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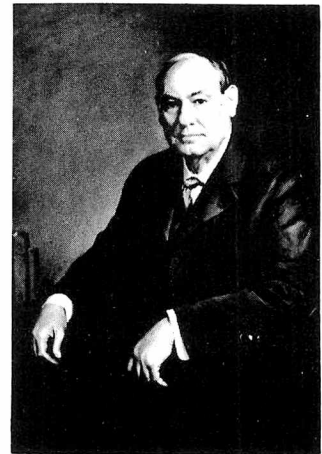
FDA PAPERS

ADVISORY OPINIONS: A HISTORICAL PERSPECTIVE

**Closing the Gap:
OTC Drugs**

**PRESCRIPTION DRUG
ADVERTISING, 1962-71**





"We are carefully to preserve that life which the Author of nature has given us, for it was no idle gift."

Harvey W. Wiley, 1844-1930

Father of the Federal Food and Drugs Act of 1906

From his commencement address
"Life and the Coming Time"
Hanover College, 1867

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But the people generally have known what they wanted and have made their wants known to the Congress. As a result there has been a progressive, if sporadic, improvement in drugs. The Drug Amendments of 1962 promised the people, for the first time, a modern system of safe and effective drugs, truthfully and helpfully labeled.

The OTC Drug Review program (see page 4) is FDA's final major step in implementing that law; thenceforth, there will be only some loose ends to tie up.

Closing The Gap:



OTC Drugs

by Charles C. Edwards, M.D.

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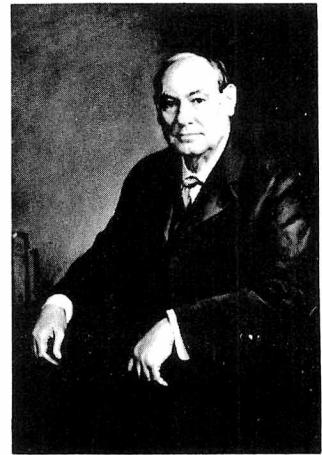
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By whatever name, their sheer number—variously estimated at 100,000 to 500,000 on the market—are

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With due appreciation of this right and full awareness of the important place self-medication occupies in the health care system, FDA has just embarked on one of the most ambitious and comprehensive programs it has ever undertaken in terms of number and volume of products involved and of consumers affected. Our ultimate purpose is to assure the public that all over-the-counter drugs on the market will be safe to use, effective for the treatment of symptoms claimed for them, and honestly, accurately, and understandably labeled.

Our announcement at the beginning of 1972 of FDA's Over-the-Counter Drug Products Evaluation Program inaugurates the final of three major steps by this Agency, which are intended to fulfill the mandate of the Congress when it enacted the Drug Amendments of 1962 requiring that all drugs, both prescription and nonprescription, be not only safe to use but also ef-



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Section 705 [375] of the Food, Drug, and Cosmetic Act.

(a) The Secretary shall cause to be published from time to time reports summarizing all judgments, decrees, and court orders which have been rendered under this Act, including the nature of the charge and the disposition thereof.

(b) The Secretary may also cause to be disseminated information regarding food, drugs, devices, or cosmetics in situations involving, in the opinion of the Secretary, imminent danger to health, or gross deception of the consumer. Nothing in this section shall be construed to prohibit the Secretary from collecting, reporting, and illustrating the results of the investigations of the Department.

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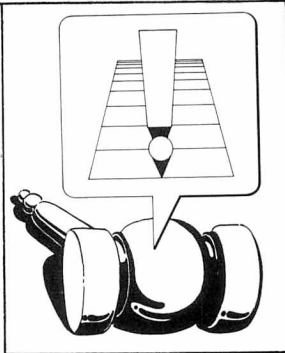
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fective for the purposes claimed by their makers.

To provide the maximum protection to the public health while moving to implement the 1962 amendments, FDA decided the first order of priority in the use of its limited resources should deal with those drugs that have the higher potential for harm. Thus we turned primary attention to the prescription drugs and those of the nonprescription drugs for which both safety and efficacy had not been established under the statutory requirements.

The first step, taken shortly after enactment of the 1962 amendments to the Food, Drug, and Cosmetic Act of 1938, was to require that all new prescription drugs, and all new over-the-counter drugs not generally recognized as both safe and effective as defined in Section 505 of the FDC Act, be proved effective as well as safe before being placed on the market.

The Agency's second step, beginning in May 1966, inaugurated its Drug Efficacy Study by an agreement reached with the National Academy of Sciences-National Research Council for the latter's review—for efficacy as well as safety—of more than 4,000 drug products that had entered the market between 1938 and 1962. The NAS-NRC review was conducted by 30 panels of physicians, all experts in their fields. The products reviewed were mostly prescription drugs, but they also included 422 over-the-counter drugs for which both safety and efficacy under Section 505 of the FDC Act had not been established. These 422 represented a broad range of products spread over practically all of the general therapeutic categories of over-the-counter drugs.

By September 1966 the NAS-NRC panels had been organized and began moving ahead with their reviews. Between October 1967 and April 1969 they sent forward to FDA a total of 2,824 reports evaluating 4,349 drug products. Upon receipt of these reports a special task force in FDA's Bureau of Drugs, called the Drug Efficacy Study Implementation (DESI) Project Office, began reviewing the recommendations of the NAS-NRC panels, preparing FDA's findings on these, and publishing them in the *Federal Register* for implementation by regulation. When all findings are published and the regulations implemented, the DESI project will be complete. Those products that comply with the statutory requirements for safety, efficacy, and correct labeling may remain on the market. Those that do not comply will be either removed from the market by regulatory action or be required to alter labeling or make other changes, such as reformulation, to conform to the regulatory requirements.

Now that the DESI project is well under control, the FDA turns major attention to over-the-counter drugs. Although the number of these products is far larger than that of prescription drugs, in most cases their active ingredients, either single or in combinations of two or more, have been estimated to be encompassed for the most part by a total of only a little more than 200 significantly active ingredients. Many of these are well-known substances that have been in use for many years and have been considered as being of low risk in terms of potential harm when taken in the established doses

or uses. This is in contrast to prescription drugs, which are more specific for treatment of disease and of higher potency. Such prescription drugs are required to be administered under the supervision of a physician, who can identify the disease before prescribing specific medication.

In moving toward assuring compliance of over-the-counter drugs with the 1962 amendments, the FDA faces a considerably different problem than that presented by prescription drugs. Some of the major differences:

- The extremely large number of OTC drugs, so large that no one can say how many are on the market, and estimates have varied from 100,000 to 500,000.

- The likeness of many OTC drugs containing identical or similar single active ingredients or combinations.

- The nature of the ingredients, which have been in use many years with few untoward side effects when labeled instructions are carefully followed.

- A great number of OTC drugs being exempt from classification as "new drugs" under both the FDC Act and the Drug Amendments of 1962, so long as labeling and composition remain unchanged and there is no finding that they lack effectiveness for the therapeutic claims made for them.

- The paramount concern of the OTC Drug Products Evaluation Program being not only to assure effectiveness, as in the DESI program, but to do so under a system by which consumers would benefit from the added protection in the shortest possible time.

Because the organization and orientation of the NAS-NRC panels reviewing the 1938-62 prescription drugs rested on therapeutic indications for specific diseases and because similar reviewing groups for OTC drugs would have faced the problem of dealing with symptoms not necessarily traceable to any specific disease, it was clear that the OTC Drug Products Evaluation would have to be planned and conducted differently than for prescription drugs.

FDA's first of two alternatives would have been to evaluate each OTC drug on a case-by-case basis and when necessary proceed against it with litigation to achieve compliance. Obviously this was impracticable, and perhaps impossible, for a number of reasons:

- There are thousands of OTC products on the market, and to proceed against each of them would require many years and would severely tax the resources not only of this Agency, but the courts, the medical experts called to testify, and the industry.

- Many of the products contain the same or similar ingredients and, although dosages may be different, are similar in nature, which would mean a great deal of repetition on a case-by-case basis in the presentation of medical and scientific evidence.

- Many of the OTC drugs undergo frequent changes in formulation and labeling, and these changes could be made even while a court case is in progress, requiring additional and in some cases protracted litigation.

- It would be difficult and possibly futile to proceed by litigation simultaneously against all manufacturers of similar preparations or their drugs, and many would

Proposed Standards for Safety, Effectiveness, and Labeling

"Safety means a low incidence of adverse reactions or significant side effects under adequate directions for use and warnings against unsafe use as well as low potential for harm which may result from abuse under conditions of widespread availability. Proof of safety shall consist of adequate tests by all methods reasonably applicable to show the drug is safe under the prescribed, recommended, or suggested conditions of use; such tests may be corroborated by reports of significant human experience during marketing. General recognition of safety shall ordinarily be based upon published studies which may be corroborated by unpublished studies and other data.

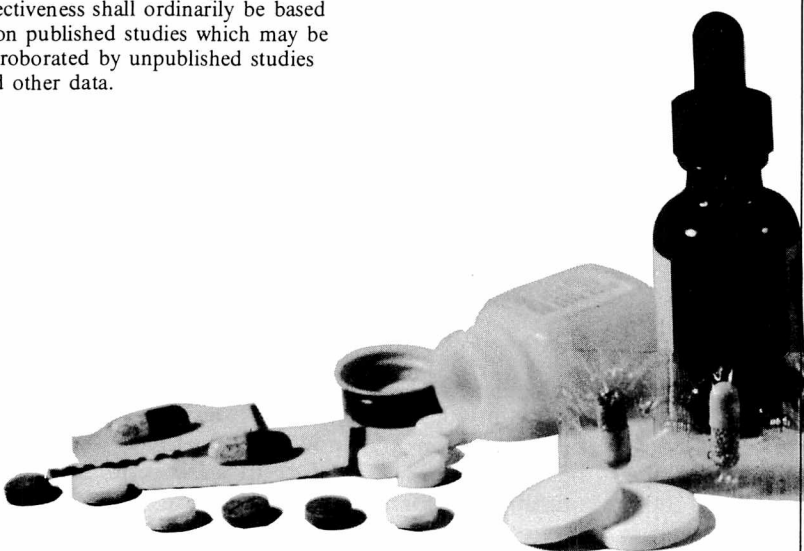
"Effectiveness means a reasonable expectation that, in a significant proportion of the target population, the pharmacological effect of the drug, when used under adequate directions for use and warnings against unsafe use, will provide clinically significant relief of the type claimed. Proof of effectiveness shall consist of controlled clinical investigations as defined in § 130.12(a)(5)(ii), unless this requirement is waived on the basis of a showing that it is not reasonably applicable to the drug or essential to the validity of the investigation and that an alternative method of investigation is adequate to substantiate effectiveness. Investigations may be corroborated by partially controlled or uncontrolled studies, documented clinical studies by qualified experts, and reports of significant human experience during marketing. Isolated case reports, random experience, and reports lacking the details which permit scientific evaluation will not be considered. General recognition of effectiveness shall ordinarily be based upon published studies which may be corroborated by unpublished studies and other data.

"The benefit-to-risk ratio of a drug shall be considered in determining safety and effectiveness.

"An OTC drug may combine two or more safe and effective active ingredients and may be generally recognized as safe and effective when each active ingredient makes a contribution to the claimed effect(s); when combining of the active ingredients does not decrease the safety or effectiveness of any of the individual active ingredients; and when the combination, when used under adequate directions for use and warnings against unsafe use, provides rational concurrent therapy for a significant proportion of the target population.

"Labeling shall be clear and truthful in all respects and may not be false or misleading in any particular. It shall state the intended uses and results of the product; adequate directions for proper use; and warnings against unsafe use, side effects, and adverse reactions in such terms as to render them likely to be read and understood by the ordinary individual, including individuals of low comprehension, under customary conditions of purchase and use.

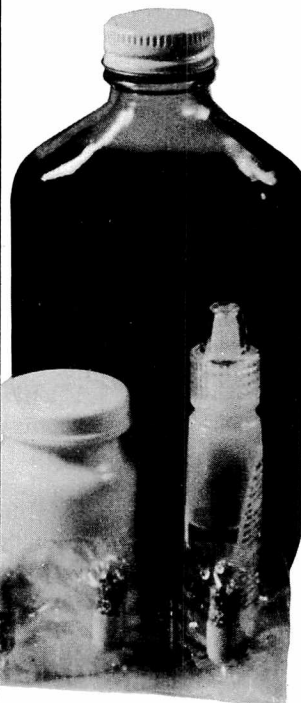
"A drug shall be permitted for OTC sale and use by the laity unless, because of its toxicity or other potential for harmful effect or because of the method of or collateral measures necessary to its use, it may safely be sold and used only under a practitioner's prescription."



The Order in Which OTC's Will Be Evaluated.

FDA plans to evaluate 25 categories of OTC drugs. The following listing indicates the order in which the Agency intends to call for data from the industry. As the Review Program develops, some realignments and/or redefinitions may become necessary. The Requests for Data and Information will be printed in the *Federal Register*. Sixty days will be allowed for submission.

1. Antacids
2. Antimicrobials
3. Sedatives & sleep aids
4. Analgesics
5. Cold remedies & antitussives
6. Antihistamines
7. Mouthwashes
8. Anti-infectives
9. Antirheumatics
10. Hematinics
11. Vitamins-minerals
12. Antiperspirants
13. Laxatives
14. Dentifrices & dental products
15. Sunburn treatments & preventives
16. Contraceptives
17. Stimulants
18. Hemorrhoidals
19. Antidiarrheals
20. Dandruff preparations
21. Bronchodilators & antiasthmatics
22. Antiemetics
23. Ophthalmics
24. Menstrual products
25. Emetics



be likely to remain on the market and others introduced to the market while similar competing products were removed.

- FDA would encounter enormous delay and difficulty in delineating and interpreting the exempting provisions of the FDC Act of 1938 and the 1962 amendments as to the date of entry into the market of the drug. The date of entry should have no bearing whatever on the safety and effectiveness of the drug and the truthfulness and adequacy of its labeling.

- There would also be inadequate consumer protection where violative products remained on the market for long periods of time while the Agency proceeded against individual drugs.

- In each and every case, FDA would be required to hew to the law's exacting requirements in documenting medical evidence to determine if the product qualified for exemption from "new drug" status.

FDA chose the second alternative. The Agency will deal with all OTC drugs through rulemaking that will establish, define, and describe therapeutic classes or categories of these products on an industrywide basis and will outline parameters for each class by means of a monograph. Those OTC drugs that meet the established standards of safety and effectiveness and are not misbranded under prescribed, recommended, or suggested conditions of use for their category may be marketed as before. Those not meeting the requirements, to continue on the market, may either file a New Drug Application for FDA approval or submit data in support of a monograph amendment.

Under this method of classifying drugs, FDA will appoint advisory review panels of qualified experts from outside the Agency to evaluate the safety and efficacy of OTC drugs, to review OTC drug labeling, and to advise the Agency on the promulgation of the monographs establishing conditions under which OTC drugs in the specific categories will be generally recognized as safe and effective and not misbranded. Separate advisory panels will consider at least 25 designated categories of drugs. The FDA will appoint these panels and a chairman of each from nominating lists submitted by organizations representing professional, consumer, and industry interests. Each panel after its study will recommend a monograph for an entire drug category. This monograph will include acceptable active ingredients and certain combinations when appropriate, acceptable dosage ranges of ingredients, acceptable indications for use, guidelines for labeling, and directions for consumer use.

General guidelines, policies, and overall definitions under which each panel will operate will be determined by FDA in consultation with the National Advisory Drug Committee, which was established by the Secretary of Health, Education, and Welfare last December 29 and will consist of 20 members selected from the biomedical and related fields, the mental health field, economics, the drug industry, and the general public and consumers. The Committee, headed by the Commissioner of Food and Drugs, will review and evaluate FDA programs and provide advice and guidance on policy matters of national significance concerning the

Agency's statutory mission in the area of drugs, such as OTC drugs, oral contraceptives, adverse drug reaction monitoring systems, and revision of New Drug Application review procedures. The OTC drug review advisory panels, in addition to advice from this Committee, will rely heavily on the Bureau of Drugs for scientific support.

Each advisory review panel will receive information from interested persons and other appropriate sources, will review and evaluate this information, and will submit its conclusions and recommendations to the FDA. This Agency will review the information and publish, in turn, *proposed*, *tentative final*, and *final* monographs in the *Federal Register* after consideration of comments and objections from interested persons under the provisions of the FDC and Administrative Procedures Acts.

Both the panels and the FDA, in determining conditions under which a category of OTC drugs is safe and effective and not misbranded, will apply defined standards of safety and effectiveness and the benefit-to-risk ratio, and will also consider combinations of active ingredients, labeling, and conditions of safety that must be met for classification as an OTC instead of a prescription drug.

Each advisory review panel will submit in its report to the FDA its recommended conditions under which OTC drugs in the category may be considered safe and effective and not misbranded; and (1) a recommended monograph covering the drug category, acceptable active ingredients (and combinations), labeling indications, warnings and adequate directions for use, prescription or OTC status, or other conditions considered necessary and appropriate; (2) a statement excluding those active ingredients, labeling claims or other statements, or conditions which have been reviewed and do not meet the standards; and (3) a statement of active ingredients, inactive ingredients, labeling claims or other statements, or other conditions for which sufficient data does not exist to recommend inclusion or exclusion from the monograph and for which further testing is therefore required. The last would be accompanied by any appropriate recommendations for further testing and time periods that may be required for testing.

The FDA's action, after review of the panel's conclusions and recommendations, will be to publish (1) a *proposed* monograph or monographs of conditions under which a category of OTC drugs is generally recognized as safe and effective and not misbranded; (2) a statement of conditions excluded from the monograph because of lack of safety and effectiveness and because of misbranding; (3) a statement of conditions excluded because of insufficient data; and (4) the full report or reports made by the panel.

The *proposed* monograph will be followed, after a round of comments, by a *tentative final* monograph on which objections will be considered and an oral hearing scheduled if warranted. The publication of a *final* monograph in the *Federal Register* will be the last step by FDA in making the monograph effective. Any further legal action contesting the regulation would be resolved by the courts. In the case of such legal actions,

FDA could at its discretion stay the effective date of all or parts of the monograph pending resolution in the courts. As in the case of all FDA regulations, monographs that have gone into effect are subject to subsequent amendment.

Both the panels and FDA will work under the defined standards (see proposed standards)—applicable to all the OTC drugs—of safety, effectiveness, and labeling. Benefit-to-risk ratio also will be considered in determining safety and effectiveness.

We estimate that the time for the work of the review panels and initial publication of proposed monographs in the *Federal Register* for all 25 classes of OTC drugs will take about three years—through the year 1974. Final implementation, of course, will take additional time. FDA has begun to organize its own special review staff for the program. I have asked Dr. John H. Moxley, dean of the University of Maryland School of Medicine, to be our chief liaison between the National Advisory Drug Committee and the review panels.

The first review panel will be on the antacids. It held its first meeting on February 22. With inauguration of the OTC Drug Products Evaluation Program on January 5, we published a notice in the *Federal Register* inviting interested persons, within 30 days, to submit safety and effectiveness data on these products as well as on any other active ingredients they wish to have considered by the panel at its meeting.

Recommendations regarding the operation of future panels will depend on the experience gained from the first panels.

We intend to insure that the only routes to the market for all OTC products will be through FDA, and each manufacturer will have a choice of two routes: (1) to comply with the FDA monograph covering his product and continue to market it without interruption or (2) to seek approval for a product not conforming to established OTC monographs through FDA's New Drug Application system or through monograph amendment. Existing products exempted at the time the 1938 and 1962 statutes were enacted may continue on the market with no problem if their formulations and labeling comply with the monograph, but if not they must reformulate or relabel as appropriate to comply.

We feel that modification by manufacturers of formulas and relabeling can solve most safety and efficacy problems that may confront the OTC drug manufacturer as a result of our review. Total removal of his product from the market is the last of a number of options open to him. We believe many basically good products in use for many years are being promoted with unjustified exaggeration or with deceptiveness. The consumer has a right to know what a product will and will not do.

We welcome information from industry in response to our notices requesting data on behavior of ingredients, dosage testing, and overall product performance. This will help us to establish reasonable efficacy standards and workable product classifications.

We invite cooperation from industry in responding to our current voluntary drug inventory announced last October 7 seeking information about all drugs for

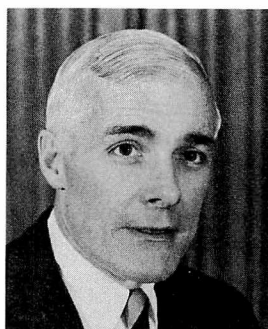
human use now on the market. The Congress is at present considering legislation that would require industry to provide this information to us.

We feel the clear guidelines for over-the-counter drugs that we expect to result from this OTC review will protect those manufacturers who have refrained from promoting their products in unethical or misleading ways. We feel that under these standards the druggist will know more about the OTC products he is selling and thus can help the consumer to select a product or products that will benefit him without subjecting him to deceptive or hard-to-understand claims or promotion that merely confuse him and possibly withhold the relief he seeks.

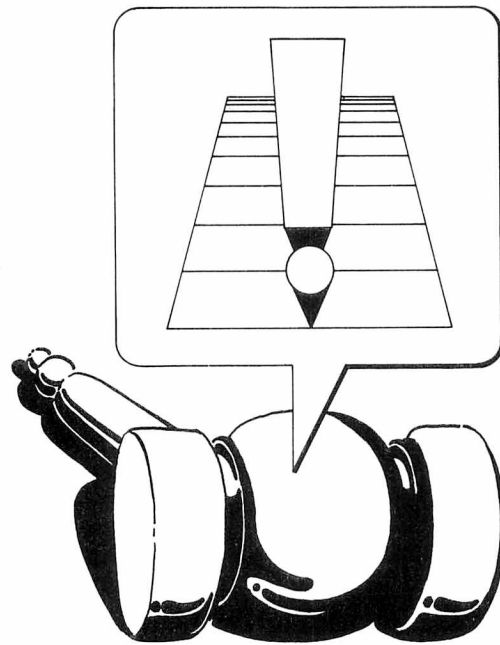
We believe also that a consumer who is made more aware of the limitations of a product through knowledge that his Government will allow only those claims that are scientifically supportable will be less likely—than in the present climate of ambiguity and exaggeration—to rely on certain of these products for treatment of illnesses of a degree and nature needing a physician's attention. Similarly, a consumer who may seek results other than therapeutic from certain classes of OTC products, will be in a better position to judge what a product can and cannot do for him.

Now that we have announced the goals we intend to accomplish and the criteria we will use to accomplish them, we expect that a positive and salutary effect on the quality of OTC drugs in the market and the methods of promoting them will begin to become evident from the time that each advisory review panel makes its recommendations to us.

When the DESI and the OTC Review program are completed, along with the related and complementary programs, the mandate of the Congress in enacting the 1962 amendments will have been realized, and we can look forward to a reasonably modern system that assures safe and effective drugs to protect the health of the public. This protection becomes more vital than ever to the consumer in an age and society relying increasingly on advances in chemotherapy to wipe out or alleviate disease. A drug supply that is safe, effective, and informatively labeled will help him to cope with threats to his health and well-being as modern life becomes more complex, the globe becomes more crowded, and the threat to environment quality raises new uncertainties concerning public health.



Charles C. Edwards, M.D.,
Commissioner of Food and Drugs.



Advisory Opinions: A Historical Perspective

by Sam D. Fine and Walter R. Moses

The industrialist J. Pierpont Morgan once remarked that his staff of a hundred lawyers contained but one who could tell him what was permitted; the others told him only what was prohibited. Advisory opinions have helped many by advising what is permitted as well as what is prohibited. You may be helped by such advisory opinions if you are a manufacturer, packer, or distributor of foods, drugs, cosmetics, therapeutic devices, household products, toys, television sets, X-ray diagnostic equipment, or other items subject to the consumer protection laws administered by the Food and Drug Administration. FDA stands ready to assist you in your efforts to comply with the laws and regulations which it administers.

Charles C. Edwards, M.D., the present Commissioner of Food and Drugs, like all of his predecessors believes in an open-door policy. Actually this open-door policy predates FDA and even the enactment of the Federal Food and Drugs Act in 1906.

The earliest published advisory opinions were called Food Inspection Decisions, a series that began July 1, 1902. Their nature and purpose were explained by James Wilson, then Secretary of Agriculture, in F.I.D. No. 44, issued on December 4, 1906:

"The opinions or decisions of this Department do not add anything to the rules and regulations nor take anything away from them. They therefore are not to be considered in the light of rules and regulations. On the other hand, the decisions and opinions referred to express the attitude of this Department in relation to

the interpretation of the law and the rules and regulations, and they are published for the information of the officials of the Department who may be charged with the execution of the law and especially to acquaint manufacturers, jobbers, and dealers with the attitude of this Department in these matters. They are therefore issued more in an advisory than in a mandatory spirit. It is clear that if the manufacturers, jobbers, and dealers interpret the rules and regulations in the same manner as they are interpreted by this Department, and follow that interpretation in their business transactions, no prosecution will lie against them."

That the pertinent Federal Department, then as now, preferred compliance on a voluntary basis is indicated by this final sentence:

"It is hoped, therefore, that the publication of the opinions and decisions of the Department will lead to the avoidance of litigation which might arise due to decisions which may be reached by this Department indicating violations of the act, violations which would not have occurred had the opinions and decisions of the Department been brought to the attention of the offender."

As might be expected, many of those inquiring have not liked the opinions they received. Some have gone to court to challenge particular opinions or even the right of the agency to publish such opinions. The courts have consistently upheld the right of the agency to publish advisory opinions and have taken note of the useful purpose they serve. Before discussing these cases,

however, let us review briefly the history of published opinions.

The Bureau of Chemistry, in the U.S. Department of Agriculture, continued to issue F.I.D.'s until June 1927. In the meantime, the Bureau had begun to issue Service and Regulatory Announcements (S.R.A.'s), of which 28 were published.

After the Food and Drug Administration (first called the Food, Drug, and Insecticide Administration) was formed, that agency continued to publish S.R.A.'s with the number bearing the prefix "F.D." Although only four of these were issued, they were often revised, the last revisions being made after enactment of the Federal Food, Drug, and Cosmetic Act (FDC Act) of June 25, 1938. Some food standards established in accord with the McNary-Mapes Amendment to the 1906 Act remained in effect until replaced by standards established under Section 401 of the FDC Act. In fact, a few of these standards in the S.R.A.'s still serve as acceptable guidelines where standards have not yet been established under the FDC Act.

Following passage of the FDC Act, FDA was flooded with requests for interpretations and explanations of the new law. Many replies were published as Trade Correspondence (T.C.'s). More than 400 of these were issued before the practice was discontinued in 1944, after enactment of the Federal Administrative Procedures Act. Opinions and interpretations were then issued more formally as Statements of General Policy or Interpretations (S.P.I.'s) published in the *Federal Register* and incorporated into Part 3 of Title 21, Code of Federal Regulations.

In addition to these S.P.I.'s, FDA issues more informal advisory opinions in the form of Compliance Policy Guides and the Fair Packaging and Labeling Act Manual which are available to interested firms and trade associations upon request to the Office of Compliance, Bureau of Foods.

Both published and unpublished advisory opinions have been involved in court contests.

The first such case was initiated in January 1909, when the Alsop Process Company filed in the Supreme Court of the District of Columbia a petition for a writ of mandamus praying "that the Secretary of Agriculture be commanded to revoke and cancel and annul" F.I.D. No. 100. The Alsop Process Company was a maker of machinery and held a patent on a process in which the bleaching of flour was "accomplished by the passage of pure air through a flaming discharge of electricity and the application of the resultant gaseous medium to the freshly milled flour as the latter passes through an agitator." In F.I.D. No. 100, the Secretary had stated that flour prepared by this process was considered adulterated in violation of the Food and Drugs Act of 1906; that after six months, during "which time the manufacturers and dealers will have an opportunity to adjust themselves to the situation," district attorneys would be called upon to proceed against violators. The Alsop Process Company claimed that

in so doing the Secretary acted "without warrant or color of law." The court, in refusing to command the Secretary "to vacate his decision, to take back what he has said," stated:

"This court cannot change the fact that the Secretary entertains this opinion, nor the fact that he intends to call on the District Attorneys to test the case in the courts. It cannot command him not to *make his opinion* and intention known and if it could it would be useless for he has already made it known, and the petitioner itself is making the fact still more widely known by this proceeding. The merits of the real question, namely, whether flour subjected to the bleaching process may be sold without violating the pure food law, is one that will ultimately be determined by the courts. In the meantime the Secretary is not violating any law in having an opinion and in telling the public what it is." (*U.S. Ex. Rel. Alsop Process Co., Petitioner v. James Wilson, Secretary of Agriculture, Respondent*. Supreme Court, District of Columbia, April 30, 1909). (Upheld by Court of Appeals, District of Columbia, June 1, 1909. 33 app. D.C. 472).

The court was prophetic in the prediction that the issue of "whether flour subjected to the bleaching process may be sold without violating the pure food law" would ultimately be determined by the courts. This issue was determined in a series of trials that led up to the oft-cited landmark decision in *United States v. Lexington Mill and Elevator Company*.

The decision of the District Court that such flour was adulterated was reversed by the Eighth Circuit Court of Appeals, and the reversal was affirmed by the U.S. Supreme Court.

The nature and effect of F.I.D.'s received further consideration by the courts in connection with the seizure of a package of coal-tar color that bore the statement, "Warranted Complies with all requirements. Quality Color," but contained salt (39.14 percent) and arsenic (20 parts per million) that exceeded tolerances for these substances in certifiable colors as set forth in F.I.D.'s. In finding this statement false and misleading in violation of the Food and Drugs Act, the District Court for the Eastern District of Illinois, on November 21, 1921, said:

"It is true, as contended by the counsel for the respondent, that the requirements put out by the Department of Agriculture upon this question are not the law, but they are a mighty good index for the court in passing upon these technical questions * * *."

In answer to the claimant's allegation that the statement was intended to refer only to the requirements of the statute, the court observed that "Maybe it did * * *," but went on to say:

"It appears from the evidence here that the purchasers generally knew or understood that the requirements meant the requirements of the Department and not the requirements of the statute. They were buying it according to the requirements put forth in the circulars of the Department."

In upholding the finding of misbranding by the District Court, the Circuit Court of Appeals for the Seventh Circuit said that the quoted statement "was intended, and would reasonably tend to convey the belief that the color was warranted to comply with the food inspection decisions of the Department of Agriculture." (*W.B. Wood Manufacturing Co. v. United States*, Circuit Court of Appeals, Seventh Circuit, January 2, 1923. 286 Fed. 84).

An unpublished advisory opinion precipitated a lawsuit in 1943. Blue poppy seeds could not be obtained by bakers during World War II. Helco Products Co., Inc., desiring to supply the bakery trade with white poppy seeds dyed blue, tried without success to convince FDA that the FDC Act does not prohibit interstate shipment of artificially colored poppy seeds properly labeled. First by telegram, then by a letter from Walter G. Campbell, at that time Commissioner of Food and Drugs, the firm was advised: "It is therefore our considered opinion that the interstate shipment of this artificially colored product under any labeling would result in an adulterated product within the meaning of Section 402(b) of the Federal Food, Drug, and Cosmetic Act, and that this violation could not be corrected by any form of labeling." The attorney for the firm then tried to get Attorney General Francis Biddle to say whether he would institute prosecution if his client shipped the seeds in interstate commerce. The Attorney General replied that he was authorized to give opinions only to the President and heads of Executive Departments. The firm then sued in the District Court for a declaratory judgment against the Federal Security Administrator (the Federal Security Agency was at that time the parent agency of FDA) and the Attorney General. When the District Court dismissed the complaint, the firm appealed the case to the U.S. Court of Appeals for the District of Columbia. In ruling that the District Court had not abused its discretion in dismissing the complaint, the Court of Appeals said, in part: "To permit suits for declaratory judgments upon mere informal, advisory, administrative opinions might well discourage the practice of giving such opinions, with a net loss of far greater proportions to the average citizen than any gain which could accrue." (*Helco Products Co., Inc. v. McNutt, Federal Security Administrator, and Francis Biddle, Attorney General*. United States Court of Appeals for the District of Columbia, No. 8344, June 28, 1943. 137 F. 2d 681).

As in the Alsop case, the issue of whether dyed poppy seeds could be shipped interstate without violating the law was ultimately decided by the courts. The District Court for the Northern District of Ohio ruled that such shipment was not illegal. The Circuit Court of Appeals for the Sixth Circuit reversed this decision. (*United States v. Two Bags More or Less, Each Containing 110 Pounds of Poppy Seeds*. 147 F. 2d 123).

In another case the court ruled that the agency cannot be compelled to give an advisory opinion.

Research Laboratories, Inc., was involved in proceedings under the Post Office fraud statutes and the FDC Act. The company brought a suit for declaratory judgment to compel the Federal Security Agency to give an opinion concerning certain proposed labeling and sales activities. In granting the Government's motion to dismiss, the District Court declared that the Federal Security Agency cannot "be compelled to give an advisory opinion in the future or to place its *nihil obstat* on some contemplated labeling of plaintiff's product * * *." (*Research Laboratories, Inc. v. Robert E. Hannegan et al.* United States District Court for the District of Maryland Civil No. 323-49, December 18, 1947).

In the 70 years that have passed since the first F.I.D.'s were issued, there have been many changes in manufacturing, processing, and distribution practices; consumer buying habits and patterns of consumption have changed drastically. To meet changing needs new laws and regulations have been enacted. Of course, advisory opinions must frequently be reviewed or updated, or sometimes rescinded. For example, in the *Federal Register* for April 9, 1970 (35 FR 5810). FDA published a notice requesting that all holders of advisory opinions granting sanctions for use of food additives not covered by specific regulations submit these for review. In the *Federal Register* for May 20, 1969 (34 FR 7922), a notice was published rescinding 89 T.C.'s that had been superseded by new legislation or regulations. If a person has a question as to whether a given advisory opinion represents present policy of FDA, he can resolve this question by asking about it. Preferably his inquiry should include a copy of the advisory opinion and any correspondence connected with it.

Delays in delivery of requests for advisory opinions may be reduced by directing the inquiry to the appropriate unit.

Requests concerning foods for human use or cosmetics usually should be directed to:

Food and Drug Administration
Bureau of Foods
Office of Compliance
Division of Regulatory Guidance BF-310
200 C Street, S.W.
Washington, D.C. 20204

Most questions concerning drugs for human use should be directed to:

Food and Drug Administration
Bureau of Drugs
Office of Compliance BD-300
5600 Fishers Lane
Rockville, Maryland 20852

However, when the question arises from a notice, proposal, or order published in the *Federal Register*, some other unit may be specified in the publication to receive correspondence.

The Bureau of Veterinary Medicine handles inquiries about animal drugs, animal feeds (including pet foods

and medicated feeds), and food additives and pesticide residues in meat and poultry products. This Bureau works closely with the American Association of Feed Control Officials, and in replying to questions about the composition or labeling of pet foods, supplies information which will help firms comply with State requirements as well as the FDC Act. Inquiries on these commodities should be directed to:

Food and Drug Administration
Bureau of Veterinary Medicine
Division of Compliance
Case Guidance Branch VM-220
5600 Fishers Lane
Rockville, Maryland 20852

Questions about compliance with the Fair Packaging and Labeling Act should be directed to whichever of the above units normally handles other inquiries about the particular commodity involved.

The Bureau of Product Safety is responsible for administering the Poison Prevention Packaging Act and the Federal Hazardous Substances Act, including the amendments to that Act known as the Child Protection Act of 1966 and the Child Protection and Toy Safety Act of 1969. Although the offices of this Bureau are at 5401 Westbard Avenue, Bethesda, Maryland, correspondence should be directed to:

Food and Drug Administration
Bureau of Product Safety
Compliance Guidance Staff PS-110
5600 Fishers Lane
Rockville, Maryland 20852

The latest addition to FDA is the Bureau of Radiological Health, which administers the Radiation Control for Health and Safety Act of 1968 and the voluntary control program for radioactive substances other than those controlled by the Atomic Energy Commission. This Bureau has promulgated performance standards for television receivers, cold-cathode gas discharge tubes, and microwave ovens. It has also published proposed performance standards for diagnostic X-ray systems and their major components. These place maximum limits on levels of radiant energy. Persons or firms who have problems with design of equipment to meet these requirements may receive help from experts within the Bureau. The Bureau also supplies advice about and interpretations of its regulations concerning record keeping and rules in connection with its other responsibilities. Questions about such problems may be directed to either the Director of the Bureau or the Director of the Division of Electronic Products, at the following address:

Food and Drug Administration
Bureau of Radiological Health
12720 Twinbrook Parkway
Rockville, Maryland 20852

Persons seeking advisory opinions from any of the above units can make consideration of their requests easier and may hasten replies by:

1. Carefully studying the applicable sections of the

law and regulations. Reprints of the laws and certain sections of the regulations can usually be obtained from the nearest FDA District Office or appropriate Bureau. The Bureau of Product Safety supplies a booklet that includes detailed suggestions for requests concerning products subject to the laws it administers.

2. Including copies of previous decisions or interpretations and related letters on the subject *unless* recent correspondence is involved.

3. Providing complete information and data such as quantitative formulas, full descriptions of processes and their effects (such as on nutritive value of foods or therapeutic actions of drugs), purity specifications, and detailed descriptions of equipment. Names used for ingredients or components of equipment or processes should be the standard current names in the United States.

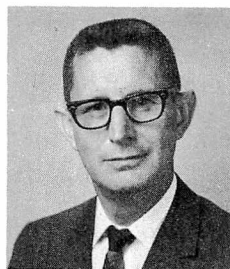
4. Stating questions clearly, frankly, and completely. The person at FDA who must consider the matter should not be asked to spend valuable time trying to guess what is wanted.

5. In requests for comment on labels, submitting only a few representative labels. FDA does not have the resources needed to provide detailed comment on all labels of a given firm.

If confirmation in writing is desired concerning any opinion given by telephone or orally in a conference, the interested person may write to FDA stating his understanding of what was said and asking for confirmation or appropriate revision of his statement of what was said.

The practice of issuing advisory opinions has stood the test of time. It has made possible better compliance at less cost to all concerned. The courts, in upholding the practice, have recognized its value.

As laws multiply and regulations become more technical and complex, the need for advisory opinions increases. To meet this need the FDA expects to continue its open-door policy.



Sam D. Fine, Associate Commissioner for Compliance, joined FDA in 1939.



Walter R. Moses, a consultant, retired in May 1970 as chief, Food Case Branch, Division of Case Guidance in the former Bureau of Foods, after 33 years service with FDA.

'In Brief Summary': Prescription Drug Advertising, 1962-71

by H. W. Chadduck

Questions arise from time to time in correspondence, interviews, symposia, and industry workshops concerning the evolution, activities, and authority of the Division of Drug Advertising in FDA's Bureau of Drugs. Considerable and continuing interest in this area has been expressed by many groups, including the general public. This article is intended to answer some of these questions and to outline this Agency's position, interpretation, and policies concerning specific requirements of the law and regulations, and to enunciate its general philosophy of regulation of the advertising of prescription drugs.

Before October 10, 1962, the responsibility for direct regulation of advertising of all domestic commodities in interstate commerce was vested by Federal statute in the Federal Trade Commission. But in the Drug Amendments of 1962, the Congress singled out prescription drugs (those available only on prescription of a licensed medical practitioner) from all other commodities and made the Food and Drug Administration solely responsible for regulating advertisements and other descriptive printed matter covering drugs of this class.

Although divested of responsibility for regulating prescription drug advertising, the Federal Trade Commission still retains primary responsibility for regulating advertisements of so-called over-the-counter (OTC) drugs and other commodities such as those appearing in television, radio, magazines, newspapers, and other media intended for the general public audience. Some extensively promoted examples of the OTC drugs are aspirin, other headache and similar pain remedies, cough preparations, antacids, "stomach upset" preparations, sleep promoting drugs, and liniments.

Because prescription drug advertising is usually addressed only to the medical profession in medical journals, direct mailings, and similar media, the general public is seldom if ever directly exposed to its impact, even though the total promotional expenditure in this area has been estimated at something around \$850 million in 1969 (25 percent of gross sales—of \$3.4 billion—rule of thumb percentage).

The Drug Amendments of 1962 imposed few general advertising requirements. In essence, the Congress decided that advertisements for prescription drugs were to *include* the identity of the drug and its quantitative composition, and were to *include* a true statement in brief summary relating to side effects, contraindications, and effectiveness.

The phrase "in brief summary" in the law led to use by the industry of the term "Brief Summary," a char-

acterization which has persisted in practice. Oversimplified, the latter requirement meant among other things that this kind of advertising was to avoid conveying a false, incomplete, or otherwise misleading impression that the advertised drug is a panacea, or even more effective or more safe than is medically justified. Note that the term "*include*" (italicized above) sets the stage for objective, as distinguished from subjective evaluations of prescription drug advertising.

Prescription drug advertising is gradually continuing to improve. Drug companies have issued 33 "Dear Doctor" remedial letters and 19 remedial advertisements.

Briefly, a "Dear Doctor" letter is one addressed to physicians that contains information regarded as important to them in their practice of medicine. A "corrective" remedial advertisement is one which appears in medical journals and carries a message to the physician reader calling his attention to defects in previous advertising in these journals.

At the request of FDA, preventive measures, initiated in 1970 and continuing, also are contributing visibly to improvements in prescription drug advertising practices. Improvement, however, has not been so extensive as to warrant relaxed vigilance or obviate the need for continuing education and liaison. Much more remains to be done.

In illustrations accompanying this article we have sought not to focus on the identities of drug producers or their product names in presenting actual examples of remedial letters and advertisements. The photographic material has been selected solely because it is illustrative of specific types of defects, corrections, or data.

Near-future consideration is indicated to assure that the advertising regulations do not become archaic but keep pace with current customs of the trade and new developments. With increased educational facilities, improved communication systems, and widespread awareness of drugs, even the general public will expect to receive more and more information about prescription drugs than is the case today. Therefore, new and significant methods must be considered across the board to meet this expanding responsibility to the public.

Audio-visual media such as motion picture films, audio-tapes, and video-tapes clearly must be dealt with, but rationally so, by our development of new policy statements, guidelines, and regulations where such media are regarded as drug labelings because of their product association. The need for improvements, particularly in this area of promotional labeling, presents challenges for FDA action in the early '70's.

Some Definitions

Sometimes terminology that has developed from the law, regulations, and customs of the trade has led to requests for nontechnical explanations of terms such as some of those found in this article. Let's discuss just a few.

Advertising—This unofficial term often applied within the context of the FDC Act and regulations is generally descriptive of all forms of drug promotion. It includes advertisements, descriptive printed matter, all forms of labeling, oral statements, in fact any form of communication calling attention of medical and other audiences to a drug product. Even the drug label and the so-called package insert have some advertising impact, whether greater or less.

Advertisements—Prescription drug advertisements subject to section 502(n) of the Act include advertisements in published journals, magazines, other periodicals and newspapers, and advertisements broadcast through media such as radio, television, and telephone communication systems.

Label—The term "label" means a display of written, printed, or graphic matter upon the immediate drug container as well as on the outside container or wrapper. This kind of interstate label, seldom seen by the public in the case of a prescription drug, is different from the kind that patients see on their prescription medicines obtained from the pharmacist.

Labeling—The term "labeling" means all labels and other written, printed, or graphic matter (1) upon any article or any of its containers or wrappers, or (2) accompanying such article.

Package Insert (Labeling)—This term is often applied to labeling on or within the drug package which bears adequate information or directions for use. Sometimes the label can accommodate the required information but more often the information is so extensive that it must be presented on a printed sheet or folder wrapped around, or in the box with the immediate container.

Promotional Labeling—This form of advertising is not specifically defined by the Act but is governed by regulations. It is the kind which has been established as "accompanying" an article. As a measure of the vast scope of promotion involved, some examples presenting drug information and distributed by or on behalf of drug producers are brochures, booklets, mailing pieces, detailing pieces, file cards, bulletins, calendars, price lists, catalogs, house organs, letters (to physicians and other audiences), motion picture film strips, lantern slides, audio tapes, other sound recordings, video tapes, exhibits (such as those at medical meetings and conventions), literature, reprints, and reference books containing drug information supplied by the manufacturer, packer, or distributor of the drug.

A Developing Need

Prior to the Drug Amendments of 1962 there was no effective control of advertisements directed to the medical profession. The Congress, in the Wheeler-Lea Act of 1938, had specifically exempted such advertising

from control by the Federal Trade Commission and, although the exemption was qualified, the FTC did not attempt to make a case in this field.

The legislative history of both the Wheeler-Lea Act and the Federal Food, Drug, and Cosmetic Act of 1938 showed that the Congress then considered physicians to be experts who did not need the protection from the impact of misleading advertising that was provided for the general public. However, disclosures before Senator Estes Kefauver's Subcommittee on Antitrust and Monopoly in 1960-61 led the Committee to the conclusion that advertising to the medical profession had resulted in serious abuses, and required new specific controls for the protection of the public.

The Kefauver hearings, which initially had been concerned with administered prices, placed prescription drug advertising and other drug promotional practices under public scrutiny because of complaints about high prices for certain prescription drugs. Advertising became involved because high-cost advertising was alleged to have affected the pricing of pharmaceutical products. Before the hearings were completed, numerous questionable advertising practices were exposed. The Congress then decided that reforms were needed because:

- Usually favorable features about a drug were presented in advertising, but side effects, contraindications, warnings, and other limitations regarding usefulness of the drug were omitted or deemphasized.
- Drugs were being promoted for uses they could not fulfill; trade names were overemphasized, often to the exclusion of common or usual names of a drug; and superlatives were used to describe the effectiveness of a drug that possessed no outstanding qualities beyond those of drugs already on the market.
- The burden of verifying footnotes, bibliographies, and testimonials in advertisements was left with the practicing physician. In practical effect, the Congress found that the busy doctor had no reasonable opportunity to evaluate the implications of advertising messages.

Representative members of the medical profession were interviewed by the Senate Committee staff. They testified as to their views about drug advertising. The attitudes of these physicians indicated to the Committee that the advertising practices of the pharmaceutical industry were open to question. Testifying members of the medical profession expressed not only skepticism but actual disbelief of advertising they had seen.

A Measure of Cost

As a measure of the continuing economic impact involved, based on a recent consolidated industry report released by the Pharmaceutical Manufacturers Association, figures for 1969 indicate that there were \$3.4 billion in domestic sales of prescription drugs in that year. This was up from 1964, for example, when sales reportedly ran to \$2.4 billion. During 1964, between \$600-\$800 million was spent on advertising and promotion by the manufacturers of these drugs. This represented roughly one quarter of the reported gross sales dollar. Although no comparable promotion dollar fig-

ures are available from the consolidated industry report, an estimate of 25 percent of sales suggests that about \$850 million was spent on the advertising and promotion of prescription drugs in 1969.

The 1962 Law and Regulations

The Drug Amendments of 1962 (sometimes referred to as the Kefauver-Harris Amendments), specifically section 502(n) of the Federal Food, Drug, and Cosmetic Act, as amended October 10, 1962, gave jurisdiction over prescription drug advertisements to the Secretary of Health, Education, and Welfare—in effect, to the Food and Drug Administration.

Briefly, the new law provided that an advertisement is required to include “a true statement of (1) the established name . . . printed prominently and in type at least half as large as that used for any trade or brand name . . . , (2) the formula . . . , and (3) such other information in brief summary relating to side effects, contraindications, and effectiveness as shall be required in regulations which shall be issued by the Secretary in accordance with the procedure specified in section 701(e) of the Act. . . .”

A prominent feature of the 1962 law is that it requires the inclusion of certain information in an advertisement regardless of whether a reader is misled by reason of its absence and regardless of the audience to whom the advertisement is directed. The term “true” has been interpreted to proscribe use of information that is false, lacking in fair balance, or otherwise misleading.

An advertising violation renders the drug misbranded under the terms of the Act and subject to seizure, and makes the drug sponsor subject to prosecution and injunction proceedings. In enacting the prescription drug advertising law, the Congress extended the jurisdiction of the Government in misbranding cases based on advertising violations to include *intrastate* distribution or offering for sale of any prescription drug. This includes stocks of drugs in possession of the responsible person (firm) and stocks distributed and still in commerce channels.

The Food and Drug Administration in February 1963, about four months after enactment of this law, proposed advertising regulations. They were simple regulations. They required that any prescription drug that had been approved through the new drug or antibiotic drug procedures provided for in the Drug Amendments of 1962 for new drugs entering the market be advertised only for conditions for which the drug had been approved. Drugs that had never been cleared through these procedures could be advertised only for conditions for which they were generally recognized as safe and effective, or for which there was “substantial evidence” of effectiveness.

The proposed regulations called for the advertisement to show, with “fair balance,” the effectiveness of the drug for the conditions for which it was recommended in the particular advertisement. The advertisement also was required to list those side effects and contraindications that were pertinent to the uses recommended in the ad and to other uses for which the drug

was commonly prescribed.

To make the “in brief summary” idea helpful to the physician, the regulations called for a complete though brief presentation of all the adverse information affecting safety, even though the small size of an ad might limit the total amount of information to be presented.

The regulations required that the information on side effects and contraindications be presented in close association with the information on effectiveness.

There was a requirement for preclearance of an ad if it had been recently discovered that the drug could cause death or serious injury, and if this were not generally known to the medical profession. To date, this mandatory preclearance procedure has not had to be invoked.

The first regulations also designated as “labeling” things such as drug brochures, mailing pieces, detailing pieces, file cards, bulletins, price lists, catalogs, company house organs, literature reprints, and reference publications intended to provide information to prescribing physicians. The basic FDC Act of 1938 already had provided authority to the FDA to regulate drug labeling, including promotional labeling.

Early Regulations Stayed by Objections

The first advertising regulations under the 1962 statute were published in the form of a final order in the *Federal Register* on June 20, 1963. The regulations were subject to formal objection by interested persons and to public hearing. It became generally known to the public that the Pharmaceutical Manufacturers Association and 44 of its member companies, the American Medical Association, and others objected to the regulations. This, of course, had the effect of staying enforcement of the regulations until a hearing could be held.

In September 1963, notice of the hearing was published on five issues that had been presented by those objecting. These were—

1. Whether the Secretary should have the authority to require “fair balance” in the advertised claims of effectiveness, side effects, and contraindications.
2. Whether the Secretary could require that the advertisement give all the side effects and contraindications of the advertised drug when the advertisement really related to only one use.
3. Whether the Secretary could limit the efficacy claims of old drugs—that is, the drugs not subject to a New Drug Application or certification—to those uses for which the drug was generally recognized as safe and effective and for which there was substantial evidence to support the claim.
4. Whether the side effects and contraindications would have to appear in “reasonably close association” with the information on effectiveness and be as prominent and conspicuous.
5. Whether advertisements would have to be precleared, even in extraordinary circumstances.

Essentially the dispute was about how much of the ad the FDA could control, about the requirement of established effectiveness as a condition for advertising

drugs not subject to new drug and antibiotic drug pre-clearance, and about the ad pre-clearance provision.

One objection was that advertisements were not educational in nature, did not have to be fully informative, and were only reminders. Another maintained that the regulations would destroy the basic purpose of prescription drug advertising. One insisted that if the regulations applied to the whole ad—not merely to the “Brief Summary”—they were illegal and lacked statutory authority. Another objected to the “fair balance” provision and to the requirement of information on side effects and contraindications for any use for which the advertised drug is commonly prescribed. One objected to the close association of side effects and contraindications with claims of effectiveness.

At a prehearing conference the FDA presented a number of exhibits—including various advertising ethics, codes, examples of current and past prescription drug advertising, and surveys of doctors’ attitudes about prescription drug advertising. A move to an actual hearing as provided by law was anticipated by the Government.

A drug trade association presented 24 questions in writing about the FDA’s interpretations of the regulations. These questions were answered by the FDA. In addition, the Agency agreed to comment on a series of current advertisements selected by the industry to provide a better understanding of the regulations.

After this action, and after some adjustments in the regulations, the industry’s objections to the regulations were withdrawn, the anticipated public hearing was called off, and the regulations were placed into effect.

Early Signs of Improvement

Even though there were objections to the regulations proposed in February 1963, advertisements began to change between February and September 1963, when the prehearing conference was held. And beginning in January 1964, when the regulations took effect, there was improvement in both the style and content of medical advertising.

An increasing number of prescription drug ads began to carry a prominent section which included side effects, contraindications, and warnings. In general this part of the ad was more or less consistent with the approved labeling and told the reader what the drug was for and what hazards could be anticipated from its use. In short, the general tone of the ads tended to change from unrestricted promotion toward more scientific information. More informative messages were now going to the physician. However, a subtle problem of significant magnitude remained. It was only through reviewing the whole ad—in depth—that the FDA found misleading practices were persisting, in less obvious ways.

Interpretive Policy Announced

The Agency found so many misleading features in prescription drug advertising that it was necessary, in November 1964, to issue a policy statement detailing the kinds of abuses being practiced and announcing

that regulatory action would follow if the practices continued. These were the kinds of abuses the Agency listed at that time:

1. Extension or distortion of the claims for usefulness beyond those in the product’s approved or permitted drug package labeling.

2. A quotation from a study that was used to imply improperly that the study was representative of much larger and general experience with the drug.

3. The selection and use of poor-quality *research* papers that were favorable to the product and the omission of contrary evidence from much better research.

4. Quotation out of context of a seemingly favorable statement in an article by an authoritative figure but omission of unpleasing data from the same article.

5. A favorable quotation from an obviously authoritative source but none from other experts in the same field who differed.

6. Use of data from papers that reported no side effects and failure to use information from other papers reporting side effects.

7. Ads constructed from data previously valid but rendered obsolete or false by more recent research.

Legal Sanctions Imposed

Action on compliance which followed final publication of the initial regulations and the policy statement on misleading practices began with efforts toward achieving voluntary compliance. These included meetings with individual firms to discuss specific advertising problems, and advisory opinion letters to companies, seminars, and lectures. Although these efforts probably had some educational benefit, they did not achieve full compliance with the principles of good prescription drug advertising. Accordingly, while voluntary compliance methods were continued, it became necessary for FDA to invoke regulatory compliance procedures. Formal sanctions provided under the law were imposed in some cases.

Early in this initial enforcement program, drug sponsors were informed of violations, called in for conferences, and requested to change their violative practices. Later the policy was stiffened and citations were issued to firms asking them to show cause why the facts surrounding misbrandings arising from improper advertising should not be referred to the Department of Justice for consideration of prosecution.

During the initial period of enforcement, six criminal and five civil cases were brought against firms on charges of false or misleading advertising (including advertisements and promotional labeling). Four of the criminal cases terminated with pleas of no contest, one with acquittal, and one case was dismissed. The average time from initiation of the action by FDA following analysis of the advertising to final disposition of the criminal case was about 36 months. In the five civil cases, the Government seized shipments of the drugs; these actions were not contested by the firms involved. In one case the seizure action was completed in about one week.

Publicity, based on court records readily available to

reporters, ensued in the news media. The impact of these seizures on the regulated industry was profound. In fact, in December 1966 two firms temporarily discontinued their advertising campaigns until they could make certain their advertising would conform to the regulatory requirements. They soon reactivated their campaigns on a revised basis.

The statutory sanctions provided under Federal law, although fundamentally punitive and therefore effective enforcement tools for that reason, were not entirely adequate to remedy misleading advertising and promotional messages within a reasonable time. These statutory sanctions have not been abandoned, of course, but have been reserved for cases where legal sanctions are preferable, based on the facts. It is noteworthy that no new case involving an alleged violation of section 502(n) of the Act has been filed in a Federal court in about 4½ years. But this should not be interpreted as precluding or making irrevocable our right to change or revise policy should circumstances warrant.

Administrative Sanctions

In February 1967 a new administrative concept of advertising correction was put into practice. This mechanism, requiring the issuance of a "remedial letter" to members of the medical profession by sponsors of advertising determined by FDA to be false or misleading, had been conceived in 1964 but never activated. However, as a result of experience primarily with civil actions involving seizures of drug shipments on the basis of advertising complaints, the concept was adopted as an administrative corrective process. Although no express statutory basis existed for requiring issuance of these remedial letters, in each case the FDA was prepared to proceed with one or more legal sanctions in the event the affected firms were unwilling to issue remedial letters by first class mail to practicing physicians (then a maximum of about 280,000 mailings). Between February 1, 1967, and July 1968, 25 "Dear Doctor" letters and one ad with an early "corrected" slant (See Figure 5) involving corrections of journal advertising and promotional labeling were issued by the affected firms to the medical profession. The cost to a company of preparation and mailing of each "Dear Doctor" letter was then estimated at around \$40,000. It is higher today, largely because of increased postage rates.

Demand for Updating Regulations

Still another step for public health protection in the prescription drug promotion area was formally initiated by FDA on May 23, 1967, following evaluation of our experience with the 1964 regulations. New regulations were drafted by the Agency incorporating policies adopted in the interim and updating and making more specific the principles laid down in the earlier rules.

The new proposals were intended primarily to interpret with greater particularity the statutory requirement that an advertisement include a true statement of information in brief summary regarding side effects, con-

traindications, and effectiveness, and to set standards for achieving fair balance—both physical fair balance and contextual fair balance. The new proposals also distinguished advertisements from labeling and listed examples in each category.

With publication of the proposed new regulations in the *Federal Register*, written comments were invited from the industry and other interested persons. Nearly a hundred were received; all opposed the proposed new rules.

In an effort to resolve questions raised in the comments, the FDA named a working group to meet with a group of representatives of the Pharmaceutical Manufacturers Association and the Pharmaceutical Advertising Club. A number of meetings were held over a period of months running into 1968. The language of the originally proposed rules was changed essentially to provide more clarity in stating certain principles.

The revised regulations were published about 13 months later in the form of a final order in the *Federal Register* of June 27, 1968. Under the General Administrative Provisions (Chapter VII) of the Federal Food, Drug, and Cosmetic Act, the new rules were subject to objections and to a public hearing on petition of any interested person.

The industry submitted a number of objections to the published regulations, which had the effect of staying some but not all of the rules. The Pharmaceutical Manufacturers Association requested a public hearing on the issues raised by its objections. Those regulations not stayed because of the PMA action were made effective 60 days after publication of the order in the *Federal Register* of June 27, 1968.

As to the remaining issues which principally would have adversely affected certain rules pertaining to *per se* violations, these were resolved by a series of conferences extending into early 1969 when further modifications were adopted, none resulting in serious loss of public health protection. Once again the request for a public hearing was withdrawn. The new regulations that had been the subject of joint FDA-industry conferences were published as a final order on June 16, 1969, about two years after the original proposal. A number of regulations concerning promotional labeling, proposed in the *Federal Register* of May 23, 1967, remained to be developed and activated in the future.

Promotional Labeling Too

Promotional labeling is regarded as advertising in the general sense because it consists of such things as brochures, booklets, mailing pieces, file cards, exhibits, literature reprints, motion picture films, and reference books such as the *Physicians' Desk Reference*, which are furnished to the medical profession by or on behalf of drug sponsors. Promotional labeling is regulated under rules issued pursuant to the basic Federal Food, Drug, and Cosmetic Act of 1938 which requires among other things that the labeling of a drug bear adequate directions for use. Regulations affecting promotional labeling have existed since 1960.

During the course of enforcement of the law and



- practically painless on injection—therapy may be initiated parenterally and then followed through orally without switching antibiotic.
- reactions rare, even for patients sensitive to penicillin—does not share antigenicity with the penicillin group of compounds.
- no serious renal or neurologic abnormalities; no ototoxicity.
- no tooth discoloration to date; case reports on nearly 1,700 patients up to 13 years of age have revealed no tooth discoloration with [redacted].

"follow-through" antibiotic
in upper respiratory infections

[illegible]

FIG. 1

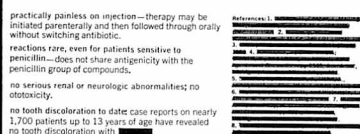
[illegible]

FIG. 2

"LIBEL OF INFORMATION FOR ..."

"...failed to include:

(A) A true statement of information in brief summary relating to the effectiveness of said drug as required by regulation 21 CFR 1.105(e) in that the advertisement lacks fair balance in its presentation and does not fairly show the effectiveness of the drug in the conditions for which it is recommended or suggested in the advertisement since the advertisement represents:

1. That therapy may be initiated parentally and then followed through orally without switching to another antibiotic but fails at this point to refer to the sensitivity study requirement contained in the labeling accepted under the certification requirements for the drug that "... in vitro sensitivity studies should be performed before ... is utilized as sole antibiotic therapy":

2. That reactions are rare, even for patients sensitive to penicillin--does not share antigenicity with the penicillin group of compounds, which representation is misleading, and fails at this point to refer to the "adverse experience" information contained in the labeling accepted under the certification requirements for the drug that "a few cases of hypersensitivity reactions such as angioneurotic edema, serum sickness and anaphylaxis have been reported";

3. That there are "no serious renal or neurologic abnormalities; no ototoxicity" and "no tooth discoloration to date" which representations are misleading in that the audience for whom the advertisement is intended is not advised at this point or with

equal prominence or in reasonably close association with this information the facts that hematologic toxicity, manifested by neutropenia or leukopenia, can occur and that the frequency of severe diarrhea is a unique feature of ... therapy.

(B) A true statement of information in brief summary concerning those side effects and contraindications that are pertinent with respect to the uses recommended or suggested in the advertisement and any other use or uses for which the dosage form advertised is commonly prescribed as required by regulation 21 CFR 1.105(g) in that the advertisement failed to include the following information from the labeling covered by the certification, or the applicable certification regulations (21 CFR 148.3 and 148.3).

1. The precautionary information that "with B-hemolytic streptococcal infections, treatment should continue for at least 10 days to diminish the likelihood of subsequent rheumatic fever or glomerulonephritis":

2. The side effect information which specifies the serious nature of the cases of hypersensitivity reactions, i.e. ... angioneurotic edema, serum sickness and anaphylaxis" and fails to identify the usual agents which should be available for emergency treatment, i.e., "antihistamines, pressor amines, corticosteroids":

3. The precautionary information that "... in vitro sensitivity studies should be performed before ... is utilized as sole antibiotic therapy".

4. The statement "other adverse reactions observed in a small proportion of patients" ... appearing in the labeling is not included and is misleadingly changed in the advertisement to read "side effects of small proportion...".

A CASE OF SEIZURE Figures 1 and 2. The representation of an early 1966 medical journal advertisement (top left) illustrates an example of certain violative situations which led to seizure of the advertised drug.

The Libel of Information (bottom left) represents a typical complaint filed by the Government in U.S. District Court against a drug alleged to be misbranded by advertising. The depicted complaint lists the alleged violations contained in the ad which misbranded certain shipment(s) of the drug involved.

Dear Doctor:

The Food and Drug Administration has asked that we call your attention to our letter of [REDACTED] which announced the coming availability of [REDACTED] (Penicillinase-resistant penicillin). The Food and Drug Administration has expressed concern that our discussion of this drug in terms of treating skin and soft tissue infections created misleading impressions concerning the proper use of [REDACTED] in its limited appropriate indications.

Therefore, we wish to specify the indications and limitations for use of this drug in detail as follows:

1. The principal indication for [REDACTED] is in the treatment of infections known to be due to penicillinase-producing staphylococci which have been shown to be sensitive to it.
2. If antibiotic therapy is considered necessary in potentially serious infections while awaiting reports of cultures and sensitivity studies, [REDACTED] may be used to initiate therapy in such patients in whom a penicillinase-producing staphylococcus is suspected. (See Important Note below.)

Important Note

Bacteriologic studies to determine the causative organisms and their sensitivity to [REDACTED] should be performed. When it is judged important that treatment be initiated before definitive culture and sensitivity results are known, the choice of [REDACTED] should take into consideration the knowledge that it has also been shown to be effective only in the treatment of infections caused by pneumococci, Group A beta-hemolytic streptococci and penicillin G-sensitive staphylococci. In serious, life threatening infections oral preparations of the penicillinase-resistant penicillins should not be relied on for initial therapy.

[REDACTED], a compound working through a similar mechanism against penicillin G-resistant staphylococci, has been available for nine years. It is a fact that strains of staphylococci resistant to methicillin have existed in nature and it is known that the number of these strains reported has been increasing. It has been demonstrated that such strains are almost always resistant to other penicillinase-resistant penicillins, such as the isoxazole group of which [REDACTED] is a member. When such a strain is isolated, use of routine antibiotic discs cannot be relied on to differentiate relative sensitivity. Such strains of staphylococci have been capable of producing serious disease, in some instances resulting in fatality. Because of this, the Food and Drug Administration is concerned that widespread use of the penicillinase-resistant penicillins in infections other than those due to penicillin G-resistant staphylococci may result in the appearance of an increasing number of staphylococcal strains which are resistant to these penicillins.

Therefore, if the bacteriology report indicates the infection is not due to a penicillin G-resistant staphylococcus, the physician is advised to continue therapy with a drug other than [REDACTED] or any other penicillinase-resistant semi-synthetic penicillin.

Indicated surgical procedures should be performed.

Contraindications:

A history of allergic reactions to penicillin should be considered a contraindication.

Information in our announcement letter, or that you may have received from one of our sales representatives, should be carefully considered in light of the preceding clarification.

We have discontinued the advertising in question. Future advertising will be appropriately modified. The drug is not available for prescription at this time. We will notify you when it becomes available.

Sincerely,

[REDACTED]
[REDACTED]

Dear Doctor:

The Food and Drug Administration has requested that we bring to your attention a recent promotional campaign for [REDACTED] Injectable ([REDACTED]) which featured a nationwide *in-vitro* hospital survey involving a comparison of sensitivity patterns of [REDACTED] Injectable and seven other antibiotics.

The FDA considers the advertising misleading in several respects such as:

The *in-vitro* chart contained in the ads, which compared [REDACTED] Injectable with seven other antibiotics, implied that [REDACTED] Injectable is clinically more effective than the seven other compared antibiotics. THE FACTS ARE (1) THAT DIRECT EXTRAPOLATION OF NONCLINICAL FINDINGS TO CLINICAL EFFECTIVENESS IS UNWARRANTED, AND (2) THAT THE ADVERTISED *IN-VITRO* COMPARISONS DO NOT CONSTITUTE A VALID BASIS FOR SUGGESTING THAT [REDACTED] INJECTABLE HAS GREATER CLINICAL EFFECTIVENESS THAN THE COMPARED ANTIBIOTICS.

The *in-vitro* chart and information contained under the ad heading, "Indications" presented *in-vitro* data results in such a way as to imply that the drug is indicated for Gram-positive bacteria, such as *Staphylococcus aureus*. [REDACTED] INJECTABLE IS NOT APPROVED FOR INFECTIONS DUE TO ANY GRAM-POSITIVE ORGANISMS.

We emphasize that [REDACTED] Injectable is approved for use only in infections due to susceptible strains of gram-negative bacteria, including *Pseudomonas aeruginosa*, and species of indole-positive and indole-negative *Proteus*, *Escherichia coli*, and *Klebsiella-Aerobacter*.

We have discontinued use of the promotional material in question and the journal advertisements in which the same themes were featured are being corrected.

Yours truly,

[REDACTED]
[REDACTED]

EVOLUTION OF THE "DEAR DOCTOR" LETTER The "Dear Doctor" remedial letter issued by drug sponsors at the request of FDA is an administrative method of correcting false or misleading information disseminated via promotional campaigns.

This nonstatutory method of correction is used to communicate without undue delay important corrective medical information directly to the physician, especially in those situations where seizure or prosecution would be too time consuming or otherwise inappropriate for adequate public health protection.

Figure 3 (above) represents one of the first "Dear Doctor" letters issued on the basis of an alleged violative promotional campaign. Compare the potential reader impact, obscurity of message, and marginal emphasis of this example with the more recent version depicted in Figure 4 (left).

Figure 4 represents a recent "Dear Doctor" letter illustrating improvements that have occurred, such as brevity, emphasis, and deletion of promotional statements that in the past were inconsistent with the remedial concept and tended to obscure the corrective message. Even the package insert has been excluded from these letters so as not to dilute the message.

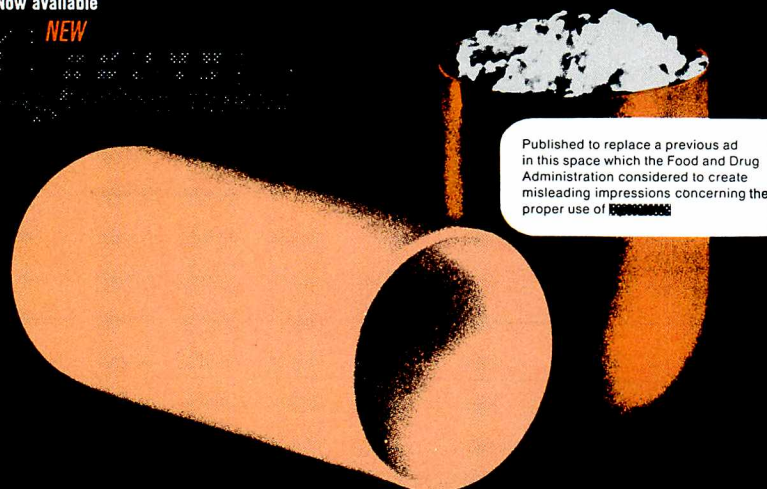
new high potency penicillin for treatment of known pen. G-resistant staph or for initiating treatment whenever this organism is suspected

Bacteriologic studies to determine the causative organisms and their sensitivity to [redacted] should be performed. When the infecting organism is susceptible to penicillin G, the physician is advised to use penicillin G, phenoxymethyl penicillin (penicillin V), phenethicillin, or other appropriate antibiotic therapy because of the possible appearance in the environment of organisms resistant to the penicillinase-resistant semisynthetic penicillins.

- [redacted] is bactericidal
- [redacted] is exceptionally well absorbed
- [redacted] is highly effective against pen. G-resistant staph
- [redacted] is low cost therapy

Now available

NEW



Published to replace a previous ad in this space which the Food and Drug Administration considered to create misleading impressions concerning the proper use of [redacted]

REMEDIAL ADS In addition to requiring the issuance of "Dear Doctor" remedial letters, FDA began the innovation of requiring the issuance of remedial advertisements. This has proved to be another effective administrative tool in bringing corrective information to the attention of the physician. In the following two examples, the "Brief Summary" has been omitted for brevity and emphasis of violative aspects.

THE FIRST REMEDIAL AD Figure 5 (above left) is representative of the first remedial advertisement. This June 1968 ad contains a "boxed" statement intended to inform the reader that it replaces one considered by the FDA to be misleading. This was a beginning, but by today's standards, this remedial concept would be considered obsolete.

EXAMPLE OF RECENT REMEDIAL AD Figure 6 (below left) represents a 1971 remedial ("corrective") advertisement showing improvements. Differences readily apparent include: prominence and enlargement of the "boxed" statement; a listing of the significant points considered to be false or misleading in the original ad and the corrective information for each statement or idea; and an absence of promotional copy. Remedial ads are now required to appear at least once in each of two issues of the journals in which the original violative ad appeared.

PUBLISHED TO CORRECT A PREVIOUS ADVERTISEMENT WHICH THE FOOD AND DRUG ADMINISTRATION CONSIDERED MISLEADING



Capsules Equivalent to 50 & 100 mgs, [redacted]

The Food and Drug Administration has requested that we bring to your attention a recent promotional campaign for [redacted] which graphically featured laboratory findings from animal studies and reported clinical results.

The FDA considers the advertising misleading in several respects such as:

THE MEASUREMENTS OF CONCENTRATIONS OF [redacted] IN ANIMAL TISSUE DEPICTED IN THE ADVERTISING WERE PRESENTED THROUGH GRAPHICS, HEADLINES AND SUBHEADLINES IN SUCH A WAY (AND WITHOUT ADEQUATE QUALIFICATION) AS TO SUGGEST THAT THE ANIMAL DATA COULD BE DIRECTLY CORRELATED WITH THE CLINICAL RESULTS REPORTED ELSEWHERE IN THE ADS.

The ads charted a number of sites or types of infection in which clinical "success" rates were claimed, but failed to disclose the effective spectrum of Vibramycin (WHICH DOES NOT INCLUDE INFECTIONS DUE TO VIRUSES AND OTHER NONSUSCEPTIBLE ORGANISMS). [See opposite page for "Brief Summary."]

The ads emphasized the lessening of lower G.I. and other side effects but failed to disclose that GASTRIC IRRITATION MAY OCCUR WITH [redacted] and that PATIENTS TAKING THE DRUG ARE SUBJECT TO THE SAME ADVERSE REACTIONS AS THOSE ADMINISTERED OTHER TETRACYCLINES.

We have discontinued the above promotional campaign and have suspended use of other similar promotional material relating to [redacted] until corrections can be made.

—the better antialdosterone diuretic

to counteract renal effects
of aldosterone
to conserve potassium
to augment other diuretics



VS.



Faster acting—

"acts within 2 hours of its administration, unlike [redacted] and a single day's administration can be given with good effect."¹

"does not reach its maximum [effect] until 48 hours or more after administration has been started."¹

Simpler dosage—

"The usual starting dosage is one capsule twice daily after meals. (An occasional patient can be started on one capsule daily.) When adequate control of edema has been achieved, the patient may be maintained on one capsule daily or one capsule every other day. . . . When it is combined with another diuretic total dosage of each agent should be lowered initially."²

Since [redacted] competitively inhibits aldosterone, the higher the aldosterone secretion, the higher the amount of [redacted] required.

"... an initial daily dosage of 100 mg. [four tablets] . . . given in divided doses, is recommended. . . . Although some patients may respond adequately to a dosage of only 75 mg. [three tablets] daily, a considerably greater daily dosage of [redacted], either alone or in combination with a conventional diuretic, may be given to achieve diuresis."³

More economical—

Average cost to patients*

	Per Capsule or Tablet (Rx # 100)	Per Day		
[redacted]	11¢	11¢ once daily	22¢ b.i.d.	
[redacted]	15¢	30¢ b.i.d.	45¢ t.i.d.	60¢ q.i.d.

*Based on published list price plus average retail markup.

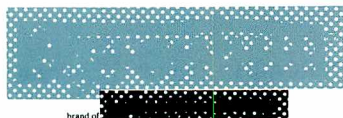
REMEDIAL PROMOTIONAL LITERATURE In addition to misleading advertisements, the Division of Drug Advertising has dealt with a number of violative promotional labeling pieces. Because of the impact of promotional literature, it became necessary to request issuance not only of remedial ads but also of remedial promotional labeling.

ONE MATTER OF CONCERN Figure 7 (above) is an example of such a promotional piece containing misleading information mailed to physicians. Shown here are only the front cover and main promotional page from the booklet.

THE REMEDY Figure 8 (below) is the remedial promotional piece issued to replace the above example. Readily to be seen are similarities with remedial ads. For example, the remedial promotional piece contains: the "boxed" statement, corrections of false or misleading statements, and other information regarded as necessary to provide a fair balance of information that was missing from the original piece.

PUBLISHED TO REPLACE A PREVIOUS PROMOTION
THAT THE FOOD AND DRUG
ADMINISTRATION REGARDED AS MISLEADING

In edema due to certain causes*



to conserve potassium

to augment the effect of
other diuretics in edema
due to certain causes*

[redacted] indicated in: edema associated with congestive heart failure, cirrhosis, nephrotic syndrome and late pregnancy; steroid-induced edema, idiopathic edema and edema due to secondary hyperaldosteronism.

The FDA has requested publication of the following
supplementary and balancing facts to correct impressions
in a recent promotion regarded by the FDA as misleading:

- [redacted] ([redacted]) is not an aldosterone antagonist. Therefore, the FDA believes that ' [redacted] ' cannot be characterized as an "antialdosterone diuretic."
- The previous advertisement referred to ' [redacted] ' as a diuretic, but did not state the indication—namely edema due to certain causes.
- Since certain other diuretics have antihypertensive actions, it could be misconstrued that ' [redacted] ' is also an antihypertensive. ' [redacted] ' is not indicated for the treatment of hypertension.
- The terms "faster acting," "simpler dosage" and "more economical" were intended to be comparisons to [redacted] only, and to no other agents. However, the FDA regards the two drugs as different in their composition and action so that any comparisons between them are apt to be misleading.

FIG. 9

**TOTAL REGULATORY ACTIONS
DIVISION OF DRUG ADVERTISING
1969-1971**

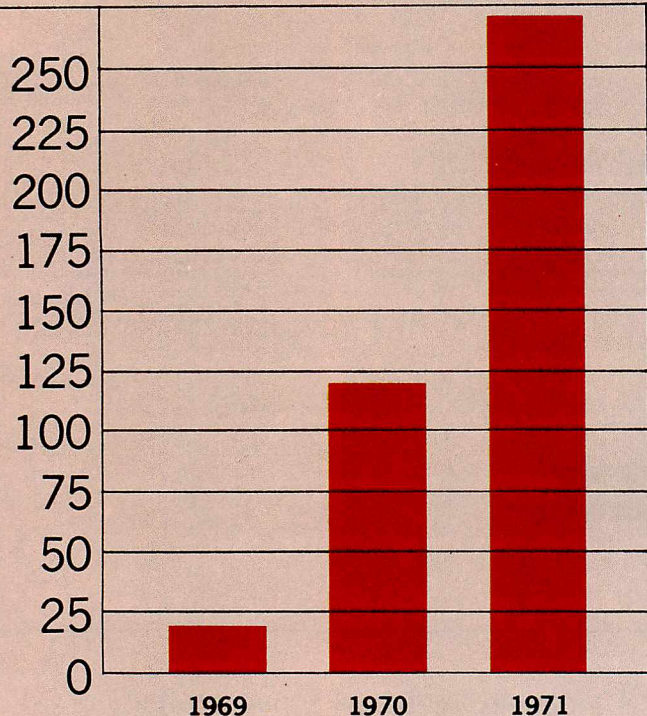
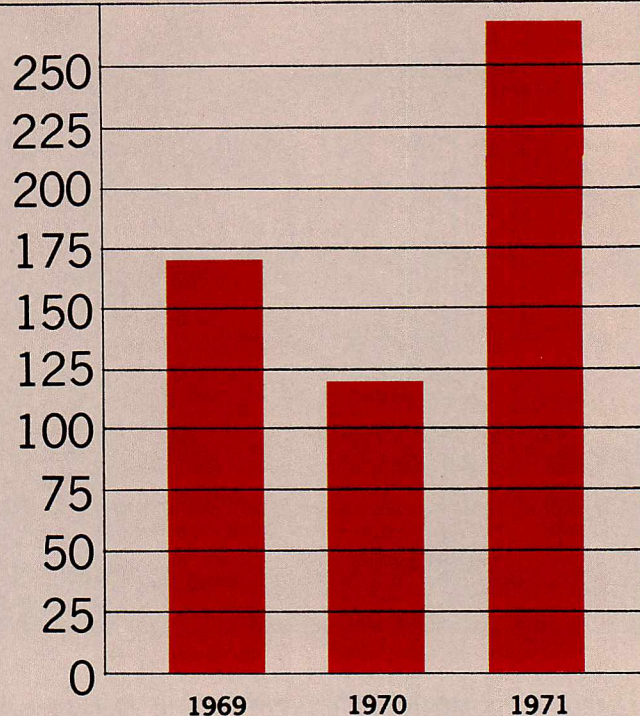


FIG. 10

**TOTAL ADVISORY ACTIONS
DIVISION OF DRUG ADVERTISING
1969-1971**



**DIVISION OF DRUG ADVERTISING
CALENDAR YEARS
1969-1971**

(1) Advertising monitored

CY 1969	CY 1970	CY 1971
5031	12,302	18,115

(2) Actions taken

CY 1969	CY 1970	CY 1971
190	260	596

KEY

(1) **Advertising monitored** includes: prescription drug ads monitored; PDR monographs, other promotional labeling and ads reviewed in-depth.

(2) **Actions taken** include: advisory and regulatory conferences and opinions provided; warning letters to industry; ads cancelled; and "preventive" letters (mass warning letters to industry).

NOTE: (See text for numbers of remedial instruments published and distributed to date.)

REGULATORY VS. ADVISORY BALANCE Figures 9 and 10 (above) represent significant regulatory and advisory actions taken by the Division of Drug Advertising during calendar years 1969-71. These bar graphs are based on actual figures in the Division's periodical reports. Taken together, actions have steadily increased during this time period. Regulatory actions include warning letters to industry, "preventive" letters, and regulatory conferences. Advisory actions include advisory letters to industry and advisory opinion conferences.

SUMMARY OF ACTIVITIES Figure 11 (below left) shows a tabulation of significant activities* of the Division of Drug Advertising from 1969-1971. These figures reflect:

(1) the number of prescription drug advertisements and promotional pieces monitored;

(2) actions taken by the Division (advisory and regulatory)

*Source: Division periodical reports

THE "PREVENTIVE" APPROACH Figures 12 through 15 (opposite page), depict examples of four "preventive letters" issued by FDA to manufacturers of various classes of drugs in an attempt to block advertising trends that were considered misleading and to encourage voluntary compliance in anticipation of preventing future regulatory action. Revised advertising trends indicate that the use of these preventive letters has been successful in blocking or modifying several campaigns which prompted their issuance and in improving the advertising for the various drug classes represented.

FIG. 11

FIG. 12

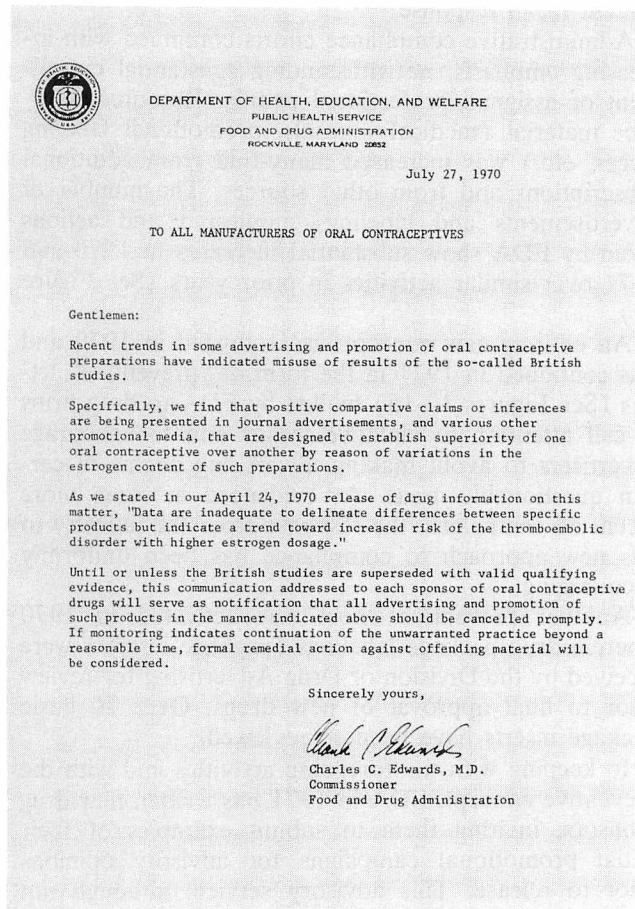


FIG. 13

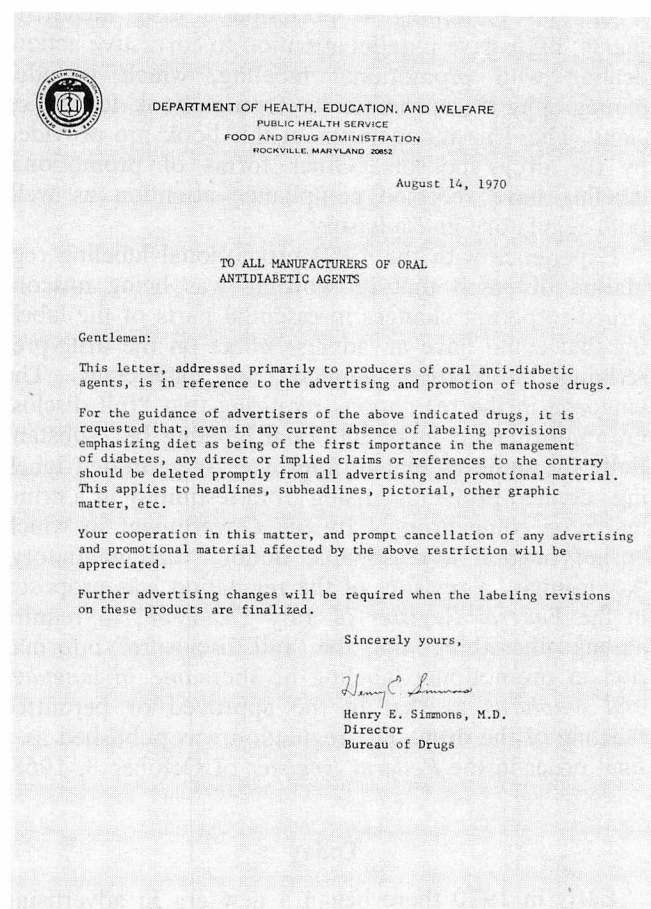


FIG. 14

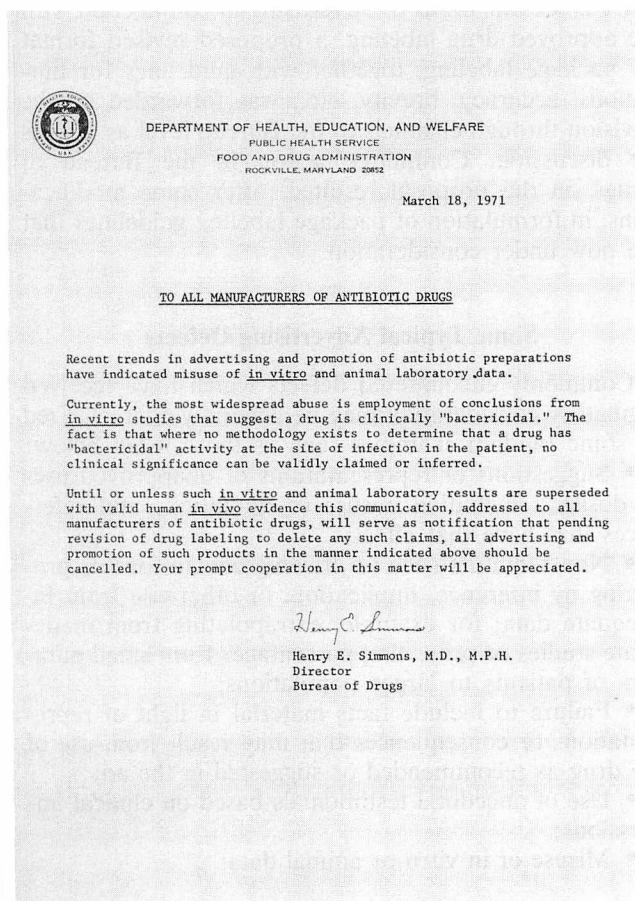
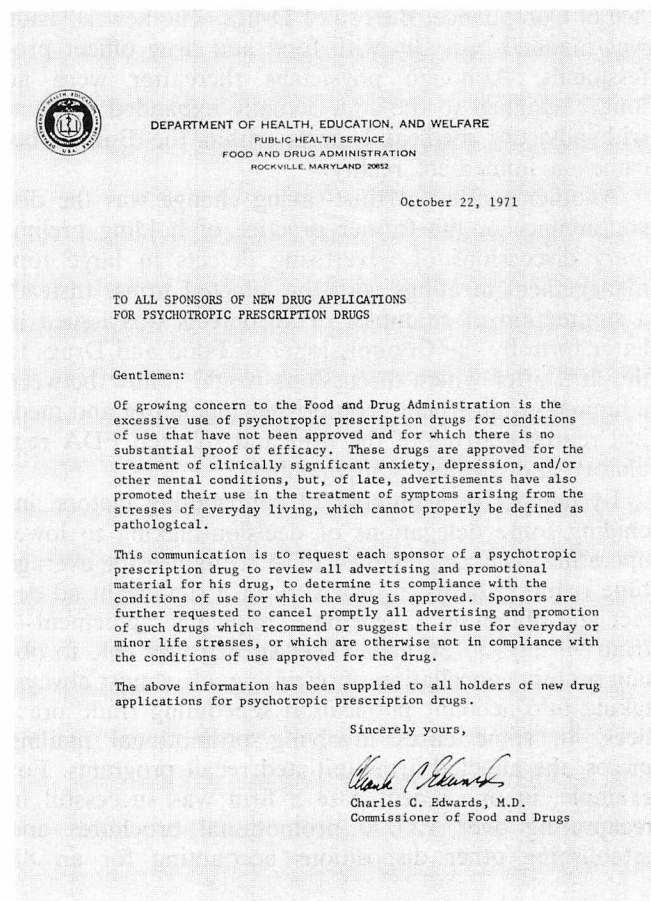


FIG. 15



regulations pertaining to prescription drug advertisements, FDA gave parallel attention to corrective actions dealing with promotional labeling, which included monographs in a prominent reference book for physicians. The drug monographs in this book are provided by the drug sponsors. Other forms of promotional labeling have received compliance attention as well, both regulatory and advisory.

Experience with the 1960 promotional labeling regulation disclosed that its wording was being misconstrued to permit changes in essential parts of the labeling that could have an adverse effect on the drug-prescribing information intended for physicians. The language in the regulations requiring that "full disclosure" information in promotional labeling be "substantially the same as that in approved or permitted labeling" created problems arising from testimony in a criminal proceeding brought by the Government in which "proof beyond a reasonable doubt" was mandatory. Accordingly, a revision of the regulation was proposed in the *Federal Register* of July 18, 1968, to require among other things that the "full disclosure" information in promotional labeling be the *same in language and emphasis* as that in the approved or permitted labeling of the drug. The regulation was published as a final order in the *Federal Register* of October 8, 1968.

Today

Early in 1970 there began a new era in advertising compliance activities and management. In March 1970, the Division of Drug Advertising was established for the first time under a permanent directorate in the Office of Compliance, Bureau of Drugs. The new Division was manned basically with food and drug officer professionals. Although physicians thereafter were no longer assigned to the unit, actually expanded contacts with advisory medical experts within the Bureau became an immediate reality.

Another significant time-saving change was the discontinuance of the former practice of holding preliminary discussions of advertising defects in large top-management meetings with the affected firms. Instead, a summation of examples of ad defects was issued in letter form by the Commissioner of Food and Drugs to the firm after which discussions would follow between a limited group usually comprising regulatory and medical representatives of the firm and selected FDA regulatory and medical staff members.

By late 1970, a number of contributing factors, including some delegations of decision-making to lower operating echelons, enabled FDA to reduce the average time required between discovery of a significant ad defect and obtaining a remedial compliance agreement—from 99 days to 36 days. The Agency was able to obtain prompt cancellation of offending ads almost always, taking into account publication scheduling trade practices. In some cases involving promotional mailing pieces, the affected firms initiated recall programs. For example, in one recent case a firm was successful in recapturing over 12,000 promotional brochures and establishing other dispositions accounting for an 88

percent recall response.

Administrative compliance efforts continued with increasing emphasis, notwithstanding substantial curtailment of assigned professional people. Resource reference material (medical journals, promotional labeling pieces, etc.) was increased many-fold from additional subscriptions and from other sources. The number of advertisements and labelings monitored and actions taken by FDA show substantial increases in 1970 and 1971 over similar activities in prior years (See Figure 11).

An entirely new concept was activated in 1970 and was continued in 1971 in the form of "preventive" letters (See Figures 12-15) mailed by FDA to drug firms to call attention to violative trends and to encourage advertisers to avoid making advertising claims in certain questionable areas. As evidenced in some more recent ad campaigns, the response from the industry to this new approach to compliance has been uniformly encouraging.

Another preventive effort was activated in 1970 wherein drug package labelings (package inserts) were received by the Division of Drug Advertising for review prior to final approval of new drugs. Over 70 basic package inserts have been so reviewed.

In keeping with the foregoing activities and with the preventive concept, FDA in 1971 has written new drug sponsors, inviting them to submit examples of their initial promotional campaigns for advisory opinions prior to release. This advisory service, although not required by regulations, has been found helpful by a number of participating firms.

In November 1970, as an outgrowth of comprehensive FDA evaluations of advertising in conjunction with the approved drug labeling, a proposed revised format for package labeling, together with guidelines for limitations, accuracy, brevity, etc., was forwarded by the Division through channels to the Bureau level as a basis for discussion. Committee action in the Bureau of Drugs on the proposal resulted, after some modifications, in formulation of package labeling guidelines that are now under consideration.

Some Typical Advertising Defects

Commonly encountered defects which have received regulatory consideration may be generally characterized by some random examples such as those listed below:

- Suggestions or representations of unapproved uses or dosages, including misuse of quotations and references that have that effect;
- Non sequiturs such as drawing conclusions or projecting by inference, implication, or otherwise from inadequate data; for example, extrapolating from inadequate studies or projecting percentages from small numbers of patients to larger populations;
- Failure to include facts material in light of representations or consequences that may result from use of the drug as recommended or suggested in the ad;
- Use of anecdotal testimonials based on clinical impressions;
- Misuse of in vitro or animal data;

- Direct or implied comparison of unlike drugs;
- Inaccurate characterizations or inaccurate limitations of drug actions, indications, or side effects by using sophistry, euphemisms, metaphors, colloquialisms, subtle syntax, exaggerations of effectiveness, minimizations of safety considerations, and hypotheses;
- Half-truths, inadequate qualifications and/or limitations regarding safety or effectiveness;
- Selection of warning or precautionary ideas in approved labeling and inversion into promotional thrusts;
- Whole or partial omissions in the "Brief Summary";
- Grouping of side effects when the labeling names side effects specifically;
- Vague, open-ended claims or suggestions of superiority;
- Representations or suggestions that a New Drug Application for a drug has been approved by FDA;
- Failure to provide the quantitative formula information required under section 502(n)(2) of the Act for *all* prescription drug advertisements. *Note:* a drug containing more than one ingredient, whether active or inactive, is not a "single ingredient drug";
- Representations or suggestions about drug products in so-called reminder ads, resulting in failure to meet the provisions exempting "reminder" ads from the requirement to present a true statement of information in brief summary relating to side effects, contraindications, and effectiveness;
- Lack of appropriate contextual and physical fair balance;
- "Hiding" the "Brief Summary" by, for instance, placing the information at the top of the page or in some other location on the page but clearly dissociated from the promotional message by use of intervening white space or some other technique; or
- Casting the "Brief Summary" in small black print on white background contrasted to the vividly colored, bold-lettered promotion, or camouflaging through use of soft-colored, poor-contrasting type; or
- Failing to appropriately "key over" to the "Brief Summary" on another page; or
- Obscuring the "Brief Summary" on a different page among other ads and articles;
- Failure, particularly by retail practitioners such as pharmacists, optometrists, and opticians, to take into account that all regulatory requirements for prescription

drug advertisements must be adhered to regardless of the intended audience, whether it is the general public, pharmacists, nurses, or others.

Epilogue-Prologue

Just as the FDA and industry approach the tenth year of experience with the prescription drug advertising provisions of the Drug Amendments of 1962, it is appropriate to reflect briefly on past developments in anticipation of future progress.

Let's take an example. Recently a violative promotional labeling piece was being discussed with a drug firm in a regulatory setting. One of the complaints about the piece was that it failed to provide fair balance both as to effectiveness and safety of the promoted drug. The sole defense offered for the omission was "but while the expression 'fair balance' is admittedly in the regulations concerning advertisements, it is not in the promotional labeling regulations and therefore fair balance should not be required in promotional labeling."

Our answer was in two parts. First, we admitted that there are a number of labeling regulations (counterparts of the advertising provisions) that remain to be published. Fair balance clarification is one. Second, we pointed out that a careful restudy of the advertising regulation relied on by the firm discloses that it reads ". . . false, lacking in fair balance, or *otherwise* misleading . . ." [italicized for emphasis]. In other words, lack of fair balance is only one example of a misleading situation. Moreover, the law itself [section 502(a)] requires that labeling of a drug not be false or misleading in any particular. The firm then agreed to provide the required fair balance in the promotional pieces.

We believe that even more progress can be expected. The advertising of prescription drugs first requires a fundamental realization that the pitch men, the old time medicine show, the hawkers, the hucksters, the shell game artists must have no place in the promotion of prescription drugs. It also requires confidence that advertising which discloses the balanced truth about prescription drugs, including their limitations of effectiveness and safety, will in the long run enhance the stature of these commodities in the marketplace. The reduction to practice of this modern concept of educational advertising presents challenges to the ingenuity and talents of advertisers. We feel that these challenges can reasonably be met.

H. W. Chadduck, director, Division of Drug Advertising, Office of Compliance, Bureau of Drugs, joined FDA at Washington in 1961.

field reports

ATLANTA Toru Ebihara, a pharmaceutical officer in the Ministry of Health and Welfare, Tokyo, Japan, and a Fellow in the World Health Organization, visited the Atlanta Field office during the week of November 22. Mr. Ebihara received orientation on FDA's regional laboratory, compliance, and inspectional operations, and observed the operation of a drug manufacturer in the regional area. Through the cooperation of the Georgia Board of Pharmacy, which made the necessary arrangements, Mr. Ebihara also visited a large retail pharmacy.

BALTIMORE The management of a large Baltimore grocery warehouse recently took voluntary action after Baltimore District inspectors, in a cooperative inspection with city health department inspectors, found heavy rodent infestation of the firm's premises. Management destroyed approximately 200,000 pounds of flour and sugar, and arranged to have nearly 180 tons of suspect sugar recrystallized. In the recrystallizing process, the sugar is run through a liquid solution that separates the pure sugar crystals from any impurities it contains. The firm has also begun an estimated \$50,000 worth of structural improvements to eliminate the rodent problem.

In a routine followup, the District recently reviewed the current status of two local firms against which complaints for injunction were filed about two years ago. The firms, one manufacturing food for human consumption and the other feed items for animals, were restrained from operating while insanitary conditions existed and from shipping violative products in interstate commerce. Neither firm has been in production since that time. The District's review showed that the animal feed manufacturer decided to abandon operations following the injunctive action and consideration is being given to dismissing the complaint against it. On the other hand, the food manufacturer reportedly has spent about \$100,000 on new equipment and to improve physical facilities in an effort to comply with the stringent requirements of the Consent Decree of Injunction.

The second phase of the personnel exchange between the Virginia Department of Agriculture and Commerce and FDA's Baltimore District (see May 1971 FDA PAPERS) was completed December 1, when Tom Price, the District's supervisory inspector, returned from a two-month detail in Richmond. Among the benefits resulting from the exchange is a new work-sharing agreement which encompasses the entire Virginia food industry for which the agencies share an obligation. Under the new agreement, the State will use the District's data processing unit for work planning and scheduling. Joint sessions will be held monthly to schedule assignments and more effectively utilize the pooled manpower.

Medicated feed inspectors from Maryland, Virginia, and

West Virginia attended a basic training course December 7-10 at the Baltimore District. The eventual commissioning by FDA of these inspectors will result in even better coverage of the feed industry in the District.

BOSTON The Federal Court for the District of Connecticut has issued a default decree ordering condemnation of approximately 10,000 pounds of furazolidone, a medicated feed premix, that has been held since May 19, 1971, when it was seized at the Davis-Edwards Pharmacal Co., Danbury. The complaint for forfeiture charged the product was a new animal drug for which the firm did not have an effective approved New Animal Drug Application.

A U.S. marshal seized 47 twenty-pound cartons of macaroni shells and 12 cases containing 12 sixteen-ounce packages of lasagna at Woonsocket, Rhode Island, where the products had been shipped by the manufacturer, Viva Macaroni Manufacturing Co., Inc., Lawrence, Massachusetts. FDA alleged the foods were insect contaminated and were prepared and packed under insanitary conditions.

BUFFALO Winthrop Laboratories, Rensselaer, New York, has destroyed more than \$300,000 worth of Pontocaine and Novocain Injectables, indicated for use in spinal conditions, after FDA found in a routine sampling that the product was decomposing and forming insoluble crystals. Some lots showed discoloration of the solution and low potency. The firm has been responsible for removing lots of these products from the market, and it expects additional stocks will be destroyed before the removal is completed.

A Buffalo District inspector maintained surveillance over voluntary destruction by Gioia Macaroni Co., Buffalo, of 165,312 six-ounce cans of tomato paste valued at about \$16,500. The article had been imported from Portugal through the ports of Chicago and Philadelphia. Numerous consumer complaints received by the importer, Gioia, and by FDA complained of the paste squirting from cans upon opening. Although the District's analysis showed no viable micro-organisms, hydrogen swells and serious metallic odor and taste were found. At least two firms that had packaged the article under private labeling returned stocks to Gioia because of the consumer complaints.

Import detentions through ports covered by Buffalo District increased during November—possibly because of diversion to and reshipment of products from Canada due to the dock strike curtailing such entries through the port of New York. The detained products included foods, cosmetics, and animal feed concentrate, with a total value of about \$61,000. The reasons for detaining

were absence of labeling, absence of mandatory labeling, inadequate labeling, filth, short weight, and failure to comply with Fair Packaging and Labeling Act regulations.

CINCINNATI Nature's forces brought about a recent detention in the District. The ship *Arthur Stone* arrived at the port of Toledo with 126,000 cases of canned foods from Taiwan. Much of the cargo was seriously damaged due to three storms the ship encountered during the voyage, causing shifting of the cargo and taking in of water. The District surveyed the damage, collected samples, and detained several lots of the canned foods.

The District has numerous cans of sauerkraut under surveillance because of an unusual problem that came to FDA's attention through a consumer complaint that the lacquer lining of a can of the sauerkraut had separated from the metal, causing a chemical reaction between the contents and the metal can. The District's investigation at the can manufacturing plant disclosed that the can was not the type intended or suitable for containing such a high acid food.

The cannery has removed the product from the market and turned the merchandise over to the can manufacturer for research and disposition. The District is trying to determine if this type of can was distributed by the can manufacturer for use with other high acid foods.

DENVER Federal, State, and industry efforts were successful in removing dangerously contaminated wheat from the marketplace before it entered human food channels. The contamination was discovered during an FDA investigation that started in response to a call to the Field Office from Montana State officials reporting the sudden and mysterious deaths of poultry and cattle on one farm. FDA Field Inspector Charles W. Scritchfield was sent to the farm to investigate. He learned that one week earlier one of the farmer's sons had entered an empty railcar and found approximately ten gallons of wheat, which he took home and fed to the poultry and cattle. Field Office analysis of the wheat showed that it was contaminated with the previous contents of the railcar—lead oxide, a poisonous substance. Through the efforts of Federal and State officials, the contaminated grain that had been carried in the car was soon located. With the cooperation of the mill where the grain was located, the officials were enabled to remove the wheat from the market.

Monetary value of Field Office seizures in November of products not in conformity with the Fair Packaging and Labeling Act totaled more than \$3,800. Foremost was the seizure in Denver of 389 gallons of olive oil valued at \$2,413 and manufactured by F. Bertoll, Lucca, Italy.

KANSAS CITY After Bastian's Wholesale Grocery Co., Joplin, Missouri, pleaded guilty to eight counts of an information charging that foods held on the premises were contaminated with rodent and insect filth and were stored under insanitary conditions, a District Court fined the partnership \$100 per count, a total of \$800. The court then suspended \$300 of the fine.

The Special Programs Branch of the Kansas City Regional Office conducted Food Service Sanitation workshops in Lincoln, Nebraska, and Des Moines, Iowa, in November. Both workshops were conducted by C. D. Brand, FDA regional food consultant. The Nebraska workshop was attended by 40 enforcement officials representing the State Departments of Agriculture and of Health, Lincoln-Lancaster County Health Department, Grand Island-Hall County Health Department, Omaha-Douglas County Health Department, South Sioux City Health Department, Hastings Department of Health, and the City of Kearney.

At Des Moines, 52 enforcement officials attended. They represented the State Departments of Agriculture and of Health, Des Moines-Polk County Health Department, and the Story County Health Department.

Lorena Meyers, District consumer specialist, recently made three radio tapes at the University of Nebraska Information Office at Lincoln to be sent to 25 radio stations throughout the State. Among the subjects covered were toys, safety of canned foods, and activities in the Bureau of Radiological Health. She also spent some time with Ann Snyder, newly appointed consumer specialist for the Nebraska Department of Agriculture, discussing FDA's consumer education program and future consumer activities the Agency plans for the State of Nebraska.

LOS ANGELES Linden Laboratories, Los Angeles, is recalling four lots of aspirin compound with codeine phosphate. All lots show an excess of free salicylic acid. In addition, two of the lots contain undeclared acetaminophen and do not contain declared phenacetin.

A lot of 1.78 million pounds of whale meat, imported from Japan and valued at \$240,000, was seized on a charge that it contained mercury in excess of FDA's action guideline of 0.5 parts per million. The lot was in the possession of a local pet food manufacturer, Kal-Kan Co., for incorporation into dog and cat food. Whales are considered endangered species under a July 30, 1970, announcement from the Department of the Interior. Since the shipment was enroute at the time of the announcement, the firm had reportedly received special permission for this last lot of whale meat to be allowed into the country.

MINNEAPOLIS Personnel of WCCO-TV, Minneapolis, returned to the District office in December to tape a sequel to a program on toy safety which the station ran during the last week in November in its series, "Consumer Affairs." The program apparently enjoyed consumer approval. The station photographed various toys at the District office, including some of the laboratory testing procedures, and the message pointed out parents' responsibility in buying safe toys.

District officials have observed a recent increase in valid consumer complaints about canned food in abnormal appearing cans. The abnormalities include swells, pinholes, and rusted cans. District investigations following such reports have disclosed frequent instances where the involved products are old stocks up to 3½ years old. This type of product is being found in re-

putable food stores and is not limited to salvage houses as heretofore. The situation seems contrary to practices of past years, when such merchandise was rarely encountered in the area's wholesale warehouses or retail stores.

NEW ORLEANS Dixie Brewing Co., New Orleans, voluntarily destroyed approximately \$7,000 worth of brewers malt after the U.S. Attorney filed a complaint alleging contamination by presence of live and dead insects and holding of the malt under conditions that might result in contamination.

The District detained an entry of Flocked Bulls, a toy, from Hong Kong because it had a removable sharp pin in the nose which could cause puncture wounds. It also had eyes, a bell, and horns that could be removed by a child and could cause possible injury by aspiration or ingestion.

Also detained because they contained amounts of leachable lead and cadmium above actionable levels were toy tea sets from Japan valued at \$6,400.

NEW YORK Irradiated frog legs shipped to Canada from a New Jersey firm will no longer be found on the tables of Canadian gourmets. Recent combined efforts of the Atomic Energy Commission, FDA Region II, and the Canadian Food and Drug Directorate resulted in discontinuance of a surreptitious operation in which frozen frog legs were being irradiated.

The operation came to light during a routine AEC inspection at a cobalt 60 gamma irradiator operating under AEC license. Because the irradiator's license when issued did not provide for such an activity, it could not be regulated by the AEC. The Commission therefore referred the problem to New York District's Newark Section (now Newark District) for FDA followup. Newark Section's inspectors investigated and found that the irradiator did not have an effective FDA food additive petition demonstrating that the irradiated product was nontoxic. The Federal law at this time states that foods can be irradiated for experimental purposes only. The firm agreed to discontinue irradiating frog legs. All the output was being exported to Canada as quickly as it was treated; consequently there was no product on hand for FDA to act against.

The business was presumed to be profitable, since Canadian import test standards for acceptance of frog legs result in a high rejection rate because of *Salmonella* contamination, and since irradiation renders the goods virtually sterile and thus free from such contamination. When advised of the problem, the Canadian Food and Drug Directorate began plans to initiate action against the Canadian distributor, since he had acted in violation of the Directorate's food additive law, which has the same requirements as the U.S. law has.

The AEC, as a result of the problem, is considering the addition of restrictive clauses in its licenses which will prohibit irradiation of foods or drugs that are not covered by appropriate approvals.

A comprehensive Memorandum of Understanding concerning the human drug industry in Puerto Rico was signed recently by Ernesto Colon Yordan, M.D., the

Commonwealth's Secretary of Health, and Weems L. Clevenger, Director of Food and Drugs, Region II, FDA.

There are some 50 drug manufacturing firms now located in Puerto Rico and another 20 plants are either under construction or in planning stages. The annual volume of drug production in the Commonwealth exceeds \$200 million. To achieve an acceptable level of consumer drug protection, maximum utilization of both agencies' resources must be made. Under the terms of the Memorandum, both partners share equal responsibilities with the intent of avoiding duplicative efforts.

Highlights of the Memorandum: Primary responsibility for surveillance and compliance inspectional and analytical coverage of each individual drug firm in Puerto Rico is borne by the health department or by FDA, but not by both as in the past. The department, utilizing its personnel who have received FDA commissions, will inspect each of the drug firms for which it bears primary responsibility at least once annually. FDA, utilizing its personnel who have received department commissions, will collect and report that data needed by the department for its licensing activities when making inspections of the firms for which FDA has primary responsibility. Continuous exchange of work schedules, inspection and analytical reports, and periodic refresher training of personnel will take place between the two agencies. When violations are encountered, the department and FDA will promote compliance by using the most effective and expedient means at the disposal of either agency under its respective authority.

PHILADELPHIA Harold W. Bryan, supervisory inspector, and Raymond P. Beaudette, inspector, of the District's resident station at Pittsburgh, manned a booth and taped several TV appearances in connection with the Consumer Fair held December 1-2 at Gimbels Department Store in Pittsburgh. The *Pittsburgh Press* on December 1 published an article featuring the booth exhibit, which showed banned and unsafe toys and quack medical devices.

The fair, sponsored by the Consumer Services Committee for the Pittsburgh Federal Executive Board, presented exhibits from 18 Federal, State, and local consumer protection agencies, as well as several private independent groups.

Mr. Bryan has received a written commendation from Harold T. Busbey, chairman of the Pittsburgh Federal Executive Board, for FDA's presentation. White House representatives have recommended that similar programs be conducted by Federal Executive Boards on a nationwide basis.

A Philadelphia bakery of specialty baking items was fined \$2,000 November 17 by Federal Judge A. Leon Higgenbotham, sitting at Philadelphia. The bakery was charged with shipping products containing insects and rodent hairs and with manufacturing the products under insanitary conditions.

SAN FRANCISCO The District acted as host at a meeting of West Coast detergent distributors December 3, which was arranged and led by representatives of the Bureau of Product Safety. John Locke, assistant direc-

tor of the Bureau, presided. Covering details of FDA problems with regulating detergents were other Bureau personnel: Jerry Donovan, deputy director, Chemical Hazards; Dr. Bob Hehir, chief, Chemical Toxicological Laboratory; and Fred Halverson, senior official, Compliance. They led the discussions on test methods and standards, formulation, graphic symbols in labeling to indicate degree of hazard, cautionary labeling, and an appropriate consumer education program.

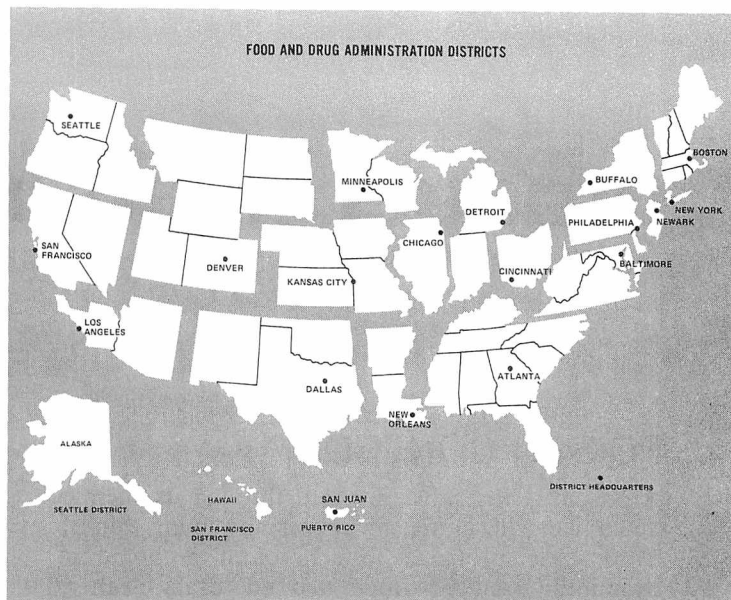
The 13 members of industry attending appeared to be genuinely interested in developing improved public safety in the use of their products.

Among a total of 97 various detentions made by the District office during November were seven entries of canned tunafish, valued in excess of \$315,000, detained because of adulteration with mercury, decomposition, or both. All the mercury-adulterated lots were exported from Japan.

SEATTLE Sanitation practices concerning food processing and food services in Alaska was the keynote of a recent workshop and of a random survey by District officials.

At the suggestion of the shrimp industry at Kodiak, Alaska, the Seattle Field Office and the National Canners Association sponsored a sanitation workshop there December 9 for 55 employees representing 13 firms in the local shrimp and crab industry. The workshop was keyed to employee sanitary practices and retort operations and was conducted by LeRoy Gomez, chief inspector, and Ed Murray, inspector, of the Seattle office.

The random survey, taken at the request of Alaska health officials, was of 33 food service establishments located in southeast Alaska. It was conducted by James L. Shoemake, FDA regional milk and food consultant,



to determine the sanitary status of the establishments and administrative problems in management of the food protection program.

Results of the survey indicate that the program in southeast Alaska is somewhat comparable to food service sanitation programs in other States. Recommendations were provided to the health officials concerning the need for additional manpower in the program, improved program planning and evaluation procedures as well as records, and adoption of the 1962 Recommended Food Service Sanitation and Code to serve as a legal basis for the program. The State health officials have indicated they are in the process of implementing these and other program changes as a result of the survey.

FDA REGIONAL AND DISTRICT OFFICES

ATLANTA 60 Eighth St., N.E.
Atlanta, Ga. 30309

BALTIMORE 900 Madison Ave.
Baltimore, Md. 21201

BOSTON 585 Commercial St.
Boston, Mass. 02109

BUFFALO 599 Delaware Ave.
Buffalo, N.Y. 14202

CHICAGO Main Post Office Bldg.
Rm. 1222/433 W. Van Buren St.
Chicago, Ill. 60607

CINCINNATI 1141 Central Pkwy.
Cincinnati, Ohio 45202

DALLAS 3032 Bryan St.
Dallas, Tex. 75204

DENVER New Customhouse Bldg.
Rm. 513/20th & California Sts.
Denver, Colo. 80202

DETROIT 1560 E. Jefferson Ave.
Detroit, Mich. 48207

KANSAS CITY 1009 Cherry St.
Kansas City, Mo. 64106

LOS ANGELES 1521 W. Pico Blvd.
Los Angeles, Calif. 90015

MINNEAPOLIS 240 Hennepin Ave.
Minneapolis, Minn. 55401

NEW ORLEANS U.S. Customhouse
Rm. 222/423 Canal St.
New Orleans, La. 70130

NEW YORK 850 3rd Ave.
Brooklyn, N.Y. 11232

NEWARK Rm. 831, 970 Broad St.
Newark, N.J. 07102

PHILADELPHIA U.S. Customhouse
Rm. 1204/2nd & Chestnut Sts.
Philadelphia, Pa. 19106

SAN FRANCISCO Federal Office Bldg.
Rm. 518/50 Fulton St.
San Francisco, Calif. 94102

SAN JUAN P.O. Box 4427
San Juan Station, P.R. 00905

SEATTLE Federal Office Bldg.
Rm. 5003/909 First Ave.
Seattle, Wash. 98104

HEW REGIONAL OFFICES I-X

BOSTON J.F. Kennedy Federal Bldg.
Boston, Mass. 02203

NEW YORK 26 Federal Plaza
New York, N.Y. 10007

PHILADELPHIA 401 North Broad St.
Philadelphia, Pa. 19108

ATLANTA 50 7th St., N.E.
Rm. 404/Atlanta, Ga. 30323

CHICAGO New Post Office Bldg.
433 W. Van Buren St./Chicago, Ill.
60607

KANSAS CITY 601 E. 12th St.
Kansas City, Mo. 64106

DALLAS 1114 Commerce St.
Rm. 911/Dallas, Tex. 75202

DENVER Federal Office Bldg.
19th & Stout Sts./Denver, Colo. 80202

SAN FRANCISCO Federal Office Bldg.
Rm. 416/50 Fulton St.
San Francisco, Calif. 94102

SEATTLE Arcade Plaza Bldg.
1321 2nd Ave., Seattle, Wash. 98101

product safety report

POISON CONTROL

A poison is any substance that through its chemical action can kill, injure, or impair any living thing. Thus, some substances found around the home in commonly used containers marked “drain cleaner,” “electric dishwasher detergent,” “baby aspirin,” “floor polish,” and “furniture wax” can be used so carelessly or thoughtlessly that they become poisons. A child who drinks turpentine stored in a soft-drink bottle, a toddler who eats baby aspirin in the belief it’s candy, a family that is overcome by the fumes from an unlighted gas heater—all are occurrences in which everyday items become poisons through accidental misuse.

Such events are common, according to Georg S. Maisel, chief of the Project and Program Development Branch in the Bureau of Product Safety, Division of Chemical Hazards. In 1970, 432 Poison Control Centers in 49 States reported 64,494 cases of improper use of medicines, 12,668 involving aspirin alone. There were 12,591 reports concerning accidental ingestions of cleaning and polishing agents, 5,617 related to cosmetics ingestions, and 4,077 concerning ingestions of petroleum products. There were reports of 5,016 cases involving poisonings from turpentine and paints and 5,771 from pesticides. It is estimated that in the coming year alone, 500,000 children will accidentally ingest toxic or potentially toxic substances.

The records show that 90 percent of all cases of accidental poisoning involve children under five years of age. Substances that most frequently cause such harm are medicines and household preparations, including cleaning fluids, soaps and detergents, insect sprays, lighter fluid, and some furniture polishes, as well as kerosene, turpentine, paints, solvents, and various other products containing lye and acids. Aspirin has been the most common single cause.

Although aspirin is still the leading item involved in childhood ingestions, it has dropped from 25.8 percent in 1965 to 19 percent in 1969. Vitamin ingestions in overdoses have risen, however, from 1.7 percent to 5.1 percent. (Although most over-the-counter vitamins represent a minimum hazard, some therapeutic prescription vitamins can cause poisonings. Therefore, all vitamins should be kept from the reach of children.) Bleaches dropped from 5.3 percent to 2.4 percent and insecticides dropped from 6.1 percent to 2.4 percent. In 1968, the last year for which death

reports are available, 284 fatalities occurred among children under the age of five from accidental ingestion of potentially toxic substances.

In 1968, drugs of abuse were responsible for 150 deaths among children under five. These substances included barbiturates, tranquilizers, and amphetamines. Although drug abuse is normally associated with young adults, the accessibility to children of these drugs makes the youngsters vulnerable to poisonings by these products.

Eleven years ago, realizing the serious nature of childhood poisonings, Congress enacted Public Law 87-319, requesting the President to designate the third week in March each year for highlighting poison prevention activities “to aid in encouraging the American people to learn of the dangers of accidental poisoning and to take such preventive measures as are warranted by the seriousness of the danger. . . .”

In 1972, the week of March 19-25 marks the 11th observance of National Poison Prevention Week. It is sponsored by the National Planning Council, formed in 1961 by representatives of the Departments of Agriculture and Health, Education, and Welfare, allied with medical, pharmaceutical, and similar groups, as well as industrial and trade associations and civic and service organizations. (Reports indicate that Spain, Italy, and Canada will conduct poison prevention activities to dovetail with this campaign.)

The theme for the week will be the startling “Search and Destroy.” “Search” is the clue word for the householder’s responsibility to seek out hazards in the home, garden, and outbuildings. “Destroy” refers to the necessity to eliminate those dangers, through “childproof” storage (accomplished by locking medicine cabinets and placing household cleansers beyond the reach of youngsters), through the proper and careful use of all medicines and household supplies, and by destroying all hazardous items when no longer needed. For example, prescription items, particularly, should be discarded once the illness for which they were prescribed is over.

It is shocking that 95 percent of poisonings to children under five occur while they are under the supervision of parents or other responsible adults. Thus, careful storage methods are critical to safety and should be varied to meet the changes in the development of children as they grow; most growing children are curious about things that glitter—pretty colored pills, bottles, and containers of all kinds.

If a child is in the crawling stage, adults should keep household products somewhere other than below the kitchen sink or on floors and lower shelves of unlocked cabinets.

If a child is toddling, parents should put away, or take along, bottles and boxes containing medicines and potentially dangerous household products when leaving the room to answer the telephone or doorbell.

If a child is able to climb, parents should be certain that all hazardous substances are on shelves completely beyond the child's ability or reach or, better yet, are locked in a cabinet or closet.

Parents should look, too, for safety packaging for those items which could cause serious injury or illness to children. The concept of such packaging was established in December 1970 under Public Law 91-601, the Poison Prevention Packaging Act. When fully implemented, it will aid in protecting children from accidental ingestion of many toxic substances by requiring safety closures and other safety packaging for certain designated products. It should be noted that some safety closures are already on the market, and parents certainly should shop for products in such packaging.

Under the law, the package must be so designed that most children under the age of five will find the container difficult to open but adults will find it relatively uncomplicated. However, the law makes provision for aged or infirm adults who might have difficulty coping with some of the special packaging. For these people, the law permits a container which can be easily opened, provided it comes only in one size and is appropriately labeled as being for use in households without young children.

It would be practically impossible to manufacture a package or closure that would prevent every single child from getting into the contents under all possible circumstances. Most children know that if their fingers won't work, their teeth might! Therefore, the law requires that the regulated packages be designed so that it will be difficult for most children under five years of age to obtain a toxic amount. For example, FDA has proposed a regulation requiring that aspirin be packaged in special containers which would make it difficult for 80 percent of children tested to open the container. It is obvious that, even with such regulations in effect, it will always be necessary for parents to provide constant supervision and observe recommended poison prevention measures.

To aid parents and other concerned adults, the National Planning Council has prepared these rules to help make a home "poison proof."

1. Keep household products and medicines out of reach and out of sight of children, preferably in a locked cabinet or closet—even a fishing tackle box or suitcase can be used. If you must leave the room for even an instant, remove the container to a safe spot or take the child and/or container(s) with you.

2. Store medicines separately from other household products and keep these items in their original containers—never in cups or soft-drink bottles.

3. Be sure that all products are properly labeled and read the label before administering. In a dark room, turn the light on to do so.

4. Since children tend to imitate adults, avoid taking medications in their presence.

5. Refer to medicines by their proper names. Never encourage children to take any medicine by calling it "candy," for later they may be tempted to eat it as a treat.

6. Clean out your medicine cabinet periodically. Get rid of old medicines by flushing them down a drain, rinsing the containers in water, and then discarding them. Do not put any container with its contents into a refuse can.

7. Keep telephone numbers handy for your family doctor, local police, and nearest hospital emergency room.

8. For some poisonings, first-aid treatment can be given at home. Therefore, every household with children should have a one-ounce container of Syrup of Ipecac for inducing vomiting when this is called for. Also, activated charcoal should be kept on hand for first-aid use. Its label indicates when this type of treatment should be used, but it is wise to check with your physician.

If, in spite of all safety precautions, a poisoning accident occurs or a possible poisoning accident is suspected, these procedures are recommended:

First, call your physician—you should get the victim under medical care as quickly as possible. If you have no physician, contact your county or city general hospital.

Second, if aspirin is involved, induce vomiting. (See Home Rule 8.) However, vomiting is not recommended if the product ingested contains petroleum distillates, caustics, or alkali. Instead, the victim should be made to drink milk or water.

Remember, furniture polishes can be dangerous. Some contain petroleum distillates which are responsible for most of the hazards associated with swallowing this kind of product. Polishes containing such distillates display warning labels.

Vomiting should not be induced if the victim is unconscious or convulsing. Additional information on poisons and Poison Prevention Week can be obtained by writing to:

National Planning Council for Poison Prevention
Week
P.O. Box 1543
Washington, D.C. 20013

The Council publishes a list of brochures, flyers, and pamphlets with information on how to secure them from Government agencies, medical and pharmaceutical groups, and civic and service organizations.

news highlights

'Child-Resistant' Aspirin Packaging Set To Become Effective in Mid-August

Final regulations have been published by FDA to protect children from accidental poisoning by requiring special "child-resistant" packages for all products containing aspirin.

In announcing the packaging order February 15, FDA reported that although the number of accidental ingestions of aspirin has dropped significantly in recent years, aspirin is still the leading cause of poisoning of children under five years of age. The regulations take effect in mid-August.

The safety standards for aspirin packaging require 85 percent closure effectiveness in tests with a specified group of 200 small children.

The Poison Prevention Packaging Act of 1970, under which the aspirin safety packaging regulation was promulgated, was enacted in December 1970. It required appointment of an 18-member technical advisory committee to consult with FDA on implementing the Act. The Committee was appointed April 15, 1971.

A testing protocol to establish standards for safety packaging was proposed July 29, 1971, published as a final regulation November 20, 1971, and became effective January 19, 1972.

FDA's action on aspirin packaging was the first in a series to implement the Poison Prevention Packaging Act.

Ban of Asbestos Fibers for Clothing Proposed After FDA Study of Hazards

The use of asbestos fibers in cloth for garments intended for general use would be banned as a hazardous substance by a regulation proposed by FDA.

Charles C. Edwards, M.D., Commissioner of Food and Drugs, said airborne asbestos fibers from the garments can be toxic when inhaled.

The regulation, proposed February 18, is being promulgated under provisions of the Federal Hazardous Substances Act. It would ban from interstate commerce all general use garments containing asbestos, but would exempt garments used for firefighting purposes.

An imported fabric containing 8 percent asbestos fibers was used to manufacture about 600,000 women's coats in late 1970. FDA's Bureau of Product Safety sponsored a simulated wearer test conducted by the National Institute for Occupational Safety and Health. The results of this study were reviewed and evaluated by a committee of nationally recognized experts on asbestos hazards.

The committee concluded that recall of the 600,000 coats was not warranted, but future use of asbestos in garments for the general public was inappropriate and presented an avoidable toxicity hazard.

FDA Asks Makers to Improve Safety Of Home Gas, Electric Cookstoves

FDA has asked stove manufacturers to improve the safety of gas and electric home cooking ranges.

The FDA made the request at a recent meeting in Washington of officials of FDA's Bureau of Product Safety and representatives of the Association of Home Appliance Manufacturers, Gas Appliance Manufacturers' Association, and Underwriters' Laboratories.

FDA officials noted that these products are not covered by legislation and that response by industry to the recommendations would be voluntary. The manufacturers and association representatives said they will explore a number of possibilities to determine the most practical ways of implementing the needed improvements.

The industry representatives were asked to consider three improvements in ranges which, FDA officials said, would substantially reduce accidental clothing ignition and resulting injury.

The recommended improvements include design changes in location of the control knobs to prevent them from being turned on accidentally; relocation of signal lights to provide a more effective warning that burners are on; and methods of insuring that the housewife uses the proper size burner to eliminate the risk of clothing ignition from contact with that portion of the burner left uncovered.

FDA Proposes Rules on Electric Toys Using House Current to Assure Safety

Regulations to set safety standards for electrically operated toys and to provide for banning those with unacceptable electrical, mechanical, or heat hazards were proposed by the FDA in the *Federal Register* of January 21.

Charles C. Edwards, M.D., Commissioner of Food and Drugs, said the proposed safety requirements for toys are intended to minimize or eliminate danger to children from electrical shock, heated surfaces, molten material, or electrically operated moving parts.

"We are also developing additional regulations to cover the mechanical hazards of nonelectrical toys," Dr. Edwards said. "When these and the regulations we

are proposing today are made final, the Agency will be able to implement effectively its toy safety responsibilities under the Child Protection and Toy Safety Act."

The proposed regulations for electrically operated toys cover trains, stoves, ovens (either heated by a light bulb or a heating unit), irons, corn poppers, candy making machines, electrical football games, cars, molding sets (plastic or lead), wood burning kits, or any other toy activated by a household line current. Separate standards are being developed for battery-operated toys.

In the past 15 months, FDA has issued final regulations banning seven classes of toys and articles intended for children's use where they were judged to have specific unacceptable mechanical hazards. These included toy rattles and noisemakers, dolls and other stuffed toys, outdoor lawn darts, caps, clackers, and baby walkers.

FDA's Bureau of Product Safety said these banning actions resulted in the removal of 250 toy products, or an estimated 2 million toys, from the market before Christmas of 1971. The Bureau's Toy Review Committee also examined approximately 800 other toys and obtained more than 100 voluntary corrections of potential hazards from manufacturers.

In addition, 122 toy manufacturing plants were inspected by Agency personnel.

An estimated 1,200 toy manufacturers produce approximately \$3 billion worth of toys each year and there are another 83,000 import shipments of toys into the United States.

The proposed regulations would require all toys intended to be operated at voltages higher than 30 volts to bear the statement: "Caution—Electric Toy." The toy's package and instructions would also carry a warning statement. Warning statements would also be required on toys employing heating devices to warn the user of "hot" surface temperatures.

Moving parts capable of causing injury would be required to be enclosed or guarded. Switches required for electrically operated toys with moving parts would be plainly marked for "Off" and would be simple to operate.

Electrically operated sewing machines would be designed to eliminate the possibility of a child's finger being pierced by a needle. Pressurized enclosures such as cylinders in toy steam engines would be equipped with automatic pressure relief devices and the toy would be required to withstand hydrostatic pressure equal to five times the relief pressure.

The proposed regulation also establishes maximum acceptable temperatures for toy surfaces accessible to the user. The temperatures are based on the type of surface, and the thermal characteristic of the material involved. Those materials having higher heat transfer rates are required to have lower surface temperatures.

Toy pots and pans and containers for holding molten compounds would be designed to prevent accidental

spillage and to have adequately insulated handles. These would also be constructed of material which would not warp or melt when heated. Paints and surface-coating materials for toys would be required to comply with FDA regulations which, as proposed November 2, 1971, would limit the content of lead and other heavy metals.

The proposal details tests and conditions under which the tests are to be performed.

FDA-Developed System Will Help More Hospitals in Bone Tumor Diagnosis

Opportunities to reduce patient radiation exposure during the use of radioactive materials in bone-tumor detection have been increased by the work of scientists at FDA's Nuclear Medicine Laboratory in Cincinnati.

The scientists, according to John C. Villforth, director of FDA's Bureau of Radiological Health, have developed a system to make possible the wider use of reactor-produced fluorine-18 as a substitute for the more commonly used strontium-85. Because of its shorter radioactive life, he noted, fluorine-18 delivers about 5 percent of the radiation dose normally delivered by strontium-85. Fluorine-18 has another advantage, he added, in that it transfers from bloodstream to bone more rapidly than strontium-85.

The key component of the system is a kit with which a technologist, untrained in radioactive materials production, can make fluorine-18 available to any hospital or clinic within a few hours travel time from a research nuclear reactor, provided the medical facility has the capability for preparing radioactive materials suitable for administration to patients.

Until development of the kit, opportunities to take advantage of the short radioactive life of fluorine-18 had been limited to a few medical institutions in the country that have reactors or accelerators in which radioactive material can be produced. Many other hospitals and clinics needed fluorine-18 production capability to prepare the material in their own laboratories for treatment of patients. Such institutions now are in a position to use the fluorine-18 kit provided the trip from reactor to the hospital can be completed in a few hours.

The advantages of using trace amounts of fluorine-18 for bone scanning have been established. Bone tumors can be distinguished from normal bone by the use of scanning devices.

The kit contains lithium-6 carbonate targets; an ion exchange column of zirconium oxide; and various reagents, syringes, and pipettes. Arrangements may be made by a hospital or clinic for irradiation of the targets at a nearby reactor. Once the targets are returned to the medical facility, the kit can be used to separate tiny amounts of fluorine-18 from the irradiated material in about 30 minutes.

The kit was developed by Kenneth L. Scholz and Dr. Vincent J. Sodd of the laboratory's research staff.

USDA, FDA Note Finding Small Amounts Of Nitrosamine in Some Processed Meats

Preliminary studies have confirmed small amounts of the chemical nitrosamine in some processed meat products, the U.S. Department of Agriculture and FDA have announced.

The findings were reported February 5 at a regular meeting of FDA, USDA, and participating scientists who are conducting research on the safety of present meat curing processes and the need to protect against botulism.

Nitrosamines are a family of chemical compounds which may be formed by a combination of nitrite and amines and which, under certain conditions, have been shown to be carcinogenic in certain species of test animals.

USDA Consumer and Marketing Service scientists reported that tests have confirmed that three meat samples had nitrosamine levels of 11 to 48 parts per billion. Two of the samples were dried beef products and one was cured pork. USDA scientists have analyzed 45 other samples with negative results. C&MS meat inspection officials said that the limited sampling program for dimethylnitrosamine was initiated immediately after preliminary research findings by USDA's Agricultural Research Service revealed traces of dimethylnitrosamine in three samples of cooked sausage products from retail markets.

Agricultural Research Service scientists said that in laboratory tests of cooked sausage products no nitrosamines were detected in the samples with nitrite at currently permissible levels. At higher than normal levels of nitrite usage, about 10 times the allowable quantity was required before the formation of nitrosamines could be detected.

FDA reported that it has analyzed more than 200 meat products, many with a multidetection procedure recently developed by FDA, which will identify 14 nitrosamines. Dimethylnitrosamine was confirmed in one ham sample at a level of 5 ppb. Preliminary studies on four different brands of bacon showed that N-nitrosopyrrolidine, a nitrosamine, was formed when the bacon was cooked in the conventional manner. Levels ranged from 30 to 106 ppb in the cooked product. The compound was not found in the raw bacon.

USDA and FDA emphasized that the significance of these findings is not known at present. Ongoing public and private research must be continued to determine under what circumstances nitrosamines are formed before any firm conclusions can be drawn.

American Meat Institute scientists reported they had made preliminary findings that demonstrated the necessity of using nitrites to prevent botulism in pasteurized canned meat products. The Institute has also initiated an additional study on bacon to determine minimal levels of nitrites needed in this food product.

USDA and FDA also emphasized the need for

further research to clarify the role of nitrites in preventing botulism before changes in curing processes are recommended. A primary purpose of the use of nitrites, which have been used in curing meats for hundreds of years, is to inhibit the growth of botulinum spores and prevent botulism.

Saccharin Removed From GRAS List, Use Restricted Pending New Studies

The FDA on January 28 removed saccharin from the GRAS (Generally Recognized As Safe) list of food additives and issued an interim, provisional regulation restricting use of the artificial sweetener while additional safety reviews are being completed.

The interim order limits saccharin use in accord with a National Academy of Sciences/National Research Council recommendation of no more than one gram per day for the average adult. One gram of saccharin is equal to seven 12-ounce bottles of the standard diet drink. A gram of saccharin is equal to 60 of the common small saccharin tablets. Each tablet is equal in sweetening to one teaspoon of sugar.

The order requires saccharin disclosure on the labels of all beverages, foods, and food mixes in which use is permitted.

In announcing publication of the new order, Charles C. Edwards, M.D., Commissioner of Food and Drugs, emphasized that the action is an interim step designed to "freeze" saccharin use at present levels pending final outcome of current research on safety of the non-nutritive sweetener.

Chronic feeding studies with saccharin in animals are being conducted in FDA laboratories and by others. Preliminary reports from one of these, Wisconsin Alumni Research Foundation, indicate no injury when saccharin constitutes 0.05 percent of the daily diet—a level comparable to the one-gram limit set by the FDA's regulation.

At much higher levels, 5 percent of the daily diet, or approximately 100 times the maximum permitted by the new regulation, some test animals developed bladder tumors. An intensive review is now under way to determine whether or not these tumors are cancerous.

Saccharin has been widely used in the food supply for more than 80 years without any evidence of harm to humans. The tentative adverse findings in rats occurred at a level roughly equivalent in humans to 875 bottles of a typical diet soft drink per day.

"The FDA, with the assistance of the NAS, will continue to weigh the evidence as it becomes available and should experimental findings demonstrate that saccharin involves a risk to public health, the FDA will withdraw approval for use of saccharin in foods," said Dr. Edwards.

"In the meanwhile, the interim food additive order adequately protects the public," he said.

state actions

DDT Residues Down The laboratory services of the Oregon Department of Agriculture report a significant reduction in traces of the pesticide DDT in cheese, milk, and butter produced in the State since 1970. According to the department's chief chemist, Virgil Hiatt, testing results from 1971 show a decrease of DDT residues not only to a level almost a million times lower than the tolerance established by FDA for milk and milk products but ten times lower than results of tests made in Oregon in 1970. Mr. Hiatt said that FDA tolerances read in "parts per million" and the department results read in "parts per billion."

New Packaging Regulation Irvin Mann, Jr., director of the Oregon Department of Agriculture, has signed an administrative order to become effective April 1 requiring that all prepackaged, sliced bacon be sold in containers that offer the consumer a clear view of a substantial portion of a slice of bacon similar to other slices contained in the package. Canned bacon and that bacon wrapped or packaged at the time of purchase are the two exceptions to the requirement. Mr. Mann said the regulation is one more step by the department to require honest and full disclosure to the consumer in the sale of food products or any other products over which the department has authority.

Kenneth Carl, administrator of the department's Dairy and Consumer Services Division and hearing officer for the two hearings preceding promulgation of the regulation on bacon packaging, said Oregon's packaging requirements would be similar enough to those of the State of Washington to enable processors to use the same packages in both States. Washington's new packaging requirements for bacon became effective January 1. Mr. Carl said the decision to adopt similar packaging requirements was made when consumers testifying at the hear-

ings in Eugene and in Portland indicated such an approach would be agreeable with them even if it meant a cost increase. The industry testified that Oregon should seriously consider following the Washington pattern if it was unwilling to await Federal action on bacon packaging.

Certification Program Dr. Glenn B. Rea, State veterinarian and administrator of the Veterinary Division of the Oregon Department of Agriculture, has announced that as of January 8, all cattle and sheep in feedlots in the State must be certified prior to slaughter as having received no feed containing diethylstilbestrol (DES), or that applicable regulations of FDA had been followed when the drug was administered. Range cattle and sheep and dairy animals came under the same regulation January 17.

DES is a synthetic hormone-like substance used in cattle and sheep production to promote growth. Under FDA food additive regulations, it is considered to be an adulterant, and DES residues must not be found in any cattle or sheep slaughtered for human consumption. As an assurance, use of the medicated feed must be discontinued seven days before slaughter; or, Dr. Rea said, the animals can be slaughtered and tissue samples sent for testing to a private or commercial laboratory acceptable to the State's laboratory services.

Although a U.S. Department of Agriculture directive explaining the mandatory DES certification program mentioned only those slaughtering plants under Federal meat inspection supervision, Dr. Rea said that it also applied to plants under State of Oregon inspection because Oregon keeps its own program up to at least the minimum standards of Federal inspection. He said details spelling out correct procedures have been circulated to all State meat inspection personnel and slaughterhouse managers and

are available from the Veterinary Division of the Oregon Department of Agriculture.

Short-weight Poultry Turkeys and capons on the way to the consumer were delayed in December by weights and measures inspectors from the Oregon Department of Agriculture, when they seized three shipments at Portland because of short weight. A 22-case lot of frozen turkey breasts was seized on December 21, and was held for word from the shipper in Minnesota as to disposal. On December 22, a lot of 168 more frozen turkey breasts shipped from out of the State was seized. By relabeling with the correct weight to comply with the State's labeling requirements, the shipper was able to get the product released and moving to market the next day.

A 32-case lot of frozen capons shipped from Iowa was seized on December 21. The lot was released to a Portland poultry processing firm for weighing and relabeling with the correct weight, with the shipper paying the costs.

False Advertising A potato packer in Oregon got into trouble with the Oregon Department of Agriculture's consumer officer, Jane Wyatt, because of the labeling content he was using to promote the sale of his product. Assuming that a large segment of this country's consumers are weight conscious, he used phrases such as "lower in calories" and "less starch" on his labels. Such labeling, he was told, is false or misleading advertising under the Oregon Food Law, which deems any advertisement of food to be false if it is false or misleading in any particular, and that violation of the law is punishable by a fine up to \$500 or imprisonment in the county jail for six months or both.

Although Oregon has no standards of identity for the described labeling and/or advertising of potatoes as lower in calories or having

less starch, Mrs. Wyatt said, the questions remain: "less starch than what?" and "lower in calories than what?"

After being alerted to the label that was being used on some of the potatoes, Mrs. Wyatt also sent letters to produce managers of several of the large chain stores, drawing their attention to the requirement of the law and advising them that any labeling containing this type of information should be discontinued within ten days.

Commissioning William Schroeder, secretary of the South Dakota Department of Agriculture, has been commissioned to act as an official of FDA. During the ceremony, Mr. Schroeder indicated his desire to continue working with FDA in the area of medicated feeds and also to have more of his personnel commissioned.

In Missouri, FDA commissions were conferred on personnel in the State Department of Agriculture's Grain, Feed, and Seed Division. They included Inspectors George Gresham, John Quinley, Wes Shelton, and Cecil Simpson, and Inspection Program Supervisor Joseph Arnold. James Dunscombe, director of the Division, and four other inspectors had been commissioned previously.

Insect-infested Foods Neighboring States recently took action against insect-infested foods. In Topeka, Kansas, inspectors from the Food and Drug Division of the State Board of Health found during an inspection of a local food warehouse that inadequate and poor storage practices by the firm had caused heavy insect infestation of the premises. The firm voluntarily destroyed 1½ tons of contaminated flour and flour products.

In Missouri, Jones D. Searcy, a sanitarian in the Kansas City Health Department, supervised the destruction of 60,296 pounds of insect-infested grits, flour, pancake mix, and cornmeal at the city landfill. The railcar containing the products had been returned to the Missouri Pacific Railroad after the consignee in Little Rock, Arkansas,

refused to accept it. Railroad officials then contacted the city health department to provide supervision over the destruction procedures.

Shellfish Program Adolph Zulk, director of the Sioux Falls Health Department in South Dakota, has agreed to institute a shellfish sampling program to supplement FDA's efforts in shellfish sanitation. Mr. Zulk, his sanitarians, and his laboratory personnel met recently with FDA's Daniel Hunt of the Agency's Shellfish Sanitation Division to discuss the shellfish sanitation program and laboratory techniques.

Wisconsin Project Leader Wisconsin has been named as project leader for a five-State survey on the use of pesticides in agriculture during 1971. A similar survey was made in 1969 and 1970, and the results provided accurate information on the amount of chemicals used in farm production. Computerized data from the current survey will be made available in February and should prove useful to both State and Federal agencies for a number of purposes.

State Embargoes The Wisconsin State Department of Agriculture has embargoed 450,000 cases of canned corn packed by two Wisconsin canning firms during the 1971 canning season. The corn, valued at about \$1.5 million, was adulterated with machinery mold and other filth. It appears that the State action will require much of the canned corn to be destroyed.

'Hot Line' Service At the special request of Wendell R. Anderson, Governor of Minnesota, the State's Department of Agriculture has established a "Consumers' Hot Line" service, to expedite action on complaints and inquiries about foods, beverages, and hazardous substances. The department's commissioner, Jon Wefald, said the service will operate in cooperation with the new Minnesota Office of Consumer Services established by the 1971 Legislature.

"This action reemphasizes that

the Minnesota Department of Agriculture is the State agency with the major regulatory responsibilities for consumer protection on all human foods, livestock feeds, and pet foods, and for a wide range of hazardous products. We are to Minnesota what the Federal Food and Drug Administration is to the Nation," Commissioner Wefald said.

A recording telephone has been installed in the department's St. Paul office to provide virtually instant consumer access to the new service. It has a special number, (area code 612) 221-6883, and is reserved solely for consumer calls. Out-of-State consumers also have the option of addressing written complaints or inquiries to: Consumers' Hot Line, 530 State Office Building, St. Paul, Minnesota 55101.

Meat Rules Revised Donald E. Wilkinson, secretary of the Wisconsin Department of Agriculture, reports that the State's meat inspection regulations have been revised. They now apply to slaughterers, processors, distributors, carriers, and retail stores engaged in the slaughtering, processing, transporting, and marketing of meat and poultry.

"While the primary impact of the revised regulations will be in the meat and poultry area, new provisions will provide uniform sanitary guidelines for other food handling operations—something the agriculture department has been striving for years to develop," Mr. Wilkinson said.

Copies of the new regulations may be obtained from the department in Madison, or from Madison, Milwaukee, Green Bay, and Eau Claire district offices.

State Prosecutes Pisano Bakeries, Redwood City, California, was prosecuted under the California State Food and Drug law after State inspection disclosed insect-infested equipment and flour. The firm was fined \$375 and placed on probation for two years.

The agency responsible for enforcing the food and drug law in California is the State's Department of Public Health.

seizures & postal service cases

SEIZURE ACTIONS charging violation of the Federal Food, Drug, and Cosmetic Act and the Federal Hazardous Substances Act are published when they are reported by the FDA District Office.

A total of 27 actions to remove from the consumer market products charged to be violative were reported in October/November. These included 18 seizures of foods: 14 involved charges concerning contamination, and 4 involved charges

concerning economic and labeling violations. Other seizures included 5 of drugs (including 3 of veterinary and medicated feed), and 4 of hazardous substances.

PRODUCT, PLACE & DATE SEIZED	MANUFACTURER (M), PACKER (P), SHIPPER (S), DEALER (D)	CHARGES
FOOD / Contamination, Spoilage, Insanitary Handling		
Cornhusks, chili pods, dried, red, whole/ Denver, Colo. 11/10/71	La Popular Mexican Foods/Denver, Colo. (D)	Held under insanitary conditions; rodent contaminated.
Fennel seed, Lupini beans/Denver, Colo. 10/20/71	Veltrie Brokerage, Inc. d/b/a Western Food Importing Co./Denver, Colo. (D)	Contain live insects; rodent contaminated (fennel seed).
Flour/Greenville, Miss. 6/18/71	The Itzig Co./Greenville, Miss. (D)	Held under insanitary conditions; rodent contaminated.
Palm hearts/Miami, Fla. 11/5/71	Shaw Foreign Trade Warehouse/Miami, Fla. (D)	Partly decomposed.
Sesame seed, hulled/Houston, Tex. 11/3/71	Davis Warehouse Co./Houston, Tex. (D)	Insect contaminated.
Soup(s), Bon Vivant/Dallas, Tex. 10/12/71	Bon Vivant Soups, Inc./Newark, N.J. (M, S)	Prepared under insanitary conditions; defective and abnormal cans.
Bronx, N.Y. 9/16/71	"	"
Bon Vivant and Ancora brands/Baltimore, Md. 10/1/71	Bon Vivant Soups, Inc./Baltimore, Md. (M, S)	"
Richmond, Va. 10/1/71	Bon Vivant Soups, Inc./Newark, N.J. (M, S)	"
Richmond, Va. 10/1/71	"	"
Landover, Md. 10/5/71	"	"
canned/Winchester, Va. 10/8/71	"	"
Roanoke, Va. 9/29/71	"	"
Philadelphia, Pa. 10/14/71	"	"
Economic and Labeling Violations		
Christmas stockings, candy-filled/San An- gelo, Tex. 11/8/71	Del-Tex, Inc./San Angelo, Tex. (D)	Not in conformity with the Fair Packaging and Labeling Act.
Chun King pepper steak dinner/Detroit, Mich. 11/5/71	RJR Foods, Inc./New York, N.Y. (M, S) (shipped from Duluth, Minn.)	" ; does not contain meat.
Marsh peaches, Fruitful Farms peaches/ Yorktown, Ind. 10/26/71	Fruitful Valley Sun/Dinuba, Calif. (M, S)	" ; short weight.
Queen olives, black pepper/Gretna, La. 11/16-18/71	Zatarain's, Inc./Gretna, La. (D)	Not in conformity with the Fair Packaging and Labeling Act.
DRUGS / Human Use		
Prescription and nonprescription drugs/ North Little Rock, Ark. 10/18/71	Spriggs Drug Store/North Little Rock, Ark. (D)	Exposed to heat, smoke, and water damage by fire in the store.
Sodium salicylate combination tablets, ECT/ Santa Monica, Calif. 8/30/71	Paul B. Elder Co./Bryan, Ohio (M, S)	The quality of the enteric coating was deficient.
Veterinary / Medicated Feed		
Medi-matic Free Choice poultry formula, Myconox Medicated/Springfield, Mo. 11/1/71	Naremco, Inc./Springfield, Mo. (D)	New animal drug without effective approved New Animal Drug Application; false and misleading label statements.
Phenylbutazone injection/Phoenix, Ariz. 9/17/71	Western Serum Co./Phoenix, Ariz. (D)	New animal drug without effective approved New Animal Drug Application.
PHEN-BUTA-VET (brand of phenylbutazone)/ El Monte, Calif. 9/17/71	Anthony Product Co./El Monte, Calif. (D) (raw materials shipped from Italy)	"

PRODUCT, PLACE & DATE SEIZED	MANUFACTURER (M), PACKER (P), SHIPPER (S), DEALER (D)	CHARGES
HAZARDOUS SUBSTANCES		
Cherry bombs/Brookfield, Mo. 10/21/71	Roy L. Deke Wholesale/Brookfield, Mo. (D)	Banned hazardous substances; lack consumer protection information required by the Fed. Hazardous Substances Act.
CONCERN, liquid laundry product/ Milwaukee, Wis. 10/27/71	H. T. Developments, Inc./Buffalo, N.Y. (M, S)	Hazardous, toxic, irritant; misbranded, label lacks cautionary statements. "
Milwaukee, Wis. 10/27/71	"	"
Mystery Love Mete:/Moonachie, N.J. 9/2/71	Knobler & Co. (Viking Import Trade Co.)/ Moonachie, N.J. (D)	Insufficient labeling of hazardous substances.

U.S. POSTAL SERVICE actions taken in medical cases as authorized in the Mail Fraud Statute (18 U.S.C. 1341) and/or the False Representation Statute (39 U.S.C. 3005) as reported by the Assistant Postmaster General — Inspection Service.

False Representation Orders Issued by Judicial Officer Under 39 U.S.C. 3005

November 2, 1971: False Representation Order issued against **Marvelex Co.**, Dept. 7516, 7471 Melrose Avenue, Los Angeles, California. Advertising and sale by mail of "Marvelex Plan," promising dramatic weight losses in only eight weeks.

November 8, 1971: False Representation Order issued against **Wilson Products, Inc.**, 26 Journal Square, Jersey City, New Jersey. Solicitations of orders and sales through the mails of "Slim-Away Plan," represented as enabling subscribers to "cure" overweight without dieting or calorie counting.

November 11, 1971: False Representation Order issued against **Na-Tan Products Corp.**, 139 Dodd Street, Weehawken, New Jersey. Solicitations of orders and sales through the mails of "Hormonex Youth Formula 21," represented as an amazing sexual rejuvenator.

November 18, 1971: False Representation Order issued against **Xrisnel, Inc.**, Dept. 897, P.O. Box 188, Osbornville, New Jersey 08723. Advertising and sale by mail of "Syntron Method," promising dramatic weight losses.

Complaints Filed by Law Department Under 39 U.S.C. 3005 (False Representation)

November 11, 1971: **Development Research**, 210 Fifth Avenue, New York, New York 10010. Solicitations of orders and sales through the mails of "Formula LDX-33," designed to nourish the sex organs and restore lost sexual interest, potency, or fertility.

December 14, 1971: **Elizabeth Saint James Co.**, P.O. Box 2065, General Post Office, New York, New York 10001. Advertising and sale by mail of "The Famous Elizabeth Saint James Method," represented as the most successful new advance in bosom building and guaranteed to add from 1-3 inches to the bustline in just eight days.

notices of judgment

NOTICES OF JUDGMENT on Seizure Actions FOOD / Poisonous and Deleterious Substances

Corn, at Topeka, Dist. Kans.

Charged 12-14-66: while held for sale, the article contained an added poisonous and deleterious substance, aflatoxin; 402(a)(1). The article was claimed by Topeka Mill & Elevator Co., Inc., Topeka, Kans. The claimant denied the charges, claimed that even in the event the corn did contain some aflatoxin, the amount of it was so minimal as to not render the corn unfit for human consumption, and even if the court should find that the corn should not be released to the claimant for human consumption, it could be released to the claimant for use as livestock feed or other nonhuman consumption purposes. The parties served interrogatories on each other. After additional litigation and sampling of the corn, the case came up on trial by the court on 10-6-70. After trial, the court found for the Government and made a number of findings of fact, among which were the following:

"The corn seized in this action contains various quantities of aflatoxin. The combined results of analyses of the quantity of corn seized in this action cannot be said to represent an average quantity of aflatoxin in the seized corn. Some portions of the corn obviously have higher concentrations of aflatoxin and other portions less. There is no method by which the corn could be mixed to insure a completely uniform distribution of the aflatoxin present.

"Aflatoxin is a toxic metabolite produced by the growth of the mold *Aspergillus flavus* (*A. flavus*). The spores (seed-like organisms) of the mold *A. flavus* are present in the soil but are not found on domestic corn in the field while still attached to the cob and covered by the husk. They may be found on corn after it is harvested and shelled.

"Aflatoxin is an added substance. It is the by-product of the growth of a mold which grows under limited conditions from spores not found on corn prior to harvesting. The substance aflatoxin is not a natural constituent of corn. * * *

"The carcinogenic effect of aflatoxin has been investigated in tests with animals. These show that aflatoxin is the most powerful known carcinogen. In rainbow trout, as little as 0.4 ppb aflatoxin in the diet produces a significant incidence of liver cancer within one year. As little as 20 ppb aflatoxin in the diet for only one day produces a significant incidence of liver cancer in rainbow trout within one year. * * *

"An acceptable quantity of aflatoxin in food for either man or other animals cannot be established by the available toxicological evidence. There is no evidence which enables science to establish a level of aflatoxin in food which would present no possibility of hazard to health in man. There is also no evidence which shows that a minimum or baseline level of aflatoxin is commonly found in foods consumed by either man or other animals. Though the World Health Organization, UNICEF, and the Food and Agricultural Organization authorized the use of foodstuffs containing up to 30 ppb of aflatoxin as an alternative to starvation, it likewise directed that the use of food containing any aflatoxin should be avoided when such uncontaminated food became available.

"The aflatoxin present in the corn seized in this action may possibly render the corn injurious to the health of man or other animals. Based on the opinion of the expert witnesses who testified in this action, man and other animals should never be exposed to any quantity of aflatoxin in the diet whenever it can be prevented." * * *

The court concluded that the corn was adulterated as charged and that the Government was entitled to a decree of condemnation and to a bill of costs against the claimant. (1)

Swordfish, whole, frozen, at San Pedro, C. Dist. Calif.

Charged 4-7-71: when shipped from waters outside of California, the article contained the added poisonous and deleterious substance mercury; 402(a)(1). Default decree ordered destruction. (2)

Swordfish, whole, frozen, at Wilmington, C. Dist. Calif.

Charged 3-30-71: when shipped from waters outside of California, the article contained the added poisonous and deleterious substance mercury; 402(a)(1). Default decree ordered destruction. (3)

Swordfish, whole, frozen, and swordfish chunks, frozen, at San Pedro, C. Dist. Calif.

Charged 4-27-71: when shipped from waters outside of California, the article contained the added poisonous and deleterious substance mercury; 402(a)(1). Default decree ordered destruction. (4)

Swordfish, chunks, frozen, at Long Beach, C. Dist. Calif.

Charged 3-30-71: when shipped from waters outside of California, the article contained the added poisonous and deleterious substance mercury; 402(a)(1). Default decree ordered destruction. (5)

Swordfish, chunks, frozen, at Wilmington, C. Dist. Calif.

Charged 4-27-71: when shipped from waters outside of California, the article contained the added poisonous and deleterious substance mercury; 402(a)(1). Default decree ordered destruction. (6)

Swordfish steaks, at Boston, Dist. Mass.

Charged 2-14-71: when shipped by an unknown shipper from Japan, the article, labeled in part "Geisha Brand Swordfish * * * Packed for Nozaki & Co. Ltd., Tokyo, Japan," contained the added poisonous and deleterious substance mercury; 402(a)(1). Consent decree authorized release to Crocker & Winsdor Seafoods, Boston, Mass., for export to original foreign supplier, Nozaki & Co., Ltd. (7)

Swordfish steaks, at Cleveland, Ohio.

Charged 2-22-71: when the following brands of the articles were shipped, namely, Geisha brand by L. N. White Co., New York, N.Y., Soseaco brand by Southern Seafood Co., Baltimore, Md., Promaresa brand by John Howley, Boston, Mass., and Ship Ahoy brand by New England Fish Co., New York, N.Y., the articles contained the added poisonous and deleterious substance mercury; 402(a)(1). Consent decree ordered destruction. (8)

FOOD / Contamination, Spoilage, Insanitary Handling

Cashews, blanched, at Detroit, E. Dist., Mich.

Charged 11-3-70: when shipped by Hollander Trading Corp., New York, N.Y., the article, labeled in part "Vita Packed Produce of India, Blanched Cashew Kernels . . . Packed by Raj Cashew Company, Quilon, India," contained insects; 402(a)(3). Consent decree authorized release to the shipper for reconditioning. (9)

Cornmeal, at Shreveport, W. Dist. La.

Charged 4-9-71: when shipped by Alford Refrigerated Warehouse, Dallas, Tex., the article contained rodent filth; 402(a)(3). Default decree ordered destruction. (10)

Dates, dried, at Thermal, C. Dist. Calif.

Charged 3-25-71: when shipped by Lyle Date Gardens (Dr. William Lyle), Yuma, Ariz., the article contained insect filth; 402(a)(3). Default decree ordered destruction. (11)

Flour and corn twists, at Chicago, N. Dist. Ill.

Charged 2-12-71: while held by Certified Grocers of Illinois, Inc., Chicago, Ill., the articles were rodent gnawed, the corn twists contained rodent-gnawed material, and the articles were held under insanitary conditions; 402(a)(3), 402(a)(4). Consent decree authorized salvaging by the dealer. (12)

Fruitcake, Clipper Carole Ann/Ye-Oldie Inn, at Salem, W. Dist. Va.

Charged 12-18-70: when shipped by Kent Bakers, Ltd., Newark, N.J., the article contained rodent and insect filth and had been prepared and packed under insanitary conditions; 402(a)(3), 402(a)(4). Default decree ordered destruction. (13)

Pecan pieces, at Cincinnati, S. Dist. Ohio.

Charged 3-3-71: when shipped by Nut Tree Pecan Co., Baconton, Ga., the article contained *E. coli* and had been prepared and packed under insanitary conditions; 402(a)(3), 402(a)(4). Consent decree authorized release to the shipper for salvaging. (14)

Pecan pieces, at Boston, Dist. Mass.

Charged 4-21-71: when shipped by Dasher Pecan Co., Valdosta, Ga., the article contained *E. coli* and had been prepared and packed under insanitary conditions; 402(a)(3), 402(a)(4). Consent decree authorized release to shipper for reconditioning. (15)

Pickles, dill, at Bronx, S. Dist. N.Y.

Charged 3-22-71: while held by Merchants Food Distributing Cooperative, Inc., Bronx, N.Y., the article contained decomposed pickles and had been held under insanitary conditions; 402(a)(3), 402(a)(4). Default decree ordered destruction. (16)

FOOD / Economic and Labeling Violations

Confection bar, Farm Boy, at Compton, C. Dist. Calif.

Charged 6-3-70: when shipped by Phoenix Famous Foods, Div. Kimbill Enterprises, Inc., Phoenix, Ariz., the article was in violation of the Fair Packaging and Labeling Act in that the quantity of contents declaration was not adequately separated from other printed label information; and the quantity of contents declaration, on the principal display panel with an area between 5 and 25 square inches, was stated in a type size less than 1/4 inch high; 15 U.S.C. 1453(a)(2), 1453(a)(3)(C)(i). Default decree ordered destruction. (17)

Fish portions, at Kansas City, W. Dist. Mo.

Charged 1-15-71: while held for sale, after being labeled by Sun-Ra Frozen Foods, Inc., the article, labeled in part "Halibut Steaks . . . Ingredients: Selected Skinless Northern Flounder . . . Packed by Sun-Ra Frozen Foods, Inc., Kansas City, Mo.," the name of the article and the ingredient statement were false and misleading, since the article was neither halibut, nor in the form of steaks, nor was it Northern flounder; the article was cut portions of fish other than halibut and was offered for sale under the name of another food, halibut steaks; the label lacked the common or usual name of the food; and cut portions of Greenland Turbot had been substituted for halibut steaks; 403(a), 403(b), 403(i)(1), 402(b)(2). Consent decree authorized release to packer for relabeling. (18)

Fry mix, Drake's, at Fort Wayne, N. Dist. Ind.

Charged 6-5-70: when shipped by Drake's Batter Mix Co., Inc., Grass Lake, Mich., the article was in violation of the Fair Packaging and Labeling Act in that the quantity of contents declaration did not appear within the lower 30 percent of the principal display panel; and the quantity of contents declaration, on the principal display panel with an area between 5 and 25 square inches, was stated in a type size less than 1/4 inch high; 15 U.S.C. 1453(a)(2), 1453(a)(3)(C)(i). Default decree authorized donation to charitable institution. (19)

Rice, instant, at Philadelphia, E. Dist. Pa.

Charged 8-4-70: when shipped by Riviana Foods, Inc., Houston, Tex., the article, labeled in part "Food Club Instant Rice . . . Distributed by Topco Associates, Inc., Skokie, Illinois," was in violation of the Fair Packaging and Labeling Act in that the quantity of contents was expressed as "Net Wt. 1 Lb. 8 Ozs." instead of "Net Wt. 24 Ozs. (1 Lb. 8 Ozs.);" and the quantity of contents declaration, on the principal display panel with an area between 25 and 100 square inches, was stated in a type size less than 3/16 inch high; 21 U.S.C. 1453(a)(3)(A)(i), 1453(a)(3)(C)(i). Default decree authorized donation to charitable/tax-exempt institution. (20)

Tomatoes, canned, unlabeled, at Gentry, W. Dist. Ark.

Charged 7-21-71: while held by Gentry Canning Co., Gentry, Ark., the article fell below the standard of quality for canned tomatoes because of excess tomato peel; 403(b)(1). Consent decree authorized release to dealer for labeling with statement of substandard quality. (21)

VITAMINS / DIETARY FOODS

MV Plus Formula #1 dietary supplement tablets, at Columbia, Dist. S.C.

Charged 8-31-70: when shipped in bulk by Lit Drug Co., Union, N.J., the valuable constituent vitamin B12 has been in part omitted or abstracted; and while held by Doctor's Specialties, Inc., Columbia, S.C., after repacking by that firm, the label statement of vitamin B12 content was false and misleading, since the article contained less than the declared amount (approx. 25 percent less); 402(b)(1), 403(a). Consent decree ordered destruction. (22)

FOOD ADDITIVES

Cheese, feta, at Watertown, Dist. Mass.

Charged 10-28-70: when shipped by Standard Importing Co., Inc., New York, N.Y., the article contained the nonconforming food additive benzene hexachloride; 402(a)(2)(C). Default decree ordered destruction. (23)

Skillets of earthenware, at Fort Worth, N. Dist. Tex.

Charged on or about 4-13-71: when shipped by Ramon C. Gonzalez, Nuevo Laredo, Mexico, the article contained the nonconforming food additive lead [which would leach out into food]; 402(a)(2)(C). Default decree ordered destruction. (24)

DRUGS / Human Use

A-P-C buffered aspirin-acetaminophen combination tablets, at La Crosse, W. Dist. Wis.

Charged 7-31-70: when shipped by Standard Pharmaceutical Corp., Elgin, Ill., the strength of the article differed from that represented by its name "A-P-C" (i.e. Aspirin, Phenacetin, and Caffeine) when the article did not contain phenacetin; the ingredient, acetaminophen, had been substituted for phenacetin; the labeling lacked adequate directions for use, since it lacked dosages for children 6-12 and 3-6 years old—501(c), 501(d)(2), 502(f)(1); and the article was in violation of the Fair Packaging and Labeling Act in that the article lacked a label specifying the place of business of the manufacturer, packer, or distributor as required by regulations; 15 U.S.C. 1453(a)(1). Default decree ordered destruction. (25)

Bardase liquid phenobarbital, hyoscyamine, hyoscine, and atropine elixir, at Atlanta, N. Dist. Ga.

Charged 5-8-70: when shipped by Parke, Davis & Co., Detroit, Mich., the article's strength was deficient, and the label statement "Each 5 cc . . . Hyoscyamine Sulfate 0.1 mg. Hyoscine Hydrobromide 0.007 mg. and Atropine Sulfate 0.02 mg." was false and misleading, since the article was approximately 18 percent deficient in total alkaloids; 501(c), 502(a). The article was claimed by the shipper and the charges were denied. The Government served written interrogatories upon the claimant. Thereafter, the shipper's claim and answer were withdrawn, and a default decree was entered ordering the article destroyed. (26)

Conjugated estrogens tablets, at Baltimore, Dist. Md.

Charged 12-7-70: when shipped by Dumont Pharmacal Co., Philadelphia, Pa., the strength of the article in respect to conjugated estrogens was deficient (approx. 16 percent); 501(c). Default decree ordered destruction. (27)

Del Tissue Freeze and Topical Anesthetic pressurized spray, at Menomonee Falls, E. Dist. Wis.

Charged 9-8-69: when shipped by Chase Products Co., Broadview, Ill., the article, labeled in part "Del Tissue Freeze and Topical Anesthetic . . . Immediate First Aid . . . Improves early return of player . . . Del Chemical Corporation . . . Menomonee Falls, Wis.," was a new drug without an effective approved New Drug Application—505(a); and the article's label lacked the established name of the drug or, in case it was fabricated from two or more ingredients, the established name of each active ingredient, the article's labeling lacked adequate directions for use, and the article's label lacked the prescription legend—502(e)(1)(A), 502(f)(1), 503(b)(4). Del Chemical Corp., Menomonee Falls, Wis., claimed the article and denied the charges. The Government served written interrogatories upon the claimant. Thereafter, a consent decree of condemnation ordered the article destroyed. (28)

Green Mountain Asthmatic stramonium-belladonna compound and Green Mountain Asthmatic stramonium-belladonna cigarettes, at Beaumont, E. Dist. Tex.

Charged 12-8-69: when shipped by J. H. Guild Co., Inc., Rupert, Vt., the labels of the articles lacked the required prescription legend; 503(b)(4). Upon motion of the shipper, who claimed the articles, the case was transferred to the District of Massachusetts. Thereafter, the claimant having consented, a decree was entered ordering the destruction of the article. (29)

Migranestick mentholated wax stick, at New York, S. Dist. N.Y.

Charged on or about 2-4-70: when shipped by Parfa Perfumerie Und Kosmetik A G, Zurich, Switzerland, the article's labeling lacked adequate directions for use for migraine headaches; 502(f)(1). Consent decree ordered destruction. (30)

Provitamin B15 (Pangamic Acid) capsules, at Fort Lauderdale, S. Dist. Fla.

Charged 9-29-70: when shipped by Krebs Labs., San Francisco, Calif., the labeling contained false and misleading claims that the article was effective as a specific treatment for arthritis and other body toxicities; that it was effective for the treatment of bowel or kidney function, allergies, and atherosclerosis, for alleviating hypoxia, for use in coronary artery insufficiency, and for relieving symptoms of

angina and asthma; that it might well play a role in prevention and treatment of cancer; and the article was a new drug without an effective approved New Drug Application; 502(a), 505(a). Default decree ordered destruction. (31)

Thyroid tablets, at Detroit, E. Dist. Mich.

Charged 4-28-70: when returned to Parke, Davis & Co., Detroit, Mich., after shipment to Cincinnati, Ohio, the article's labeling lacked adequate directions for use and was not exempt therefrom, since it lacked required information under which practitioners could use the drug; 502(f)(1). Default decree ordered destruction. (32)

DRUGS / Veterinary

Leamycin oxytetracycline HCl injectable, at Clovis, E. Dist. Calif.

Charged 4-28-70: when shipped by Kem Vet, Inc., Fremont, Nebr., the article was a new animal drug without an effective approved New Animal Drug Application; 501(a)(5). Default decree ordered destruction. (33)

Myconox medicated additives for feed and for water for poultry, at Selbyville, Dist. Del.

Charged 7-11-68: when shipped by Naremo, Inc., Springfield, Mo., the articles were new drugs without effective approved New Drug Applications; the articles contained the nonconforming food additives methylosaniline chloride and sodium propionate with directions for use for mixing (one article) in water and (other article) in feed for the control of avian mycosis in broilers and market turkeys, fatty liver syndrome, in poultry and avian leucosis complex in poultry; the name "Myconox," the bag and case label statements, and statements in accompanying printed promotional material contained false and misleading claims for the control of avian mycosis in broilers and market turkeys; the control of fatty liver syndrome in poultry; and the control of avian leucosis complex in poultry; and the labeling of the articles lacked adequate directions for use for their intended purposes; 505(a), 402(a)(2)(C), 502(a), 502(f)(1). The article was claimed by the shipper and the charges were denied. Subsequently, the shipper's claim and answer were withdrawn and a default decree of condemnation was entered. (34)

MEDICAL DEVICES

Batronic Ventilaid electric stimulator, at Worland, Dist. Wyo.

Charged 11-13-70 and amended 12-2-70: when shipped by Batrow Laboratories, Inc., Branford, Conn., the name of the article, "Ventilaid," and statements in its labeling were false and misleading as to the adequacy and effectiveness of the article for pulmonary ventilation and emergency breathing conditions; its labeling lacked adequate directions for use, and it was dangerous to health when used as directed, since it was ineffective for its intended purposes and by reason of its ineffectiveness, reliance upon its use would serve to delay or deny proper respiration or resuscitation measures in those life threatening situations where immediate emergency aid was needed; 502(a), 502(f)(1), 502(j). The shipper claimed the article and moved that the case be removed to a district of reasonable proximity to the claimants' principal place of business. Thereafter the case was removed to the District of Massachusetts. The court ordered the parties to submit proposed stipulations. The claimant failed to submit proposed stipulations and failed to indicate agreement or objection to the proposed stipulations submitted by the Government and mailed to claimant. The Government moved to strike the claimants claim and answer and moved for a default decree of condemnation and destruction. The Government's motion was granted and default decree ordered destruction. (35)

Copper bracelets, at Fort Lauderdale and Port Everglades, S. Dist. Fla.

Charged 7-6-70: while held by British Imports, Inc., at the above locations, after being repacked, the article was accompanied by labeling which was printed by the dealer and which contained false and misleading claims for preventing muscle fatigue and acidity and relieving cramps and rheumatism; 502(a). Default decree authorized delivery to the Food and Drug Administration. (36)

Theramic model A-6 DT 40 electronic instrument, at Minneapolis, Dist. Minn.

Charged 3-17-70: when shipped by Dynapower Systems Corp., Los Angeles, Calif., the labeling of the article contained false and misleading claims for the treatment of infections, otitis media, fractures, bone and tissue healing, smooth muscle spasms, bursitis, arthritis, low back pain, sinusitis, prostatitis, Meniere's syndrome, hypertension, certain inflammations, angina, hemorrhoids, and other diseases, and the labeling lacked adequate directions for such uses; 502(a), 502(f)(1). Default decree authorized release of device to FDA for display and other such purposes. (37)

Relaxacizer electric muscle-stimulator, at San Francisco, N. Dist. Calif.

Charged 8-18-70: when shipped, the accompanying labeling contained statements which represented and suggested that the device was safe for use by a layman, which statements were false, since the labeling failed to reveal that the device was capable of aggravating many preexisting conditions and otherwise injuring the user; the labeling did not and cannot bear adequate directions for safe use by a layman; the labeling lacked adequate warnings against unsafe use; and the article was dangerous to health when used as directed in the labeling; 502(a), 502(f)(1), 502(f)(2), 502(j). Default decree authorized delivery to FDA for exhibit and testing purposes. (38)

Respirators, 3 seizure actions, at New Port Richey, Tampa, and St. Petersburg, M. Dist. Fla.

Charged 7-1-69, 7-3-69, and 7-3-69: when shipped by Crown Products Co., Cleveland, Ohio, or Eldee, Cleveland, Ohio, the article, labeled in part "Res-Q-Aire Emergency Respirator Ready to Use—Easy to Use—Portable . . . For Every Breathing Difficulty," bore the name "Res-Q-Aire" and contained statements on the carton, attached card, and accompanying brochures which were false and misleading as to the adequacy and effectiveness of the article as a means of resuscitation for emphysema, bronchial asthma, and other therapy; the article's labeling lacked adequate directions for use and such could not be written, the article's labeling lacked adequate warnings against use involving obstructions, aspirated objects and dentures, and involving children where the volume of air would be excessive, and the article was dangerous to health when used as directed by its labeling; 502(a), 502(f)(1), 502(f)(2), 502(j). Default decree ordered destruction. (39)

HAZARDOUS SUBSTANCES

Jetex solid-fuel pellets, at Los Angeles, C. Dist. Calif.

Charged 8-8-68: when shipped by Aristocrat Distinctive Miniatures, Newark, N.J., the article, which was toxic and was a flammable solid, was a banned hazardous substance, since it was a toy which was a hazardous substance; 2(q)(1)(A). Default decree ordered destruction. (40)

Optical frames, at Philadelphia, E. Dist. Pa.

Charged 3-15-68: when shipped by Osaka Optical Material Co., Ltd., Osaka, Japan, and S. Barundo, S.A., Madrid, Spain, the article, which contained cellulose nitrate, was a flammable solid, and lacked a number of required conspicuous label statements—2(p)(1)(D)(E)(I)&(J); and the article was a device whose quality fell below its purported suitability for wearing upon the face, in that it was not suitable, since it was flammable—501(c). The article was claimed by Swank Optical Manufacturing Co., Inc., Philadelphia, Pa. After the service of interrogatories upon the claimant, the claimant consented to a decree of condemnation permitting export to original foreign suppliers. Subsequently, an amended consent decree of condemnation ordered the article destroyed. (41)

NOTICES OF JUDGMENT on Criminal Actions

FOOD

Church Point Wholesale Grocery Co., Inc., Church Point, W. Dist. La.

Charged 9-5-69: flour was held in a building accessible to rodents and was contaminated with rodent filth; 402(a)(3), 402(a)(4). Guilty plea; fine. (42)

Y. Hata & Co., Ltd., Honolulu, Kahului, and Hilo, Dist. Hawaii.

Charged 11-27-70: at Honolulu rice and flour were held in a building accessible to rodents, birds, and insects; at Kahului lima beans and flour were held in a building accessible to rodents and insects; and at Hilo rice was held in a building accessible to rodents, birds, and insects; and the articles were contaminated with rodent, bird, and insect filth; 402(a)(3), 402(a)(4). After the court denied the corporation's motion to dismiss and to suppress evidence, the corporation pleaded guilty and was assessed a fine and court costs. (43)

McCraw Candies, Inc., and Ben Cohen, secretary-treasurer, Farmersville, E. Dist. Tex.

Charged 1-6-70: when shipped, Taffy candy (count 2) and Peanut Patty candy (counts 3 & 5) contained rodent hairs (count 2) and insect filth (counts 3 & 5), and such candy had been prepared and packed under insanitary conditions—402(a)(3), 402(a)(4); and peanuts (count 1) were held in a building accessible to rodents and insects and were exposed to contamination by rodents and insects—

402(a)(4). The individual pleaded guilty to count 1, was sentenced to 1 year imprisonment, which was suspended, and was placed on probation. The corporation pleaded guilty to counts 2, 3, & 5, was fined \$3,000, of which \$2,000 was suspended, and was placed on probation. (44)

New York Bakery, a partnership, Albany, N. Dist. N.Y.

Charged 10-29-69: when shipped, hard rolls contained fly fragments and rodent hairs and had been prepared and packed under insanitary conditions; 402(a)(3), 402(a)(4). Guilty plea; fine. (45)

Rose Frozen Shrimp, Inc., and Ken Takiguchi, manager, Los Angeles, C. Dist. Calif.

Charged 11-12-70 by grand jury: Qik Fry brand breaded tantai shrimp were held, prepared, and packed under insanitary conditions and were contaminated by bacterial filth; 402(a)(3), 402(a)(4). Guilty plea by corporation; fine. Guilty plea by individual; fine suspended and probation. (46)

Supreme Dairy Products Co., t/a Aledo Cheese Co., Eugene Alleman, president, and Wendell Alleman, secretary-treasurer, Aledo, S. Dist. Ill.

Charged by grand jury on or about 8-25-70: when shipped cheddar cheese contained insect filth; 402(a)(3). Guilty plea by corporation; fine. Guilty plea by individuals; probation. (47)

Union Grove Milling Co., Inc., and Leonard G. Keller, secretary-treasurer and general manager, Union Grove, W. Dist. N.C.

Charged 8-17-70: when shipped, flour contained insect filth and had been prepared and packed under insanitary conditions; 402(a)(3), 402(a)(4). Guilty pleas; corporation fined; and individual sentenced to 1 year in jail which sentence was suspended on condition that defendants' mill should not engage in business until reinspected and approved by the Food and Drug Administration. (48)

DRUG

Owen E. Brosam, and partner, in Nutritional Progress Scientific Co., Logan, Dist. Utah.

Charged 6-5-62: when shipped, an article of drug, labeled in part "Mineral Life Active Ingredients Silicon . . . Major Ingredient . . . This is a natural mineral. Not compounded by man. Nutritional Progress Scientific Co. . . Logan, Utah," was accompanied by pamphlets entitled "MINERALIFE And What It Means To You" and "MINERALIFE Eject Death From The Temple," and leaflet entitled "College Of Knowledge News Letter Sept. 1960"; and such accompanying labeling contained false and misleading claims for cancer, constipation, premature aging, heart trouble, shortness of breath, tiredness, arthritis, tumor, ulcers, diabetes, restoration of youthfulness, promotion of relaxation and calmness, and other therapy; 502(a). The two partners in the firm pleaded guilty and Brosam was placed on probation. Prior to sentencing, the other partner disappeared during an airplane flight from California to Utah; it appeared that he had been killed in an airplane accident; and, thereafter, the court dismissed the case as to him. (49)

NOTICE OF JUDGMENT on Miscellaneous Action

Foods for special dietary uses, suit for declaratory judgment and injunction, New York, S. Dist. N.Y.

Charged 6-10-68 by National Dietary Foods Association, Inc., of Illinois; and National Food Drug and Cosmetic Association of Manufacturers and Distributors, Inc., New York, N.Y.; in suit for declaratory judgment and injunctive relief against HEW Secretary Wilbur Cohen and FDA Commissioner James L. Goddard: that the defendants failed to assign initially or within a reasonable time a hearing examiner for an administrative hearing upon proposed regulations relating to foods for special dietary use; that when a hearing examiner was assigned, he was not a hearing examiner at the time that he was assigned; and that the hearing examiner's designation and assignment to the proceeding was contrary to the Administrative Procedure Act, was contrary to the congressional purpose and intent, was a violation of the plaintiffs' rights, and constituted a denial of due process of law.

The Government opposed the plaintiffs' action, and the plaintiffs moved for a preliminary injunction enjoining FDA from continuing to conduct the hearing. On the motion for preliminary injunction, the court said:

"The procedure for the appointment and assignment of Hearing Examiners is set forth in 5 U.S.C. § 3105:

"Each agency shall appoint as many hearing examiners as are necessary for proceedings required to be conducted in accordance with sections 556 and 557 of this title. Hearing examiners shall be assigned to cases in rotation so far as practicable, and may not perform duties inconsistent with their duties and responsibilities as hearing examiners." (Emphasis added.) Construed in *Ramspeck v. Trial Examiners Conference*, 345 U.S. 128 (1953).

In *Ramspeck, id.*, the CSC considered it practicable to assign cases to examiners who were, according to their classification, qualified to handle the specific matter, taking into consideration the complexity of the case, together with the experience and ability of the available examiner. Defendant therein contended, inter alia, that such practice did not conform to the terms of the statute in that it did not require application of the mechanical rotation method. The Court, addressing itself for the first time to the scope of discretion contemplated by the phrase "in rotation so far as practicable," held that the Act contemplates the exercise of reasonable discretion on the part of the agency in its selection process, and that the classifications which the CSC had made were a permissible modification of the rotation rule. The decision in *Ramspeck, id.*, is consistent with Congress' intent as to the application of the "in rotation" requirement:

"The requirement of assignment of examiners in rotation prevents an agency from disfavoring an examiner by rendering him inactive, although examiners may be permitted to specialize and be assigned to cases for which they have so qualified."

"Plaintiffs do not contend that Hearing Examiner Harris is biased or incompetent, but merely insist upon a rigid and mechanical application of the rotation method of selection. Neither legislative history nor judicial interpretation supports such a construction, in this case. See *Tractor Training Serv. v. F.T.C.*, 227 F.2d 420, 423-24 (9th Cir. 1955). Considering the increased caseload before the FDA, the scope of the present proceedings, the fact that FDA had only one Hearing Examiner, and the degree of discretion permissible under 5 U.S.C. § 3105 regarding the selection process, it is the opinion of this Court that the FDA acted in consonance with the statutory mandate. To require the application of the mechanical rotation method where the agency employs but one examiner would not be at all 'practicable.'"

"Plaintiffs' reliance upon *Federal Home Loan Bd. v. Long Beach Fed. Sav. & Loan Ass'n*, 295 F.2d 403, 409-10 (9th Cir. 1961) to support the proposition that the CSC, and not the agency, select the Hearing Examiner is ill founded. In that case, the Court of Appeals held that where one agency desires to borrow an examiner from another agency selection by the CSC is necessary. The present case represents a situation in which an agency is hiring an additional examiner rather than temporarily borrowing one; therefore, the 'borrowing statute' relied upon in *Federal Home Loan Bd., id.*, is here inapplicable.

"While a closer adherence by the FDA to the Congressional scheme might in some ways have been more expeditious, the Court finds sufficient adherence thereto so as to require the denial of plaintiffs' motion. *Pharmaceutical Manufacturers Ass'n v. Gardner*, supra at 282.

"Even assuming, arguendo, that a reasonable probability of success in the main action exists, plaintiffs have failed to show the necessary irreparable harm that will befall them but for the granting of the requested injunctive relief. *Sperry & Hutchinson Co. v. F.T.C.*, supra at 144.

"Accordingly, plaintiffs' motion for preliminary injunction is denied."

Thereafter, pursuant to stipulation between the parties, the action was discontinued without prejudice and without costs. (50)

Notices of Judgment are given pursuant to section 705 of the Federal Food, Drug, and Cosmetic Act and section 13 of the Federal Hazardous Substances Act. Notices of Judgment report cases involving seizure proceedings, criminal proceedings, and injunction proceedings. Seizure proceedings are civil actions taken against goods alleged to be in violation, and criminal and injunction proceedings are against firms or individuals charged to be responsible for violations. The cases generally involve foods, drugs, devices, cosmetics, or hazardous substances which were alleged to be adulterated or misbranded or otherwise violative of the law when introduced into and while in interstate commerce, or while held for sale after shipment in interstate commerce.

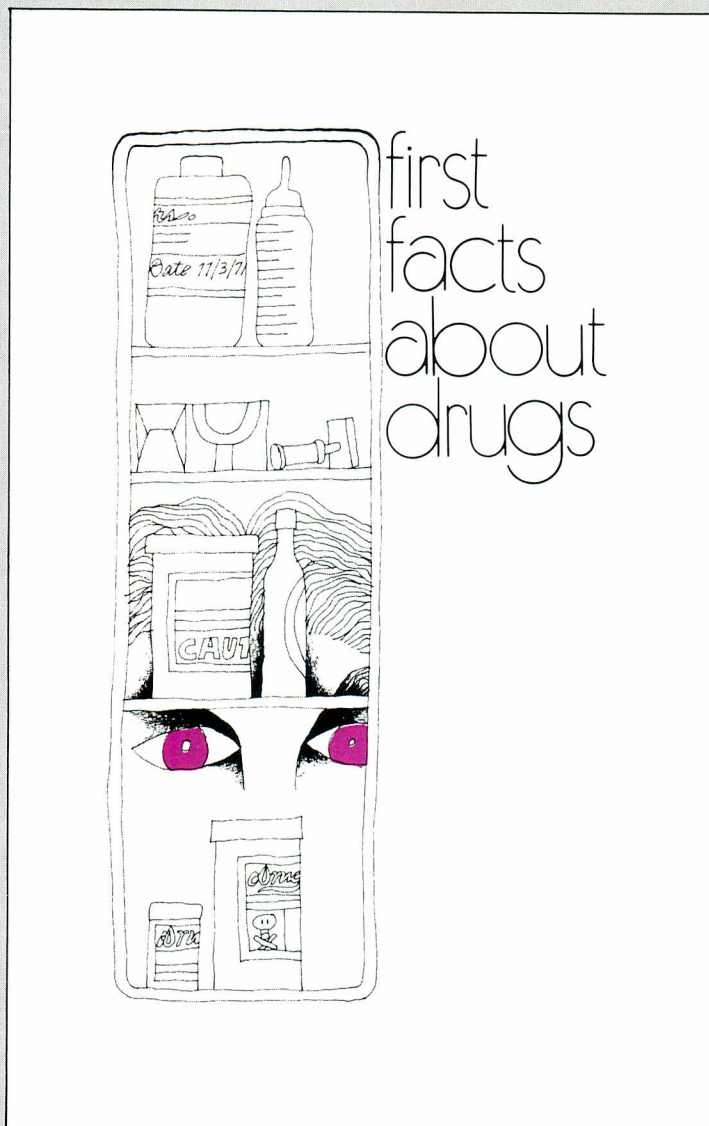
Notices of Judgment are prepared by Food, Drug, and Environmental Health Division, Office of the General Counsel, DHEW.

Published by direction of the Secretary of Health, Education, and Welfare.

Charles C. Edwards, M.D., Commissioner of Food and Drugs

Washington, D.C. February 1, 1972

What Everyone Ought To Know About Drugs



Whether we use drugs seldomly, frequently, or not at all—we should all know some basics about them. FDA has prepared a booklet that tells the consumer, in 15 easy-to-read pages, the "First Facts About Drugs."

It talks about how to use drugs safely and how Federal laws protect us from unsafe or ineffective drugs. The booklet is for sale at 25 cents a copy. Order Stock Number 1712-0137 from the Superintendent of Documents, Government Printing Office, Washington, D.C. 20402.

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Announcements

USP PROPOSES CHANGE The United States Pharmacopeia has informed firms that manufacture nitroglycerin tablets of proposed changes in packaging and labeling requirements of the drug. The Committee of Revision is considering the following: Manufacturers must package nitroglycerin tablets in tight containers, preferably glass. A container shall hold not more than 100 tablets. The labeling must indicate that the tablets are to be dispensed in the original, unopened container. The labels of all containers, including those on the container dispensed to the patient, must bear a statement directing the user to keep the tablets in the original container, and to close tightly between uses.

The U.S.P. notified the FDA in a letter dated January 5 of its intent to modify requirements on packaging and labeling for nitroglycerin. In that letter, Dr. Thomas J. Macek, director of revision for the U.S.P., said, "Because improper packaging may lead to inadequate medication in some critical cases, and thus is unsafe, it is believed that U.S.P. has an obligation to exercise an unusual responsibility in order to assure proper packaging of this drug until it is consumed by the patient." U.S.P. says the FDA has agreed with these actions, and plans to impose similar requirements for other, nonofficial dosage forms of nitroglycerin.

The Committee of Revision will declare its final decision in an Interim Revision Announcement to the U.S.P. approximately April 1, and any changes to be implemented will become effective approximately four to six months after the I.R.A.