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Food Drug Cosmetic Law JOURNAL

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

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TO THE READER

About This Issue. — This month's JOURNAL contains two Charles Wesley Dunn Memorial Lectures. These lectures were created in honor of the late Mr. Dunn, who was one of the founders and the first president of The Food Law Institute, Inc. *Tobias G. Klinger* spoke at the University of Southern California Law School on April 9, on the subject of "Ours Is a Government of Laws—Laws, Laws, Laws." He remarked that in recent years, regulations pertaining to food and drugs have "seemed to take on the characteristics of a veritable population explosion in statutory and regulatory terms." However, it is his belief that if industry "can demonstrate its own responsibility and its ability to control and regulate itself, and even suggest necessary legislation and regulation, the men in our government . . . will, . . . be happy —and even eager—to permit and encourage such a wholesome trend to grow and develop." Mr. Klinger, whose comments appear at page 252, is a former Assistant United States District Attorney and former president of the Federal Bar Association of Los Angeles. A Washington, D. C. attorney, *H. Thomas Austern,* presented the second lecture at the New York University School of Law on May 6. On the subject of "Drug Regulation and the Public Health," he discussed the side effects and contraindications of Congressional committee *post hoc* medical judgments. This timely article begins on page 259.

Two industry lawyers discussed weights and measures trend and developments at the annual conference of the Central States Association of Food and Drug Officials. The Head of the Commercial Division, Law Department of Swift & Company, *Harvey L. Hensel,* told of the importance of uniformity in that field, while recent developments in weights and measures labeling was covered by *George M. Burditt,* a Chicago attorney. These papers appear at page 274 and page 279.

In an article beginning on page 290, Commissioner George P. Larrick describes the FDA's efforts to improve controls in frozen foods.

The story behind our country's present drug law is reviewed by *M. L. Yakowitz,* who is Director of the Division of Case Supervision, Bureau of Regulatory Compliance, Food and Drug Administration. In a paper appearing at page 296, he traces the evolution of drug laws in this country from the 1906 Act to the present.

Ralph G. Smith explains the government's control of new drug testing and introduction in an authoritative paper starting on page 305. Dr. Smith is Director of the Division of New Drugs, Bureau of Medicine, Food and Drug Administration.

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Ours Is a Government of Laws—Laws, Laws, Laws

By TOBIAS G. KLINGER

Tobias G. Klinger, of the Los Angeles Bar, Delivered the Charles Wesley Dunn Memorial Lecture at the University of Southern California, on April 9, 1964.

I FEEL DEEPLY HONORED to have been invited to give the Charles Wesley Dunn Memorial Lecture this year, and wish to express my personal appreciation to the Food Law Institute in establishing these lectures at five leading law schools in honor of Mr. Dunn, and to the University of Southern California Law School. I was privileged to meet Mr. Dunn personally only on a few occasions—too few—but as I mention his name I am keenly reminded of the impression of strength and grace and character which he made upon me and which seemed to emanate from him at all times and in all circumstances. He was one of those rare individuals who combined in himself those qualities both of intellect and spirit, of mind and principle, which we associate with our finest human beings.

Tribute to Charles Wesley Dunn

Mr. Dunn was without question the Dean of, and universally considered the foremost authority in, the field of Food and Drug Law. His activity and his accomplishments in this growing, expanding and dynamic area are so numerous and pervasive that merely to list them would take more than the time we have available this afternoon. Nor, I believe, would he wish this time spent in this way, for his intense and wide-ranging interest in this field was not limited to its purely

legal aspects, although, certainly, he did not neglect that vital part of it.

His establishment of The Food Law Institute, the promotion of graduate instruction in food and drug law, and his many authoritative legal works and publications testify to his interest in the law far more eloquently than any words of mine. But he did not seek to analyze the language of a particular statute or the precedent established by a particular judicial decision as solely a legalistic matter as so many lawyers have a tendency to do. He saw it all as a part of the fabric of our society, as an integral part of the world in which we live, and, more important, as the kind of a world and the kind of a society in which we would like to live. His guiding principle was not at any time a narrow, partisan one favoring industry as against government, nor was his opposition at any time to any proposed legislation or regulation blind or emotional in character. He favored and supported those measures and those proposals which were in the public interest even though they called frequently for the increased regulation of the firms and industries he so ably represented as a private lawyer.

Nor as I read his biography did he consider the government as some alien, antagonistic entity to be fought at all times and on every front, right or wrong—an attitude, unhappily, all too common today. Instead, as his service on the National Citizens Advisory Committee on the Food and Drug Administration and the Attorney General's National Committee to Study the Antitrust Laws demonstrates, he recognized that *the* government was *our* government and he attributed to its members the same sincerity of purpose which he himself had. As one publication so accurately put it,

> Many of the changes in the industry's status reflect his stubborn persistence, skilled negotiations and unwavering arguments which he used to drive, force, coerce and lead industry into accepting new positions, usually on a common ground with government regulatory agencies.

Prediction for More Rather Than Less Regulation

It is in this spirit, in the true spirit of Charles Wesley Dunn as I interpret that spirit, that these remarks are made—and I hope will be understood. We are all aware of the increasing proliferation of statutes, rules and regulations. They seem to be steadily expanding in almost geometric proportions in all fields of activity. That this has been true in the field of Food and Drug legislation, we here certainly know only too well. Since 1938 there has been a steady march and increase in the amount, variety and complexity of legislation and

regulations pertaining to foods and drugs. It has in recent years seemed to take on the characteristics of a veritable population explosion in statutory and regulatory terms. And the end is not yet in sight. If anything, given the existing situation and assuming that the forces at work will continue, it is a safe prediction that there will be more rather than less regulation. This may not be *particularly* true of the field of food and drug regulation—for the same thing is taking place in many other areas—but it is certainly true in the field of foods and drugs.

The limitations of time—not to mention my own limitations—do not permit an examination of all the forces at work which are accelerating and spurring this trend. The constantly growing complexity of our society and industrial practices, the increasing dependence of the great mass of our population upon others for supplying everything which goes in or on our bodies, are facts which are well known and show no signs of abating. The individual consumer or user is not able to protect himself and in the absence of some intervening protector, the only alternative is government regulation.

Thoughtful observers in the Food and Drug field deplore and condemn the ever-increasing volume of complex laws and regulations in this field and the concomitantly growing power vested in the FDA. There is virtue in deploring this trend and calling attention to it so that to the extent possible it will be slowed, or at least will not grow more rapidly than the public need requires. But I suggest that no amount of pointing with alarm alone, however sincere, and no amount of nostalgic yearning, however intense, for simplicity and nonregulation will stem the growing tide of statutory and administrative regulation. To reverse a familiar line from a well-known popular song, "Wishing *won't* make it so." To say that it must stop or that it should stop is simply a King Canute-ism. It didn't work for him a thousand years ago and it won't work any better now.

The explanation is not found, as some suggest, in an extension of Parkinson's law to the effect that statutes and regulations by a natural amoeba-like process beget more statutes and regulations. Nor do I believe that it can be explained satisfactorily by the assertion that administrative agencies such as the FDA are constantly seeking to expand their jurisdiction and power merely for the sake of asserting greater influence over a greater area. There may possibly somewhere be a grain of truth in each of these alleged explanations which have by now become clichés in our political lexicon. But if there is such

grain of truth, it has not been fairly proved. It is arrived at by noting the trend of increasing and expanding regulation and control and assigning to it the explanation of a natural process or bureaucratic ambition, without examining in each instance the history and background affecting a particular statute or rule.

Majority of Laws Enacted to Meet Particular Problems

I believe that it is far more fair to say, and supportable by evidence, that the great majority of the laws and regulations which have been enacted and promulated in the Food and Drug field are enacted and promulgated to meet particular abuses or problems, usually widespread in character, which rather directly affect the public welfare. This can be documented far more completely than any Parkinsonian or self-generating expansion-of-administrative-jurisdiction explanation can be. Frequently, the particular event which results in the enactment of what appears to be a far-reaching piece of legislation is a dramatic and tragic one. It is well known that the Food, Drug and Cosmetic Act of 1938 was finally enacted by Congress, after languishing there for several years, as the result of the Elixir Sulfanilomide episode which caused 107 deaths in this country. The Drug Amendments of 1962 were making little meaningful progress in Congress until the Thalidamide disaster dramatically revealed to Congress and the American public the dangerous practices which the existing drug laws permitted.

These, of course, are dramatic examples with which we are all familiar, but the same underlying forces are constantly at work and in my view produce the great bulk of the legislation and regulation which so many of us wish was unnecessary. Again, let me emphasize that proposed legislation and regulation which extends the area of control and increases administrative power should be carefully but responsibly scrutinized to determine whether it is responsive to a need which actually exists and is reasonably calculated to meet the problem at which it is aimed considered in its true dimensions. By that I mean, that sweeping legislation and regulation encompassing broad new areas should not be enacted to meet relatively minor problems. They should be seen and measured in their true perspective, and dealt with accordingly.

Nature and Congress abhor a vacuum, and both move in to fill it. What I have been saying is that it is this extension of a physical law to government which more readily and, I submit, logically explains

the phenomenon of greater and greater regulation. The answer, if there is one, is suggested by the physical law I have mentioned, namely, fill the vacuum before nature or Congress does. In short, legislation and regulation in the Food and Drug field can be reduced only to the extent that the specific and urgent problems relating to consumers' welfare in this area can be minimized or solved by industry itself.

Self-Regulation of the Salmon Canning Industry

There are doubtless many ways in which this can be done, and in specific areas it has been done. The self-regulation of the salmon canning industry through arrangements worked out by the National Canners Association in cooperation with the FDA is an outstanding example of such self-regulation—self-regulation which has benefitted both the industry and the consumer, has greatly reduced, if not eliminated, the need for governmental enforcement action in this area, and has thus at the same time provided a welcome reduction in the work load which the FDA carries. Self-regulation represents a challenge of vital importance to the industries which come within the jurisdiction of the Federal Food, Drug and Cosmetic Act, but a challenge which is at the same time complex and difficult to meet. It requires an industry which is sufficiently well organized and sufficiently motivated by principle to be able to control the relatively few among them who create most of the difficulty. It is axiomatic that bad cases, that is, cases with difficult facts, produce bad law. It is equally true that the few in each industry who disregard the consumer and reduce the free competitive system to the law of the jungle, create the problems and difficulties which affect all the others. Can industry regulate itself? Even if it were admitted that it cannot by its very nature do so entirely, I believe that to a considerable extent, and in specific areas, it can. The effort, in any event, must be made, or the rising flood of legislation and regulation will continue inexorably and inevitably to rise.

Differences of Opinion Between FDA and Industry

Much of the regulation under the Federal Food, Drug and Cosmetic Act and related legislation is based upon scientific data or qualified professional and scientific opinion. There are differences of opinion between the FDA and various industries as to the scientific accuracy or validity of some of the positions which the FDA has

taken upon which some of its regulations, both promulgated and proposed, are based.

This appears to be particularly true in the field of dietary food supplements, with which I am somewhat familiar. Thus, to take only two points, it is generally believed and urged by honest and respected members of this industry that the FDA is not correct in declaring that the average American diet supplies all the vitamins and minerals which an individual needs, and in declaring that the minimum daily requirement is sufficient in cases where such a minimum has been established. The same difference of opinion certainly exists in other areas as well. The answer—again, if there is one—is not for industry merely to reiterate and restate the difference of opinion which exists, but to do something affirmative on an organized industry-wide basis about it, namely, to do the scientific research and obtain the valid scientific evidence—if it exists—to support the industry's position.

Some work has certainly been done along these lines as a recent syndicated article by Dr. F. J. Stare of the Department of Nutrition, Harvard University, makes clear. In the article to which I refer Dr. Stare points out that while we have sufficient food of sufficient variety adequately to nourish every citizen in this country, the last annual report of the National Vitamin Foundation contains evidence that many Americans of all ages and socio-economic brackets have food intakes that provide nutrients below the amounts considered desirable. This is significant and points the way. Here, again, it is not sufficient to curse the darkness; the bright searching light of scientific and clinical inquiry should be turned on ever more brightly by industry itself. To the extent that this is done, valid differences of scientific opinion can be validly resolved; to the extent that it is not done, the scientific views and opinions of the FDA will necessarily prevail, largely by default.

Conclusion

We like to say that ours is a government of laws and not of men, and it is from this oft-stated principle of our system of government that the title of these remarks is taken, but like so many statements of principle which seek to encompass great meaning in a few words, it is only partly true. Our laws are proposed, considered and enacted by *men*, and they are thereafter administered and enforced by *men*. Anyone who thinks that all legislation in this field emanates from the FDA and that Congress rolls over and plays dead whenever the

FDA lifts its finger, should read the series of articles entitled "Annals of Legislation" recently appearing in the *New Yorker Magazine* describing the struggle waged almost single-handedly by the late Senator Kefauver for the enactment of the 1962 Drug Amendments. If industry, wherever possible, can demonstrate its own responsibility and its ability to control and regulate itself, and perhaps, from time to time even suggest the legislation and regulation which its own research and fair appraisal convinces it are necessary, the men in our government, both Congressional and Executive, will, I am satisfied, be happy—and even eager—to permit and encourage such a wholesome trend to grow and develop. **[The End]**

WRINKLE-SMOOTHING SKIN LOTION SEIZED

A quantity of wrinkle-smoothing skin lotion was seized by the Food and Drug Administration on charges that the lotion is a New Drug not covered by an approved New Drug Application being marketed under false claims. United States marshals seized over 35 cartons of the product April 30, 1964, in possession of a dealer at Baltimore, Maryland. Also seized was a quantity of promotional material.

Papers filed in the Federal District Court at Baltimore made the following charges:

(1) The product is a New Drug not generally recognized as safe and effective by qualified experts for prolonged, continued use for removal of wrinkles and no New Drug Application has been approved under the Federal Food, Drug and Cosmetic Act.

(2) The product is misbranded because its labeling is false and misleading when read by the ordinary consumer. The government charged that the labeling presents an exaggerated statement of what the drug will do and a misleading statement of how it works.

Middle-aged women are led to believe that "this is a newly discovered article produced after years of research which will immediately and dramatically eliminate all her wrinkles, including crowsfeet, puffy under-eye circles, laugh, frown, smile and throat lines, through its action of tightening, firming, moisturizing, freshening and toning her skin, that this facial and neck skin improvement can be accomplished in minutes and will last for hours . . . that the drug has the capacity to provide a youthful appearance to the skin. . . ."

The government charged that actually the product has only a temporary effect on wrinkles, that regular applications do not provide any permanent benefits, that the drug has no astringent action adequate to draw the skin and eradicate wrinkles or provide the other claimed effects, including making the skin youthful again.

(3) The drug is fabricated from two or more ingredients and its label fails to bear the established name of each active ingredient.

FDA said the promotional material seized included streamers, leaflets, cards, placards, booklets and a display board.

Drug Regulation and the Public Health

SIDE EFFECTS AND CONTRAINDICATIONS OF CONGRESSIONAL COMMITTEE POST HOC MEDICAL JUDGMENTS

By H. THOMAS AUSTERN

The Second Annual Charles Wesley Dunn Lecture on the Food and Drug Law at New York University School of Law Was Delivered by Mr. Austern on May 6, 1964. Mr. Austern, of the Washington, D. C. Law Firm of Covington & Burling, Is an Adjunct Professor at the New York University School of Law.

IN OCTOBER 1962 Congress finally enacted the sweeping Drug Amendments Act of 1962,[1] a bill that had provoked intensive controversy for more than three years.[2] Yet it was ultimately passed by the unanimous vote of both the House and the Senate [3]—a unanimity that, so far as I know, had never before been achieved in major legislation, not even a declaration of war.

Those who have read, in recent issues of the *New Yorker*,[4] Richard Harris's colorful, extensive, and not always accurate "Annals of Legislation," know that final passage was triggered by the episode involving thalidomide, the sedative which produced limbless babies when administered to women in early pregnancy.

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[1] P. L. 87-781, 76 Stat. 780 (1962), FOOD DRUG COSMETIC LAW REPORTS ¶ 550-¶ 611 (codified in scattered sections of 21 U. S. C.).

[2] The controversy started with the Kefauver pricing hearings in 1959, and proceeded through the submission of Senator Kefauver's bill, S. 1552, 87th Cong., 1st Sess. (1961), the hearings on the bill, to the committee and floor consideration of the measure.

[3] 108 *Congressional Record* 17422 (1962) (Senate roll-call vote); 108 *Congressional Record* 21092 (1962) (House voice vote); 108 *Congressional Record* 22041 (1962) (Senate voice vote on conference report); 108 *Congressional Record* 22325 (1962) (House roll-call vote on conference report).

[4] Harris, "Annals of Legislation—The Real Voice" (parts 1-3), *The New Yorker*, March 14, 1964, p. 48; March 21, 1964, p. 75; March 28, 1964, p. 46.

The drama of a pregnant Arizona television announcer publicly deciding whether to go to Japan or to Sweden for an abortion, followed later by the horrible pictures of phocomelia babies born abroad, excited public pressure to which Congress readily responded.

To those who are intrigued with American politics, I might mention that in the same year 41,130 Americans were killed in automobile accidents [5] and that no federal legislation emerged on that problem, even though Congress did in 1962 require that all future television sets would have to embody UHF reception.[6]

As Professor James Harvey Young has observed, the 1962 Drug Amendments were but another illustration of the etiology of American public health legislation—change, complexity, competition, crusading and compromise built on catastrophe.[7]

Paradoxically, on thalidomide and American catastrophe had been averted by a refusal to permit marketing under the authority of the then-existing law; [8] and the loopholes in the investigational testing of new drugs were being administratively closed before the 1962 Drug Act was passed.[9] One does not denigrate Dr. Frances Kelsey's Distinguished Service Medal by noting that she got it by an authorized refusal to act.

Debate on many of the provisions incorporated in the 1962 statute still continues, particularly on its detailed administrative implementation in the areas of prescription drug advertising and labeling,[10] the availability of procedural safeguards, and the futility of judicial review.

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[5] *World Almanac and Book of Facts*, p. 305 (Hansen ed. 1964).

[6] See Communications Act of 1934, Sec. 303(s), added by Act of July 10, 1962, Sec. 1, 76 Stat. 150, 47 U. S. C. Sec. 303(s) (Supp. IV, 1963).

[7] Young, "Social History of American Drug Legislation," in *Drugs in Our Society*, p. 217 (Talalay ed. 1964).

[8] See Federal Food, Drug and Cosmetic Act, Sec. 505, 52 Stat. 1052 (1938), as amended, 21 U. S. C. Sec. 355 (1958), FOOD DRUG COSMETIC LAW REPORTS ¶ 71,051-¶ 71,069; 21 CFR Sec. 130.4(c)(1)(a), FOOD DRUG COSMETIC LAW REPORTS ¶ 71,304; Sec. 130.5(a) (Supp. 1962), FOOD DRUG COSMETIC LAW REPORTS ¶ 71,305.

[9] Proposed revised regulations on investigational new drugs were published on August 10, 1962, 27 *Federal Register* 7990 (1962); the final day for comments was October 10, 1962, the date of the passage of the Drug Amendments of 1962. The regulations were published in final form on January 8, 1963, 28 *Federal Register* 179 (1963), effective February 7, 1963; corrected 28 *Federal Register* 319; amended 28 *Federal Register* 5048, effective May 21, 1963; 28 *Federal Register* 10972, effective October 12, 1963.

[10] See *Abbott Laboratories v. Celebrezze*, FOOD DRUG COSMETIC LAW REPORTS ¶ 40,119, Civ. No. 2737, (DC Del. April 30, 1964), striking down FDA regulations, 21 CFR Sec. 1.104(g), FOOD DRUG COSMETIC LAW REPORTS ¶ 3404; Sec. 1.105(b), FOOD DRUG COSMETIC LAW REPORTS ¶ 3405, requiring the concurrent display of generic and trade names in labeling and advertising.

Litigation over excess assertion of detailed authority on "grandfathered" old drugs may be expected.[11] These nice questions can be pursued by the specialists, and competence in this field of public law is now indeed a legal specialty.

This afternoon, however, I should like to examine with you two recently developed trends that perhaps probe deeply into public policy and which should concern every student of government, indeed every citizen interested in his own health and that of his family.

The first is the danger of Congressional public nonmedical tinkering with and second-guessing on the difficult and delicate administrative job of clearance and withdrawal of prescription drugs. The second is the curious, and I think perhaps hazardous phenomenon of documentary congestion and possible administrative paper indigestion that may be building up in the Food and Drug Administration. In some measure, both of these are related by-products of what has happened since October 1962.

To focus our inquiry, we must first fix in mind some of the underlying policy and procedural predicates embodied in the statute. We must examine, all too briefly, what is decided when a newly discovered drug is either given or refused licensed availability to the medical profession. We must also understand who makes that decision and the nature of the institutional determination.

Complete Licensing Control Authorized by New Amendments

As to the first, the present law embodies complete licensing control. No prescription for a new drug may be written by a licensed physician unless the FDA authorizes it to be prescribed.[12] No proprietary drug may be sold over the drugstore counter for self-medication unless the FDA permits it to be marketed.

Elsewhere I have endeavored to describe the full swing of the pendulum, in the federal regulation of foods, cosmetics and drugs,

[11] The scope of the "grandfather" protection, Drug Amendments of 1962, Sec. 107(c)(4), 75 Stat. 789, FOOD DRUG COSMETIC LAW REPORTS ¶ 581, is neatly posed in the proposed regulations recently issued by the FDA, 29 *Federal Register* 2790 (1964), FOOD DRUG COSMETIC LAW REPORTS ¶ 80,057, calling for annual reports from all drugs marketed under new drug applications prior to June 20, 1963.

[12] See Federal Food, Drug and Cosmetic Act, Sec. 503(b), FOOD DRUG COSMETIC LAW REPORTS ¶ 70,193; Sec. 505(a), FOOD DRUG COSMETIC LAW REPORTS ¶ 71,051, as amended, 21 U. S. C. Secs. 353(b), 355(a) (1958), as amended, 21 U. S. C. Sec. 355 (Supp. IV, 1962).

from the policing format of 1906 to the full licensing trend of today, as well as the basic change from making the manufacturer responsible for the safety and wholesomeness of his product—subject to severe penalties and criminal prosecution under concepts of absolute liability —to the working postulate of today where prior government clearance, irrespective of actual safety, is first required.[13]

Prescription drugs are unique. They may be purchased and used only if a qualified, licensed doctor in turn writes a prescription. They are advertised only to the medical profession. Doctors are presumably competent to diagnose a patient's disease, to determine the need for therapy, and to select remedial medication. Between the taker of the drug and its vendor always stands his physician.[14]

Theoretically, it might be argued that the decision whether to administer any drug to a patient, to determine for that patient whether its potential good outweighs any possible hazard, should rest alone with the professionally trained and licensed doctor without the intervention of a federal agency.

If the doctor can be trusted to diagnose the disease, perhaps he should be trusted to have enough knowledge and skill to pass upon the relative safety and efficacy of the drug he prescribes.

But that bridge has been crossed by the Congress. It serves no useful purpose to argue whether organized medicine has abdicated to the government, or whether much of the statute and many of the new regulations seem to be predicated inescapably on the proposition that many doctors are perhaps incompetent, indifferent, or unhappily uninformed.

Commissioner Larrick's Observations

As recently stated by Commissioner Larrick, someone must decide these questions, and under federal law that responsibility now lies with the FDA.[15]

In exercising it, that agency does not assume that the general practitioner is always professionally alert or fully informed. As Commissioner Larrick puts it,

[13] Austern, "Expertise in Vivo," 15 *Administrative Law Review* 46, 49-52 (1963).

[14] Garai, "Advertising and Promotion of Drugs," in *Drugs in Our Society* 189, 193-94 (Talalay ed. 1964).

[15] Larrick, Statement before the Subcommittee on Intergovernmental Relations of the House Committee on Government Operations, March 24, 1964, at p. 7.

The Government must consider:

not just *a* patient with *a* disease process; not just the skills of *a* physician, including his ability to arrive at a correct diagnosis, his awareness of recent scientific discoveries relating to the drug, and his willingness to read the labeling of the new drug, to perform the tests prerequisite to its safe use, and to take the time to make other observations required for proper use of the medication.[16]

With commendable candor, Commissioner Larrick admitted that the government must judge

the hazards likely to be encountered when the drug is employed:

by physicians of varying skills and abilities, in patients with a multitude of disease processes, many occurring concurrently, and in patients incorrectly diagnosed or inadequately tested with accepted laboratory procedures.[17]

Perhaps there are some disappointed clients who might well endorse the adoption of similar protective rules for the legal profession based on like apprehensions about the comparable skills of lawyers. Debates as to professional levels of competence are always invidious.

Criticism of the medical profession can best be left to doctors. In the current May *Harper's*, Dr. Theodore Sanders wields a nice scalpel on his colleagues.[18] He tells of the doctor who discovered in the middle of the night that the toilet in his house was not functioning. He called his plumber—who was annoyed at being awakened and asked to come right over. Said the plumber to the doctor: "Just drop two aspirins down the drain—and call me in the morning if it isn't better."

FDA Determines Safety and Effectiveness

Nevertheless, for better or worse, under the law no new drug may be licensed for prescription unless the FDA is satisfied that it is both *safe* and *effective* for the particular use in the hands of the run-of-the-mill busy doctor.

The legal experts who closely dissect the statute will tell you that the FDA must make this decision only on "substantial evidence," consisting of adequate and well-controlled investigations that would satisfy "experts qualified by scientific training and experience to evaluate" the drug, and that this hard-fought statutory language is a meaningful limitation on arbitrary refusals.[19] Nevertheless, everyone will admit that there is very wide latitude for decision.

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[16] Work cited at footnote 15, at p. 12.

[17] Work cited at footnote 16.

[18] Sanders, "The Easy Chair: What Doctors Can Do To Cut the Cost of Medical Care," *Harper's*, May 1964, at p. 16.

[19] Federal Food, Drug and Cosmetic Act Sec. 505(d), as amended, 21 U. S. C. Sec. 355(d), FOOD DRUG COSMETIC LAW REPORTS ¶ 71,057; see S. Rept. No. 1744, 87th Cong., 2d Sess. 17-18 (1962); S. Rept. No. 1744, 87th Cong., 2d Sess. pt. 2, at 6 (1962); H. R. Rept. No. 2464, 87th Cong., 2d Sess. 8 (1962).

Congress often legislates in absolute terms. But the administrative decision whether to permit or to forbid the availability of a drug for use by doctors involves relative values. No scientific or medical judgment in this area is ever wholly right or wrong. No drug is absolutely safe. If it were, it perhaps would not cure anything.

What is involved is a three-step operation: determining the therapeutic benefit that will be derived; determining the risks in the indicated use; and then deciding whether on all of the available facts the potential benefit outweighs the risk and should on balance lead the FDA to license the drug for use.

The first two tasks are usually not too difficult unless there are incomplete facts. The third involves judgment and the level of apprehension that is to operate as the criterion.

Possible Adverse Side Effects of Drugs

Here one gets into hard decisions that are incredibly difficult to make. Human beings are complicated organisms, genetically and structurally often very different, and when sick, they do not always react in the same way.

Any drug may encounter an idiosyncrasy in someone. An injection of penicillin may sometimes cause immediate death, but that does not mean that all forms of penicillin will be forbidden because the lives saved far outbalance the occasional fatality.

No matter how widely tested, all of the possible adverse reactions do not come to light until a new drug is widely used after it has been licensed. One must balance the benefit, the hazard of ignorance, and the availability of other drugs for a particular disease.

Even more, even where much is known about possible adverse side effects, the FDA must determine whether bold and adequate warnings to the doctor will adequately minimize the risks.

Illustration of This Point

Let me illustrate: There is a well-known and potent broad-spectrum antibiotic. For typhoid fever and certain other diseases it is a specific. On the other hand, it is implicated in a dangerous and sometimes fatal blood condition. The safe use of this drug requires that the doctor carefully watch his patients and continuously make

certain blood studies.[20] It was charged that despite warnings from the manufacturer and in the medical journals, many doctors would still prescribe this antibiotic without regard to the dangers of its use.[21]

Should the drug be allowed? Should it be withdrawn, or the warning labels amplified? Should its distribution be limited only to hospitals where stricter controls might be exercised?

In this case, the FDA, after twice consulting panels of medical experts, concluded that the drug should still be available because it was needed, but insisted upon stern and stringent warnings at the very top of the doctor's desk reference card.[22]

Another Situation

In another case, a valuable X-ray diagnostic aid was authorized in 1958. It visualized gall bladders, and was a valuable aid in determining whether surgery was necessary, and made for better surgery. But it was also risky where kidney disease existed and was credited with some fatalities.[23]

In this second case the FDA decided that widespread warning letters to doctors would not be enough, and asked that the drug be withdrawn from the market. It did so even though its own medical staff believed that if the kidney function were first tested, and the specific instructions followed by the doctor, the product was still a safe and useful drug.[24]

Thus, the FDA must evaluate not only the manufacturing controls, not only the composition and action of the drug, and balance the benefits against the risks, but do so against the prevailing standards of the medical profession, its diligence, and the likelihood that the doctor will read the warning instructions and follow them.

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[20] Larrick, cited at footnote 15, at p. 7; *Hearings on Interagency Coordination in Drug Research and Regulation Before the Subcommittee on Reorganizations and International Organizations of the Senate Committee on Government Operations,* 88th Cong., 1st Sess., pt. 4, at 2033 (1963) [hereafter cited as "Humphrey Interagency Coordination Hearings"].

[21] See "Humphrey Interagency Coordination Hearings," cited at footnote 20, at 1984-2049.

[22] See "Humphrey Interagency Coordination Hearings," cited at footnote 20, at 2005-07; Larrick, cited at footnote 15, at p. 7.

[23] "Humphrey Interagency Coordination Hearings," cited at footnote 20, at 2049-80.

[24] *Hearings on HEW Appropriations for 1965 Before a Subcommittee of the House Committee on Appropriations,* 88th Cong., 2d Sess., pt. 1, at 210 (1964).

Of course, the FDA must first decide whether at the outset it has enough information on which to act. Its demands in this respect have multiplied exponentially over the past decade. A new drug application today may involve more than ten fat volumes of clinical data, apart from vast details on manufacturing methods and controls.[25] This is the beginning point for the time and arduous effort required in analyzing data, and contributes the documentary congestion to which I shall refer later.

Adverse Reactions to New Drugs

Next, of course, there must be, and there now has been developed, better machinery for the rapid collection and evaluation of adverse reactions to new drugs that come to light only with their general use.

Hindsight is often the resort of the uninformed. What has caused a fatality is not always clear—and it is often easy to assign blame to a drug where some other undiscovered factor may have operated. To balance the reported few instances of trouble against the reported many cases of successful and often lifesaving cures, takes both medical skill and cool courage.

FDA's Medical Staff Discussed

Of course, this must be an institutional decision by the FDA. It has medical staffs, numerically inadequate in past years, but now being improved and amplified. It can resort to outside panels of medical experts. It must separate and judge the various disciplines and emphases of its chemists, toxicologists, pharmacologists, and physicians. Ultimately, those who administer the whole operation must make the final decision.

No one would deny that the FDA needs the best men. Doctors interested in research are often more drawn to the National Institutes of Health and to the universities. As has been said, a research doctor far prefers to be on the frontiers of medicine than being a traffic cop on the beat.[26] Suggestions have been advanced that the federal government might rotate its scientists between research and control jobs.[27]

But what cannot be escaped is that the FDA, as the authorized arm of the federal government, is deciding when and which newly

[25] Larrick, cited at footnote 15, at p. 14.

[26] Cutler, "Practical Aspects of Drug Legislation," in *Drugs in Our Society* 149, 157 (Talalay ed. 1964).

[27] For example, see the work cited at footnote 26.

discovered medicines may be given by doctors to the American public. If it is timid or inefficient, it can block medical advance and foreclose prolonging or saving human lives. If it is lax, it will not discharge the responsibility Congress has given it.

Ideally, the FDA ought to be willing courageously to exercise its best judgment—assuming the risks of error with the hope of saving lives as anticipated—while at the same time insuring that there is a constant flow of information to keep its decisions up to date.

But the FDA cannot accomplish that task if Congressional committees in heavy-handed fashion either intrude upon, or by hindsight publicly second-guess, administrative action.

In a democracy, no agency of government operates in a vacuum. Commissioner Larrick has observed:

> We seek to make decisions about drugs solely on the basis of scientific considerations. But over a period of time, the direction of Government's decisions will inevitably be influenced by public reaction.

And he added that public judgments

> are not necessarily consistent with scientific facts. They are not always logical. They can be and sometimes are arbitrary. Even so, neither the Executive nor the Legislative Branches of the Government can long ignore them.

He concluded that

> If it should become the overwhelming public view that society should drastically limit the risk no matter how much good a drug can do, then we would be forced to remove from the market many drugs whose good far outweighs their harm. Carried too far such developments could seriously impede the progress of medicine.[28]

Necessarily, an administrative official must be restrained in his public observations. A law professor is sometimes freer to criticize.

Over the past three years there has been increasing evidence that constant Congressional committee intrusion into this area and the accompanying scare publicity may be a major hazard.

The Pressure of Uninformed Public Opinion

Two drugs—the famous thalidomide and the notorious krebiozin—strongly demonstrate that uninformed public opinion can force judgment and evoke regulatory control contrary to scientific knowledge.

Thalidomide was a sleeping compound. Except for pregnant women, it was undoubtedly a safe, valuable prescription drug. Since

[28] Larrick, cited at footnote 15, at p. 13.

it had no lethal dose, it could be given even to people with suicidal tendencies. With stringent and strong cautionary labeling against its prescription for women of child-bearing age, a judgment that it could be available for prescription might have been made.[29] But the public reaction to its unfortunate consequences, when permitted for unlimited use in Europe, resulted in its absolute prohibition in this country.[30]

I doubt that any doctor would today admit having it in his possession, and its unfortunate use abroad almost alone supported the passage of the 1962 Drug Amendments, most of the provisions of which had no direct bearing on the problem of thalidomide.

Krebiozin

Krebiozin represents an opposite public reaction in a health area as emotionally charged as that involving thalidomide.

Involved here was another product, an alleged cancer cure, never cleared for general public distribution through a new drug application. It had nonetheless been distributed as an investigational drug for over ten years and had been used by possibly hundreds of persons all under the care of licensed practitioners. After the passage of the Drug Amendments of 1962, and the final promulgation of revised FDA rules governing investigational products, the distributors of Krebiozen withdrew the investigational plan called for by the new regulations. They were required to halt the interstate distribution.[31]

When that occurred or appeared imminent, sizeable demonstrations were mounted in front of the White House. Indeed, some of the pickets had to be forcibly removed when they failed to obey the regulations governing picketing of the White House.[32]

Sixteen senators, who had unanimously supported the Drug Amendments of 1962 and the tightened rules for clinical testing, then introduced bills to exempt Krebiozin from the 1962 Amend-

[29] The writer obviously is not competent to make any medical judgments. The suggestion in the text speaks as of 1962. Recently there has been a report in the *British Medical Journal* about some experiments by Dr. Cecilia Lutwak-Mann in which thalidomide was administered to male rabbits and apparently caused a diminution in fertility. It was further reported that these results need not necessarily be applied to human beings. 85 *Science News Letter* 296 (1964).

[30] *Hearings on HEW Appropriations for 1964 Before a Subcommittee of the House Committee on Appropriations,* 88th Cong., 1st Sess. pt. 1, at 363-65 (1963) (thalidomide chronology).

[31] *Hearings,* cited at footnote 24, at 203-07.

[32] *Washington Post,* June 5, 1963, p. B-10.

ments and to require the National Institutes of Health to run independent tests of the value of Krebiozin.[33]

In this instance, a full report of investigations made by the FDA, backed by the National Institutes of Health, demonstrated the apparent composition and lack of effect of Krebiozin, and, for the time being, ended the controversy.[34]

Congressional Committee Hearings

Now let us look at Congressional committees. Since 1962 two committees, one in the House and one in the Senate, have pursued, some would say harassed, the FDA unmercifully.[35] They have considered in public hearings earlier FDA consideration and action on not less than ten prescription drugs subject to new drug controls including continued extensive inquiry into Krebiozin.[36] They have sought to review by illuminated hindsight almost every step in the earlier administrative consideration.

The kind of testimony accepted by these committees, and often promptly distorted in headlines, has ranged from confidential FDA files through newspaper clippings, magazine articles, personal communications, and a random conglomeration of every type of unverified report and hearsay evidence that might be imagined.[37]

Very often at these hearings there will be present, in addition to a host of reporters seeking to gratify public concern about health and drugs, a single senator or congressman and one or two committee staff lawyers or investigators. The spectacle of a young medically-untrained staff man interrogating medical experts—and ragging hard-working administrative officials—is often not edifying.

One might well question the long arm of Congress—from whom appropriations must be obtained [38]—being freely used to demand the production of technical files and documents and the preparation of

[33] S. J. Res. 101, 88th Cong., 1st Sess. (1963).

[34] See *Hearings,* cited at footnote 24, at 205-07.

[35] The two committees involved are the Subcommittee on Reorganization and International Organizations of the Senate Committee on Government Operations, operating pursuant to S. Res. 27, 88th Cong., 1st Sess. (1963), 109 *Congressional Record* 320 (1963), and the Subcommittee on Intergovernmental Relations of the House Committee on Government Operations.

[36] Among the other prescription drugs considered have been Chloromycetin, Enovid, Flexin, Kevadon (thalidomide), Librium, MER/29, Miltown, Orabilex, Parnate and Percodan.

[37] See, for example, "Humphrey Interagency Coordination Hearings," cited at footnote 20, 1436-63, 1502-27.

[38] See Harris, *Congressional Control of Administration, passim* (1964).

extensive explanatory medical memoranda on questions which, it is fair to say, neither the committee staff nor its members are competent to make judgments.

Perhaps you will agree that if those who must exercise administrative judgment in these difficult and delicate areas of drug control are constantly to be hauled up, interrogated, sometimes publicly pilloried, and inescapably have their judgment questioned, serious results may follow.

The loss of time and energy and the disruptive distraction from the onerous daily job hardly needs elaboration. I do not know whether an official count is kept, but I would suggest that a very substantial portion of the total time of top FDA officials—and certainly its Medical Bureau engaged in new drug controls—has been taken up with the preparation for and appearance before these Congressional committees.

The more troublesome effect may be on the process of decision. The FDA can always avoid future trouble by always refusing clearance. There is also available the official escape hatch of saying that there is inadequate data on which to judge.

One can hardly be blamed for deferring a difficult decision when the consequence for being wrong may be later public debate about his medical competence and his acuity, along with public embarrassment and unhappy publicity years later—all based largely on hindsight and distortion.

In the meantime, the drug not cleared because of these apprehensions might have saved lives and cured illnesses for thousands. Dr. Kelsey won her medal for refusing to authorize the marketing of thalidomide. No one ever got a medal for courageously clearing a drug on a balanced judgment as to benefit and hazard.

Finally, it is difficult to read the headlines and newspaper reports [39] on these hearings without becoming concerned that they may produce public apprehension about all new drugs, and may in turn lead to loss of confidence both in the FDA and in the medical profession as a whole.

Headlines magnify the fundamental health neuroses which most of us harbor. The news story heralded through the country that

[39] See, for example, *Washington Daily News,* April 29, 1964, p. 1 ("Charge Firm Withheld Data Linking Drug to Deadly Liver Damage"; this charge and the accompanying article related to a drug that had been removed from the market two and one-half years earlier).

Drug X killed or injured one or two people seldom points out that it was successfully used to save hundreds or thousands of others.

Congressional investigatory powers of course serve an important function in American government. No one would suggest that the Congress has no right to investigate the conduct, indeed the particular decisions, of any federal agency. Time and again these committees have done immeasurable good.

Suggestion Offered to Minimize Harmful Publicity

Nevertheless, in areas involving the national security, it is well-recognized that Congressional committees should operate only in executive session, and that the delicacy and importance of the area being scrutinized preclude publicity and headlines.

The conduct of the Central Intelligence Agency is not publicly ventilated. The details of operations of the Department of Defense are very often explored by Congressional committee under accepted security rules. Committees dealing with many aspects of atomic energy maintain the privacy of what is reported to them.

I suggest to you the desirability that in the area of new drug control which we have been considering, these same considerations might be applicable.

If they are not, and the present tendencies continue, there may be considerable ground for the apprehension that potentially valuable and important life-saving medicines—whose over-all benefit outweighs the possible or disclosed risks—will be foreclosed or long-delayed in being made available to those who need them.

Current FDA Operations

My second point is a brief addendum on current FDA operations.

We have seen the importance of securing a prompt and continuing flow of all information on adverse reactions that may come to light in the general use of any drug. The need for getting that information is recognized as cardinal by everyone.

The American Medical Association has recently expanded its efforts to secure prompt reporting.[40] The FDA will soon, by contract and voluntary agreement, have almost one thousand hospitals reporting

[40] See "Humphrey Interagency Coordination Hearings," cited at footnote 20, at 1753.

directly to it on all adverse drug reactions. Its Adverse Reaction Reporting Branch scans hundreds of medical journals and reviews some 58,000 reports annually received from other sources.[41]

Moreover, the FDA leans to a great extent on its statutory authority to require manufacturers to report all adverse reactions they learn about in investigational work and from any other source. Indeed, there appears to be a feeling that if the FDA gets everything reported, the problem will be solved.

Lately, there has been, in a series of overlapping regulations, a vast amount of duplication. Even after a drug has been authorized for general prescription use following clinical investigation, the manufacturer is asked to continue to report to the Investigational New Drug Branch.[42] The manufacturer must also report to the New Drug Surveillance Branch, both annually and wherever anything significant comes to light.[43]

Documentary Congestion Is Possible

Some of those interested in New Drug controls are beginning to worry whether a complete state of documentary congestion may result. There is some evidence that the sheer mass of the documentary flow may lead to delayed, and even lost consideration of the significant.

Computer and electronic retrieval techniques are being discussed, but their effective adaptation to this vast task will undoubtedly be costly and complicated.[44] Moreover, a computer is only as good as its factual input, and I doubt that it can make sensitive medical judgments.

Under the Act, the FDA has a broad discretion in the amount and type of reporting it can require. The current tendency, possibly in response to Congressional second-guessing, is to require everything. The wisdom of doing so is open to question.

From the point of view of the manufacturer, this system may be a mechanical burden, but it affords the opportunity to throw much of the responsibility upon the FDA. Prosecuting a drug manufacturer for failing to differentiate the significant hazard from the insignificant

[41] Saiger, "The Food and Drug Administration Information Center on Adverse Reactions and Hazards," 19 FOOD DRUG COSMETIC LAW JOURNAL 235 (1964).

[42] See 21 CFR Sec. 130.3(a)(5) (1963), FOOD DRUG COSMETIC LAW REPORTS ¶ 71,303.

[43] 21 CFR Sec. 130.13(b) (1963), FOOD DRUG COSMETIC LAW REPORTS ¶ 71,313.

[44] Saiger, cited at footnote 41; Larrick, cited at footnote 15, at pp. 15-16.

will be very difficult indeed where he has regularly filed every report with the FDA.

FDA has been criticized for not ferreting out adverse reports when some drug manufacturers failed promptly to turn them in. It runs the hazard of deeper criticism if a report occurs in a roomful of documents and is not gotten to for a long time. From the standpoint of effective regulation, it might be better to minimize these reporting requirements to avoid duplication, and to forestall documentary indigestion.

I do not know whether the drug industry would prefer having the entire responsibility for reporting only the significant adverse reactions placed upon it. Since the FDA has now established a vast machinery for the collateral flow of information on adverse reactions, that change might better serve the public interest.

Conclusion

In closing, I hope that not too many of you will feel that the advertised title of this lecture was a false and misleading label wholly without proper indication of how narrow would be its legal thrust and therapeutic claim.

Necessarily, this area of new drug control is an intricate mosaic of statutory provision and voluminous regulations. Some food and drug lawyers have lamented that the half-life of alert expertise in this field may be only six months, and checking for the latest revision has become a daily requirement. As in all food and drug regulation, there is the vast substratum of informal correspondence and rulings that make up the bulk of daily regulatory activity. Backing up all of that is the tremendous bulk of complicated clinical and scientific material. To discuss merely the possible impact of Congressional hindsight tinkering and publicity, or of probable documentary congestion in the FDA, is somewhat like pointing to a minor distortion in a very large painting.

At the very least, I hope that the discussion has suggested that the practice of law in this area has become a demanding, difficult, but highly intriguing specialty in the expanding field of public law.

[The End]

Industry Lawyers Look at Weights and Measures Trends and Developments

Importance of Uniformity in the Weights and Measures Field

By HARVEY L. HENSEL

Harvey L. Hensel, Head of the Commercial Division, Law Department of Swift & Company, Delivered This Talk at the Central States Association of Food and Drug Officials Annual Conference 1964, Boyne Falls, Michigan, May 15, 1964.

DURING THE LAST TWELVE MONTHS weights and measures laws and regulations have been in the national spotlight. Industry lawyers and representatives, who in the past have worked on problems such as food additives and pesticides, have devoted a large share of their time this year to the weights and measures field. Mr. Burditt will talk to you regarding what these recent developments have been. First, however, I would like to talk to you about the subject that has caused the weights and measures laws to receive so much attention this year. This subject is uniformity and its importance to all interstate manufacturers of food and other packaged commodities.

I know it is obvious to all of you that a very large per cent of food that is sold today is produced by manufacturers who, at one plant, manufacture food that is sold in many states. Unless this manufacturer is going to adopt the very inefficient procedure of having a separate production line for each state in which he sells, he must have uniformity in the application of the weights and measures laws to his labels and package contents. I might add that even trying to produce separate products for separate states does not guarantee compliance with nonuniform state laws. An outstanding example of this is the Michigan Comminuted Meat Law. This law requires different labeling and different ingredients than the sausage laws of other

states. Since chain stores distribute to various states from one central warehouse, it is very difficult to guarantee that only Michigan sausage will be distributed in and sold in Michigan.

Interstate Manufacturers Desire Uniform Laws

I would now like to discuss for a moment the various types of uniformity in the weights and measures field that an interstate manufacturer feels should exist. The first type of uniformity desired is that of uniform laws in all the various states. Since states, like people, have different personalities, it is not easy to persuade all 50 states to adopt the same law. Nevertheless, substantial progress has been made in this direction. As of this time, 14 states have adopted the model law which has been recommended by the Association of Weights and Measures Officials. Three other states are presently considering adopting the model law. In addition to the model law, it is also necessary that the regulations under the law be uniform. At the present time 14 states have also adopted the model regulations recommended by the National Association.

Unfortunately, it is not enough to merely adopt a model law and regulations on one particular occasion. If uniformity of laws and regulations is to be achieved, whenever there is a change in the model laws or regulations these changes must also be adopted by the states. Mr. Burditt will describe for you some of the important changes in the model law and regulations being considered at the present time.

Uniformity Is Necessary Between Federal and State Laws

Another area where uniformity is necessary is between the federal laws regulating the sale of food and the state laws governing the same products. Occasionally, these laws are in direct conflict with the result that a manufacturer is unable to sell his product, even though it is a completely wholesome one, until such time as he is able either to obtain court relief or to have the laws changed. For example, the Federal Food and Drug Administration requires that all vegetable fat frozen desserts be marked on the carton as "imitation ice cream." On the other hand, some state laws specifically prohibit the use of the word "ice cream" on a dessert made from vegetable fat. It is easy to see that it is impossible to use both the phrase "imitation ice cream" and at the same time not use the words "ice cream."

Another federal-state conflict presently being litigated concerns ice cream that meets the federal standard but not a higher state stand-

ard. Can a state stop the sale of such a product? Under these circumstances the Borden Company obtained a temporary restraining order against the Secretary of Agriculture of the State of Iowa. The matter has been in litigation in the federal court for several years and is still not resolved.

Conflicts of this type have also occurred in the weights and measures field. One question, being litigated in a federal court at the present time, is whether a product that has been properly weighed and labeled in accordance with the federal law covering the product, can be prevented from being sold in a state because the state weights and measures law has requirements different than those of the federal law.

Differences in Enforcement of Weights and Measures

Another area where uniformity is very desirable is that in the enforcement of weights and measures laws. Some states are noted for their rigid enforcement of weights and measures laws. It is no secret that Michigan definitely falls in this class. On the other hand, other states are very lax in their enforcement of these laws. As lax enforcement encourages lax compliance, the possibility exists that some manufacturers may comply with the laws where they are enforced and not comply where they are not enforced. Once this attitude is adopted by even a small percentage of companies, an added competitive burden is placed on companies that feel that laws should be complied with regardless of the enforcement procedures of a particular state.

Differences Also Exist Within State

We not only find differences in enforcement from state to state but also within a state. Weights and measures officials are sometimes part of either city or county governments with little or no control at the state level. Situations often exist where a particular city or county has a very strict enforcement or interpretation of weights and measures laws even though the rest of the state has an entirely different program for enforcing and interpreting the same law.

Occasionally we find enforcement directed at a particular company, or at out-of-state manufacturers, and not against local manufacturers. This is, of course, lack of uniformity in the worst sense of the word. I would like to emphasize, however, that in my experience, this type of nonuniformity or discrimination has been very rare.

Suggestions for Uniform Enforcement

I cannot leave this field of uniformity of enforcement without mentioning a few things which I feel should be complied with by all weights and measures officials in making uniform enforcement of their laws. First, I think there should be a uniform recognition of the principle of shrinkage or evaporation as it applies to products which are so affected. I certainly recognize that the application of this principle by weights and measures officials is extremely difficult for the simple reason that what is unavoidable shrinkage for one product is not unavoidable shrinkage for another product. In addition, what is unavoidable shrinkage for one product under one set of facts concerning distribution and transportation is not unavoidable shrinkage for the same product under different methods of transportation and distribution. Nevertheless, (1) unavoidable shrinkage does occur in many products, (2) the principle is recognized in the weights and measures laws of all the states, and (3) the principle is recognized in the Federal Food, Drug and Cosmetic Act. Therefore, even though difficult to administer, the principle should be followed in enforcing weights and measures acts. Unfortunately, there is probably more lack of uniformity in the application of this principle by weights and measures officials than in any other area. Furthermore, it is my opinion that the provisions of the model law and regulations on unavoidable shrinkage do not give proper recognition to this principle as it applies to interstate shipments. Moreover, they are not in accord with the federal food and drug laws and regulations on this subject. It is my opinion that these sections of the model law and regulations should be appropriately amended.

Secondly, I feel that there is room for more uniform application of the way the tare weight of packages is computed. If the product is one in which there is evaporation, we feel that the dry tare should be used and not the wet tare. The methods used in computing the tare should be uniformly applied and should be known not only by the inspectors but also the manufacturers.

Lastly, I think any publicity given to weights and measures enforcement should be handled with care. If there is evidence of a deliberate scheme to violate the weights and measures laws, publicity may be an effective tool of the enforcement officials to bring this to the public's attention. On the other hand, publicity given to a minor and possibly accidental violation of weights and measures laws can damage the reputation of a national manufacturer without accomplishing any useful purpose.

One final comment on the subject of uniformity. It is often true that even though you want something very badly, there is a limit to the price that you are willing to pay for this desired object. This is certainly true in the case of the desire of manufacturers for uniformity in weights and measures laws and enforcement. Certainly uniformity is extremely desirable and a goal worth working hard to achieve. But even for this worthwhile goal, there are certain prices which most manufacturers are not willing to pay. Some of these are: (1) elimination of the principle of unavoidable shrinkage, (2) the substitution of strict federal control for control at the state level, and (3) adoption of laws and regulations which would require the use of the same size boxes and the same size, style, type and placement of labeling information by all manufacturers. Regardless of the fact that the current popular song on conformity indicates that we are all using the same boxes, the manufacturer still desires the right to use artistic measures to try to have his box and label more attractive than his competitor's.

Conclusion

In conclusion, I want you to know that manufacturers generally consider the role played by weights and measures officials as an extremely important one in keeping the confidence of the public in the product that they produce. There is no doubt that within the last year the recognition of the importance of weights and measures officials by companies generally, as well as the public, has greatly increased. I am sure that as these officials perform their important tasks, it is to their best interest, as well as that of industry, that uniformity always be kept in mind. **[The End]**

PESTICIDE REGISTRATION CHANGES BECOME LAW

The bill to amend the Federal Insecticide, Fungicide and Rodenticide Act (S. 1605) by eliminating the protest registration and making other changes was signed by President Johnson on May 12, 1964, becoming P. L. 88-305.

In a brief statement accompanying the signing, the President paid tribute to Rachel Carson, whose book has been considered a definite factor in spurring enactment of the legislation, and indicated his approval of additional testing which may be required under the amended law. It will also be recalled that elimination of protest registration was advocated by the President's Science Advisory Committee, Life Sciences Panel, in its Report on the Use of Pesticides (FOOD DRUG COSMETIC LAW REPORT No. 10, Part I, May 10, 1963). Full text of the Act as amended appears in FOOD DRUG COSMETIC LAW REPORTS, ¶ 840.

Industry Lawyers Look at Weights and Measures Trends and Developments

Recent Developments in the Field of Weights and Measures Labeling

By GEORGE M. BURDITT

George M. Burditt Is a Member of Chadwell, Keck, Kayser, Ruggles & McLaren, in Chicago. He Delivered This Talk at the Central States Association of Food and Drug Officials Annual Conference 1964, at Boyne Falls, Michigan, on May 15, 1964.

POKING FUN AT UNIFORMITY is a popular sport, and one which is frequently justified. For example, if Hart Bill thinking prevails, our food "little boxes" will inevitably be made of ticky-tacky, and even though there may be green ones and red ones and pink ones and yellow ones, they'll still be made of ticky-tacky and they'll all look just the same. But Harvey Hensel has just convinced me of the extreme desirability of uniformity, at least in the field of weights and measures laws and regulations and their enforcement.

Actually, Mr. Hensel and many others of us in industry have been working with Mr. Littlefield and several other state weights and measures officials for the last several months to bring about uniformity in one important area, the area of labeling requirements on packaged commodities. As Mr. Hensel indicated, I would like to review briefly with you this morning the efforts made by industry to cooperate with the Committee on Laws and Regulations of the National Conference on Weights and Measures of which Mr. Littlefield became chairman in June 1963, in proposing amendments to the Model Law and Model Regulations recommended by the National Conference.

Desirable and Undesirable Goals

But before I get into the story of developments of the last few months, I'd like to emphasize the clear distinction made by Mr. Hensel

between *uniformity* of laws and regulations among the states on the one hand—a highly desirable goal—and regimented *conformity* of design of packages on the other hand—an equally highly *undesirable* goal. In other words, while it is important to consumers, as well as to officials and industry, that the laws and regulations in Michigan be as similar as possible to the laws and regulations in Illinois, it is equally important to consumers that those laws do not so completely regulate package design and size and shape that our free enterprise system is compromised. Ticky-tacky packages that all look just the same clearly do not promote consumer interest.

Industry's Efforts to Achieve Maximum Protection for Consumer

So what I would like to talk about today is in a sense industry's efforts, in cooperation with state weights and measures officials and the National Bureau of Standards to achieve maximum and equal protection for the consumer, whether she lives in Boyne Falls, Michigan or Buffalo Valley, Tennessee, without depriving her of the tools she needs and likes to have in her daily shopping.

The National Conference on Weights and Measures has drafted and adopted a Model Weights and Measures Law analagous to the Model Food and Drug Law recommended by AFDOUS, and has drafted Model Regulations to be promulgated under the law. This Model Law has several important labeling provisions. Perhaps the most important is Section 26, which provides:

Sec. 26. *SAME: PACKAGES: DECLARATIONS OF QUANTITY AND ORIGIN: VARIATIONS: EXEMPTIONS.*—Except as otherwise provided in this Act, any commodity in package form introduced or delivered for introduction into or received in intrastate commerce, kept for the purpose of sale, or offered or exposed for sale in intrastate commerce shall bear on the outside of the package a definite, plain, and conspicuous declaration of (1) the identity of the commodity in the package unless the same can easily be identified through the wrapper or container, (2) the net quantity of the contents in terms of weight, measure, or count, and (3) in the case of any packaged kept, offered, or exposed for sale, or sold any place other than on the premises where packed, the name and place of business of the manufacturer, packer, or distributor: *Provided,* That in connection with the declaration required under clause (2), neither the qualifying term "when packed" or any words of similar import, nor any term qualifying a unit of weight, measure, or count (for example, "jumbo," "giant," "full," and the like) that tends to exaggerate the amount of commodity in a package, shall be used: And provided further, that under clause (2) the director shall, by regulation, establish (a) reasonable variations to be allowed, which may include variations below the declared weight or measure caused by ordinary and customary exposure, only after the commodity is introduced into intrastate commerce, to conditions that normally occur in good distribution practice and that unavoidably result in decreased weight or measure, (b) exemptions as to small packages, and (c) exemptions as to commodies put up in variable weights or sizes

for sale intact and either customarily not sold as individual units or customarily weighed or measured at time of sale to the consumer.

The Model Regulation also has important labeling provisions. Section 6 provides:

PROMINENCE AND PLACEMENT.—All information required to appear on a package shall be prominent, definite, and plain, and shall be conspicuous as to size and style of letters and numbers and as to color of letters and numbers in contrast to color of background. The declaration of identity, if required, and the net quantity statement shall appear on the principal display panel of the package. The name and address of the manufacturer, packer, or distributor shall appear either on the principal display panel or on any other appropriate panel. Any required information that is either in hand lettering or hand script shall be entirely clear and equal to printing in legibility.

The Committee on Laws and Regulations of the National Conference is charged with keeping the Model Law and Regulations up to date. In February 1963 this committee recommended that Section 26 of the Model Law be amended to require the director of weights and measures to prescribe by regulation

. . . the minimum type size, style and placement of any statement required by this section to appear on the package.

This would have made it mandatory for the director to regulate the *size* and *style* of type and *location* of the name of the product, the net quantity statement, and the name and address of the manufacturer, packer or distributor.

The committee also recommended that Section 6 of the Model Regulation be amended to require that the name of the product, the net quantity statement, and the signature appear on the principal display panel of the package, and to require that the net quantity statement be no smaller than a specific size, depending on the area of the principal display panel, in accordance with the following scale:

Area of Principal Display Panel	Minimum Height of Net Quantity Statement
0-15 sq. in.	1/16 inch
15-30 sq. in.	1/8 inch
30-60 sq. in.	1/4 inch
60-120 sq. in.	3/8 inch
120-240 sq. in.	1/2 inch
240-480 sq. in.	3/4 inch
Over 480 sq. in.	1 inch

Any deviation from this scale would be a per se violation of the regulation.

Needless to say, these extreme recommendations were a long step down the road to ticky-tacky. A strong industry contingent appeared at the National Conference in June, 1963, and vigorously protested the proposal at the open meeting of the Committee on Laws and Regulations. The Committee very courteously and cooperatively listened to the industry's views and changed its recommendation, so that the final committee report states:

> . . . The Committee is exhibiting its agreement with the strong consensus of those representatives of the packaging industry, trade associations, and weights and measures agencies who appeared before it during the Committee's open hearing. It is the Committee's view that definitive type sizes need to be developed and agreed to as either legal stipulations or administrative guidelines for designers of packages and package labels. The Committee is impressed, however, with the strong representations made by many delegates from the industry that time, cooperation, and collaboration will be necessary before a completely acceptable solution can be realized. The Committee, therefore, recommends that the Office of Weights and Measures of the National Bureau of Standards initiate during the coming year a serious technical study in this area and, working with qualified representatives of the packaging industry, develop specific recommendations for the consideration of the Committee.

This report was accepted by the Conference. Note, however, that this matter of location and prominence of type size is still on the agenda of the National Conference. And note also that industry is specifically invited to cooperate with the National Conference in suggesting solutions to these problems.

The Problem of Uniformity Among States

The States of North Carolina,[1] Virginia,[2] Pennsylvania,[3] and New York [4] and the Dominion of Canada [5] have already acted in this area

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[1] Notice to All Manufacturers, Processors, and Packers of Products Which Are Marketed in Package Form, Issued by the *North Carolina* Department of Agriculture, Weights and Measures Division, July 26, 1961:

"Net Content Specifications

". . . this office concludes that the following specifications will satisfy the PURPOSE and INTENT of the Law and Rules and Regulations of the North Carolina State Department of Agriculture, to wit:

"1. That the net content declaration appear on the principal label, main panel, or face, preferably at the top, in a contrasting color and not be obscured by crowding or by color, or by other legend—Said label, panel, or face being the one which is customarily displayed by the vendor within the view of a prospective purchaser.

"2. That the letters or figures that comprise the net content declaration be of a height not less than 3 per cent of the height of the package or ⅛ inch, whichever is greater."

[2] Notice to All Manufacturers, Processors, Packers of Products Sold in Virginia in package form, Issued by Commonwealth of *Virginia,* Department of Agriculture and Immigration, Division of Regulatory Services, after the December 17, 1962 meeting of the State Board of Agriculture and Immigration:

(*Footnotes continued on next page.*)

of minimum type size. California,[6] pursuant to a unique statutory requirement, is going to hold a hearing in the near future, and other states have the matter under active consideration. To compound the problem, only Virginia and Pennsylvania have similar type-size scales for the net quantity statement. Five of the six jurisdictions have different requirements.

Meetings to Discuss Solutions

As industry became aware of this two-headed problem of nonuniform super conformity—nonuniform among states but with the

"Subject: Labeling of Commodities in Package Form for Sale in Virginia.

"In an effort to assist the industry in complying with the Virginia Weights and Measures Law and Regulations relating to package marking, this office makes the following recommendations:

"1. The name of the product and the net quantity of the contents in the package in terms of weight, measure, or numerical count must appear on the principal display panel of the package in a plain, definite, and conspicuous manner and in contrasting color. The name and address of the manufacturer, packer, or distributor may appear on the principal display panel of the package or at some other plain and conspicuous place on the package.

"2. The declaration of net content on a package *should be* displayed thereon in Bold-Face Type and not less than—

"(A) one-sixteenth of an inch in height on packages, the principal display panel of which has an area of 10 square inches or less.

"(B) one-eighth of an inch in height on packages, the principal display panel of which has an area of more than 10 but less than 40 square inches.

"(C) one-quarter of an inch in height on packages, the principal display panel of which has an area of 40 but less than 100 square inches.

"(D) three-eighths of an inch in height on packages, the principal display panel of which has an area of 100 but less than 400 square inches.

"(E) one inch in height on packages, the principal display panel of which has an area of 400 or more square inches.

"(F) On packages in which the quantity statement is expressed in a fraction of a unit of weight or measure, all parts of the fraction must be equal in prominence to quantity statements on packages expressed in whole units.

"(G) Because of the design, shape, and size of some packages, it is desirable for the quantity statements to appear on the package in more than one place.

"It must be remembered that the above recommendations are to be used only as a guide. The determining factor of a label meeting the requirements of the Law and Regulations is whether or not the quantity statement expressed on a label is definite, plain, and conspicuous when considered in relation to other printing, art work, and color of the label."

[3] Notice to All Packers, Processors and Distributors, Issued by the Bureau of Standard Weights and Measures, *Pennsylvania* Department of Internal Affairs, August 21, 1963:

"We are recommending type sizes for net content declarations in order to aid compliance with the marking requirements. It is hoped that these recommendations will help in more clearly defining the meaning of prominence, definite, clear and conspicuous as they apply to quantity statements. Labels which meet the type size recommendations will be considered as satisfactory provided that the quantity statement is not obscured by other printing, art work, or color of the label.

(*Footnotes continued on next page.*)

threat of ticky-tacky packaging—a series of meetings was held to discuss possible solutions. A small group met in Pittsburgh at the time of the annual meeting of the Pennsylvania Weights and Measures

"The boldface type size recommendations and the nearest letter press type equivalents are as follows:

Size of Principal Display Panel	*Height of Lettering*	*Type Size Equivalents*
10 square inches or less	1/16 inch	6 point
More than 10 but less than 40 square inches	1/8 inch	12 point
40 square inches but less than 100 square inches	1/4 inch	18 point
100 square inches but less than 400 square inches	3/8 inch	24 point
400 square inches or more	1 inch	72 point"

[4] Notice To Whom It May Concern, Issued by the Bureau of Weights and Measures, *New York* Department of Agriculture and Markets, November 29, 1963:

"Section 221.7 of such rules and regulations requires that a net quantity statement appear on the principal display panel and that such quantity declaration be prominent, definite and plain and conspicuous as to size and style of letters and numbers and as to color of letters and numbers in contrast to color of background.

"To assist manufacturers, processors, distributors, packers and sellers of commodities to comply with the rules and regulations, the Commissioner makes the following recommendation as to the minimum size of type to be used for quantity declarations:

"(1) 1/16 inch in height on a principal display panel of an area of 20 square inches or less;

"(2) ⅛ inch in height on a principal display panel of an area of over 20 square inches to and including an area of 120 square inches;

"(3) ¼ inch in height on a principal display panel of an area of over 120 square inches to and including an area of 400 square inches;

"(4) ½ inch in height on a principal display panel of an area of over 400 square inches.

"It is pointed out that the above recommendations are to be used as a guide only. The determining factor of compliance with the rules and regulations is whether or not the quantity declaration appears on the principal display panel in a definite, plain and conspicuous manner when considered in relation to the printing, color of the label and art work."

[5] Food and Drug Regulations issued by the Department of National Health and Welfare, Ottawa, *Canada,* August 17, 1960:

"Sec. B.01.005

"(b) a declaration of net contents on a package of food shall be deemed to be clearly and prominently displayed thereon if it is in boldface type and not less than

"(i) one-sixteenth of a inch in height on packages the main panel of the label of which has an area of twenty square inches or less;

"(ii) one-eighth of an inch in height on packages the main panel of the label of which has an area of more than twenty but not more than forty square inches;

"(iii) one-quarter of an inch in height on packages the main panel of the label of which has an area of more than forty but not more than one hundred square inches; and

"(iv) three-eighths of an inch in height on packages the main panel of

(Footnotes continued on next page.)

Association. Subsequent meetings were held in Chicago and New York attended by important representatives of the food and packaging industries. The Legal Committee of the Grocery Manufacturers of America reviewed the matter thoroughly at a second meeting in New York City. A very large meeting was held in San Francisco. Finally, an open *ad hoc* Industry Committee, under the chairmanship of Frank T. Dierson, general counsel of the Grocery Manufacturers of America, was organized at a meeting in Washington December 1963. James Bell of the National Canners Association is Vice Chairman of the Com-

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the label of which has an area of more than one hundred square inches."

[6] *California* Business and Professions Code, Sec. 12606 (Chapter 903, Laws 1963):

"12606. Whenever any commodities are sold in containers, the net quantity of the contents of the container shall be plainly and conspicuously marked, branded, or otherwise indicated on the principal display panel of the container or on a label or tag attached thereto; provided that containers, circular in cross-sectional area, may contain the statement of net quantity on either the principal display panel or on an area immediately adjacent thereto, which area shall be equivalent to not less than 20 percent of the entire label, or on the top of the container if the cross-sectional area is not less than the cross-sectional area of the bottom of the container. The size of the markings shall be governed by the area of the display panel, or the area of the label or tag attached.

"The director shall establish necessary rules and regulations to carry out the design of this chapter. Any such rule or regulation, or amendment thereof, shall be adopted and promulgated by the director in conformity with the provisions of Chapter 4.5 (commencing with Section 11371) or Part 1 of Division 3 of Title 2 of the Government Code.

"The provisions of this section do not apply:

"(a) To containers while being used for the delivery of a food which, in accordance with the practice of the trade, is to be processed, labeled, packed or repacked on premises other than where originally placed in such containers.

"(b) To transparent wrappings, devoid of any words, letters or numerals, used as a means of protecting the commodity, when the weight or count of the contents, or any portion thereof, is accurately determined at time of, and for the immediate purpose of, sale.

"(c) To an unlidded container when the weight of the contents, or any portion thereof, can be accurately determined at the time of, and for the immediate purpose of sale, by the seller at the request of the buyer, on a weighing device installed for the purpose on the premises of the seller and sealed in accordance with the provisions of this division.

"(d) To an unlidded container when the count of the contents, or any portion thereof, is accurately determined at time of, and for the immediate purpose of, sale.

"(e) To containers of fruits and vegetables, when the quantity is expressed in terms of count as required by the provisions of Chapter 2 (commencing at Section 781), Division 5 of the Agricultural Code, and the count is accurate with no tolerance below the actual count allowed.

"(f) To containers of petroleum products where the net quantity of the contents of such containers is plainly and conspicuously marked, branded or otherwise indicated on the side or top thereof."

mittee, and John Speer of the International Association of Ice Cream Manufacturers is Secretary.

The *ad hoc* committee has the broadest possible membership and has at all times been open to anyone else who would like to join. It is at present composed of scores of members representing virtually every major national food association, many associations which represent industries selling packaged commodities other than food, several important packaging material associations, and, of course, a great many representatives of individual companies. The cooperation of such a diverse group, and their sincere efforts to promote consumer interest, have been most encouraging to witness.

A Drafting Subcommittee was appointed at the December meeting to prepare and circulate a questionnaire with recommendations as to the industry positions, and to summarize the answers for presentation to the Committee on Laws and Regulations of the National Conference, all of which assignments were accomplished in time for final review by the full Industry Committee at a meeting in Washington in February. The Industry Committee then made its report to the Committee on Laws and Regulations.

Industry Committee Report Makes Four Points

(1) The quantity statement should appear on the principal display panel, unless the principal display panel is under four square inches in size or unless the package is an industrial-type package, such as a drum of lard.

(2) "Principal display panel" means that part of a label most likely to be presented, displayed or examined under customary conditions of purchase.

(3) Rules governing type size should be advisory and should be based on the area of the principal display panel with 1/16 inch for panels of 0-25 square inches, 1/8 inch for panels from 25-120 square inches, ¼ inch for panels 120-400 square inches, and ½ inch for panels over 400 square inches.

(4) Adequate time should be given to use up old labels and redesign new labels.

Recommendations of Committee's Tentative Report

This Report was presented to Mr. Littlefield's Committee in February, and last month the Committee's Tentative Report was made

public in the announcement of the 49th National Conference on Weights and Measures. The Tentative Report makes several recommendations:

(1) No amendment should be made in the Model Law or Model Regulations at the June 1964 Conference, but state officials should issue administrative rulings to the effect that conformance with the standards set forth in the Committee report will be considered to fulfill the label requirements of the state statute and regulation. Primarily because of the complexity of the problems with which we are dealing, and because of the importance of making certain that the proposals are exactly as they should be before a statutory or regulatory amendment is recommended, many of us in industry concur in this recommendation, provided that uniformity is not thereby jeopardized.

(2) "Principal display panel or panels" is defined

> . . . that part, or those parts, of a package that is, or are, so designed as to be most likely displayed, presented, shown, or examined under normal and customary conditions of display and purchase.

This definition, when read with paragraph 3(d) of the report, does not appear to be significantly different from the Industry Committee's recommendation or from current law, and many of us in industry have no objection to it.

(3) The quantity statement regulations would be effective as to all package labels printed or ordered after July 1, 1964—two weeks after the National Conference adjourns—and as to all packages, including reusable containers, as of July 1, 1966. This time schedule seems to many of us in industry to be too short, and we therefore will presumably urge the Committee on Laws and Regulations to reconsider the Industry Committee's proposal. The industry proposed that the type size and placement provisions of the proposed regulation be effective immediately upon promulgation as to (a) all labels redesigned thereafter, and (b) all labels prepared from plates, dies, cylinders, etc., made thereafter, and two years after promulgation as to all other labels except single use or reusable containers originally filled within the two year period.

Rules for Quantity Statement

The third paragraph of the Tentative Report also lays down a number of rules for the quantity statement:

(a) It must appear on all principal display panels and must be parallel to the base of the package. The intent of this suggestion is

undoubtedly sound, but exceptions should be made for round labels or lids and further clarification is probably necessary.

(b) The net quantity statement must be in bold face or equivalent type. Many of us in industry feel strongly that the kind of type used on packages must be left to our package designers provided, of course, that the type is prominent and contrasts with the background.

(c) The net quantity statement must be in a color which contrasts with the background, of course a sound requirement, and

(e) It must meet a minimum type-size scale similar to that recommended by the Industry Committee, except that no minimum is provided if the principal display panel is less than four square inches.

Subparagraph (d) of the third paragraph of Mr. Littlefield's report lays down specific rules for measuring the area of the "principal display panel." On rectangular containers, the area of the principal display panel is "the product of the height times the width." On cylindrical containers, the label of which covers the entire cylindrical surface, it is "the product of the height times ⅓ the circumference." On envelopes, sacks, bags and other flat containers it is "the total printed area or ⅓ the total flat area, whichever is greater." And on containers with either a distinctly identifiable label area or with the label information directly applied to the surface of the container, it is "the total actual area of the label or label space." These are interesting but new concepts which merit substantially more consideration than has been possible in the few weeks since the Tentative Report was published. For example, no provision is made for a label on a glass jar which covers only a portion of the height but all of the circumference of the jar.

Subparagraph (f) lays down a novel rule that "the quantity statement shall be presented in an area free from other printing or marking, and such area shall extend in all directions from the statement in dimension not less than twice the height of the numbers and letters of the quantity statement." The result is that the larger and therefore the more prominently your quantity statement appears, the more blank space you have to leave around it. It seems to me that if this proposal is adopted, package designers will be forced to put the quantity statement in the smallest permissible size, a result directly contrary to what the Tentative Report and the Industry Committee are trying to accomplish.

The Industry Committee is now polling its members for comments on the Tentative Report of Mr. Littlefield's Committee, and these

comments will be presented at the open meeting of the Committee on Laws and Regulations on June 15th.

One of the most important results of these last few months has been the exceptional cooperation between weights and measures officials and industry representatives. I personally very much appreciate the courtesy and consideration which Mr. Littlefield and his Committee have extended to us in industry and I hope that the weights and measures officials have the same degree of respect for us as we have for their integrity and ability. The inevitable result will be promotion of the interest of consumers through better, and uniform, weights and measures laws and regulations—without ticky-tacky. [The End]

REPORT ON "TRANQUILIZING" DRUGS

"Tranquilizing" drugs are misnamed and show broader effects than previously suspected, according to a recent report by scientists at the National Institute of Mental Health, Public Health Service, Department of Health, Education and Welfare.

New evidence indicates that the phenothiazines, the most widely used of the "tranquilizers," improve the passive, withdrawn, apathetic patient even more than the agitated, abusive one. The drugs' action, therefore, is broader and more versatile than is presently outlined in standard medical texts.

This finding was reported by Dr. Jonathan C. Cole, Director of the Institute's Psychopharmacology Service Center, at a Veterans Administration Psychiatric Conference held recently in Kansas City, Missouri.

His conclusion was based on a nine-hospital collaborative study of 340 patients, financed and directed by the Service Center. It showed that the following symptoms which are considered fundamental to schizophrenia are the most improved by the phenothiazines: poor social participation, poor self care, confusion, indifference to environment, and hebephrenic gestures (grimacing and giggling).

Psychiatric teams which evaluated patients with these symptoms after six weeks of drug therapy found them markedly improved. "In contrast," Dr. Cole added, "hostility, agitation, anxiety, and ideas of persecution—symptoms which are usually regarded as 'target symptoms' for tranquilizing therapy—although influenced by the drug treatment, were not affected to as great a degree."

"During the past dozen years," he said, "the phenothiazines have been stereotyped as 'ataractics' or 'tranquilizers,' the implication being that their dominant action is to calm excited patients by relieving the patient's anxiety. . . . We have presented evidence to confirm that phenothiazines . . . have a wide variety of clinical effects beyond tranquilization."

The drugs were shown to act in two ways, according to the study's coordinator, Dr. Solomon Goldberg. They alleviated the patient's pretreatment symptoms, and prevented the development of other schizophrenic symptoms the patient did not have before treatment. The authors conclude that the drugs seem to have a general alleviating and preventive anti-schizophrenic action, and can be used appropriately for a wide variety of schizophrenic patients.

The Challenge: Improving Controls in Frozen Foods

By GEORGE P. LARRICK

The Following Paper Was Presented Before the National Association of Frozen Food Packers' Meeting in Chicago on March 20, 1964. Mr. Larrick Is Commissioner of Food and Drugs.

A BASIC, CONTINUING PROBLEM confronting both the food industries and the Food and Drug Administration is the necessity for assuring ourselves that innovations in food processing and packaging are accompanied by adequate controls to assure food safety. In an industry, such as yours, where there has been such a dynamic growth in the volume and variety of products and in new processing and packaging methods, the need for such controls and an interest in their improvement is a major industry challenge and obligation. From the inception of a new product—in product development—to the delivery of the finished product to the consumer, the frozen food industry and allied interests can and do apply control procedures. How to improve them requires the application of technological know-how on your part, aided by research from industry and government. I propose to discuss some of the controls in effect and some which we are convinced can be improved to cope with present or potential problems.

Efforts to Control Bacterial Contamination of Foods

Bacterial contamination of foods, including frozen foods, from such organisms as staphylococci and salmonellae, needs particular attention. Total bacteria counts and coliform determinations are not enough. The 1959-1960 joint Association of Food and Drug Officials of the United States—industry survey of bacterial contamination of frozen precooked foods, in which FDA cooperated, was a start in pointing up the problem of insanitary conditions, temperature abuses, and other factors contributing to high bacterial counts. As a result of this survey, your association began a program of sanitation seminars. You prepared an information booklet for these seminars entitled, "Five Steps to Sanitary Quality of Frozen Foods." This was a fine

program, but the stress placed on the improvement in operating practices is one that needs constant reiteration and special vigilance. In this area you have the tools—in many cases, simple ones such as adequate handwashing facilities. Yet it is desirable that these be supplemented by a bacteriological test program if the efficiency of your procedures is to be checked out.

Routine bacteriological controls are not sufficient to detect potentially pathogenic microorganisms which may be present in raw ingredients. Since 1959, the stepped-up research and surveillance programs by government and industry on salmonellae have made us aware of the importance of this group in many foods, particularly those containing poultry and egg ingredients. Many frozen precooked foods are in this category. We have initiated a program whereby, through educational and appropriate regulatory means, we hope to stimulate egg breakers and food manufacturers using egg products to eliminate salmonellae from their products. We have noted with interest the efforts of one trade association (the Institute of American Poultry Industries) to set up and operate a salmonellae control program for its members.

Thus, bacteriological methods such as those for detection of staphylococcus enterotoxin and salmonellae which only a short time ago were essentially research tools are today available to the industry and the government bacteriologist for control and regulatory purposes. We know that the extent to which some in industry adopt these methods is influenced by the attention given to the problem by FDA and state and local officials. Yet a food manufacturer's interest in the safety of his products must and does continue as the principal motivation for improving his controls.

Detection of Pesticide Residues

Pesticide residues in frozen foods are a problem requiring unique controls where raw agricultural commodities of a perishable nature are purchased. FDA and state regulatory and surveillance programs on pesticide residues on raw agricultural commodities reveal that only a small incidence of samples bear illegal residues. The prudent frozen food packer, however, does operate his own competent control system. When feasible, this includes a close check of a grower's spray schedule supplemented by use by the laboratory of rapid screening methods to test samples of crops shortly before or upon delivery to the plant. Since FDA has pioneered in the development of many of the currently used pesticide residue methods, we will assist your association or

individual firms which wish to learn more about rapid screening and multiple detection methods.

An ever-present problem, both for the frozen food packer and FDA, is the care employed in adding just the right amount of a direct food additive for which there are tolerance limitations. There is a basic assumption in the use of these that the food manufacturer will take the necessary precautions to avoid misuse. When a regulation limits an additive in the finished food to several parts per million, only good controls employed in batch after batch provide the necessary assurance that the additive present is within legal limits.

Plant Inspection

When our inspectors visit your plant—about once every two years on the average—they need to know how good your controls are so we can evaluate how you are carrying out your responsibility day in and day out. Where our inspectors find there is a likelihood that your employees used an additive in excessive amounts or have used an additive which is not authorized for the particular food involved, they will point this out to management. By reporting these observations to you, FDA feels that you are then able to check immediately and eliminate an unsafe situation on future production. However, if you have already shipped products which may contain an unsafe additive, the FDA must take the necessary steps to assure removal of illegal lots from channels of consumption.

Problems which could arise from incidental additives in foods through packaging materials and equipment are eliminated where the manufacturers of such materials and equipment go through the premarketing clearance regulations under the Food Additives Amendment. The food packer himself should have few control problems in this area, as far as safety is concerned. The research required to prove the safety of these materials has been quite expensive for the petitioners in many cases. Members of the packaging industry have done a fine job in clearing their materials and they, as well as the consumer, have benefitted in the process. A spokesman for the flexible packaging industry recently pointed out how this industry had benefitted. Thus, for the first time many firms took a really close look at the ingredients and processes they had been using for years. As a result of this examination, some food packaging materials were improved and manufacturing economies effected. Many firms were introduced to advanced scientific methods—such as infrared spectroscopy and gas chromatog-

raphy. These methods were then available in solving other industry problems.

Improper Handling of Food After It Leaves the Manufacturer

All along there has been recognition that much of the packer's care and controls may be cancelled out by improper handling of the frozen product after it leaves the manufacturing plant. We are well aware of your association's pioneering efforts in pointing out the need for proper temperature controls in every phase of transportation and handling—trucks, railroad cars, warehouses, and wholesale and retail establishments. Additionally, the Association of Food and Drug Officials of the United States has done a great deal of work in this area in the development of that organization's model code for handling frozen foods.

We recognize that there are differences of opinion as to precisely what controls should be imposed, including some who would prefer a completely voluntary operation. We see no responsible disagreement, however, that the objective is to see that the frozen food package is properly handled all the way to the consumer. It is our hope that, with this common objective, means can be worked out so that there will be no question but that those who mishandle the frozen food products will stand accountable for their actions. We think it is highly desirable for this regulation to be exercised by local authorities, rather than to let some sensational accident precipitate federal regulation at the level of retail sales.

There are other problem areas where controls can be improved. One is that frozen foods packed in metal cans, labeled simply "Keep Frozen," are mistaken by consumers for a canned or nonperishable food. Consideration should be given to a standard, conspicuous marking for such frozen food containers, thus reducing the chance for consumer error. Another is the possible use of defrosting indicators as a check on proper temperature maintenance of the packaged frozen food.

Food labeling and packaging problems are of considerable concern to consumers today and this concern, of course, is reflected by all groups that have a responsibility to the consumer. More and more top management people in the food industry are examining their packaging procedures to eliminate deception. More attention is being given to such critical areas as vignettes which may mislead, net contents declarations, ingredient statements, servings per package, and product claims.

There is no question in my mind that most frozen food packers do make an effort to label and package their products honestly. But the problem is this—how to maintain a fair, ethical packaging standard for one's products in the face of competition from the firm that doesn't maintain such standards. The packer who uses misleading "gimmicks" in the labeling or in the fill of his packages reaps extra profit, and as you are aware, FDA has not been very successful in controlling certain deceptive packaging practices.

The growing interest in matters involving the consumer's welfare is certainly emphasized by the appointment of Mrs. Esther Peterson as a Special Assistant to the President. Honest packaging has been a matter to which she has repeatedly referred.

Consumer Education Programs

Over the past few years, the FDA has given increasing attention to consumer education. An informed consumer is a bulwark against false claims, be they from the food faddist or from the overenthusiastic promoter of a new food product. We have given consumer education increased emphasis by setting up a Division of Consumer Education in our new Bureau of Education and Voluntary Compliance. This division has already expanded our consumer information program—using on a regular basis, for the first time, the mass media of TV and radio; preparing study materials for high school science teachers to reach tomorrow's homemakers; and issuing concise memos to consumers on subjects which consumers frequently ask us about in the hundreds of letters we receive daily.

I am happy to note that your association is also conducting a consumer education program.

Recently our Division of Consumer Education issued a consumer memo inviting consumers to participate in the hearings to be held on standards for frozen raw breaded shrimp products. The memo contained a brief summary of the established definitions and standards of identity and the specific matters to be taken up at the hearing. It has always been our aim to obtain adequate consumer representation at these hearings and this type of educational publicity may help us to do so.

The FDA's recent reorganization recognized not only the importance of consumer understanding, but of an informed industry by establishing a Division of Industry Advice in the Bureau of Education

and Voluntary Compliance. Its function is to concentrate on a broad program of promoting voluntary compliance by the regulated industries with the various statutes enforced by FDA.

Within this division, the Industry Information Branch works primarily with industry trade, professional and farm groups. It provides them with informational materials, such as leaflets, film strips, etc., explaining FDA's policies, procedures and regulations. Acting as liaison, the branch determines which compliance problems the industry considers of prime importance and assists the industry groups in preparing informational materials to cope with such problems. Thus, trade associations, such as yours, can play a key role in preparing and distributing information that promotes compliance with the pure food laws.

The Advisory Opinions Branch of this same division assists individual firms and industry groups with immediate compliance problems offering written comment on proposed product labeling, the application of regulations to particular products, and, of course, our doors are always open to all who want to come in or telephone to talk over their problems.

The challenge—to assure the safety of innovations in frozen foods—is one shared by your industry and FDA. Recent amendments of the food and drug law show a basic trend toward making it more of a preventive statute, by requiring premarketing clearance, for example, for food and color additives, rather than a merely punitive one. To achieve maximum prevention of violations requires improved controls by industry in all aspects of production and marketing. As I have pointed out in a recent article:

> Industry is quite capable, in my judgment, of making enforcement proceedings virtually unnecessary except for the incorrigible fringe of deliberate violators.

[The End]

PRESCRIPTION DRUG NAME REGULATIONS HELD INVALID

The "established name" drug regulations, which require that the established name of a prescription drug accompany each appearance of the trade name on any label, labeling, or advertising of a drug, are invalid, according to the United States District Court in Wilmington, Delaware. The court held that Congress, in enacting Section 502(e)(1) and 502(n), intended to put an end to the practice of mentioning the generic name of the drug in an inconspicuous place, and to implement that purpose it required that the established name should be printed "prominently." But it had no intention of requiring that the established name appear every ime the trade name is mentioned.—*Abbott Laboratories v. Celebrezze,* FOOD DRUG COSMETIC LAW REPORTS ¶ 40,119.

The Evolution of the Drug Laws of the United States, 1906-1964

By M. L. YAKOWITZ

This Article Was Delivered at the Pharmacy Congress Sponsored by the College of Pharmacy of St. John's University, Jamaica, New York, on March 17, 1964. Mr. Yakowitz Is Director of the Division of Case Supervision, Bureau of Regulatory Compliance, Food and Drug Administration.

THE STORY BEHIND our country's present drug law has a great deal of historic significance and it is a pleasure to discuss this interesting story with you. It may be noted at the outset that this particular piece of Americana holds interest not only for persons working in the drug field, but also for professional historians. Thus, at the Seventy-Seventh Annual Meeting of the American Historical Association, held in Chicago on December 30, 1962, there were a number of prepared papers dealing with the history of the Federal Food, Drug and Cosmetic Act.

One of the speakers at the 1962 meeting of the American Historical Association made a most illuminating comment when he stated that the evolution of America's food and drug laws is a remarkable example of "the adaptation of democratic institutions to modern industrial society." By this, the historian obviously meant that each of the food and drug laws passed by Congress, beginning with the original Federal Food and Drugs Act of 1906, has represented a practical step by our national legislature to deal with important problems that arose out of the rapidly developing technology of the present century, and the accompanying social changes. The proof of this is evident when we consider the problems that arose in the drug field, and how Congress dealt with them in the Federal Food and Drugs Act of 1906, the basic Federal Food, Drug and Cosmetic Act of 1938, the Durham-Humphrey Amendment of 1951, and the Kefauver-Harris Amendments of 1962.

Early Problems

At the turn of the century, two important problems were recognized in the drug field. These were the undeclared presence of morphine and other narcotics in proprietary remedies and the outrageously extravagant claims made for drug products sold to the public. The Federal Food and Drugs Act of 1906 dealt with the first problem by requiring that if a product contained any morphine, opium, cocaine, heroin, or certain other potent substances, the label had to declare the presence and amount of such ingredient. As to the problem of unwarranted therapeutic claims it was hoped this could be dealt with by a provision of the 1906 law which stated that a drug was misbranded if its labeling contained any false or misleading statement "regarding such article, or the ingredients or substances contained therein."

Sherley Amendment

Unfortunately, the language in the 1906 law intended to prevent false therapeutic claims was found defective by a Supreme Court decision in an important test case. It was not until Congress passed the Sherley Amendment in 1912 that there was a definite basis in the law for curbing false claims. The Sherley Amendment stated that a drug was misbranded if its labeling contained "any statement . . . regarding the curative or therapeutic effect of [the] article . . . which is false and fraudulent."

As time went on, it became recognized that the pioneer law of 1906, even with the Sherley Amendment of 1912, was not satisfactory for dealing with problems in the drug field. For example, the government could take action against extravagant therapeutic claims only if it could prove that the claims were "false and fraudulent." To prove a fraudulent intent is usually a very difficult matter. In many contested court actions, the government was able to prove the medical claims were false, but lost the case because it could not prove a fraudulent intent. In brief, it could and did happen that an ignoramus who marketed a wholly unscientific preparation for treating serious disease was immune from action under the law because it was impossible to prove a fraudulent intent. The paradoxical result was that the ignoramus was saved from punishment by his own ignorance!

"Elixir of Sulfanilamide" Tragedy

An important defect in the 1906 law was that it did not prevent the marketing of new products without prior testing to determine the

effects of the new preparation. This latter point was strongly impressed on the public and Congress by the "Elixir of Sulfanilamide" tragedy. For the lesson it provides regarding the drug field of 25 years ago, it is worthwhile relating the story of this drug.

Sulfanilamide was the first of the sulfonamide group of drugs used for treating infection, including internal infection. For several years after its introduction in 1936, sulfanilamide was probably the most important single drug available to physicians. It was distributed by many firms in solid preparations, such as tablets and capsules, but was not available in a liquid preparation because of its tendency to decompose in solution.

In an endeavor to develop a stable solution of sulfanilamide, one drug firm set its chemist the task of finding a solvent in which sulfanilamide does not decompose. By testing the reaction of sulfanilamide with a large number of liquids from every conceivable source, including solvents used in the paint and varnish industry, the firm's chemist was successful in finding a solvent, diethylene glycol, in which sulfanilamide is both soluble and stable. Successful in its "research," the firm flavored and sweetened its diethylene glycol solution of sulfanilamide to form a palatable "elixir" and commenced marketing the product.

Unfortunately, no thought was given by the firm to the possibility of toxicity from the new solvent. This oversight had tragic consequences. Diethylene glycol is quite toxic and more than 100 persons died from consuming the diethylene glycol preparation.

The "Elixir of Sulfanilamide" occurrence hastened enactment of a modernized food and drug law that had been pending as a bill in Congress for five years. Shortly after the "Elixir of Sulfanilamide" episode, Congress enacted the pending bill, but first inserted a provision requiring proof of safety before a "new drug" could be marketed. Thus was born the famous Federal Food, Drug, and Cosmetic Act of 1938.

1938 Law's Major Provisions

The major drug provisions of the law enacted in 1938 were as follows:

(1) A drug was in violation of the law if the therapeutic claims made for it were false or misleading—the government no longer had to prove that the sponsor had a fraudulent intent before the government could take action to have the article removed from the market

and the sponsor prosecuted; (2) the government was given limited authority to conduct factory inspections to obtain information about the procedures used by the manufacturer; (3) medical devices were for the first time brought under FDA's jurisdiction; (4) the label of every drug had to state the name of each active ingredient and state the amount of certain potent substances as specified by the Act; and most important, (5) a "new drug" could not be marketed unless the sponsor filed with FDA a new-drug application containing convincing evidence that the drug was safe for the intended purposes.

The 1938 law did not specifically class any drug as a "prescription drug." However, it gradually was recognized that some "old" drugs, and many "new" drugs, are not safe for unsupervised use by the general public and that such drugs should be available to the public only on the prescription of a licensed practitioner. In 1951, Congress enacted the Durham-Humphrey Amendment which divides drugs into two broad classes: (1) articles which are safe for use without medical supervision and which may therefore be sold as over-the-counter drugs; and (2) articles which are not safe for unsupervised use and which are therefore restricted to dispensing on the prescription of a physician. This second category of drugs must be labeled with the legend "CAUTION—Federal law prohibits dispensing without prescription."

As this audience knows better than most groups, there has been a great increase in the number of new drugs in recent years. This has had a tremendous impact on the practice of medicine, a fact which is pointed up by the statistic that almost 50 per cent of the drugs dispensed today were not available six or seven years ago. With this rapid development of the drug industry, some problems arose which received attention by Congress, culminating in the Kefauver-Harris Drug Amendments of 1962.

Some of the problems dealt with by the Kefauver-Harris enactment are: (1) questionable effectiveness of new drugs; (2) use of advertising that emphasizes claims of benefit but fails to reveal the possibility of adverse side effects; and (3) questionable practices in the distribution and testing of investigational new drugs. The Kefauver-Harris enactment constitutes a major revision of the drug provisions of the Food, Drug and Cosmetic Act and it is therefore worthwhile considering each provision of this new law.

Registration

Under the new law, persons and firms engaged in the manufacture, repacking, or relabeling of drugs must "register" annually with FDA. This registration requirement applies to those engaged in intrastate business, as well as those engaged in interstate business.

We have issued a simple form for use in registering. The registrant is required to provide his name and the address of his establishment and, in addition, is asked to provide information about the type of operation conducted by him, the class of drugs that he handles, and the size of his establishment.

Foreign drug firms will be permitted to register under regulations which, when promulgated, will include procedures for inspection or other arrangements that will enable a determination to be made as to the conditions under which their products are manufactured.

The new law requires that FDA inspect every registered drug establishment at least once every two years. Also, the new law specifically adds consulting laboratories doing analytical work for drug firms on a fee basis as establishments subject to inspection.

Factory Inspection

The new law strengthens the inspection provisions in the case of establishments that manufacture or deal in prescription drugs. Such establishments must make available all files, records, and process and control information, etc., that have a bearing on possible violation of the law with respect to prescription drugs. Financial data are exempt from this new requirement.

Manufacturing Controls

Proper manufacturing of drugs requires highly qualified and trained personnel, adequate manufacturing facilities and special laboratories for checking on ingredients, partly processed batches, and finished drug preparations, etc. Under the pre-existing law, FDA lacked specific jurisdiction over the manufacturing procedures used by drug firms—we were able to take action against a poorly made drug only after the product was sampled in interstate commerce and the sample was found by our laboratory tests to be actually subpotent or not of the proper purity.

The Kefauver-Harris law enactment overcomes this deficiency by specifically requiring that the facilities, methods and control proce-

dures used by a firm in manufacturing a drug must conform with "current good manufacturing practice." We have promulgated regulations to serve as guidelines for the drug industry.

Drug Names

The Kefauver-Harris enactment coins a new phrase, the "established name," meaning the nonproprietary name by which a drug or drug substance must be designated on the label. For substances that have been available for years, it will turn out in most instances that the "established name" is the name that is already familiar as the "common or usual name" of the substance. However, the Secretary of Health, Education and Welfare is authorized to designate the "established name" of any substance when this is desirable in the interest of usefulness and simplicity.

Prescription Drug Advertising

The new law requires that any advertisement for a prescription drug must provide the same ingredient information that is required to appear on the label of the drug, plus a "brief summary relating to side effects, contraindications, and effectiveness." Enforcement and regulation making under this new provision are assigned to FDA.

The obvious objective of this portion of the law is to require prescription drug advertisements to give adequate information regarding the composition of the drug and to have the advertiser provide the physician with a fair and balanced picture of the "good" and the "bad" of the drug. The regulations promulgated by us require that the claims made in the advertisement must be truthful and must be combined with appropriate information regarding the side effects and contraindications of the drug.

New Drugs

Under the pre-existing law, an article was regarded as a "new drug" if it was not generally recognized by medical experts as safe for the intended use. Such a product could not be released for marketing until the sponsor filed with FDA a new-drug application containing convincing evidence that the drug was safe for the intended purposes. Under the new law, the definition of the term "new drug" has been expanded, so that now a product must be cleared with us if it is not generally recognized by qualified experts as both safe and effective for the intended use. The sponsor must submit satisfactory

evidence of safety and effectiveness before we may "approve" the new-drug application.

Products that were cleared under the safety provisions of the pre-existing law have until October 10, 1964, as a grace period, but by that time, the sponsor must file substantial evidence of effectiveness for the product.

If the sponsor fails to do this, the new law authorizes us to take action against the drug by withdrawing approval of the new-drug application. Proposed regulations were just recently published.

The Kefauver-Harris enactment contains several other important provisions affecting new drugs. For example, we are now authorized to require manufacturers and distributors of new drugs to submit reports of adverse effects, etc., with respect to such drugs, even after the article has been cleared through the new drug procedures. The purpose of this particular requirement is to enable us to obtain all available information regarding newly discovered adverse effects, etc., so that new warnings may be required in the labeling and advertising for the drug, or, if necessary, the drug may be forced off the market.

The Kefauver-Harris enactment contains provisions dealing with the procedures under which an investigational new drug may be distributed for test purposes. The regulations that we have adopted require that the investigational new drug must be adequately tested in lower animals before it is administered to human beings in clinical trials. Also, in accordance with the Kefauver-Harris enactment, our regulations require that the sponsor of the new drug must have the investigator certify that the investigator will inform the patient that the drug being administered is an experimental article and that the investigator will obtain the consent of the patient or the patient's representative, except in those instances in which the investigator concludes that this is not feasible, or, in his professional judgment, is contrary to the best interests of the patient.

Some other requirements of the investigational new drug regulations that are of interest are these: The sponsor of the investigational new drug must submit to us the name and a summary of the training and experience of each investigator, with an outline of the planned investigations. Further, if the sponsor intends to charge the investigator for the new drug, he must provide a full explanation of why this is necessary.

Antibiotic Drugs

Under the pre-existing law, only antibiotic products containing penicillin, streptomycin, bacitracin, chlortetracycline, or chloramphenicol, or derivatives of these antibiotic substances, were subject to certification. Full certification required that a sample from each batch of the antibiotic drug had to be submitted for testing in our laboratories, and a certificate for the particular batch was issued by us if the drug had the proper potency and purity, etc. Under the Kefauver-Harris enactment, all antibiotic drugs intended for use in humans will be subject to the certification procedures. However, this new law authorizes us to establish exemptions, so that a particular antibiotic drug, even though intended for use in humans, may be exempted from batch certification if the manufacturer can comply with the exempting provisions.

Veterinary Drug Preparations

Most of the provisions of the Kefauver-Harris enactment apply to veterinary drugs as well as to drugs intended for human use. However, the only antibiotic drugs for veterinary use that are subject to certification are those containing penicillin, streptomycin, bacitracin, chlortetracycline, or chloramphenicol, or derivatives of these five antibiotic substances.

A significant change in the veterinary drug field brought about by the Kefauver-Harris enactment relates to medicated feeds containing stilbestrol or other ingredients which are known to be capable of inducing cancer when administered in a particular fashion. Under the new law, it will be permissible for us to approve new-drug applications for medicated feeds containing such substances if the available evidence shows that the medicated feed does not adversely affect the health of the animal and does not leave a residue of the drug in the edible portions of the animal or in any food, such as milk or eggs, produced by the animal. Proposals to market such medicated feeds must also be cleared under the "Food Additives" provisions of the Act.

In closing, it is pertinent to note that each time the food and drug laws of this country have been improved to bring the control of drugs in line with technological advances, there have been those in the regulated industry who have feared that the change in law would stifle industry or would stifle research. This view was expressed in the writings and statements of some industry representatives following enactment of the Kefauver-Harris law. However, the fact of the

matter is that through the years, as industry has improved its practices in order to meet up-to-date requirements in the laws and regulations, the industry has benefited immeasurably. This point is well recognized by the more thoughtful members of the drug industry.

Thirteen years after the Food, Drug and Cosmetic Act of 1938 was enacted a major drug house published a book titled *The Odyssey of Modern Drug Research* in which it stated with regard to the effect of the 1938 law that:

> [T]he entire industry settled down to observing the law and the complex regulations issued under the wide enforcement powers granted to the Food and Drug Administration. And in the course of doing so, the manufacturers—some willy, some nilly—found themselves compelled to increase their scientific and technical personnel, to accumulate a vast body of medical evidence on which to launch their products, and in general to apply the principles of rational therapeutics to all their works.

Our confidence in the high principles and good sense of the industry leads us to anticipate that as time goes on, all members of the drug industry will regard the Kefauver-Harris law as a valuable enactment that will stimulate further infusion of scientific procedures into drug manufacture and use. Most of the forward-looking members of industry have already reached this conclusion regarding the law.

[The End]

REVISION OF ICE CREAM STANDARDS

Leading ice cream manufacturers have proposed several amendments to the Federal Definitions and Standards of Identity for ice cream and related frozen desserts. The proposals would make the following changes in the standards: (1) Revise labeling requirements to establish guidelines by which the name given a particular flavor of ice cream would be determined by the kind and amount of natural and/or artificial flavoring it contains; (2) Permit the use of concentrated cheese whey or dried cheese whey for supplying not more than 25 per cent of the nonfat milk solids in ice cream, and permit the use of a modified skim milk meeting certain prescribed requirements.

Cheese whey is now permitted as an optional ingredient in fruit sherbets, and its use must be declared on the label. The ice cream firms proposed to repeal this requirement and also to permit the use of whey in ice cream without label declaration. On its own initiative FDA proposed that if whey is made an optional ingredient for ice cream, then its use should be declared on the label of ice cream as well as on the label of other frozen desserts.

In addition to spelling out how the flavor of an ice cream is to be determined and declared, the proposed amendments also specify the relative size of letters to be used. Two proposals were offered for designating seaweed stabilizers by the names used in the food additive regulations.

FDA invited interested persons to submit their views in writing within 60 days to the Hearing Clerk, Department of Health, Education and Welfare, Rm. 5440, 330 Independence Ave., S. W., Wash., D. C.

Government Control of New Drug Testing and Introduction

By RALPH G. SMITH, M. D.

Dr. Smith Is Director of the Division of New Drugs, Bureau of Medicine, Food and Drug Administration. This Is the Paper He Presented at a Symposium of the Carl Neuberg Society for International Scientific Relations in New York City on April 15, 1964.

THE OPPORTUNITY TO APPEAR AS A SPEAKER at a symposium of this renowned society is much appreciated. The subject assigned to me is one with which I have been concerned for the past 14 years. Although this is a relatively short time, it covers more than half the period during which the government of this country has played a role in the testing and introduction of new drugs.

Prior to the 1938 Federal Food, Drug and Cosmetic Act, the government had no control over the introduction of new drugs. It was only after they were in interstate commerce that they were subject to such provisions of the then-existing Act that covered adulteration and misbranding. Although the need of further controls was recognized by those intimately concerned with the regulation of drugs well before 1938, it required a major drug disaster to arouse the public and Congress to the same state of recognition. More than a hundred people died because an "elixir" was made with diethylene glycol and the product was not tested for toxicity.

Limitations of the 1938 Act

The Act which was passed at that time required clearance of a new drug before marketing. The clearance, however, applied only to its safety when used as directed in its labeling. It was not necessary for the distributor to show that the labeling claims for efficacy were valid. It is true that, in the administration of this law, it was necessary to give some consideration to efficacy which could not be entirely divorced from safety. From the practical standpoint, it was also necessary to recognize the concept of relative safety. No active

drug is absolutely safe. The degree of hazard allowed had to be considered from the standpoint of therapeutic value. Many new drug applications were approved, however, with notification to the applicant that approval did not include the claims made for its efficacy.

The 1938 law also provided for the promulgation of regulations to control the shipment of a new drug for investigational purposes before it was approved for marketing. The regulations demanded only a very limited degree of control of investigational drugs. Before their shipment, it was required that the sponsor obtain a signed statement from the investigator to the effect that he would use the drug only for investigation and that he had the necessary facilities for it. Records of shipment had to be kept, which were subject to inspection by the Food and Drug Administration, along with the investigators' statements.

Although there were expressions of concern that these controls would interfere with the development of new drugs, subsequent experience showed that this did not occur. The two decades which followed showed enormous expansion in this area. The new drugs which were introduced replaced, to a large extent, those which were previously used as therapeutic agents. Moreover, the requirements of the law stimulated the support of new drug investigation and the development of improved manufacturing procedures.

Over the course of these years, it became evident that there were important deficiencies, particularly in the existing controls for investigational drugs and in the required procedures for the handling of new drug applications. Abuses of the investigational drug regulations occurred, some of which may be cited. There were instances of commercialization of drugs under the investigational label. The widespread distribution of investigational drugs occasionally served the purpose of premarketing promotion, rather than of valid investigation. Failure of investigators to report or to adequately report their studies was not unusual. This was to the detriment not only of the FDA, but also of industry.

Although the present regulations were first published for comment in August 1962, two months before the passage of the Kefauver-Harris amendments, the thalidomide disaster had already occurred. As the 1939 Act was precipitated by the Elixir of Sulfanilamide episode, the 1962 regulations and amendments to the Act were made acceptable by thalidomide.

A few weeks ago, the Commissioner of Food and Drugs in his testimony before a Congressional committee stated that legislation and regulations merely reflect the growing needs of our society. Quoting further:

> Neither the Legislative nor the Executive Branches of the Government can successfully impose requirements upon drug research and use that are significantly in advance of the requirements the public, including the scientific community, consider proper. Nor may they fail to provide for the controls the public, including the scientific community recognizes as desirable.

Federal Controls for Testing and Introducing New Drugs

Under what federal controls are new drugs actually tested and introduced today? I am sure that most of you are familiar with them and it is not feasible to even cite all the details at this time. The following, however, is an outline:

Prior to the distribution of a new drug for tests in man, the specific sponsor of the investigation is required to submit to the FDA certain specified information. This includes:

(1) The name, dosage form, components and quantitative composition of the drug.

(2) A description of the chemical structure, if known, and the source and preparation of any new drug substance and the methods used to insure the identity and uniformity of the new drug.

(3) Adequate information on preclinical testing to show that it is reasonably safe to initiate the proposed clinical studies. This requirement arises from the obvious need to conduct adequate tests in animals before starting human trials.

(4) The labeling or other information to be furnished to investigators. It is evident that the clinical investigator must have sound information as to prior tests to make his decisions about dosages to employ, and hazards and side effects to look for in clinical trials.

(5) The name and a summary of the training and experience of each investigator or expert.

(6) An outline of the planned investigations which may be submitted by phases. We recognize the necessity of a considerable degree of flexibility, particularly in the stages of clinical pharmacology where it is most needed.

(7) If the drug is sold, a full explanation of why such is necessary. In certain instances there may be justification for charging for an investigational drug. However, the government should have

the facts, so that it may reach its own decision as to whether sale of the drug represents premature commercialization.

(8) The regulations also provide that neither the sponsor nor any person acting on his behalf shall disseminate any promotional material representing the investigational drug to be safe or useful for the purposes for which it is under investigation. This provision was prompted by instances of extensive promotion of new drugs distributed under the investigational legend. In consideration of this point in the proposed regulations, fear was expressed that this would prevent the presentation or publication of scientific papers or reporting of such in the lay press. It has been clearly stated that it is not the intent to do so or to prevent full exchange of scientific information. This has become evident during the short period since the regulations have become effective.

Information Required from the Investigator

How do the regulations affect the investigator? He is required to submit the following information to the sponsor:

(1) A statement of his education, experience and the facilities he will employ in the investigation.

(2) An outline of the plan for his investigation.

(3) Statements showing he understands the conditions governing the use of investigational drugs, including the maintenance of records and the submission of reports to the sponsor.

Some investigators have felt no obligation to submit reports and some distributors have exerted little effort to obtain them. Making the submission of reports a condition for receiving the drug should go far in correcting this. We have heard comments to the effect that the burden of producing required records and reports will discourage some physicians from participating in investigations. This may happen in some instances. However, the failure to record and report results of the investigational use of drugs for the benefit of the medical community may lead to a repetition of drug injuries and deaths that may otherwise be avoided. There is reason to be concerned that in some drug investigations favorable experience is reported and unfavorable experience forgotten.

The sponsor also is required to inform all investigators and FDA of findings suggesting any hazard in use of the drug and to discontinue the investigation and recall outstanding stocks of the drug if the investigations adduce facts showing that there is substantial doubt

that they may be continued safely. The prompt dissemination of findings of adverse effects may give them early significance which would not otherwise occur if they remained as isolated observations, possibly without identification of the drug as a causative agent. The sponsor, of course, must receive such reports from the investigator who commits himself to report promptly any adverse effect caused by, or probably caused by the new drug. If it is an alarming reaction it should be reported immediately.

The statement which the sponsor obtains from the investigator is required to include a commitment that he will not supply the new drug to any other investigator not responsible to him, or to clinics, for administration to human beings. This is designed to prevent unauthorized distribution of the investigational drug to those who may not be aware of its unestablished safety and who may use it without adequate precautions.

Patient Consent Provision

Of particular interest, also, if the patient consent provision included by Congress in the new legislation and repeated in the regulations. It is required that the manufacturer or sponsor of the investigation obtain a certification from an investigator that he will inform any human being or his representatives (including controls) that the drug is being used for investigational purposes and obtain his consent for such use except where the investigator deems it not feasible or, in his professional judgment, contrary to the best interests of such human being. This requirement merely reflects the long-standing belief by our society and others that patients who are being used as experimental subjects should first give their consent. There has been much criticism of this requirement, but basically it is not new. The same requirement has been set forth in codes of medical ethics over a period of years and is recognized to common law. It may be even less restrictive than the latter in that it allows the physician to forego it under certain circumstances.

After submission to FDA by the sponsor of the new drug of the required information—Notice of Claimed Investigational Exemption for a New Drug—it may be shipped to investigators and the investigation may proceed without prior approval. The Commissioner may terminate the exemption if he cannot conclude from the information and data submitted that it is safe to continue it or if the conditions of the investigation are not met.

These regulations became fully effective on June 7, 1963. The need for more strict control of the investigation of new drugs had been widely recognized by many in the pharmaceutical industry and also by numerous investigators. Some expressed the view, however, that the regulations went too far, demanded too much, and required time, trouble and expense to the extent that new drug investigation would be seriously hampered.

Difficulties Encountered by Investigators

The industry did rise to the occasion. Although many investigations were at least temporarily discontinued, we have received to date some 1600 "Notices." The impact on investigators, although somewhat delayed, was also very evident. Industry was conditioned to government controls by over two decades of experience with the new drug procedure. Investigators were not. The previous investigational drug regulations affected them so slightly that they were only vaguely aware of the government somewhere in the background. The new controls and obligations constituted a novel experience in spite of the fact that many of the more competent had been complying with the spirit expressed in them in most respects in the past.

The regulations also affect many investigators who are working on their own clinical problems, rather than those of industry. This is the case if the study involves an investigational drug obtained by interstate shipment. Although they are free to act as sponsor for their own investigation, they may not understand how to do so. Many have difficulty in obtaining the drug or chemical which they wish to investigate through reluctance of the supplier to assume any degree of responsibility, understandably so in certain instances. Troubles were often accentuated by misunderstandings and lack of information.

The situation is undoubtedly improving and I am sure will continue to improve. In this, our Advisory Committee on Investigational Drugs has played no small part. It has been possible to simplify some procedures while still complying with the regulations. Irrespective of what is done, communication is a problem. It is hoped that the Investigational Drug Circular will alleviate this. The first number was published on February 20 of this year and more will follow. Announcement was made of the acceptability of a simplified "Notice" for investigations involving the use of a drug as a research tool to study normal or altered bodily functions and also for early clinical investigation of drugs of therapeutic potential. Other points, prompted by questions we have received, were clarified.

The period of adjustment is by no means over, but advances are being made.

Change in Procedures

There has also been significant change in the procedure for clearing a drug for commercial marketing once the clinical tests have been completed.

The outstanding change in the new drug application procedure is the requirement that an application include substantial evidence of effectiveness of the drug in the conditions for which it is recommended. Furthermore, its labeling must not be false or misleading in any particular. There is no doubt that the effectiveness provision will prevent the marketing of some new drugs for which applications are made, and it will without doubt result in decisions not to submit applications for some drugs after they have been investigated. As stated above, many new drug applications have been cleared in the past which did not include substantial evidence of effectiveness. It is a matter of conjecture as to what proportion of these would have passed the test if a serious effort had been made to obtain the evidence.

This requirement will necessitate better planned and conducted investigations than in the past. It may prolong the period of investigation, but I'm not sure that this is necessarily so. Maybe delay can be avoided by better planning. It is recognized, of course, that the availability of competent investigators is a problem. It can be done. Applications have been approved since October 1962.

During the next few years both industry and FDA are going to learn a lot about evidence for effectiveness. A variety of situations are going to be encountered, some of which will not be simple. Well-controlled investigations which yield data which can be evaluated statistically are not always feasible. Both FDA and industry will need the best expert advice available on occasion. I know that we are taking steps to obtain it.

I have not gone beyond the subject of new drug testing and introduction and there are several aspects of these areas which have not been considered, such as the extension by the Kefauver-Harris Amendments of the certification procedure to all antibiotics and the changes in procedure in handling new drug applications. In adhering to the subject, I have not discussed the changes in control of drugs after they have been introduced. Suffice it to say that they have been notably increased.

Government Control in Other Countries

Government controls over the investigation and introduction of new drugs are increasing in other countries which have such controls, as in Canada, and are being introduced into many countries which have not had them. In the United Kingdom, a strict voluntary (on the part of industry) control system has recently been instituted without legislation. New Zealand now has a new drug law similar to ours which it is beginning to administer.

Many other countries have varying degrees of control and others have legislation under consideration. The degree of supervision is often limited by available facilities. Communication between nations in the area of drugs is increasing. This is facilitated by the activities of the World Health Organization and the annual World Health Assembly. Certainly all nations are aware of the necessity of some degree of governmental supervision and each one is becoming familiar with the world-wide situation. International uniformity of controls will not be achieved in the foreseeable future, but there is movement in that direction. **[The End]**

PERMANENT INJUNCTION PROHIBITING MANUFACTURE OF TRANQUILIZER

A permanent injunction has been obtained prohibiting a Sayreville, New Jersey firm not registered under the Food, Drug and Cosmetic Act from future manufacture of meprobamate, a tranquilizer.

The firm, located in an old chemical plant on a dirt road in the country near Sayreville, was unknown to the Food and Drug Administration, Department of Health, Education and Welfare, until two FDA inspectors, acting on information, went to see the firm's manager late last March.

Inspection revealed quantities of urethane and aluminum isopropylate, all materials used to make meprobamate, plus some 2,700 pounds of meprobamate powder, enough to make an estimated $275,000 worth of meprobamate tablets at retail prices. The New Jersey Bureau of Food and Drugs obtained an embargo and removed all drugs on the premises.

The injunction complaint filed by the government charged that the firm failed to register as a pharmaceutical manufacturer under the Food, Drug and Cosmetic Act, as amended by the Kefauver-Harris Drug Amendments of 1962. The complaint also charged that no New Drug Application has been approved for the interstate shipment of meprobamate by the firm, and that the firm initially refused to permit inspection of part of its premises as required by the law.

Judge Arthur S. Lane of the Federal District Court at Trenton, New Jersey, signed a temporary restraining order on March 26 against the firm, prohibiting distribution of unfit drugs and ordered a hearing on an order to show cause why the firm should not be permanently enjoined. The defendants later consented to the permanent injunction, which was signed by Judge Lane on May 15, 1964.

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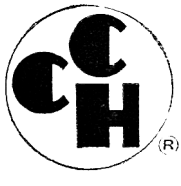

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