehensive bill with pre-clearance requirements will pass.

It also would seem that Commissioner Edwards has not had sufficient time to formulate a position on this subject, and it is going to be difficult for FDA to make a comprehensive recommendation in the near future unless this problem is given top priority. There are many other problems which appear to be higher on FDA's priority list than devices. If legislation is passed this session, it is my guess that it would have to be a result of industry's efforts.

The idea of private industry providing the initiative in seeking legislation that will control the products it manufactures may seem incongruous. Nevertheless, industry may do just that. Among other reasons, industry has a unique opportunity to exercise leadership and responsibility in the legislative area instead of having to react defensively, which is often, if not usually, the case.

As you all are aware, many of our public health statutes and regulations have as their genesis tragic occurrences. As a result, many of the statutes we have today were passed in extremely emotional atmospheres. Fortunately, that is not the case now with devices.

Representatives of industry, government, the Congress, and the consumer all seem to agree that some kind of legislation would be desirable. The only issue seems to be whether pre-clearance is neces-

[9] *Journal of the American Medical Association*, Dec. 1, 1969 at 1745.

sary and whether it could actually be against the public interest. I am not attempting to advocate any specific proposals at this time, but there are some very persuasive arguments that pre-clearance requirements are premature and that legislation short of pre-clearance would obviate such a time-consuming and costly process.

Voice of the Consumer

In any kind of legislative debate in Washington today, there is one voice that is getting louder and louder. That is the voice of the consumer. Such a comment, I know, immediately conjures up in the minds of many the self-styled spokesmen for the consumer whose motives and facts may be suspect. Nevertheless, whether you like it or not, the voices of the kind of people who participated in the recent Consumer Federation of America's Consumer Assembly in Washington, D. C. are being heard by the Congress and will be heard more and more in the future.

This so-called consumer voice may be heard from many different people and organizations, such as the President's Special Assistant for Consumer Affairs, and state and private consumer groups, many of which may not even agree among themselves. But the fact that they may not all agree does not seem to detract from the attention they are getting and the impact they are making. It is time for industry to be realistic about what both political parties and all levels of government recognize—consumerism now is a legitimate and powerful movement.

For that reason, and considering what appears to be a reasonable atmosphere for all concerned at the moment, I think industry should seize this opportunity to invite representatives of some of these consumer groups, including especially the most vocal critics of industry, to sit down in a working, shirt-sleeve type conference to discuss the complications and problems that must be considered in legislation of this kind. But mere discussion is not enough. To be more than window-dressing, such a conference must produce agreement by industry on points that concern the consumer groups. Total agreement is unlikely—but there must be some agreement. Such a dialogue would be an opportunity to establish a rapport in an altogether-too-rare unemotional atmosphere. And it is also an opportunity for consumer groups to find that they can work with industry toward common goals. It would be an impressive accomplishment if device legislation could pass with the support of consumer groups, government, and industry—with industry leading the way. **[The End]**

Drug Dating

By MORRIS AARONS

Mr. Aarons, a New York Attorney, Is General Counsel for the National Association of Pharmaceutical Manufacturers.

THE FOOD, DRUG AND COSMETIC ACT (201g) defines a drug as an article intended for use in the "diagnosis, cure, mitigation, treatment or prevention of disease in man and animal." In order to serve its purpose, there must be reasonable assurance that the drug meets appropriate standards of identity, strength, quality and purity. This, of course, is inherent in the fact that the methods, facilities, and controls used in the manufacture, processing, and packing of the drug are adequate to preserve these standards until it is used. This is referred to as the stability of the drug. Expiration dating is intended to express stability or, more appropriately, the instability of a drug.

The issue in the industry is whether the label of every finished dosage form of drug shall contain an expiration date. The present Good Manufacturing Practice (GMP) regulations call for expiration dating only "when needed"—the proposed GMPs, however, require that stability shall be "expressed as an expiration date with related conditions of storage on the drug label."

I think it is important to remind you that all biological products, antibiotics and insulin have statutory requirements for expiration dating. Furthermore, the new drug application (Paragraph 8p.) requires submission of an expiration date(s) that will be used on the label—or the applicant must justify its absence. It is clear that the interest of the Food and Drug Administration (FDA) in the stability of drug preparations is quite specifically expressed in the text of the Food, Drug and Cosmetic Act, and the regulations promulgated under it.[1]

[1] Food, Drug and Cosmetic Act, Sections 501, 502, 505, 506, 507, and 304; also, Good Manufacturing Practice Regulations 133.8(a)-133.9 and 133.13; and, Pub'ic Health Service Act Title 42, Section 73.

"Equally unequivocal is the fact that the scientists of the regulatory agency, like those of us who bear the burden of compliance rather than enforcement, have been unable to 'devise a formula which will guarantee all the answers to the demonstration of the stability of the drug.' "

No one can argue that in the interest of safety and effectiveness, the procedures employed in drug manufacturing, distribution, storage and dispensing should reasonably assure the integrity of the drug at the time of use. However, the virtuous objective expressed in the time-worn cliche: "Quality must be built into the product," is not always attained despite extreme efforts made by industry.

The Stability Factor

There are so many significant factors that may bear on stability as, for example, temperature, pH factor, particle size, moisture, air oxidation, method of sterilization, diluents, preservatives, containers, closures, light, and the presence of certain trace materials, that achievement of zero defects is truly an impossible dream.

"Testing the stability of pharmaceuticals is designed to determine quantitatively and/or qualitatively the changes which the products undergo during storage. The changes can involve chemical composition and physical characteristics, both of which are usually well-defined and are of proper order in a newly-made drug product of high quality. Changes in these features are signs of deterioration or instability of the drug, and measurement or evaluation of them from time to time provides an insight into the stability of the product."

Changes involving physical characteristics raise no real problem, since such changes may be detected simply by organoleptic observations. These physical parameters include odor, taste, physical appearance—such as separation of emulsion or suspension, cracking of a coating, gradual development of color, appearance of cloudiness or a precipitate, evaporation, fogging or coating of the wall of the container, and others. Industry does not find fault with testing the stability of pharmaceuticals, but with the desire that stability shall be expressed as an expiration date on all drug labels.

Dr. Lloyd C. Miller, recently retired Director of Revision of United States Pharmacopoeia said at a seminar in November, 1967:

> The conservative attitudes on expiry dating requirements of the compendial revision committees reflect in part the recognition of the problems that dated products in general pose, and of the position that a product should be considered stable until proven otherwise. It also reflects a paucity of data on keeping qualities of USP and NF[2] products. This lack is being met gradually, so that the related problem arises of correlating the data.

[2] National Formulary.

The requirement for dating pharmaceuticals has been under consideration by the different segments of the pharmaceutical community for some time. Putting such a requirement into effect would entail many problems and impose a hardship upon the manufacturer in a situation where there is serious doubt whether the benefits that might be derived exceed the disadvantages. Expiration dating is understandable in instances where the drug or drug preparation is known to be unstable, but other than that, there is no need for dating of stable preparations.

There is no serious problem where the product is stable because generally, the manufacturer will only produce a supply which can be sold and delivered within a three- to six-month period; the wholesaler will only purchase an amount he will need for turnover in three to six months; and the pharmacist or retailer will ordinarily purchase only an amount that will sell within a reasonable time. This is rational, practical, and statistically valid.

The Cost Factor

It is a well-accepted principle of business that a large inventory is an unnecessary investment of capital, costly, and could be a precarious practice. There may be particular instances when a dealer overbuys or incorrectly calculates his needs and is overstocked with merchandise which will take a longer period to sell than usual. There may be other situations, but these are the exception—and you don't make general rules for the exception.

A requirement to date all pharmaceuticals will unduly raise the cost of drugs to the consumer—particularly to those who can least afford it. With the steady increase in costs of materials, labor, and taxes, in addition to the costs of complying with the constant changes under GMP regulations, there is no justification for raising costs even higher by instituting the unnecessary requirement of dating pharmaceuticals.

I believe it is an accepted fact that virtually all products are subject to deterioration of some sort with the passage of time, but that the extent and rate vary widely among different drugs. Today, however, the more sophisticated methods, facilities and controls used in the manufacture, processing, and packaging of a drug, the specifications prescribed in the official compendia, and the guidelines set forth in the present GMPs, as well as other quality control regula-

tions, should adequately preserve the identity, strength, quality, and purity of most dosage form drugs during their normal shelf-life.

A different situation exists where the drug is known to have limited stability. The present GMPs, providing for "suitable expiration dates to appear in the labeling of the drug *when needed*," give the FDA all the power it needs to enforce expiration dating on drugs that should have it.

The Storage Factor

At any rate, how good is the correlation between what is predicted by a given procedure, and what happens when the drug is marketed? All the innumerable factors at variance with pampered in-house studies of the shelf-life of a drug or formulation make such studies almost inconsequential. The following statement appropriately poses the dilemma: "In attempting to isolate the variables which control the stability of a pharmaceutical preparation, and therefore, the selection of an appropriate expiration date, the manufacturer discovers very soon that, aside from label warnings, he can do little about the proper handling and storage of his products by others; that is,—wholesalers, physicians, nurses, community and hospital pharmacists",[3] and add to that list, shippers, and the consumer himself.

Aside from the problems of natural declining potency, deterioration and degradation processes, let us consider some of the uncontrollable factors disturbing the stability of drugs in the market, such as:

1) Storage temperature and conditions
2) Environment
3) Human frailties
4) Unknown variables
5) Shipping conditions in the various stages from manufacture down to consumer, such as:
    a) The kinds of vehicle or vehicles used
    b) Temperature and changes of temperature
    c) Time element before delivery
    d) Care in handling, holding, and delivering
6) Rotation of drugs by wholesalers and retailers
7) Transfer of the product by the pharmacist from manufacturers' container to others which may not meet official requirements

[3] Jack Cooper, October, 1965.

8) The well-closed, carefully packaged container of the manufacturer which no longer exists after initial use of the product by the pharmacist

9) The abuse of the product when it comes into the hands of the consumer;

and a myriad of other conditions.

If expiration dates are to appear on the label of all drugs, it will almost require the manufacturer to make drugs to order, instead of in bulk. This would not be progress, but regression.

Dating of all drugs would be commercially and economically unsound because the pharmacist would not purchase an item unless it contained the longest expiration period, and the consumer, likewise, would resist purchasing a product unless the full period of expiration had yet to run. This would pose a very serious problem in selling and in consumer acceptance. This resistance by the pharmacist and the consumer against short-expiration-period merchandise would be of such magnitude that the traffic in returning merchandise would become unmanageable and extremely costly.

Another serious problem would arise from the lack of qualified technical personnel to do the testing that would be required by thousands of manufacturers for many thousands of drug preparations. Further, each and every time that a formulation is changed, even minutely, or a different container is used, new batch stability studies would have to be started all over again—a never-ending procession. And, there is no assurance that the FDA would not require batch-to-batch studies. Even if these studies could be automated to a great extent, automatic equipment would not be available for a long period of time.

I believe that the chief problem lies with: 1) the failure of some pharmacists and wholesalers to rotate their inventory so as to dispose of the merchandise in relation to the date of purchase, and 2) the pharmacists' failure to dispose of old, open-bottle prescription drugs, either by returning them to the manufacturer, or by throwing them away. This problem can be successfully alleviated, at much less cost, by educating the wholesaler and pharmacist. Just because the pharmaceutical manufacturer is most susceptible under the stringent controls of the Food and Drug Act does not mean that he should be held responsible for the acts of the entire health community. It is not unreasonable to expect the pharmacists, hospital organizations, and physicians to bear their share.

Expiration dating of drugs has been under consideration for years, and has generally been resisted because it isn't workable and does not warrant the effort or cost, except in instances where the drugs are known to be unstable or to have limited stability. And with respect to these latter drugs, expiration dates, to a great extent, have already been required and supplied. Drugs on the market have been and are being examined constantly by the FDA in their laboratories in St. Louis and the various regional districts around the country. The results do not show stability to be a serious problem.

In any event, between using the date of manufacture or expiration dating, if the need be shown, the former is favored by many under a coded system. Adequate directions relating to storage would be necessary, and defining storage conditions, in itself, would raise many insoluble questions.

Conclusion

The NF has already undertaken to include a complete list of storage temperature terms and definitions. As stated in the NF Board News Release of July 11, 1969:

"In announcing the NF Board action, Dr. Edward G. Feldmann, Director of the National Formulary, stated that 'The stability—or rather the inherent instability—of many of today's complex and potent drugs requires more rigidly defined storage conditions. The general availability of efficient refrigeration and air-conditioning equipment now makes it possible to provide more carefully controlled storage temperatures for pharmaceutical products at all levels of drug distribution. The NF Board considered that these revisions would provide much needed preciseness and would bring the respective definitions into greater accord with present-day usage and practice.'"

Establishing the requirement for expiration dating, particularly of the drugs contained in the official compendia, should be the prerogative of the revision committees or the appropriate boards of the USP and NF.

The National Association of Pharmaceutical Manufacturers Technical Committee had reviewed the proposed GMP regulations, and during our discussion, an argument was made that opposition would be a futile gesture if the large or competitive companies would use expiration dates, since this could be a competitive advantage. Although this may be true, at least it would be a voluntary act and would not be by force of regulation.

It is my conclusion that a general requirement for expiration dating of all pharmaceuticals will not serve the best interests of all concerned, and particularly, the consumer interest. **[The End]**

FDA Procedures

By WILLIAM R. PENDERGAST

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"FDA PROCEDURES" is a title which is certainly not particularly eye-catching or one normally calculated to insure a full house. The reason why I have been asked to speak on this subject is, of course, the special committee which I chaired to recommend improvements in the Food and Drug Administration's (FDA) hearing procedures. I shall discuss that committee's progress at a later point, but I think that the program title given to me is a license to travel somewhat farther afield than that one aspect of FDA procedures.

All who have been dealing with the FDA in the last few years know full well just how important the procedures by which an agency such as FDA functions are. It is obvious that the procedures by which FDA conducts its business largely determine whether that agency is fair and just both to the consuming public which the FDA is designed to protect, and to those companies and industries which are regulated by FDA. The so-called procedural niceties by which an agency operates are not just neat formalisms which we lawyers find comfortable and intriguing. They are far more important than that, an importance which has been put in proper perspective by various Justices of the Supreme Court who have pointed out, for instance, that "procedural fairness and regularity are of the indispensable essence of liberty . . ."[1], and that "the history of liberty has largely been the history of observance of procedural safeguards."[2] Clearly, sound procedures are the stuff by which due process is assured and therefore deserves our closest study. As I said, this has been strik-

[1] *Shaughnessy v. United States Ex Rel Mezei,* 345 U. S. 206, 224 (1953) [dissenting opinion].

[2] *McNabb v. United States,* 318 U. S. 332, 347 (1943).

ingly apparent in the activities at FDA within the last two years. I shall discuss but two areas. The first is the administrative hearing on the dietary regulations. The second is the method by which the National Academy of Sciences-National Research Council (NAS-NRC) drug evaluations have been implemented by FDA.

Lack of Adequate Procedures: Vitamin Hearing

The vitamin hearing is a tragedy, a veritable litany of administrative failures and lapses. For reasons not easily apparent, the FDA chose, in this one proceeding, to very closely regulate many separate and diverse industries and interests. The food industry is affected, the dietary supplement industry is affected, the health food industry is affected, the drug industry is affected, every consumer who is concerned about his dietary intake is affected, and, in fact, the nutritional status of the entire population will be affected by the outcome of this hearing. Long before the hearing ever began the chief counsel for the agency acknowledged that it would be a hard-fought battle.

In spite of all this, the hearing regulations in existence at the time the hearing began were hopelessly inadequate for such a mammoth undertaking. There were no guidelines for the hearing examiner as to how to control a proceeding with 110 parties, each one with different and diverse interests, opposing regulations which may raise literally thousands of separate fact and scientific issues. There were no guidelines for marshalling the mass of evidence which was to come forth, for controlling cross-examination while protecting the rights of parties, or for any of the other literally thousands of procedural problems which could and indeed have arisen in this hearing. There were, simply, no controls. On other aspects of this hearing, I can only say that the procedural failures of FDA in providing for a machinery by which to conduct this hearing were only compounded by the appointment as hearing examiner of a man with no prior experience as a hearing examiner and no experience at all in the intricacies of food and drug law or regulations. Mr. Harris has made a tremendous effort to overcome the many problems he has faced, but it is obvious that, in what must be the most important hearing of the last quarter-century at FDA, the public interest would have been better served by a more experienced man.

Procedures for FDA Implementation

The vitamin hearing is an example of the lack of adequate procedures. The procedures which have evolved for the implementation of the NAS-NRC reports are the other side of the coin. Here, too many procedures were devised to implement the reports without giving the companies involved adequate opportunity to contest FDA's action. Let's look at what has happened. The NAS reports are all in and have been for some time, but the companies are not being told the results except in small doses as announcements in the *Federal Register* are made. This is obviously very poor procedure, and I am happy to note that the Federal Court in Delaware has pointed up the confusions in this implementation of the NAS reports. The court says "while the Commissioner asserts that it would create serious confusion to release all these panel reports immediately, the drug companies have indicated substantial concern about the possible future action which may be taken against their drug products based on the unreleased panel reports."[3] He implies that this inadequacy should be reformed.

The *Pharmaceutical Manufacturers Association* (PMA) case, from which that quotation was taken, deals with another aspect of FDA-NAS-NRC procedures. We all know that last September FDA published regulations describing what, in FDA's opinion, was substantial evidence of a drug's efficacy, and ruling out any other tests or data which do not meet FDA's own, self-designated, standard. In order to obtain a hearing on an FDA proposal to take a drug off the market, a company had to demonstrate that its proposed evidence met FDA's criteria. Such regulations obviously have a tremendous impact upon the industries, but the FDA chose to use a procedural method for publishing them which deprived the industries of any opportunity to show to the FDA the illegality of these regulations, the fact that they are scientifically unsound, or even the fact that FDA does not itself follow them.[4] Instead, the agency chose to assert that these regulations are merely procedural and that no one is entitled to comment on them.

Fortunately, the Federal Court in Delaware, in the lawsuit brought by PMA, disagreed and said that regulations of such import should, under the Administrative Procedure Act, be published for comment

[3] *PMA v. Finch, et al.*, CCH FOOD DRUG COSMETIC LAW REPORTS ¶ 80,292, DC Del 1970 (January 16, 1970) page 22.

[4] Footnote 3 above, pages 16 and 17.

so that the agency can have the benefit of all the views of the industry before publishing them in final form. The Court did not say that the regulations were wrong, although other courts have their doubts. The agency was enjoined from enforcing these procedural regulations.[5]

Without discussing the merits or the legalities of the regulations, we can note what all this tells us about poor administrative procedures. The first NAS evaluation was made public in a *Federal Register* announcement on January 23, 1968.[6] Since that time, now almost exactly two years, not a single drug has been removed from the market on the grounds of ineffectiveness, absent the consent of the manufacturer. No hearings have been held to determine whether FDA's assessments of efficacy are accurate, and apparently the machinery has ground to a halt. Evidently, FDA believes that the hearing regulations and procedures provided for in the law are the culprits and responsible for this delay, for quite clearly, the action in regard to the antibiotic combinations and the September 19 regulations were procedures designed for the sole purpose of cutting companies off from hearings. Now it seems that these procedural innovations are themselves the cause for still further delay. FDA decided that this delay was being caused by the hearing mechanisms provided in the Act. Whether we think hearings are proper or not, or whether a drug company can ever win a new drug revocation hearing is beside the point. The point is that the agency decided on its own to deprive the industry and the public of what appears to be a statutory right to hearing without the slightest consideration of the philosophy and requirements of the Food and Drug Act or the Administrative Procedure Act. The result has been even more delay. The industry quite properly challenged this action, and now the agency, operating under court order, must devise new regulations and afford the industry an opportunity to comment. This will delay everything further.

I don't think anyone can say that this sort of delay is in the public interest. If there are drugs which are on the market which are genuinely ineffective, the 1962 Drug Act requires that they be removed. How much simpler it would have been two years ago, instead of trying to throw out hearings altogether, to have held a series of hear-

[5] *PMA v. Finch, et al.*, footnote 3 above, page 27.

[6] 33 *Federal Register* 818, January 23, 1968, Food, Drug and Cosmetic Docket FDC-D-112.

ings right away. Whatever drugs were involved would be long gone from the market by now, if the FDA prevailed, and the rest of the industry would have seen that the FDA could put on a case and that it either is or is not good enough to convince a hearing examiner and ultimately the courts. If that had been accomplished, and I think it could have been long ago, I am sure that other companies would have taken a long, hard, look at determining whether or not to fight an FDA revocation proceeding. In short, I think if the agency followed traditional procedures available to it and pushed them with administrative control and dispatch, we would be in a much better situation than we are today. As it is, the agency is now fighting several lawsuits, the regulations for controlling hearings are in limbo, and drugs which FDA says are ineffective are not being removed from the market. In short, the whole process is at a virtual standstill. All I am suggesting, is that sound procedural mechanisms, both in the law and in the regulations, are our best safeguards and best assurance that the law will be followed. Loose procedures, such as in the vitamin hearing, or new and novel procedures which violate the Administrative Procedure Act, such as in the NAS-NRC situation, only delay matters and accomplish nothing. It is not by accident that lawyers are conservative when it comes to changing procedures. First of all, tested procedures are usually within the scope of the law and, secondly, having been subject to the test of time, they function. These are the goals of sound administrative procedures and goals which I would hope FDA will seek to put into effect. The PMA decision of January 16th gives FDA an opportunity, in the case of the NAS-NRC situation, to reform its procedures and to provide a mechanism which grants the statutory hearing with dispatch and fairness. If, as FDA suggests, they want summary judgment procedures, then I favor them, if done properly, as in federal courts, where the hearing examiner can weed out the true case from the sham litigation. Such innovations follow traditional precepts of the civil courts and could be implemented without the delays caused by the September 19th regulations.

Under such a procedure, once a hearing is requested the examiner would conduct a pre-hearing conference at which time the issues

would be discussed and then either party could file a motion for summary judgment asserting that there are no genuine issues of fact. If the position were properly justified the hearing examiner could enter an order to that effect. If, however, there were genuine issues of fact, the hearing would proceed in the usual manner.

Committee Recommendations

This brings us to the recommendations which our Committee made, all of which deal with methods for improving the conduct of FDA hearings. Their purpose is to provide a means for the examiner to control the hearings, to make it expeditious, and, most importantly, to insure that they are fair. I shall not detail our recommendations, but mention just that one applicable to my last statement. We have recommended that no employee of the Department of Health, Education and Welfare (HEW) or FDA who participates in the conduct of a hearing should be allowed to participate in the decision. While this recommendation deals with 701 hearings, it is obvious that it is applicable to all hearings, and this recommendation will insure that FDA people who take a fixed position regarding a drug will not decide whether or not we have successfully contested their case. Our recommendations were forwarded to the Council of the Administrative Law Section of the American Bar Association last October, and that Council endorsed them with modifications. The Council then authorized the presentation of these recommendations to FDA and recommended their adoption as soon as possible. They were forwarded to Secretary Finch and the Commissioner of FDA early in December, and their receipt has been acknowledged by the General Counsel of HEW. As of today, we have had no further word as to their opinion about these proposals. I want to state that we are ready to do everything we can to make the FDA procedures sound, reliable and equitable, and that we shall cooperate in any manner possible to achieve those ends. **[The End]**

Intensified Drug Inspection Program

By WARREN E. WHYTE

Mr. Whyte Is Senior Attorney for Abbott Laboratories.

IN EARLY 1968, the Food and Drug Administration (FDA) announced the Intensified Drug Inspection Program (IDIP), and subsequently, a high-level FDA official revealed FDA's purposes and reasoning for the IDIP. We heard that FDA had concluded that some systems had to be devised to counteract the continued failure of many drug firms to bring their operations into compliance with good manufacturing practices, and to counteract the continued high incidence of subpotent and other improperly compounded and labelled drugs on the market. FDA considered four alternatives to remedy this situation: batch-by-batch certification; product licenses for each drug manufactured; resident inspectors placed in each drug plant; or intensified inspections. According to the "Pink Sheet," FDA felt that it might lack statutory authority for the first three alternatives, so they opted for IDIP.

To understand FDA's purposes in initiating IDIP, we must recall Dr. Goddard's promise to Senator Nelson that FDA would be able to assure *by 1970* that all drugs manufactured in the United States are in compliance with all applicable standards.

Dr. Goddard, then FDA Commissioner, also explained in May, 1968, the priorities for a drug manufacturer receiving an intensified inspection. He said priority would be based on marketplace impact and would be measured by dollar volume. A significant history of recalls, seizures, injunctions, prosecutions and in-plant violations would also be important. Thus, if your client has not as yet received an IDIP he can probably stand a little taller, although there are indications that FDA is not necessarily following these guidelines today.

The basic concept of IDIP is that it will give the FDA an opportunity to obtain an in-depth overall understanding of a drug manufacturer's operations. It will also afford FDA an opportunity to study the manufacture of selected products in considerable depth. There is also the concept that this is a cooperative program for the benefit of both the government and industry. As a result of Abbott's intensified inspection, and numerous conversations with the FDAers, we are convinced that this is truly their attitude and their policy. Nevertheless, FDA has also made it clear that regulatory actions may result if FDA is not ultimately satisfied with the practices of the manufacturer and the changes he makes pursuant to their recommendations. The fact that, of the first twenty-two IDIPs completed, four resulted in suits for injunctions, clearly demonstrates that this is not idle talk.

I think it might be helpful, for those of you who have not been involved in an IDIP, to review the manner in which it is handled in practice. I will also give my suggestions as to the role of the attorney in this procedure.

I must preface my remarks, however, by mentioning that my experience is limited to the Chicago District of FDA. I understand from discussions with my New York brethren, and with attorneys in other areas, that IDIPs are handled differently in different Districts.

Unlike the usual FDA factory inspection, where the inspector shows up unannounced at the door with a Notice of Inspection, the IDIP is preceded by an invitation to a meeting at the FDA District Office. In our case, we discussed the matter with attorneys for several other drug manufacturers who had already commenced their IDIPs. From such input, and from the information that our regulatory people had obtained from their counterparts, we were able to plan what we would seek from FDA in the way of understanding the conduct of the inspection. FDA requested that our President attend the meeting. However, as a lawyer, I have basic concerns about personally involving top management in plant inspections in view of the *Dotterweich* holding concerning corporate officials. At the meeting, we were introduced to the two inspectors who would conduct the IDIP, and were given a brief presention on FDA's philosophy and purposes in conducting such an inspection. We then discussed the ground rules for the inspection. If discussing "ground rules" for an FDA inspection sounds a little unusual to those of you who are more accustomed to the routine type of plant inspection,

I would concur. But IDIP is not a routine inspection. We are aware, and I think FDA is too, that the IDIP is probably beyond the several "reasonable" constraints of Section 704. I feel reasonably certain that one could terminate an IDIP as being beyond FDA's statutory inspection powers, and not be found to have been wrong by the courts. Thus, I think FDA is willing to discuss mutual understanding as to the scope of the inspection—both parties have the desire to have the inspection proceed as smoothly as possible.

Points of Understanding

Upon returning from our meeting, we prepared a letter to the District Director setting forth twelve specific points of understanding on the scope of the inspection. We felt that such written communication was important, since it could be used as a reference if any disputes arose later with the inspectors or the district officials. Also, we wanted to establish a few legal positions quite clearly.

I will review some of our major points:

1. We identified the Senior Inspector so that we would know at all times who was in charge. We also stated that as we had only two liaison persons available, and since we required that an inspector be accompained by a company representative at all times, we must request a limitation on the number of FDA personnel in our plant at any one time.

2. We identified our liaison representatives. We required that these persons be contacted whenever the inspectors entered the plant, and that the inspectors not go anywhere on our premises without these men. All requests for information were to be directed to these two men, and FDA was not to make any contacts with any other employees without their approval.

3. We stated that the inspection was to pertain to compliance with current Good Manufacturing Practices (GMPs) or other applicable legal standards. The present GMP regulations were to be the guidelines for FDA, and any proposed additions to those regulations were not to be relied upon until they become final. As you know, substantial amendments to the GMP regulations have been proposed by FDA, and we do not want to get involved in discussing them until they become final.

4. We stated that any "significant deviations from GMP" be reported to us in writing. FDA concurred. I think that this is helpful not only in identifying alleged major problems, but

that FDA would have real difficulty in basing a GMP suit on any violations which they had not communicated to us in writing. We also requested weekly meetings to discuss the inspection made during that week, and for FDA to give us notice of the areas to be inspected during the following week. FDA concurred.

5. In connection with the waiver of statutory rights problem, we stated that we would regard IDIP as one continuing inspection, but that we would require a separate notice of inspection for each additional inspector, or from an inspector if he was absent from the plant for more than five consecutive working days.

6. We determined that a serious problem is the availability to FDA of the written reports that many companies prepare as a part of their self-inspection programs. I suspect that most of your clients have such self-inspection programs, and that you have thought about the problems of discovery of those reports. We informed FDA that they would not be given the reports. FDA replied in an equally direct manner that they are subject to Section 704 inspection. However, they haven't asked for them as yet.

7. We requested, and FDA agreed, that we be given copies of the analyses of any samples within twenty-four hours of the availability of the results to FDA.

8. We requested that any disagreements between us and the inspectors could be taken immediately to the District Director. He agreed. The purpose of this was to have it clearly understood that it is proper procedure for us to appeal to the District Director in the case of any disputes with the inspectors. We have had no such disputes during the IDIP.

9. We requested that every effort be made to expedite the completion of the IDIP. We have been disappointed in this regard. Our IDIP has now dragged on for over a year. I would suggest seriously to those who have not begun an IDIP to attempt to reach a fairly concrete understanding with FDA as to its maximum duration. Certainly, a long drawn-out plant inspection is a burden to a manufacturer, and the extent of that burden must be seriously weighed by the attorney advising his client concerning participation in an IDIP or similar inspection. We stated that we reserve the right to terminate the IDIP at any time. In response, FDA simply stated that they recognized this as an inspection authorized under Section 704 of the Act.

10. Finally, we stated that our cooperation with the IDIP is to be construed as neither a waiver of any of our Constitutional rights, particularly those under the Fourth Amendment pertaining to searches, nor as a waiver of any of our rights pursuant to Section 704 of the Act.

Statutory Authority

In that regard, a few brief observations about Section 704. Of course, FDA's inspection rights in a manufacturer's plant are based primarily on this section. Personally, I find it one of the more fascinating sections of the statute. I think it extremely important that all attorneys for pharmaceutical manufacturers be conversant with the legislative history of Section 704 in order to understand fully the import of several of the terms used there. The history leading up to the enactment of the Wolverton Amendment in 1953 is most enlightening. This amendment was proposed as a result of the *Cardiff*[1] decision of the Supreme Court in which certain aspects of the factory inspection authority were declared unconstitutional. The 1953 Amendments to Section 704 were originally intended to provide only statutory authority for compulsory factory inspection. However, the legislative history clearly indicates that the scope of such inspections was seriously studied by the Congress, and that the wording of Section 704, as amended, is intended to prescribe the extent of the inspection authority. I recommend the article by Charles S. Rhyne and Eugene F. Mullin, Jr. in the January, 1954 Food Drug Cosmetic Law Journal[2] for a comprehensive discussion of the congressional hearings and reports and their real import.

We all know that Section 704 states that inspections are to be "at reasonable times," "within reasonable limits," "in a reasonable manner," and are to be "completed with reasonable promptness." The use of the word "reasonable" at four different places is not mere surplusage. The legislative history clearly shows that Congress intended these words to act as limitations on FDA's inspection authority. The history also discusses various types of items that are to be subject to inspection, and items that are not subject to inspection. It also indicates that the listing in Section 704 of specific things to be inspected was intended as a limitation on FDA's authority, despite the presence of more general terms such as "to inspect."

[1] *U. S. v. Cardiff*, 344 U. S. 174 (1952).

[2] "Inspect What? A Study in Legislative History," p. 18.

The 1962 Drug Amendments, of course, enlarge the scope of inspections insofar as prescription drugs are concerned. However, there are provisions in that amendment to Section 704 which do not seem to receive too much attention. The amendment states that "records, files, papers, processes, controls, and facilities" *bearing* on whether prescription drugs are adulterated or misbranded, or may not be manufactured, or introduced into interstate commerce, "or otherwise bearing on violation of this Act." Therefore, as I read it, FDA may not inspect all of these documents pertaining to prescription drugs unless they can demonstrate that such documents bear on a violation of the Act. In order to do this, they must produce something tangible that indicates that a violation of the Act may have occurred.

The Attorney's Role

What is the attorney's role in the IDIP? I see it as three-fold.

First, all involved company personnel must be given guidance as to the statutory scope of FDA's inspection authority. Abbott Laboratories does this through the use of policy statements for our manufacturing divisions, distribution centers and sales representatives. Of course, during an inspection there will be numerous requests to the attorneys for opinions as to whether a specific FDA request for information or documents should be granted.

The attorney's second function is to be alert as to whether the cooperative and educational aspects of the IDIP have turned into an effort to gather evidence on which to base a lawsuit. Since FDA has already initiated several injunction suits resulting from IDIPs, that possibility must always be kept in mind. In such an event, of course, the cooperative attitude of the manufacturer in supplying information and documents would have to be seriously reevaluated. The attorneys at Abbott do not ordinarily accompany the inspectors, but we attempt to keep abreast of the trend of an inspection by obtaining periodic reports from our liaison personnel who are highly experienced, and who would be sensitive to such an unfortunate turn of events.

Finally, the attorney must deal with the tricky problem of waiver of Constitutional and Section 704 rights. The Supreme Court, in *Camara*[3] and *See*[4] held, in effect, that FDA may not enter a manu-

[3] *Camara v. Municipal Court*, 387 U. S. 523 (1967).

[4] *See v. City of Seattle*, 387 U. S. 541 (1967).

facturer's premises without a search warrant if the manufacturer elects to stand on his Fourth Amendment rights. The Court held that governmental inspection searches were unreasonable within the meaning of the Fourth Amendment, and that any statute providing for penalties for refusal to permit such an inspection without a proper warrant is unconstitutional. I presume that takes care of Section 301(f) of the Food and Drug Act. However, the question arises concerning the circumstances under which we may be held to have waived that right by voluntarily consenting to an FDA inspection. The *Stanack*[5] decision gives us some direction in this regard. In this case, it was held that even though the company had permitted an FDA inspection to commence, the company could subsequently refuse to supply certain records without having waived their Fourth Amendment rights. It is also important, I think, to maintain the position that you have not waived your rights pursuant to Section 704. If the facts should demonstrate that you had voluntarily consented to an inspection *without limitation,* then, possibly, it could be held that you could not limit the inspection to the scope of Section 704. Thus, I think it is necessary to establish clearly with FDA that the IDIP is a Section 704 inspection. Moreover, I think it is wise to obtain Notices of Inspection at proper intervals reciting that the inspection continues to be under Section 704.

Conclusion

In conclusion, there have been many inspiring statements both by FDA and by industry representatives as to the great purposes and expected accomplishments of IDIP. FDA, we are told, is going to help us make better drugs and to assist us in bringing our manufacturing operations into "compliance." We, in turn, are going to allow FDA to assure the American public that the drug industry is producing quality products in compliance with all applicable standards. These are indeed laudable objectives. However, the IDIP effort has already fallen far behind FDA's original schedule. When such inspections will be completed at the originally-reported 250 target companies, or at the more than 1,000 drug manufacturers in the United States, is anyone's guess. Only at that far distant date will we be able to venture opinions as to whether IDIP was a success.

[The End]

[5] *U. S. v. Stanack Sales Co.*, 387 F. 2d 849 (3rd Cir., 1968).

How the Chemical-Pharmaceutical Industry Views the Government's Patent Policy

By HOWARD I. FORMAN

Mr. Forman, Author, Contributor and Advisor in the Area of Patents, Is a Patent and Trademark Counsel of Rohm and Haas Company.

A PREREQUISITE TO CONSIDERING the views of the chemical-pharmaceutical industry regarding the government's patent policy is to understand what that policy is. Fortunately, we have a fairly expository statement of that policy, and it is applicable to all federal agencies not subject by statutory law to other requirements.

After more than 85 years of avoiding the issue of establishing a definitive government patent policy each time it chanced to be raised in the executive, congressional or judicial branches of the federal government, on October 10, 1963 President John F. Kennedy came to grips with the increasing problem, and he published his Memorandum and Statement of Government Patent Policy, stating that:

> The prudent administration of government research and development calls for a government-wide policy on the disposition of inventions made under government contracts reflecting common principles and objectives, to the extent consistent with the missions of the respective agencies. The policy must recognize the need for flexibility to accommodate special situations.

Having thus stated the purpose or need for such a policy, President Kennedy specified the policy in broad outlines. One of its major provisions is that the government shall, with some rare exceptions, normally obtain exclusive world-wide rights to inventions made in the performance of government contracts, subject to a non-exclusive right in the contractor, in essence where: (1) the principal purpose of the contract is to make something for a commercial use, particularly

a governmentally-required use; (2) the principal purpose involves the public health, welfare or safety; (3) the subject of the contract involves research into a field which has been mainly the province of government-funded investigation; or (4) the contractor is to operate a government-owned research facility or coordinate the work of others. In another of the policy's major provisions the contractor normally would retain exclusive rights, subject to the government's non-exclusive license, where the work builds upon existing knowledge or technology in which the contractor has special competence and an established non-governmental, commercial position.

In the first posture, the government takes title in situations where the facts and the equities appear heavily weighted in the direction of considerable government investment in terms of funds and public welfare interests. In the second posture, the contractor takes title in situations where the contractor's investment prior to taking the contract appears so heavily weighted as to over-balance the contribution which the government makes to the new project. These two postures are reflections of what has been called the "fairness and equity" approach to resolving the question of whether the government or the contractor should keep title, the resolution being predicated on the compromise viewpoint that, except where public welfare is involved, title should belong to the party which has made the major investment to the projects leading to the inventions in question.

Departure from the "Fairness and Equity" Approach

In a departure of major importance from the purely expedient "fairness and equity" approach, the Kennedy statement of government patent policy makes it possible for the contractor to keep title where the interested government agency is satisfied that the public interest is best served by permitting the contractor to acquire title if he gives promise of making the inventions available to the public within a reasonable period of time. In certain situations, the policy recognizes that to encourage utilization of the inventions, and the potential contributions to the public welfare, are at least as important as seeking to prevent alleged "give-aways" of government rights to the inventions based upon the investment the government may make in paying for research contracts incident to which inventions are made.

Less than two years after the Kennedy Memo and Statement was promulgated, Senator John L. McClellan, as Chairman of the Senate Judiciary Committee's Subcommittee on Patents, Trademarks and Copyrights, held hearings on S. 1809 (89th Congress) a bill he had

introduced under the designation "Federal Invention Act." On the opening day of those hearings, June 1, 1965, he said:

> In recent years the Congress has frequently considered the inclusion of patent provisions in legislation authorizing new Government research programs. However, not every agency is subject to specific statutory patent policies and diversities of patent practices developed among the various departments and agencies.
>
> From the attention which Congress has given to this subject it is clearly its intent that the basic guidelines of Government patent policy should be determined by the Congress. In an effort to find a basis for a reasonable solution of this complex question, I introduced, during the 88th Congress, S. 1290. After the introduction of my bill, President John F. Kennedy issued a memorandum of Government patent policy. I then indicated that I regarded President Kennedy's statement as a constructive contribution which would be of considerable assistance, *but that the need for legislation persisted. I believe subseqent events have amply confirmed the desirability of Congress discharging its constitutional responsibility in patent matters by enacting a comprehensive Government patent policy.* (emphasis supplied)

S. 1809 resembled the Kennedy Memo and Statement very closely. After extensive hearings lasting a total of seven days in June, July and August 1965, the bill was reported to the Senate Judiciary Committee which also acted on it favorably. But it failed to be considered by the entire Senate prior to the expiration of the 89th Congress and so it expired along with that Congress at the end of 1966.

In September 1966 the Committee on Government Patent Policy of the Federal Council for Science and Technology initiated a study of the effects of the Kennedy Memo-established government patent policy. The stated object was to secure information which would help the President and Congress decide as to what policy changes, if any, should be made. Harbridge House, Inc. of Boston was commissioned to make that study which was completed and a final report submitted in May 1968. The Harbridge House study and report was an outstanding piece of work. Many case studies and other investigations confirmed the conclusions reached by earlier researchers reported on by the Patent, Trademark and Copyright Research Institute of The George Washington University, and which helped to form the basis for the government patent policy established by the Kennedy Memo. It did, moreover, point up the need for liberalizing that policy so as to make the invention-utilization concept an even more dominant part of the policy than it had been originally.

Industry's Views on Government Patent Policy

The stage is now well set for a return to the legislative arena, a return to the Congress which, as Senator McClellan pointed out,

is responsible under the Constitution for enacting a comprehensive patent policy. Since that policy, if it does come up for legislative consideration in the near future, is likely to closely parallel both the provisions of the Kennedy Memo and the McClellan Bill, S. 1809 referred to earlier, to determine the views of the chemical industry concerning the policy is relatively simple. Since most of the major segments of the industry testified regarding S. 1809, a review of that testimony will give a fairly clear picture of the industry's position. A personal check, made in the past few months by the present author, has disclosed that each of the industry segments reported on has made no change in its position since presenting its testimony in 1965.

Referring first to the Manufacturing Chemists' Association, whose membership consists of approximately 194 U. S. corporations accounting for over 90% of the productive capacity of the chemical industry in the U. S., it supported S. 1809 with suggestions that only a few minor amendments be made to clarify the bill's language. Moreover, the spokesman for MCA expressed a belief that "a uniform national policy concerning ownership of inventions made during Government-sponsored research is necessary because the huge size of Government research demands a coherent and well-considered approach to the many and ever-growing facets of Government-sponsored research."

The American Institute of Chemists testified that it approved the principle underlying S. 1809, its spokesman saying: "Basically we are in favor of the establishment of a uniform national policy concerning property rights to inventions resulting from Government-sponsored research and development. Further, we favor that legislation which will, in most cases, permit the contractor to take title to patents resulting from the contract research. . . . We feel that an overall Government title policy will work against the best interests of the public as a whole. I may say that public interest is the only basis on which these decisions are properly made. We believe that a license policy, or modification thereof as provided in S. 789 and S. 1809, will be most likely to result in maximum benefits for the Nation as a whole."

The Pharmaceutical Manufacturers Association (PMA), a trade association of 136 manufacturers producing over 90% of the nation's prescription drugs, with certain specific suggestions for amendment, favored S. 1809, stating: "The intent of S. 1809 . . . is to recognize and follow the principle that many inventions will not reach the public unless exclusive rights in some form are provided. To this we subscribe on the basis of philosophy and in terms of practical experience

as it has unfolded particularly during the past few years." PMA's basic exception to S. 1809 and to the Kennedy Memo concerns the provision in both that the government normally takes title in contracts where the object is to explore into fields of direct concern to the public health, welfare or safety. Holding this provision to be unwise, PMA contends that "when the purpose of a contract is to explore the fields of public health, welfare, or safety, we think it is even more important, rather than less important, to encourage the perfection and marketing of the inventions. We do not believe that any different economic principles should apply because an invention results from such contract."

The wisdom of this objection was singularly noted in the Harbridge House report when in 1962 the pharmaceutical industry almost entirely refused to cooperate with the National Institute of Health's (NIH) Medicinal Chemistry Screening Program. This was due to an NIH requirement that drug manufacturers agree to yield title to inventions they made if the government's grantee investigator participated in the conception or reduction to practice of the inventions. However, in 1969 the Department of Health, Education and Welfare (HEW) abandoned that policy, thus setting the stage for resumed collaboration with the industry and university researchers.

The American Association of Colleges of Pharmacy (AACP), whose representative testified that it consists of 74 member colleges engaged in scientific research, appeared to favor S. 1809 with the exception of Section 4 thereof. The objection regarding Section 4 was that the requirement that the government take title where the invention relates to health would shut off the cooperation given by pharmaceutical manufacturers in screening drugs made by researchers in federally-funded pharmacy colleges. The AACP favored modifying Section 4(a)(2) of S. 1809 so as to treat inventions in the health field no differently than inventions in all other fields in order to stimulate incentives to developing health inventions.

The American Chemical Society (ACS), whose representative pointed out that "it is the largest membership organization devoted to a single science in the entire world", found S. 1809 generally acceptable but also opposed Section 4(a)(2) of that bill. The ACS representative said on this point: "If incentive for investment is necessary to make inventions available to the public in other areas—in a better paint or a better fiber or a better rubber—it should certainly be available to stimulate development in such vital areas as health, welfare and safety. So we believe that there is no reason to

exclude this very important area from the benefit of the incentive provided by the patent law."

The American Institute of Chemical Engineers (AIChE) did not testify at the McClellan committee hearings. It has formed an ad hoc committee to keep its council informed on patent matters, but has to date published no position in connection therewith.

I would suggest that AIChE would do well to study the government's patent policy and to develop its position in that area of interest. I submit it is past time for Senator McClellan to resume action on the equivalent of his S. 1809, preferably amended in view of the Harbridge House Report, new HEW regulations on exclusive licenses, plus the specific amendments to the Kennedy Memo and Statement which in late 1968 were recommended to the Federal Council for Science and Technology by its Committee on Government Patent Policy (based on the Harbridge House findings and experience gained in five years of operating under the Kennedy Memo).

As Senator McClellan himself said when he opened the hearings:

> . . . events have amply confirmed the desirability of Congress discharging its constitutional responsibility in patent matters by enacting a comprehensive Government patent policy now.

The chemical/pharmaceutical industry, in its separate and collective testimony favoring McClellan's S. 1809, with relatively minor exception, agreed with him in 1965. Nothing in the past five years appears to have happened which should change the view expressed by Senator McClellan or by the chemical/pharmaceutical industry. The only events concerned with government patent policy in that period of any significance were the publication of the Harbridge House Report, the change in HEW policy described previously, and the issuance in November 1966 of the Report of the President's Commission on the Patent System. The President's Commission, in its Recommendation No. 32, decided not to make specific recommendations regarding government patent policy because that question was "being considered actively elsewhere in the Executive Branch and by Committees of the Congress." But it expressed the hope that:

> . . . any action Congress may take in this regard will promote the purposes of the patent system to encourage invention and innovation and the resulting economic development and benefits.

All three actions were harbingers of the legislatively enacted comprehensive government patent policy which Senator McClellan had said was highly desirable. The chemical/pharmaceutical industry, which agreed with him, would do well to remind the senator of his own statement and urge that he back it up with action *now*!

[The End]

Reasonable Grounds, Substantial Evidence, and Law and Order

By VINCENT A. KLEINFELD

Mr. Kleinfeld, a Member of the District of Columbia Bar, Read This Paper at a Meeting of the National Association of Pharmaceutical Manufacturers on February 5, 1970.

"REASONABLE GROUNDS, SUBSTANTIAL EVIDENCE, and Law and Order" is a rather peculiar title, but I believe it is apropos. The situation which came to pass with the creation of the National Academy of Sciences-National Research Council (NAS-NRC) panels, and the problems which arose after the receipt of the panel reports, seemed rather unusual to everyone except, possibly, to attorneys in private practice who had specialized in food and drug law. I do not know of any others who did not find it somewhat strange that a drug such as Panalba, after many years of use with continuous approval by the Government as to safety and efficacy, and with the reputation it possessed among thousands of reputable physicians and internists of being a valuable addition to their armamentarium, could be removed from the market without a hearing. It appeared to many that, even if the law did not require a hearing, one would be granted because of the history of the drug. It seemed clear, however, that Congress had provided for hearings.

For a considerable time prior to the refusal of the Government to grant hearings after adverse panel reports, one of the few legal specialists in the food and drug field had prophesied that this would come to pass. He had pointed out in a number of speeches that as the years passed, there was a growing disinclination on the part of the Food and Drug Administration (FDA) to grant hearings, and that this would probably extend even to the revocation of an approved

new drug application. Like Cassandra, however, who was cursed by the gods so that her accurate prophesies would never be believed, his predictions were not accepted. This vitally important change in the basic philosophy of the Government was understandable, for it was based on the fact that in most instances, the Food and Drug Administration had considered the pertinent data, come to a definite conclusion, and felt that the public good required swift action.

Why does part of the title of this paper contain the words "law and order"? It is because I still believe in what used to be the basic principles of democracy: that if you did not like a law you sought to repeal it, and that if additional legislation were needed, this was brought to the attention of Congress. If these views make me a member of the establishment, I plead guilty to the soft impeachment.

The new drug section of the Food, Drug and Cosmetic Act provides, in part, that the Secretary of the Department of Health, Education and Welfare, after due notice and an opportunity for a hearing have been given, shall withdraw approval of an approved new drug application if he determines that there is a lack of substantial evidence that the drug will have the effect it purports to have, or is represented to have, under the conditions of use prescribed, recommended, or suggested in the labeling. With respect to antibiotics, the Act declares that any interested person may file a petition with the Secretary proposing the repeal of any antibiotic regulation. The Secretary is directed to give public notice of the proposal, and an opportunity for all interested persons to present their views. Thereafter, any interested person may file objections, specifying the changes desired, stating reasonable grounds for the changes, and requesting a public hearing. The Secretary is then directed to hold a public hearing.

It may be noted, somewhat parenthetically, that although "substantial evidence," as defined in the new drug section, consists of adequate and well-controlled investigations, including clinical investigations by experts qualified by scientific training and experience to evaluate the effectiveness of the drug, this definition is not contained in the antibiotic section. As stated, the antibiotic section does provide that reasonable grounds must be shown by the company seeking the hearing, and I do not quarrel with this. But I do not see how "reasonable grounds" can be equated with "substantial evidence."

The NAS-NRC Panels

What occurred in connection with the establishment of the NAS-NRC panels, and subsequent to the completion of their reports, is worthy of some discussion. The Food and Drug Administration requested the NAS-NRC to establish panels of experts to determine whether new drugs which, prior to 1962, had been approved by FDA only as to safety, were effective. This was done because the Drug Amendments of 1962 had added the criterion of effectiveness to that of safety. Although the criterion of efficacy had been included prior to 1962 with respect to antibiotics such as Panalba, the opinion of the NAS-NRC as to these drugs was also sought. FDA requested that one of four ratings be given to every drug which was evaluated: effective, probably effective, possibly effective, and ineffective.

The panels, who were "predominantly physicians with academic affiliations," took it upon themselves to add other categories, "Effective, but . . . " and "Ineffective as a fixed combination." The latter class was established primarily to deal with combination antibiotics. This was based upon what the panelists stated was a basic principle of medical practice—that more than one drug should be administered for the treatment of a given condition only if the physician is persuaded that there is a substantial reason to believe that each drug will make a positive contribution to the effect he seeks. This appears to have been the panel's original decision, not that of FDA.

From information which has been gathered through a number of sources (including the testimony of panel members whose depositions were taken in litigation), it does not appear that all the panels, before reaching their conclusions, gave the same consideration to a number of drugs that they would have required from anyone attempting to establish their effectiveness. There is some evidence that, in some instances, the examination could not fairly be called exhaustive. The final NAS-NRC report stated that, in a number of areas of drug action, there was no agreement on what constitutes a well-controlled investigation. Further, the report quoted a statement made by the former General Counsel of the Department of Health, Education, and Welfare, with respect to the meaning of substantial evidence, that:

> This provision states that there must be a bona fide responsible and adequately based medical judgment in support of efficacy before a drug may be put on the market, but if this condition is met, a minority opinion may prevail.

The legislative history does not reveal that Congress intended that clinical experience should be ignored, or that rather inflexible criteria of efficacy be established.

The final report declared that "The final arbiter of the value of a drug is the consensus of the experience of critical physicians in its use in the practice of medicine over a period of years." The report pointed out the interesting fact that, in some instances, the panels had based their judgments on " 'the informed judgment of the panel,' rather than upon evidence available in the medical literature. This phrase should not be read to mean that these judgments of the panels are based only on the experience of the clinical experience of its members, but rather that, in the opinion of its members, they also reflect a consensus of the experience of their peers." Apparently, only the panels are qualified to take clinical experience into consideration. It appears to me and, more important, to many highly qualified internists and other specialists, that it is, in fact, unscientific to ignore a lengthy history of clinical effectiveness. As a matter of fact, it is important to realize that, although "substantial evidence" is defined in the statute, the term "adequate and well-controlled" is not.

The Evaluation of Panalba

In December of 1968, FDA published a statement in the *Federal Register* with respect to Panalba. The statement pointed out that the NAS-NRC panel involved had evaluated the product and found it ineffective as a fixed combination; that is, not more effective than one of its ingredients, for the indications specified in the labeling, and that the Government concurred there was a lack of substantial evidence that each ingredient in the combination formula contributed to the claimed clinical effect. It is to be noted that this criterion cannot be located in the Drug Amendments of 1962 or its legislative history. FDA stated that it intended to initiate proceedings to take the product off the market. All interested persons who might be adversely affected were invited to submit any pertinent data.

In May of 1969, another notice was published which declared that there was a lack of substantial evidence that each ingredient contributed to the efficacy of the product, and that the use of the product presented an unwarranted hazard. Since the order stated that it would be effective in thirty days, the manufacturer of Panalba sued for an injunction and a declaratory judgment to restrain the enforcement of the order. The Court granted a preliminary injunction.

Subsequently, in August of 1969, FDA published a further order reviewing the data submitted by the manufacturer, and concluding that no substantial evidence of effectiveness as a fixed combination existed, and that the manufacturer had failed to show reasonable grounds for an evidentiary hearing. An innovation was provided in giving the manufacturer an opportunity to make an oral presentation to the Commissioner. I do not see how one can possibly equate such an "oral presentation" with a hearing where there can be examination and cross-examination of witnesses. No one, of course, relishes being cross-examined, and a hearing frequently consumes time, but I know of no better way to get at the truth. In any event, the request of the manufacturer of Panalba for an evidentiary hearing, in which it could cross-examine members of the NAS-NRC panels with respect to any inferences to be drawn from the reported literature, was denied on the ground that a hearing would serve no purpose other than delay.

About a month later, still another order was published. In a paragraph referring to the manufacturer's "insistence upon an evidentiary record," FDA stated that:

> The NAS-NRC classification of Panalba as ineffective as a fixed combination was simply a way of stating that there is no substantial evidence that the drug will have the effectiveness it purports and is represented to possess. . . . The time has come to end the marketing of these combination drugs which fail to meet the legal standards of effectiveness and which involved a significant and unacceptable hazard in the light of the failure of proof of effectiveness.

It is important to note that the Secretary did not find "that there is an imminent hazard to the public health," in which case he could have acted immediately and given the manufacturer prompt notice and afforded it an opportunity for an expedited hearing.

At the same time, regulations promulgating new and detailed requirements of proof of the efficacy of a drug were published in the *Federal Register*. A restrictive definition of "adequate and well-controlled investigations" of efficacy was created. This included such data as "the methods of quantitation" utilized in the efficacy studies and "the methods of recording and analyzing the patient's response to variables." There is nothing in the legislative history of the 1962 Amendments which indicates, in my opinion, an intent of Congress to authorize the limited definition of well-controlled studies also specified in the new requirements. I doubt that many drugs now on the market, even many of those recently approved, could meet these extreme requirements. In any event, these new require-

ments were published without providing industry or the scientific community with any opportunity to comment on them, and a United States District Court recently held that this had violated the Administrative Procedure Act.

The manufacturer of Panalba did not accept the last order of the Commissioner. The product had been on the market for over a decade. It had been approved both as to safety and efficacy for many years, and more than 2,000 batches had been certified. It had been widely prescribed by thousands of qualified physicians. The only recourse of the manufacturer, therefore, was to institute an action for a declaratory judgment and an injunction against the Government for the purpose of obtaining a hearing at which, through the process of examination and cross-examination, it could seek to establish that there was substantial evidence of effectiveness. When other companies were similarly denied a hearing, they, too, instituted similar actions in various courts.

The Government's Approach

The approach of the Government is, fundamentally, that it may equate "reasonable grounds" for holding a hearing with the criterion of "substantial evidence" at the hearing. This, to me, is a most unusual approach. When a hearing is requested, the company involved must show reasonable grounds, and this makes sense. But Congress did not say that FDA must be satisfied that substantial evidence has been presented in order to hold a hearing. It appears to me that if, for example, a petitioner submits, out of an abundance of caution, the affidavits of highly-qualified experts that they have examined the data and have concluded that there is substantial evidence, a hearing must be granted since reasonable grounds have been shown. It may well be that doctors A, B, C and D, both within and without FDA, have earnestly concluded, after real consideration, that in their opinion, there is no substantial evidence. On the other hand, if doctors E, F, G and H, also qualified, have concluded otherwise, how can the issue of substantial evidence be resolved, other than by holding a hearing at which all of the scientific facts can be thrashed out? To make "reasonable grounds" and "substantial evi-

dence" mean the same thing is not, in my view, what Congress intended.

As a matter of fact, if the Government's position is correct, there never will be any hearing, under any circumstances. This is because if the Government determines that, in a request for a hearing, reasonable grounds have not been shown because "substantial" evidence has not been presented, there cannot be a hearing, as in the case of Panalba. On the other hand, if data is presented which FDA determines is included within the term "substantial evidence," then, similarly, there is no point in having a hearing, inasmuch as the statutory criterion of "substantial evidence" has, in fact, been met.

The Panalba case is before a high court, and presumably may end up in the Supreme Court of the United States. In the food and drug field, no experienced lawyer will dare to prophesy that, no matter how firmly he feels about a legal problem, the courts will accept his opinion. There have been strange holdings indeed in this legal area, where the courts almost desperately attempt, in most instances, to accept the Government's position in order to close what they believe to be gaps in the law, and thus increase consumer protection. In the present situation, however, the courts may well determine that approving the refusal to grant a hearing is not necessary to close such a gap.

An interesting point to be considered is what would have happened if the Government had given the manufacturer of Panalba a hearing. A hearing could have been held in thirty days. The hearing would probably have been concluded in a few weeks. The effect of granting a hearing would have had a strong effect on the manufacturers of other drugs which FDA wished to remove from the market. As I see the situation, a number of these latter manufacturers would have fallen by the wayside for one reason or another. Many of the lawsuits now pending in the various courts would not have been instituted. As indicated, the scientific questions would have been determined in a relatively short period of time. The hearings certainly would not have been similar to the monstrous special dietary foods hearing. Perhaps most important, orderly procedures and due process would have been followed. **[The End]**

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