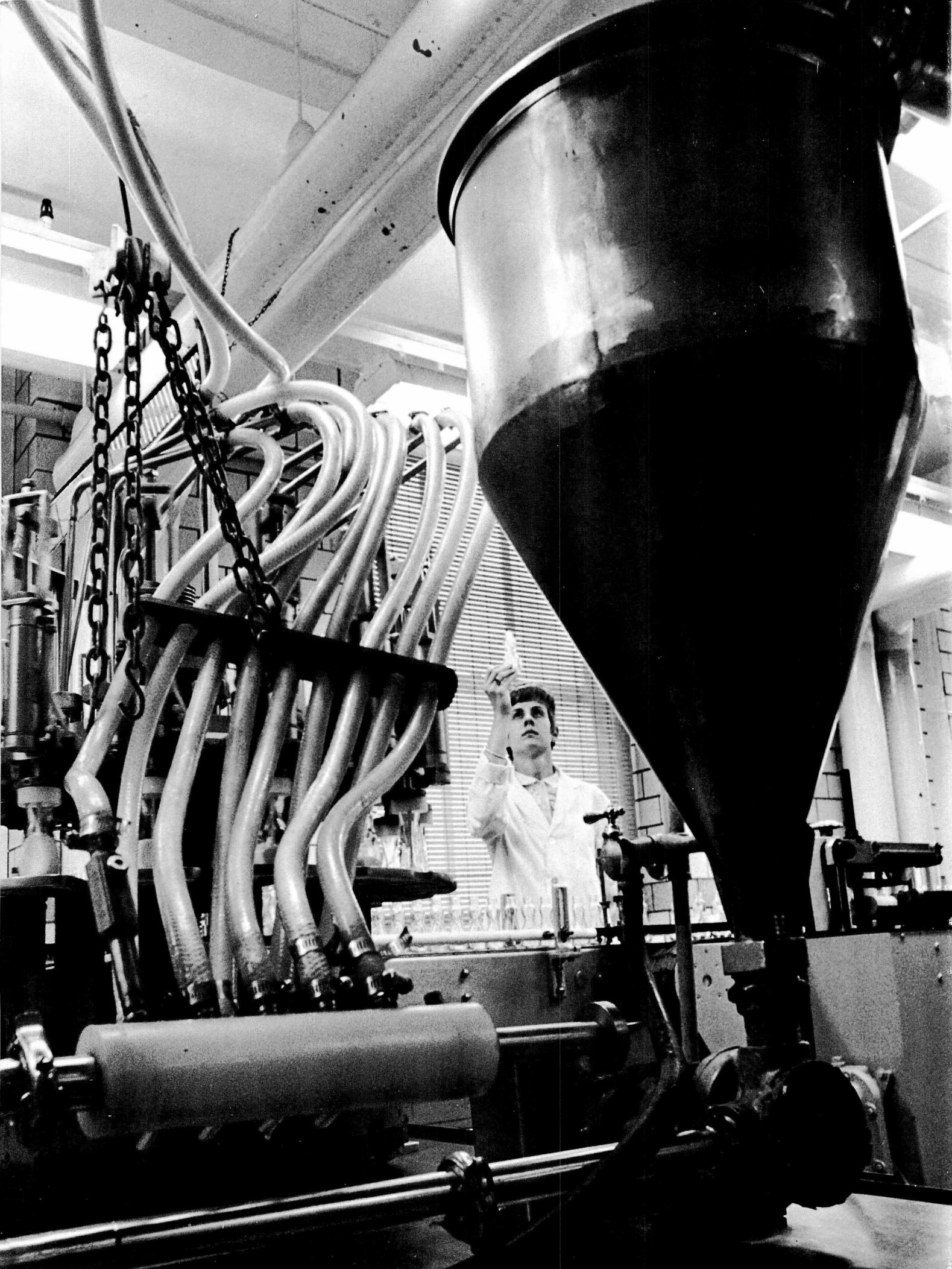


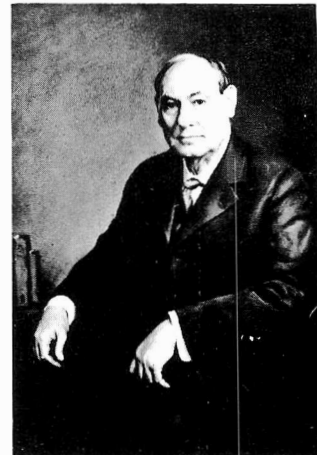
JUNE 1971

FDA PAPERS

**CONTROL GUIDELINES
FOR IND'S AND NDA'S**

**SANITARY SHELLFISH:
Keeping a Step Ahead**





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

Basically, what the Food and Drug Administration expects in Investigational New Drug (IND) and New Drug Application (NDA) submissions is data adequate to show that the drug will be safe and efficacious when used. It must be kept in mind that the FDA reviewer bases his evaluations primarily on what is presented by the sponsors and applicants. Therefore, it is important to present complete data in a well organized and clearly stated manner.

Existing regulations under the Food, Drug, and Cosmetic Act clearly provide for controls to assure the proper identification, quality, purity, and strength of a new drug; as written, however, the regulations do not necessarily spell out the essential criteria needed in making the judgment on a particular new drug. In a recent FDA survey it was found that more than five out of every six New Drug Applications submitted were incomplete or not approvable. Approximately 90 percent of the rejected NDA's lacked sufficient data in the manufacturing and controls area.

To eliminate incomplete and not approvable applications caused by a lack of understanding of the requirements by applicants, appropriate committees were set up respectively by the Pharmaceutical Manufacturers Association and FDA to work jointly in preparing guidelines that would be helpful to sponsors and applicants submitting the required information for IND's and NDA's. The guidelines published in this issue (see page 4) are the culmination of months of consideration and consultation between these industry and Government representatives. All who have reviewed the guidelines firmly believe they mark a definite step forward in aiding sponsors and applicants to prepare and submit the proper information required with regard to manufacturing and controls, thus expediting the processing of submissions to the benefit of the industry, the Government, and ultimately the public.

Because of the very important role drugs play in the life of man, every effort should be expanded to maintain the quality of drugs at all times. This tremendous effort can be accomplished only by the full cooperation of everyone connected with drugs. These guidelines represent just that type of industry-Government cooperation needed to achieve this objective.

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

quotes

"Another prediction I can make is that there will be increasing interest in Congress in new legislation regulating the sale of medical devices.

"There are many new medical devices coming on the market, and we have no idea how they are being tested, if they are being tested at all. There have been cases of outright quackery, as in the case of a machine which, it was claimed, would reduce weight—and reduce weight only on certain selected parts of the body—without any exertion on the part of the 'patient.'

Under existing law, which allows us to move on cases of misbranding or adulteration of a product, we were able to get this device banned. But when we can act only in cases of misbranding or adulteration, then we can act only after the product is in the hands of the consumer."

John Jennings, M.D., associate commissioner for medical affairs, FDA, to the Midwestern Pharmaceutical Advertising Club Annual Seminar, Chicago, May 13, 1971.

"The problem here is not efficacy but advertising. All too often basically good products with long and useful histories are being altered, added to, reformulated, and reshaped with no purpose but promotional advantage. And promotion all too often is being conducted in ways to make a snake oil salesman green with envy.

"I can sympathize with the competitive pressures which perpetuate this situation. At the same time, I understand the frustrations of a public besieged with claims and counter-claims, with testimonials, and with doubtful assertions of comparability.

"When drug promotion reaches the point where antacids are offered like martinis and laxatives are implied as essentials to everyday happiness, then the time has come to take a good hard look at the entire situation."

Charles C. Edwards, M.D., Commissioner of Food and Drugs, at the Proprietary Association Annual Meeting, White Sulphur Springs, West Virginia, May 10, 1971.

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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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guidelines recommended by PMA, FDA committees to help drug
sponsors develop required application data.

Sanitary Shellfish: Keeping a Step Ahead Two FDA technical 15
service units perform investigations and give technical
help to States and industry to assure that shellfish are
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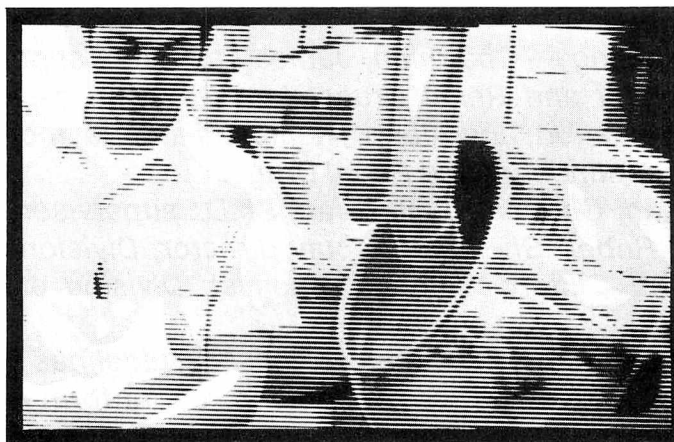
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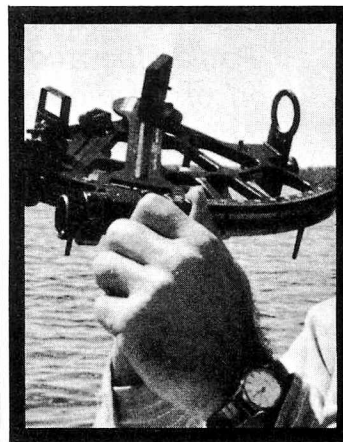
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Guidelines: Manufacturing and Controls for IND's and NDA's

The Food and Drug Administration, after several months of consideration and consultation with the Pharmaceutical Manufacturers Association, has adopted a comprehensive set of guidelines to assist drug sponsors and applicants in developing information required by FDA for Investigational New Drugs (IND's) and New Drug Applications (NDA's).

The guidelines were worked out in March by a PMA Guidelines Committee, representing the association, and an FDA Guidelines Committee, and were approved in late April by Henry E. Simmons, M.D., director of the Bureau of Drugs. They are the culmination of work that began in June last year with a meeting of FDA representatives and PMA's Steering Committee to develop a solution to the problem of deficiencies found by the Agency in information submitted in IND's and NDA's covering manufacturing and controls. The guidelines are expected to reduce the number of deficient IND's and NDA's submitted to FDA and thus expedite the processing of submissions to the benefit of the industry, the Government, and the public. Both the industry and Government committees met several times separately and jointly to work out the final draft of the guidelines.

The PMA Guidelines Committee includes: Chairman, George Poos, Ph.D., McNeil Laboratories; Barry Bloom, Ph.D., Pfizer Laboratories; Les Lueck, Ph.D., Parke-Davis Co.; Edward Schumann, Ph.D., Upjohn Co.; and Paul Sinnotte, Ph.D., Merck Sharp and Dohme.

The FDA Guidelines Committee, headed by Armand R. Casola, Ph.D., chief chemist, Bureau of Drugs, consisted of three subcommittees as follows:

Specifications and Tests — Chairman, Dennis Kertesz, Ph.D., supervisory chemist, Division of Metabolic and Endocrine Drugs; Leon DeMerre, Ph.D., acting supervisory chemist, Division of Dental and Surgical Adjuncts; Rachel Silk, chemist, Division of Neuropharmacological Drugs; and Richard Sobell, chemist, Division of Metabolic and Endocrine Drugs.

Packaging and Labeling — Chairman, James Langston, supervisory chemist, Division of Cardiopulmonary and Renal Drugs; Lee Geismar, assistant to the director, Office of Scientific Evaluation; and Albert Thompson and Raymond Scharmach, chemists, Division of Cardiopulmonary and Renal Drugs.

Stability — Chairman, Charles Kumkumian, Ph.D., supervisory chemist, Division of Anti-Infective Drugs; Robert Sheffield, deputy director, Division of Product Research and Surveillance; and Clifford Sinopoli, chemist, Division of Dental and Surgical Adjuncts.

In addition to publication in FDA Papers, these "Guidelines for Manufacturing and Controls for IND's and NDA's" will be available in reprint form and will be distributed by the Bureau of Drugs.

General Considerations. Existing regulations clearly provide for controls to assure the proper identification, quality, purity, and strength of a new drug; however, as written, the regulations do not necessarily spell out the essential criteria needed in making the judgment on a particular new drug.

It is the purpose of this paper to assist the sponsor and/or applicant in making the necessary judgments to assure that the information submitted will, indeed, meet the requirements of the regulations.

We are dealing with submissions both to IND's and NDA's. The progression from an original IND submission to all of the material that is submitted in a New Drug Application is a sequential event. Based on the information submitted in an original IND, the sponsor expects to begin with clinical pharmacology (phase 1 and early phase 2) in a limited number of human subjects and patients. The sponsor's primary objective should be to provide evidence of safety and some indication of clinical efficacy prior to making his decision to proceed into expanded trials. In the original IND submission, emphasis should be placed on controls of the raw materials and primarily the new drug substance with the understanding that modifications of the method of preparation of the new drug substance and modifications and additions to the dosage forms are highly probable and that final specifications cannot be anticipated or expected. It is also understood that such modifications would be correlated with previous and present studies.

As the development of a new drug progresses and as the sponsor continues to gain experience both in the clinic and in the laboratory, he supplements information in the IND so that at the time of NDA submission, the new drug is completely controlled. In the following discussion, the section "IND Submissions" refers primarily to the initial IND submission and information needed for early investigational stages. The section "NDA Submissions" covers the information needed for the New Drug Application.

IND Submissions

The following guidelines should be followed in considering the information required by parts 2-5, Form 1571:

Part 2: A complete list of components present in the drug including the new drug substance.

Part 3: Quantitative composition of the drug, including reasonable variations to be expected during the investigational stage. Information is to be submitted if new dosage forms (e.g., capsules in addition to tablets, reformulation of tablets, etc.) are brought into investigational usage. These submissions should describe the name of each ingredient and provide quantity ranges per unit dosage form. It is expected that as dosage form additions are put into effect, adequate controls will be supplied.

Each formulation which reflects a new dosage form, a change in the potency, and/or a significant excipient

change, should receive a formulation number. Batch numbers will continue to be used as a method of identifying individual batches. Both formulation and batch numbers should be correlated with clinical studies in which they are used.

Part 4: The source and preparation of the new drug substance involves a description of the synthesis, extraction, isolation, and purification of the new drug substance.

These will normally be provided as flow sheets giving structural formulas (where known), reagents, catalysts, and a general description of solvents and conditions. Illustrative examples of preparative details are helpful to enable the reviewer to better evaluate the nature of the substance being studied. If scientific publications or patents are available, they should be included if pertinent. It is understood that such details are based on early knowledge about the drug, and the sponsor is not bound to employ the same method in subsequent studies as better ones become available, but the IND should be updated accordingly.

It is expected that during phase 3 most of the chemical development work on the new drug substance should be completed and thus the description of the synthesis should approach NDA requirements.





Appropriate controls over the new drug substance should be exercised (see next section).

Part 5: Methods, facilities, and controls used for the manufacture and processing of the new drug to establish and maintain appropriate standards of identity, strength, quality, and purity as needed for safety and to give significance to the clinical investigations made with the drug.

a. Raw Material Controls:

1. *New Drug Substance:* Controls are necessary to determine the identity, quality, purity, and strength of a new drug substance. In the first stages of development, a new drug substance interim reference standard should be prepared with which all batches of the new drug substance used in biological work will be compared. The interim reference standard should be of the highest purity that can be attained by reasonable effort and should be thoroughly characterized to assure its identity, strength, and purity. If the interim reference standard is prepared by a different method, this method should be described. Criteria to be applied for characterization of the reference standard or the new drug substance should be: physical properties such as color, odor, general description; appropriate physical constants such as m.p., b.p., refractive index, and optical rotation; structural formula, empirical formula, molecular weight, and such information which substantiates the proof of structure of the drug substance. It is recognized that this may not be feasible for certain complex substances such as products of natural origin although every effort should be made to adequately characterize such substances.

The applicant should utilize appropriate analytical tests such as elemental analysis, i.r., u.v., n.m.r., and mass spectroscopy as well as applicable functional group analyses together with their interpretation. Suggested tests for purity include thin-layer, gas, liquid, or paper chromatography; phase solubility analysis; and differential scanning calorimetry. Subsequent comparisons of batches using the interim reference standard as a criterion of high purity should be made in such a way as to provide sound scientific evidence that the batches do not differ significantly from each other. The underlying rationale upon which the comparison of batches is made should be explicitly described. The actual methods and tests used, including acceptable limits, and the results obtained should be recorded. The need for various tests may change as experience is gained and the reliability and significance of each test becomes apparent. In a typical case, sufficient experience should have been accumulated during phase 3 to allow the establishment of complete specifications for the NDA.

2. *Other Ingredients:* Specifications for acceptance and test methods used for each lot of material should be supplied (see NDA section).

b. Manufacturing and Processing, Packaging, and Labeling:

Appropriately detailed descriptions of the preparation of the finished dosage form which include the amounts of each ingredient, equipment, packaging, and labeling procedures and conditions used should be supplied together with a description of containers and their treatment prior to use.

c. *Laboratory Controls for Finished Dosage Forms:*

In order to lend significance to the proposed studies, laboratory controls for the dosage form should include all specifications, chemical and physical, for acceptance of each lot. Assay procedures, including actual calculation of results and specific identity tests for the presence of the new drug substance in the finished dosage form, should be described. The assay method for the new drug substance should be specific, if such a method is available. If not available, additional tests to demonstrate purity should be included. Also included, when applicable, should be detailed methodology (test doses and procedures) for sterility, pyrogens, and safety tests. Acceptance standards for large batches or by phase 3 should approach NDA standards including information concerning the statistical precision and accuracy of the methods. Raw data including sampling information should also be provided at this time.

The use of placebos and comparative drugs that are frequently employed as an integral part of the investigation of a new drug should be controlled and documented, including the submission of information to fulfill all *applicable* requirements under parts 1-5 and 7. If commercially available drugs are used, it will usually suffice to identify the product by its name, including dosage form and quantitative declaration, and source; however, if such drug is altered in any way, for example, by reformulation or repackaging, full details of these operations and the related controls information should be provided.

d. *Stability:*

A description of the studies and data obtained from them on the stability of the new drug substance and the dosage forms should be submitted as it becomes available. For further guidance in this important area, refer to the NDA section.

e. *Control Numbers:*

An explanation should be given of the significance of formulation numbers and of batch control numbers used in the manufacturing, processing, packaging, and labeling of the drug including those that should appear on the labels of the finished drug.

Part 7: Investigational Label Requirements: Labels for investigational drugs are subject to the same general requirements of the Act and regulations applicable to prescription drugs. However, some label requirements are not appropriate for investigational drugs and are by policy exempted. The exemptions include the Rx legend and the recommended, or usual, dosage when this has not yet been established. The labels are required to bear the following:

1. The statement "Caution: New Drug—Limited by Federal (or United States) law to investigational use."

2. A quantitative statement of the active ingredient(s). Active ingredients must be declared by the established name if there is one, or if none exists, by a code designation such as a letter-number combination. (It is recommended that the sponsor seek the assistance

of the USAN Council in developing an established name for a new chemical entity at an early date.) The full chemical name of the drug and structural formula where known should appear in the informational labeling or brochure supplied to each investigator.

Inactive ingredients of drugs for other than oral use are required to be declared on the label or, in the case of insufficient space, in the informational material supplied to each investigator.

Inactive ingredients in injectables must be declared quantitatively except as specified in regulation 1.106 (b). Other ingredient information, such as the declaration of those substances listed in section 502(e) of the FDC Act, is applicable to investigational drugs the same as for drugs in commercial channels.

3. A statement of the quantity of contents in the container.

4. An identifying lot or control number.

5. A warning statement for habit-forming drugs, radioactive drugs, etc.

6. The drug abuse control symbol for drugs which have been determined to be subject to the drug abuse control provision.

7. The name and place of business of the manufacturer, packer, or distributor.

For drug supplies intended for double-blind studies, all necessary precautions should be observed so that in their movement in interstate commerce they are in compliance with the labeling requirements of the Act and regulations and their identity maintained at all times. For example, the use of "tear-off" labels attached to each immediate container is one possible approach.

The "tear-off" portion of the label should, of course, contain the required information discussed above. Following shipment, the "tear-off" portion of the label should be removed and retained by a neutral party at the point of use of the drug. The "permanent" portion of the label should be designed to preserve the blind character of the study. However, the label content along with the identity of the investigator, patient name, and instructions should be sufficient to enable prompt breaking of the code and acquiring all pertinent information on the specific material involved if this becomes necessary. Actual copies of the labels that appear on the investigational drug should be submitted.

NDA Submissions

1. *Components:* All the components of the drug should be listed, including the inert ingredients and those that are used in the synthesis or preparation of the new drug substance. The latter should be included regardless of whether they undergo chemical change or are removed in the process, using structural formulas where necessary for specific identification. Reasonable alternatives may be listed for excipients provided that there is adequate supporting information to justify them. Quite often a proprietary or trade name is utilized as the sole means of identification for certain ingredients

such as flavors, perfumes, and colors. When such an ingredient is used, the trade name should be followed by a complete quantitative statement of its composition. As it frequently happens, this information is considered to be a trade secret, in which case, it may be furnished directly to the Administration by the supplier in order to preserve confidentiality.

2. *Composition*: The quantitative composition of the new drug dosage form should be stated in terms of quantities of all the active and inert ingredients per unit dose, e.g., per tablet, per gram, or per milliliter. It is also required that the batch formula should include the names and amounts of any components that will not appear in the finished product. In addition, any predetermined or calculated excesses of ingredients over label declarations should be designated as such and the percent excess clearly indicated.

Proposed variations in quantities of ingredients should be reasonable and realistic. Examples of unreasonable and unrealistic variations are:

a. Intentional wide variations in the amount of an active ingredient when the product specifications should guarantee a tolerance of not less than 90 percent nor more than 110 percent of the labeled amount.

b. The proposal for limits of 90-105 percent when a 10 percent excess of the active ingredient is stated.

c. The proposed (and unacceptable) variation of 0 to 100 percent of quantities of inactive ingredients. In the case of proposed wide variation in the limits, adequate data for justification should be submitted.

d. Proposed limits that are too narrow when a relatively imprecise assay method must be used.

It should be understood that the formulation should be prepared with the intent to provide not less than 100 percent of the formula amount of active ingredient.

As a last point the applicant must carefully note whether there is any disagreement in the statements of composition between one part of the application and another. If such exist, then these discrepancies must be reconciled before it can be concluded that all parts of the application refer to the same drug formulation.

3. *Facilities and Personnel*: This requirement is clearly described in the new drug application form and the adequacy of this information may be determined by means of a factory inspection. To supply this information, it is recommended that a Master File be established for each facility and its technical and professional personnel. In NDA submissions, there should be specific reference to pertinent sections of the master file(s). Such information is useless unless it is on a current basis and should be routinely updated at no less than annual intervals.

4. *Synthesis of the New Drug Substance*: Description of the method of preparation of the new drug substance must serve to permit evaluation of the proposed specifications for it, and delineation of its structure. When the new drug substance is shown to be a highly purified compound, well characterized by its chemical and physi-

cal properties, the description of its preparation should include sufficient detail to enable a determination of whether suitable tests exist to limit the content of possible impurities.

Flow charts which specify intermediates, types of reagents and ranges of reaction conditions used, supplemented by a more detailed description of the synthetic step affording the final intermediate and the new drug substance should be provided. Emphasis should be given to methods of purification, especially when noxious impurities or unwanted isomers are encountered. Occasionally it is desirable to employ several different synthetic routes that lead to the preparation of a common or pivotal intermediate. It is necessary that such independent synthetic sequences be described in adequate detail and that the pivotal intermediate be subject to rigid specifications in order to avoid overlooking undetected or vagrant impurities. In general, greater degrees of latitude should be taken early in the synthesis and wherever the rigor of control specifications justifies it.

If the new drug substance is a complex mixture, such as a natural product prepared by extraction or fermentation, whose characteristics are not adequately defined by properties readily determined in laboratory test procedures, the method of preparation used must be described in considerable detail, as a part of defining the identity, strength, quality, and purity of the new drug substance.

In general, yield information may not be necessary but it may prove helpful in assessing the adequacy of control procedures employed.

5. *Raw Material Tests and Specifications for the New Drug Substance*: The acceptance specifications and test methods submitted for a new drug substance should be adequate to assure its proper identity, strength, quality, and purity from batch to batch. The guiding principle here is that one or two highly discriminating tests for identity and purity are better than a whole battery of less specific tests.

An infrared spectrum can be an excellent specific identity test, as for example, when determined as a dispersion in a crystalline solid. Properly designed thin-layer, paper, and gas chromatographic tests are good measures of purity and also provide strong supporting evidence for identity. When any of the chromatographic tests are used, there should be included a complete description of the method including solvent systems, materials used for the packing of columns, operating conditions, and calculations involved.

The specific data that may be assembled to support statements of identity and purity are variable. Practical considerations such as instrument availability, cost, and special skills available together with professional judgment will usually determine the selection.

It should be noted that a given methodology array is not to be regarded as invariant or recommended. Each molecule has its distinctive features and unique prop-



erties that may preclude some methods or may require the application of other combinations.

In support of the specifications, an interpretation of the underlying data and an explanation of how the specifications adequately assure the identity, purity, quality, and strength of the new drug substance should be provided.

A good specification should provide a composition material balance. A specific assay for the new drug substance should be combined where indicated with limit tests for solvents, inorganic impurities, heavy metals and precursors, by-products, and degradation products so that within the limits of precision for the assays the total will account for 100 percent.

When physical properties such as solubility and the nature of crystalline or amorphous particles can affect the physiological availability of the drug, they should be seriously examined and included in the specifications where pertinent. Of vital interest in this area is the existence of the new drug substance in an optically active form which necessitates the inclusion of criteria for the control of optical isomer content.

The methods and standard of acceptance should be clearly detailed in the application to permit duplication and verification in our laboratories. In addition, an analytical method for determining the new drug substance, using a reference standard where applicable, should be submitted for use in regulatory drug analysis.

When the new drug substance is the subject of a monograph in an official compendium, it may be sufficient for the applicant to state that it is purchased as U.S.P. or N.F. grade, indicate the supplier and/or

manufacturer, and provide assurance that each lot will be tested according to, and will meet all specifications of, the appropriate compendium.

The various chemical and physical methods and tests used to establish the integrity of a reference standard should be described. The reference standard should be of the highest purity that can be attained by reasonable effort and should be thoroughly characterized to assure its identity and purity. If the reference standard is prepared by a different method, this method should be described. Criteria to be applied for characterization of the reference standard or new drug substance should be: physical properties such as color, odor, general description; appropriate physical constants such as m.p., b.p., refractive index, and optical rotation; structural formula, empirical formula, molecular weight, and such information which substantiates the proof of structure of the drug substance.

The applicant should utilize appropriate analytical tests such as elemental analysis, i.r., u.v., n.m.r., and mass spectroscopy as well as applicable functional group analyses together with their interpretation. Suggested tests for purity include thin-layer, gas, liquid, or paper chromatography; phase solubility analysis; and differential scanning calorimetry. In general, it is expected that these tests and methods for the reference standard will be far more comprehensive than those used in the routine control of the new drug substance.

6. Raw Material and Specifications for Inactive Ingredients: As for the active ingredients, the tests and specifications for the inactive ones should be appropriate, described in sufficient detail, and adequate to



assure their identity, strength, quality, and purity.

If an ingredient is recognized in an official compendium, it should be shown that the article complies with the specifications established for it, i.e., state the tests run routinely by the applicant on each lot. If color additives are used, they should be from FDA certified batches and so stated. Non-Compendium material should contain information as follows:

- a. Description
- b. Identity Test
- c. Assay Procedure with specification limits, where applicable.
- d. Heavy Metals Test with specification limits, where applicable.
- e. Physical Property Tests such as melting point range, boiling point range, acid value, ester value, pH, and/or any other physical test(s), which *significantly* contribute(s) to further substantiating the properties of the material. Comparison should be made to a reference standard material where necessary.

Since the applicant is responsible for the integrity of the finished product which he manufactures, the most prudent course for him is to check each raw material by methods adequate to determine its identity, strength, and purity. If, however, he wishes to rely on his supplier and/or manufacturer for a major part of the necessary control and content himself, for example, with an identity test, such control may be used.

However, under these circumstances, it would be necessary for the applicant to assure the FDA that either he or the supplier and/or manufacturer does employ all the methods pertinent to establish the iden-

tity, strength, quality, and purity of the material, and the supplier and/or manufacturer guarantees to the purchaser that the article meets the specifications.

As a final comment on raw materials, it should be stated that good control includes not only the establishment of sound standards and appropriate test methods but the application of these methods to properly selected representative samples.

7. Manufacturing, Processing, Packaging, and Labeling: The description of the manufacturing process for the final dosage form should be given in detail. The final dosage form is usually not a chemically pure single entity, but must be a highly reproducible, stable composition with constant physical and chemical properties.

The information to be submitted for these operations should be coherent and well organized in order to permit a meaningful review and verification. Each step should be clearly and precisely described to include:

- a. The amounts of all ingredients, the actual operating conditions and equipment to be used together with the controls utilized;
- b. Appropriate details of the container treatment prior to use;
- c. Complete details of product sterilization procedures, when indicated, including data to support the adequacy of the procedure;
- d. The method of sampling;
- e. Procedures for final testing for the release of each batch of drug should be carried out on adequately representative samples of the finished drug;
- f. The labeling procedure and the type of labels to be used;

g. Provision for checking the quantitative yield of the finished drug just before it is packaged into final containers for comparison with the theoretical yield and for reconciling any discrepancy that may arise;

h. Provision for checking container, closure, or other component parts of the drug package;

i. Repetition of quantitative check for labeled packages;

j. Provide for adequate examination or laboratory testing of adequately representative samples of finished products after packaging and labeling to safeguard against any error in the finished operations.

In many instances other firms perform parts of the manufacturing, packaging, and labeling operations. It is required that they submit signed statements which adequately detail their operations, together with the commitments that will be met. These will be included in the applications. Drug Master Files or other documents to be incorporated by reference should be duly authorized by the particular firms involved.

With regard to any manufacturing controls changes planned by the holder of a DMF, it is incumbent upon him to inform the applicant (or sponsor) of the changes within the meaning of the confidentiality of information regulation. The applicant (or sponsor) in turn must notify the FDA of the change through the accepted NDA or IND procedures. The references regarding any changes should be specific as to the pertinent sections involved.

8. *Analytical Controls, Specifications, and Test Procedure for the Finished Drug:* To assure that the dosage form has the identity, strength, quality, and purity stated in the labeling, the applicant should adopt or develop well-defined standards for each active component of the drug and appropriate methods for their determination. The use of suitable methods from official compendia or other established procedures is recommended.

Other tests or important requirements, depending on the type of dosage form, should be included as necessary, such as:

a. Weight variation for tablets, capsules, and other solid dosage forms;

b. Content uniformity for tablets, capsules, sterile solids, and suspensions;

c. Disintegration times for tablets and capsules;

d. Dissolution test for tablets and capsules;

e. Homogeneity;

f. Clarity, presence of particulate matter, preservative assay, isotonicity, pH determination of liquids;

g. Sterility of ophthalmic solutions;

h. *In vitro* release pattern, together with appropriate specification limits and test procedures for sustained release preparations;

i. Sterility, non-pyrogenicity and container fill of injectables;

j. Physical characteristics such as color, appearance, odor, shape, hardness, coding, etc.;

k. Leakage test for ampules and aerosols;

l. Metering tests, specifications (if metered dosage) and container pressure for aerosols;

m. Particle size and resuspendibility;

n. Completion of solution for reconstituted solutions;

o. For sutures: Elongation at breaks, diameter, tensile strength—straight pull and knot pull, and handling characteristics (flexibility, fraying).

With regard to methods for the laboratory test procedures of samples, complete description should be given including the rationale of the method, calculations, derivation of factors; spectrophotometric absorption curves should indicate concentration of the sample, and if the baseline method is used, it should be so stated.

The methods should meet certain minimum basic criteria, such as an adequate degree of accuracy, precision, and specificity. Thus, if the assays themselves are nonspecific, then specific identity tests should be included.

In order for the applicant to arrive at a conclusion concerning the suitability of the methods, he should determine their precision and accuracy and submit the raw data on which they are based.

The methods and standards of acceptance should be clearly detailed in the application in order to permit duplication and verification in our laboratories. In addition, an analytical method for determining the new drug substance in the dosage form, using a reference standard where applicable, should be submitted for use in regulatory drug analysis. For this purpose it must not include the use of any formulation blank or arithmetic correction to compensate for any inactive component interference.

Alternate assay methods may be submitted for control purposes provided equivalency to the regulatory assay has been shown.

Consideration should be given to the possible need for comparative bioavailability studies of finished dosage forms. This need may arise when supplementing approved NDA's with formulation changes or when applicable in filing abbreviated NDA's.

9. *Stability Studies and Container Information:* To assure its safety and effectiveness, a pharmaceutical product must retain its identity and purity for the entire shelf life of the product. Assurance that the drug dosage form in its container will be suitably stable for the anticipated shelf life must come from an accumulation of data on the packaged drug. These stability data involved selected parameters which, taken together, form a stability profile. Information from initial and subsequent tests performed on drug substances, the various dosage forms, and containers provides the basic data upon which the stability profile of the pharmaceutical product is constructed.

A stability profile is needed to demonstrate that the rate of change of stability-indicating characteristics is less than a specified amount over a finite period of

time. Environmental factors such as temperature, humidity, and light are useful in hastening or accelerating a rate of change and usually are necessary to complete a stability profile.

For products and drug substances which have been shown to exhibit no significant rates of change of stability-indicating properties either under normal or exaggerated conditions over an extended time period, a less detailed stability profile may suffice.

Emphasis must be placed on the initial study of the drug substance, dosage form, and packaging material coming in contact with the product. Drug substances should be subjected to exaggerated conditions for any possible effect on purity and homogeneity. If degradation occurs under conditions that might be anticipated in the formulation and use of the drug substance, then the degradation product or products should be characterized and excluded or controlled by assay methods. Adequate information should be submitted with respect to the characteristics and testing of containers, closures, or other component parts of the drug package to assure their suitability for the intended use. Information especially for plastic containers, metal tubes, and aerosol containers has a direct bearing on the entire problem of stability. Since a drug may absorb toxic impurities or accumulate hazardous particles from its container or it may react with the walls of the container or be absorbed by the container, tests to define any of these possible problems should be carried out.

Contamination with micro-organisms or foreign matter can occur through the container or its closure.

Thus, in designing the stability studies for drugs, some of the many factors which should be investigated and evaluated include: temperature, moisture, pH, susceptibility to oxidation and light, excipients, chelation, trace metals, solubility, compatibility, methods of sterilization, container, and closure. Those factors found to be critical for a particular drug should be investigated thoroughly.

Temperature, of course, is a parameter of prime importance when considering stability studies. The range of controlled laboratory storage conditions that have been used and reported is quite broad, beginning at below freezing and rising to above 50° C. Intervals normally studied are 5-10° C, controlled room temperature, ambient room temperature, 35-40° C, and 41-50° C. It must be realized that several weeks at 50° C is strictly speaking not an accelerated test considering temperatures in the summer in various parts of the country and what might be expected to be found in the holds of ships, military depots, or in trucks or trains.

Samples of the drug selected for stability studies should be packaged and stored in the same manner as the drug will be marketed in the finished package and, of course, on batches with the quantitative composition intended for use.

Dosage forms studied in a "reference" container and exposed to a range of environmental conditions may yield useful information.

Accelerated studies combined with basic stability information on the new drug substance, dosage forms, and containers are useful and acceptable to support expiration dates both in the original submission and for changes in the synthesis of the new drug substances, changes in formulation of the dosage form, and changes in the container and packaging of the commercial product.

To facilitate the evaluation of a stability profile in the determination of the anticipated shelf life of a product, the applicant should include a full description of the analytical method used, its accuracy and precision, and other considerations. The method of best fit, copies of the graphs plotted as well as a complete explanation of techniques employed in the extrapolation and curve fitting should be included. If the Arrhenius equation is used to estimate the shelf life, a minimum of four points should be used unless full justification is provided for the use of a lesser number. In the presentation of accelerated stability data, ambient data on the particular dosage form in the same container should be included.

However, any proposal based on accelerated or on less than a full stability profile should be accompanied by a commitment containing the substance of the following:

1. Stability studies will continue on the drug. If the present studies do not include production batches, then studies on production batches should be made a part of the commitment.

2. The data will be submitted to the FDA (Bureau of Drugs) as available (or at specified time periods).

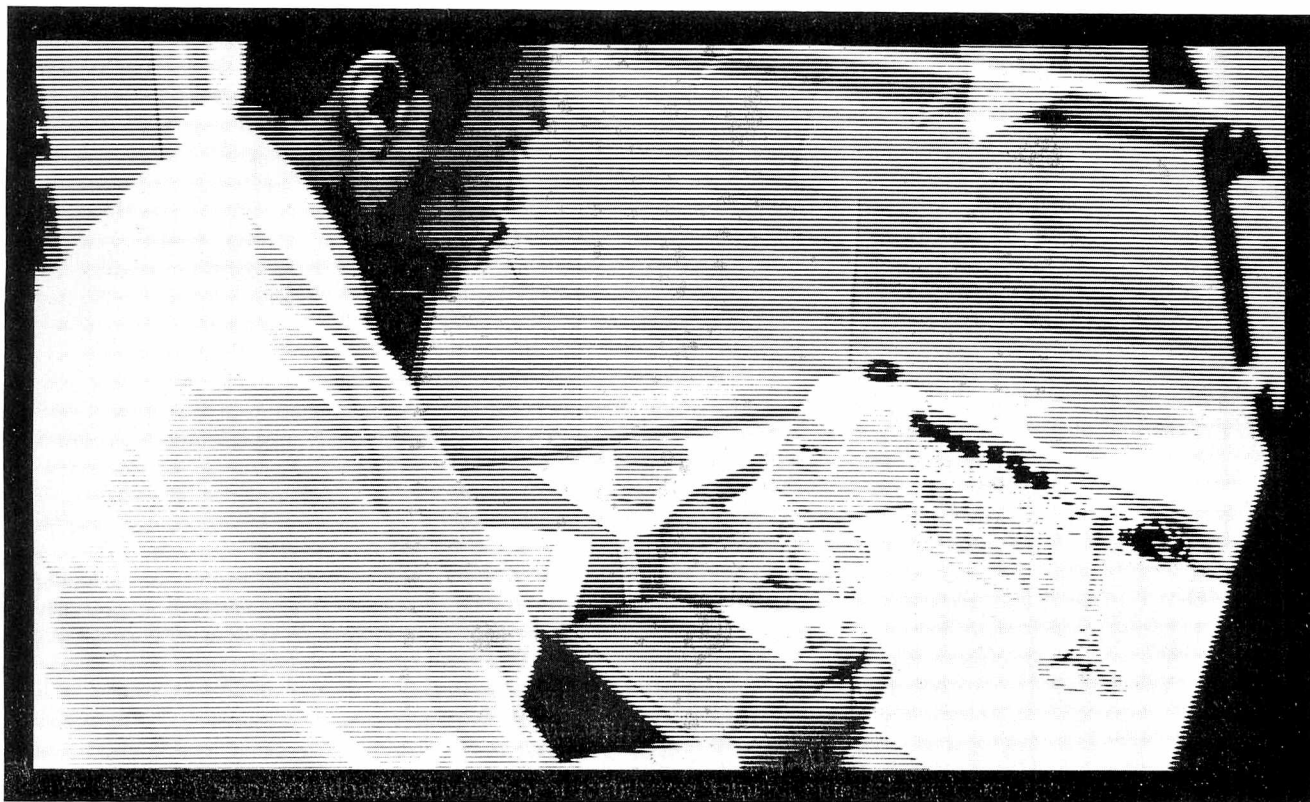
3. Any lots falling outside the approved specifications for the drug will be removed from the market.

There is an increasing use of plastic containers due to the many advantages offered by plastics as packaging materials; however, plastics have distinct disadvantages as drug containers. Ingredients added to the polymer to perform a specific function during fabrication or application such as plasticizers, lubricants, mold release agents, coloring agents, anti-oxidants, and binding or anti-static agents may result in the leaching of a component of the plastic into the drug product, a migration of a component of the drug product through the walls of the container, binding or absorption of certain ingredients of the drug preparation with the plastic, or degradation, oxidation, or precipitation in the drug product resulting from transmission of oxygen, carbon dioxide, or other gases through the plastic into the drug system.

The only certain approach to determine the suitability and safety of a plastic substance for use in a container is to conduct appropriate tests.

Testing guidelines for plastic containers, closures, or other component parts for parenterals are as follows:

- a. The N.F. and U.S.P. include test procedures for the physico-chemical evaluation of plastic containers. The tests are based on the extraction of specified amounts of plastic by various extracting media under specified



conditions of time and temperature. Such tests are useful in controlling and defining the nature of various chemical impurities and additives that result from the manufacturing process and which might have a deleterious effect on the drug. Many physical properties may render the plastic unsuitable for use in fabricating containers intended for the storage of pharmaceuticals. This may be caused by either the toxic properties of the additives or their deleterious effects on the stability of the stored drug preparations.

b. There are a number of physical and chemical test techniques utilized to identify and characterize compounds, including infrared (by ATR), ultraviolet, NMR, and thermogravimetric methods.

As appropriate, molecular weight may be determined by secondary methods such as solution or melt viscosity. Molecular weight and molecular weight distribution can also be obtained by gel permeation chromatography. Data regarding the polymer linearity, degree of crystallinity, permeability, stiffness, and softening temperatures are determined as appropriate for the particular usage. Data on film or sheet thickness, ash, and heavy metals may also be necessary.

c. In the complete testing of plastics, the following parameters may need consideration:

1. Effect of moderate degrees of cold (0°C) and heat (45°C) on some plastics, or even sterilization temperatures, if applicable.

2. Water vapor and light transmission variations among "similar" plastics.

3. Degradation of some plastics (for example: polyvinyl chloride) under exposure to heat and light.

- d. After a plastic has successfully passed through a screening program of physico-chemical tests, it should then be tested for specific uses. When it appears that a plastic has the desired chemical and physical attributes and a suitable composition, it should be tested biologically. While this testing is necessary to determine the safety of a plastic, it can also be used to detect incompatibilities not found by other means.

- e. In connection with the overall suitability of plastics for use as pharmaceutical containers, the U.S.P. and N.F. also contain biologic test procedures for plastics. These tests provide a useful means for determining the presence of undesirable substances such as residues from the polymerization process, plasticizers, stabilizers, anti-oxidants, pigments, and lubricants.

- f. A New Drug Application should also include the following information about a plastic container:

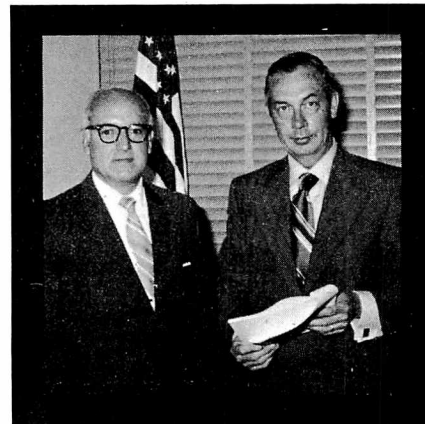
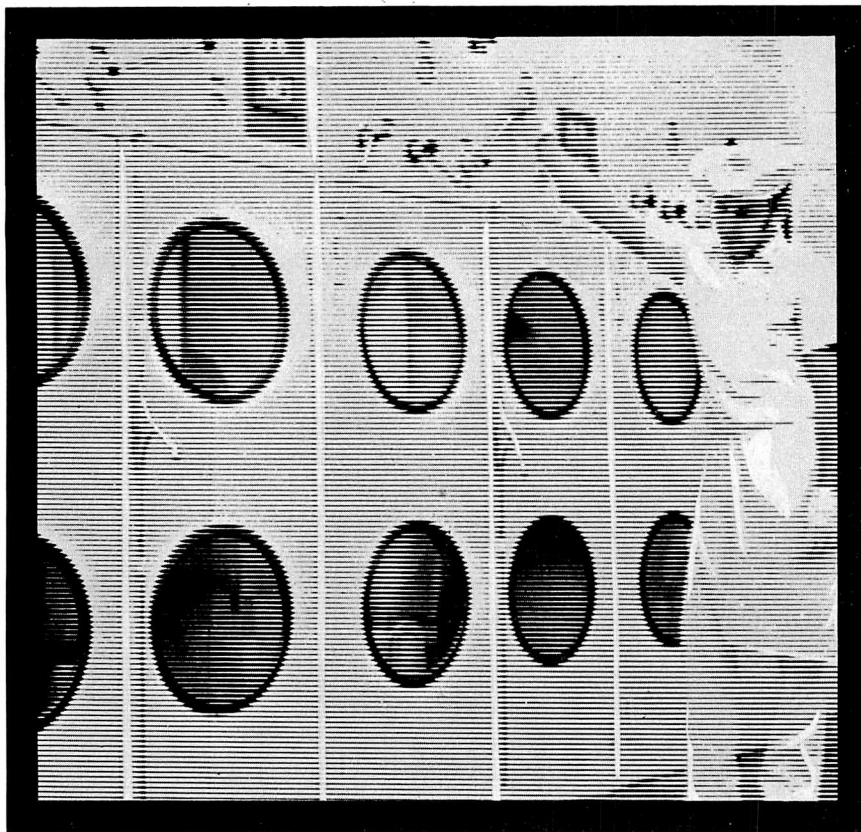
1. A complete statement of the composition and method of manufacture of the resin and plastic furnished by the plastic manufacturer to assure uniformity from batch to batch.

2. A full description of the analytical controls used, including the plastic specifications and test procedures to insure batch to batch identity, quality, and purity.

The above guidelines should also be applied, in general, to rubber closures. The N.F. includes a section for testing of rubber closures for injections.

Testing guidelines for plastic containers, closures, or other component parts for non-parenterals are as follows:

- a. A complete statement of the composition and method of manufacture of the resin, plastic, and fin-



Chairmen of the Government and industry committees that prepared the guidelines are Armand R. Casola, M.D. (left), chief chemist, Bureau of Drugs, and George Poos, Ph.D., McNeil Laboratories, representing the Pharmaceutical Manufacturers Association.

ished container to insure uniformity from batch to batch.

b. A full description of the analytical controls used, including the resin, plastic, and finished container specifications and test procedures to assure uniformity from batch to batch.

c. Parameters that need consideration are effect of moderate degrees of cold (0°C) and heat (45°C), or even sterilization temperatures; water vapor and light transmission; and degradation under exposure to heat and light.

In addition, the testing guidelines for parenteral plastic containers should be applied in part or in whole according to the dosage form involved and method of administration (ophthalmic solutions, ointments, creams, liquids, tablets, capsules, etc.).

As a final note on the stability data needed for an acceptable finished product, the assay must not only be quantitatively accurate but must also be sufficiently specific to differentiate between the unaltered drug and its possible degradation products. On any preparation for which the assay method has not been demonstrated to be specific for the undegraded drug, it will be necessary to use sensitive qualitative or quantitative tests for degradation products.

Tests and important requirements to be used in stability testing of specific dosage forms are covered under Part 8, Analytical Controls. It should be understood that the tests and assay methods used in stability studies should be highly discriminating so that the max-

imum opportunity will be provided to detect changes in active ingredients and excipients.

After the original NDA has been approved, supplemental applications may be submitted providing for changes. If the change is one that requires prior approval, adequate data should be submitted to assure the integrity of the drug. The amount and type of data depends upon the proposed change and background data available in the NDA.

If the change is of the type that comes under regulation 130.9(d)(3), such as removal from the finished dosage form of an ingredient that has been found to be unsafe, some stability data should be submitted along with a commitment to continue the study (see commitment requirements previously given in this section). When possible, sufficient data on the recommended storage conditions should be submitted to allow enough lead time to accomplish any required removal from the market.

10. *Samples:* Instructions are detailed in Form 356H concerning the number and type of samples to be submitted with an application and the analytical data required to accompany them.

Requests for waivers should be accompanied by good reasons such as the availability of the material as a U.S.P. item.

In the event the application proposes tests involving an impurity reference preparation (such as a Foreign Steroids test), samples of the latter should be included to expedite the validation of methods.

shellfish sanitation

Keeping a Step Ahead

by J. David Clem

*"Mother, may I go out to swim?"
"Yes, my darling daughter;
Hang your clothes on a hickory limb,
And don't go near the water!"*

The kind of frustration expressed in this childhood rhyme is not unlike that felt sometimes by shellfishermen who sail over contaminated oyster and clam beds. To harvest any of these polluted shellfish would be illegal, could be the cause of serious illness if eaten, and could deal their industry a severe blow.

Two technical service units of the Food and Drug Administration Bureau of Foods' Division of Shellfish Sanitation are busy throughout the year performing scientific investigations and working out technological problems that will help FDA, State officials, and the shellfish industry to make sure that shellfish that are harvested come only from clean waters.

The oyster and the popular clam varieties, delights of the epicure and housewife, are something more to public health and pollution control officials. Not only is the shellfish a prized seafood item, but it is one of the most accurate natural indicators known in gauging the hygienic quality of the water in which it reproduced and grew. Those who didn't know this 46 years ago found out the hard way, decades before environmental contamination became a subject of intense national concern.

Shellfish feed by pumping the salty and fresh water mixture that surrounds them through their gills and filtering food and any other substances contained in the water into their digestive systems. The visceral mass or meat of a shellfish will reflect the quality of the water it inhabits; ergo, polluted water means polluted oysters and clams. It was this basic ecological relationship that became starkly apparent in 1924-25 when the country experienced a typhoid fever epidemic totaling 1,500 cases and claiming 150 lives, all resulting from the consumption of oysters saturated by sewage.

This critical event galvanized Federal and State public health officials and the shellfish industry into action which created and has perpetuated the National Shellfish Sanitation Program that protects the consumer of today. This program and how it operates under the direction of what is now the Division of Shellfish Sanitation was described in "Certified Shellfish" in the May 1969 issue of FDA PAPERS. Reprints of this article are available from the Division on request.

Although the shellfish industry, various official agencies of the shellfish-producing States, and the FDA share responsibility for administering this program, the real key to its success lies in their unanimous and un-deviating acceptance of one major premise: The source

of the shellfish—the producing area—must be free of any contamination that would make the product unsafe as food. Although shellfish are subject to many of the same precautions and safeguards required by Federal and State law in the processing and distribution of other foods, the National Shellfish Sanitation Program places primary emphasis on an earlier stage—the source—to assure that the watery beds where shellfish grow are unquestionably free of contamination.

This philosophy assumes special importance because a combination of factors make shellfish unique as a food in the American diet. Oysters and clams are eaten raw by many people, as fresh from coastal waters as they can get them. Most recipes call for only superficial cooking so that the whole animal does not receive intense heating. Typical of these recipes are oyster stews, steamed clams, or fried oysters. Traditional safeguards used for retort-processed foods are absent in the shucking and packing of shellfish for market. Thus it can be seen that if the shellfish concentrates undesirable substances in its system from its aquatic environment, the consumer is quite likely to receive the same substances unaltered in the seafood dishes served. This is why it is so important that only certified shellfish be purchased and that the responsible State control agencies continue to apply all the necessary controls.

Throughout the Nation specific coastal waters have been designated where approved shellfish can be harvested by the industry. It is the job of the respective State control agencies to keep these classifications of approved growing areas current to reflect changing conditions. All coastal States follow a uniform set of criteria for the water classifications as outlined in the Manual Operations of the National Shellfish Sanitation Program. In judging the adequacy of the classifications the State control agency considers the most unfavorable pollution and the worst hydrographic conditions. As a further measure safe or approved areas are separated from obviously polluted areas by buffer zones or sections of clean water to provide additional factors of safety. The Division takes the view that even the most perfect of manmade protection systems can go wrong, and recognizing this possible eventuality and preparing for it may avert disaster. There is, for instance, "no such thing as a 'fail-safe' sewage treatment system today," as one FDA official puts it, noting that besides mechanical breakdowns, natural disasters, and human error, there are also other human factors to contend with, such as strikes and negligence.

It is important for FDA to maintain a cadre of specialized shellfish sanitation personnel who can render technical assistance, provide investigational capabilities, train State and Federal public health workers, and plan and evaluate sanitary surveys of shellfish growing areas. The array of public health threats to the safe use of shellfish is growing in complexity and demands a con-

stant vigil to keep a step ahead of new threats in our marine environment. This is largely what the Division's technical services units are all about.

The two TSU's—at Davisville, Rhode Island, and Dauphin Island, Alabama—are responsible for performing sanitary engineering evaluations and technical services to help provide State agencies of shellfish-producing States with the necessary scientific and technical capabilities to assure that the conditions under which shellfish are produced meet sanitation requirements set forth in the Manual of Operations. This assistance is extended through the regional shellfish consultants in FDA regional offices.

The Northeast Technical Services Unit, at Davisville, Rhode Island, gives support to shellfish-producing States on the upper Atlantic seaboard and the Pacific Coast: Regions I (Maine, New Hampshire, Massachusetts, Rhode Island, Connecticut), II (New York, New Jersey), III (Pennsylvania, Delaware, Maryland, Virginia), IX (California, Hawaii), and X (Oregon, Washington, Alaska).

The Gulf Coast Technical Services Unit serves the lower Atlantic seaboard and the Gulf Coast States: Regions IV (the Carolinas, Georgia, Florida, Alabama, Mississippi) and VI (Louisiana, Texas).

Although these are the general regional responsibilities, each of the TSU's may provide special assistance outside its assigned regions, particularly since each has special capabilities in some areas of engineering and science. For instance, the Northeast TSU, which has a professional staff of eight and is headed by James L. Verber, a senior oceanographer of the Public Health Service, has extensive experience and training in the fields of sanitary engineering and oceanography. The Gulf Coast TSU, which has a professional staff of five and is headed by Albert H. Story, Ph.D., a PHS senior sanitary engineer, has expertise in marine biology and sanitary microbiology.

There are geographical and shellfish industry differences, which are reflected in the scientific and technical support available at each unit. The Northeast TSU is generally concerned with a larger variety of shellfish: several species of clams, including two offshore species; oysters; mussels; and geoducks. The Gulf Coast TSU is concerned mainly with the Eastern oyster, *Crassostrea virginica*. The Northeast unit has a greater problem with the potential contamination implicit in the heavy concentration of industry and population along the upper Atlantic seaboard. One aspect of this problem concerns the common practice of dumping industrial and domestic waste on the continental shelf. The effect of this dumping on the sanitary quality of off-shore shellfish has been the subject of study by this unit. Of most concern at present are two species of clams taken from ocean beds in the Atlantic. They are the surf, or sea clam, harvested from certain ocean areas since 1958 at depths of up to 80 feet, and the ocean quahog, taken at depths of 80 to 200 feet. These clams, principally the former, make up 43 percent of total U.S. oyster and

clam production in 1970. Only the muscular parts are edible and are the largest source of fried clams and chowders and stews. At present the surf clam is harvested off the shores of States in Region II, with some in Regions III, and the ocean quahog almost completely off Rhode Island, in Region I.

FDA has established two closed areas to the harvest of shellfish off the Atlantic coast—one off the New York Bight area and the other off the mouth of Delaware Bay. Of the 39 million tons of sewage sludge and other types of wastes disposed of in the Atlantic annually, 45 percent (17.65 million tons) are dumped in these two sites. Areas within a six-mile radius of these two sites have been designated as closed areas for the harvesting of shellfish. Under an agreement with FDA, the Coast Guard patrols these areas routinely and identifies the vessels and home ports of violators so the FDA can intercept them in port for appropriate action. The Northeast TSU has plans for studying the effect on shellfish of other dump sites in a continuing program to assure a safe product.

The units carry out a variety of activities in support of the National Shellfish Sanitation Program's objectives. Both units help train Federal, State, and foreign personnel in shellfish sanitation through classroom lectures and practical field demonstrations. They provide the Division with literature reviews on current subjects, prepare critical evaluations of studies performed by other agencies, and develop proposals for changes in the Manual of Operations based on new experiences and scientific advances. They participate in studies to collect surveillance samples of shellfish and record important associated data such as climatic conditions and physical parameters of water quality. Each unit has its own marine sampling devices and small boats for access to isolated estuarine study areas. Many times they find it necessary to design their own equipment to do a particular job either because none is available commercially or because they can do it for less cost.

In 1966 a compilation was made of the Nation's commercial shellfish growing areas. The inventory showed that of the 10 million acres of water supporting the reproduction and growth of commercial quantities of shellfish approximately 2 million acres was closed because of pollution, conservation, or some other resource control concern. This project, coordinated by the Northeast TSU, has been termed the National Register of Shellfish Growing Areas. The question today is whether we are losing more important shellfish areas through increasing pollution of our coastal waters or whether pollution control efforts are arresting this trend. We expect by October of this year to complete a second Register that will indicate the trend over the past five-year period. Preliminary information suggests we are holding about the same amount of acreage nationally but that important local changes have affected certain segments of the industry.

Another major task of the units is to review engineering plans by municipalities for the construction and

operation of sewage treatment facilities. This work is coordinated with the Environmental Protection Agency under the Federal Water Pollution Control Act, as amended, for public financial assistance. If such facilities are built near shellfish growing areas they can adversely affect the sanitary quality of the shellfish. The TSU's offer suggestions and recommendations in the design and construction of these facilities to minimize this effect. We are presently developing guidelines with EPA to assist consulting engineers in the optimum design and operation of these facilities for the protection of shellfish growing areas. These technical service units have participated in chlorinated pesticide and heavy metals studies for several years and are continuing work in these two areas. One of the more current problems of concern is the effect of toxic hydrocarbons on the health hazard potential to consumers of shellfish. An estimated 600 oil spills per month have been reported in coastal waters of the United States. Up to the present time only two States have closed shellfish areas because of oil contamination. Plans are now being made to study the overall problem of oil pollution and its effect on shellfish quality.

The field service capability of the Northeast Unit was curtailed recently when a fire destroyed the mobile bacteriology laboratory. The trailer lab is being replaced by a motorized laboratory that will increase this service capability. The motorized laboratory will include capacity for freezer storage of shellfish and bottom sediment samples for later chemical or radiological analysis. One of the primary needs of the Northeast Unit is to acquire the capability to conduct chemical analyses for heavy metals and other types of industrial chemical wastes. At the present time, most of the samples collected by the units for chemical analysis are being examined in EPA laboratories. Our engineers have long been interested in developing ways to improve the efficiency of chlorine contact tanks for better disinfection of sewage effluents affecting shellfish growing areas.

The Gulf Coast Unit's professional staff and equipment are oriented toward marine biology and microbiology. Some aspects being investigated by this unit are rapid methods for counting indicator organisms in samples of seawater and shellfish, more reliable methods for determining the extent of *Salmonella* contamination in estuarine water, and the survival and die-off rates of indicator organisms and pathogens in estuarine waters. Other problems being considered for study include health hazards associated with growing area contamination from waterfowl; the effect of paper mill discharges on shellfish growing quality as reflected in changes in microbiological indicator populations; the public health aspects of commercial development of the brackish water clam, *Rangia*, which grows profusely along the Gulf Coast; and the cooling rates of oysters packaged in commercial containers.

Although the assistance the two units extend to State officials is usually in the form of information and training and the State is responsible for carrying out its own

regulation and enforcement, there are times when the Federal Government people will pitch in and provide more substantial help to a State beset by special difficulties, even doing legwork, if necessary.

For instance, two such efforts were made by the Gulf Coast TSU when States had trouble with resurveys of shellfish areas, which are required each 10 years by the Shellfish Sanitation Program's Manual of Operations, or oftener if circumstances warrant.

These resurveys consist of evaluating all actual and potential pollution sources on an estuary and its tributaries and their distance from growing areas; the effectiveness and reliability of sewage treatment works; the presence of industrial wastes, pesticides, or radionuclides that would cause hazards to a shellfish consumer; and the effect of wind, stream flow, and tidal current in distributing polluting materials in the growing area.

Early in 1970, Florida asked for help in resurveys of two shellfish areas of roughly 30 miles each of shoreline—Apalachicola Bay and the coastal area north and south of Cedar Keys, both on the State's Gulf Coast side. All five of the Gulf Coast TSU's professional staff spent two seven-day weeks at each place setting up sampling stations and taking and analyzing samples, conducting shoreline studies looking for pollution sources, and carrying out hydrographic studies.

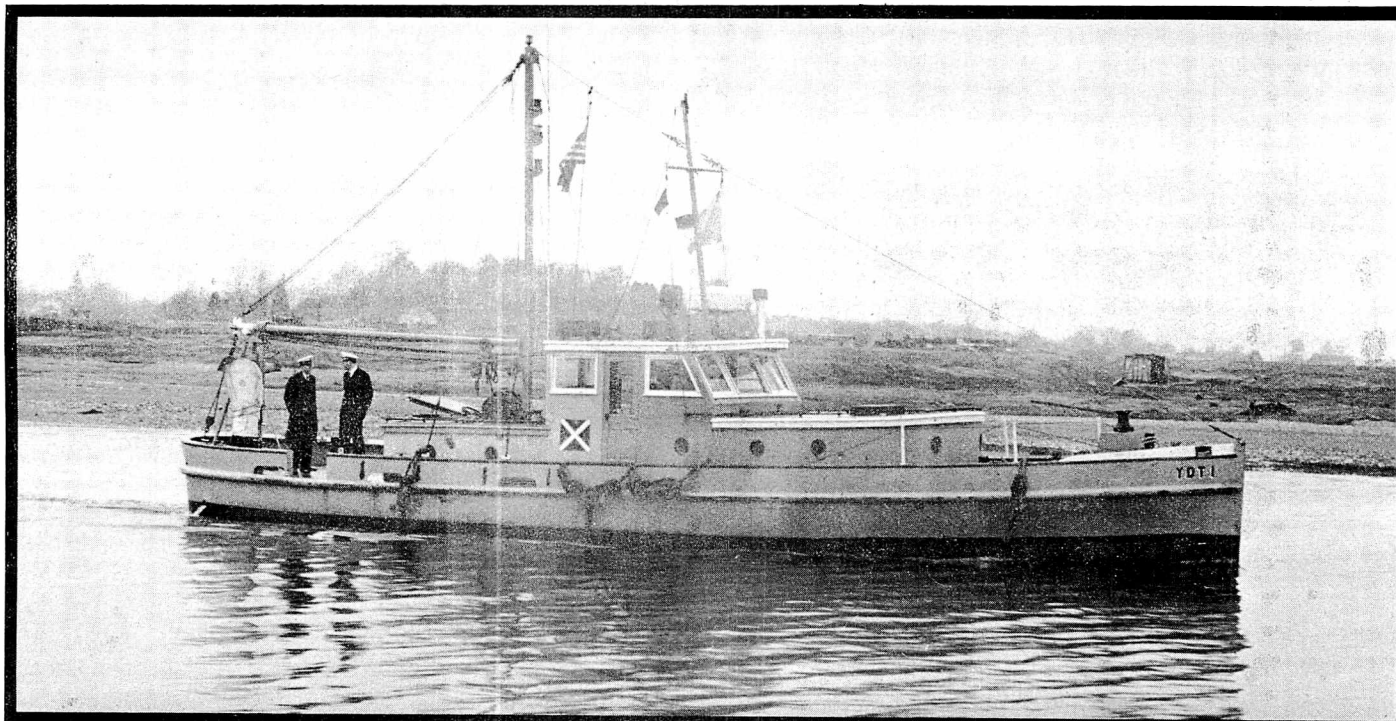
When Hurricane Camille laid waste to the Mississippi Gulf Coast in the fall of 1969 the Unit began helping officials with a resurvey of that State's entire 75 miles of coastline.

The hurricane had devastated most of the shoreline restaurants, oyster shucking and fish processing houses, and marinas, and the sewage systems of most of the coast cities were completely or partly destroyed, with sewer line breaks everywhere. Members of the unit's staff worked in teams with State officials, checking to see if the sewage systems and sewage treatment facilities of the shoreline establishments and of the municipalities had been rebuilt properly. They also checked to determine the effect on shellfish beds of the increased flow of several sewage systems to which new houses or communities had been added in the rebuilding. The project was just completed recently and took a total of about 60 man-days.



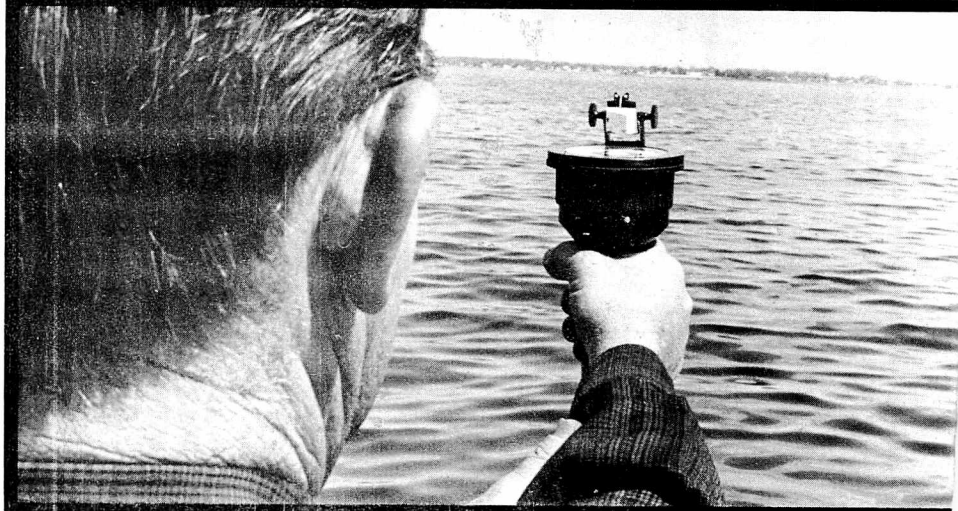
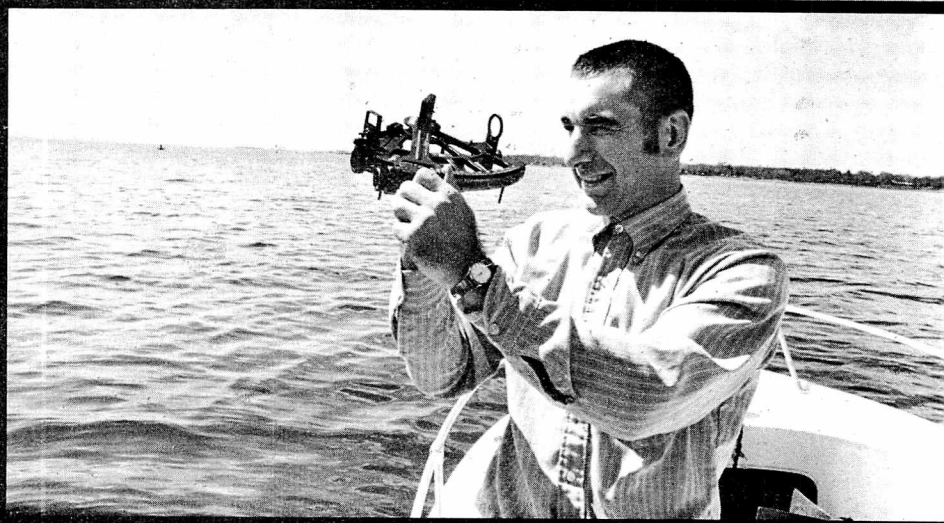
J. David Clem, director, Division of Shellfish Sanitation in the Office of Food Sanitation, Bureau of Foods, joined FDA in 1968 and had served in the Public Health Service Commissioned Corps from 1961 as a sanitary engineer assigned to shellfish sanitation activities.

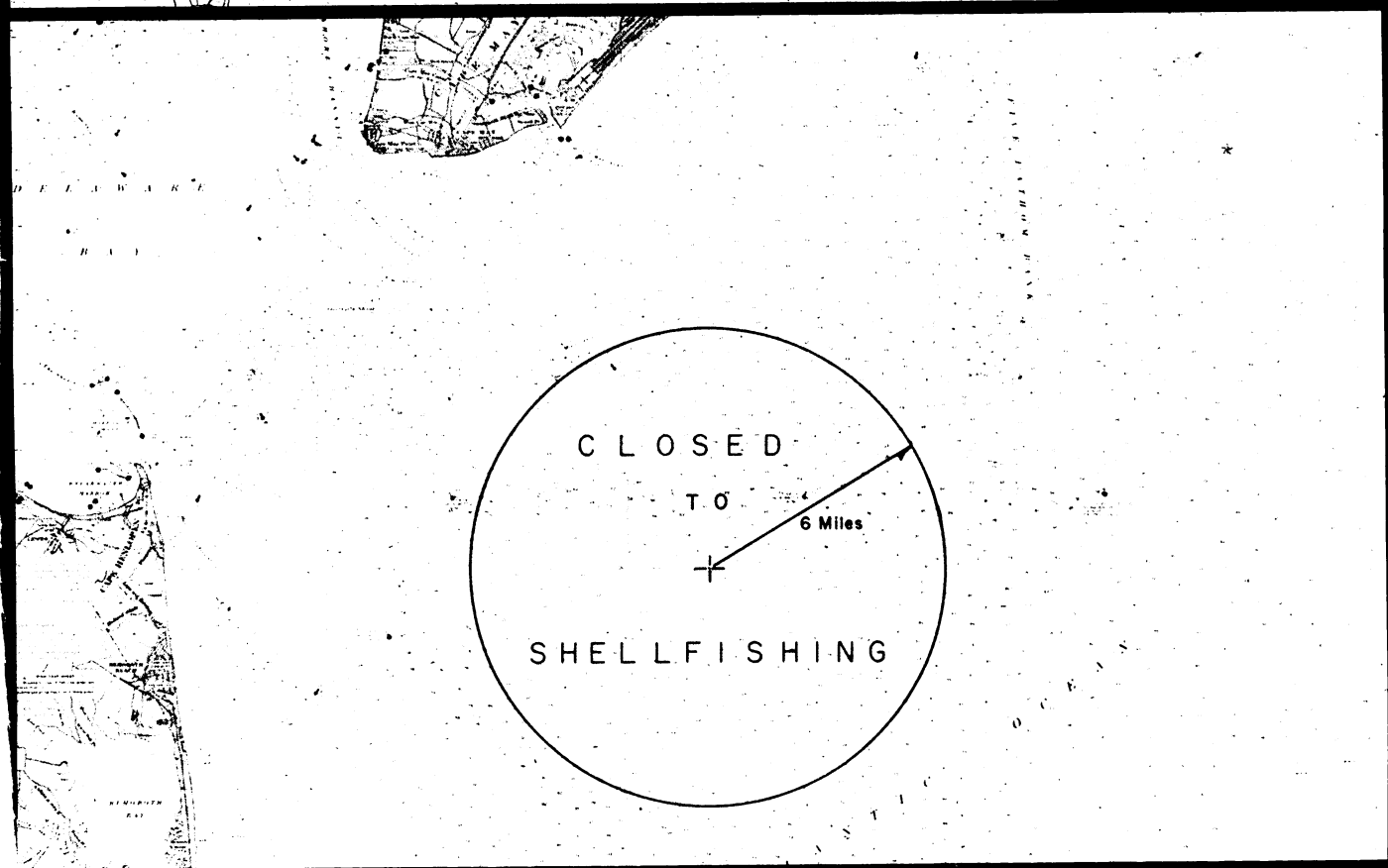
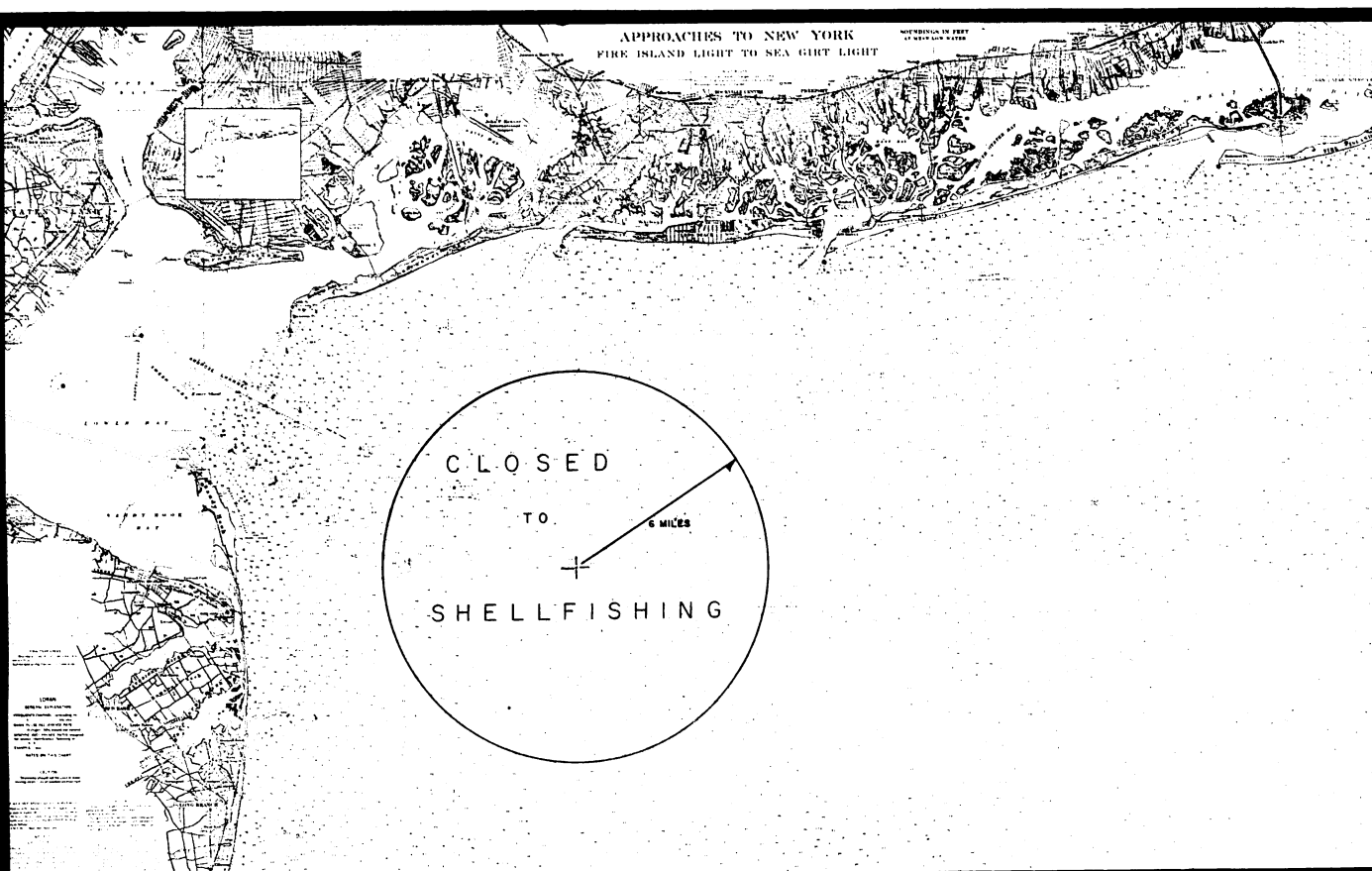
Navigation and Charting



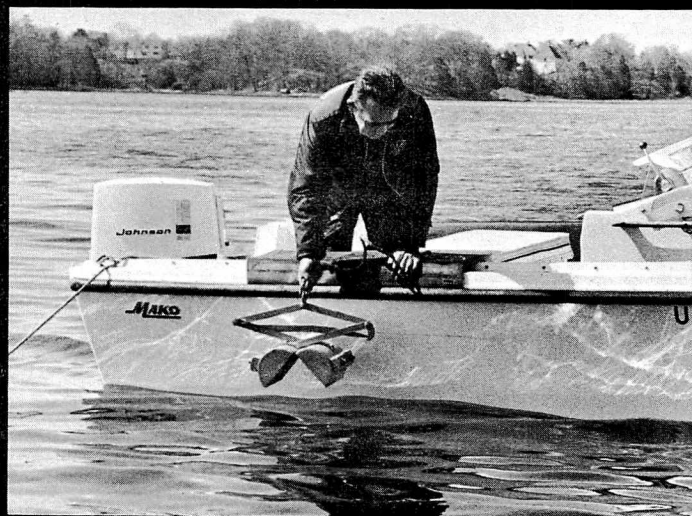
In their work, TSU staff professionals assessing shellfish waters are often called upon to be sailors as well. The flagship of the Division's "fleet" of boats is the Benjamin W. Brown (top), originally commissioned in 1937 as a PHS quarantine vessel and used at the Northeast TSU for offshore work where the water is too rough for smaller boats. The 65-foot, 40-ton, twin-diesel-powered craft is borrowed by U.S. Navy divers for submarine repair work. A sanitary engineer is shown using a sextant (middle) to get a shoreline bearing, and a marine biologist uses a hand-bearing compass (bottom) to determine his boat's position on a nautical chart, in both instances for location of sampling stations.

These charts (far right) of Atlantic Ocean areas off the New York Bight (top) and the mouth of Delaware Bay (bottom) show designated sites (centers of circles) where huge quantities of sewage sludge are dumped throughout the year. The areas within the circles, each circle having a radius of six miles, have been closed to the harvesting of ocean clams.





Marine Biology



Marine biologists of the Division's TSU's need to know how shellfish are affected by their environment and about the ecological conditions under which they grow. A marine biologist uses tongs (top left) to collect oysters for various types of analysis and lowers a Petersen dredge (top right) to collect bottom sediment to be examined for other marine organisms associated with shellfish ecology and for physical and chemical properties. Two marine biologists (middle) use a small dredge to collect oysters for microbiological analysis. In his office a marine biologist uses a planimeter on a nautical chart (bottom) to measure areas of shellfish growing waters.



shellfish sanitation



Eastern oyster



Surf or sea clam



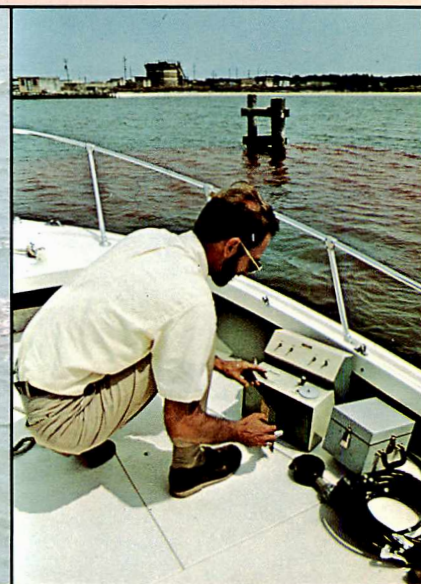
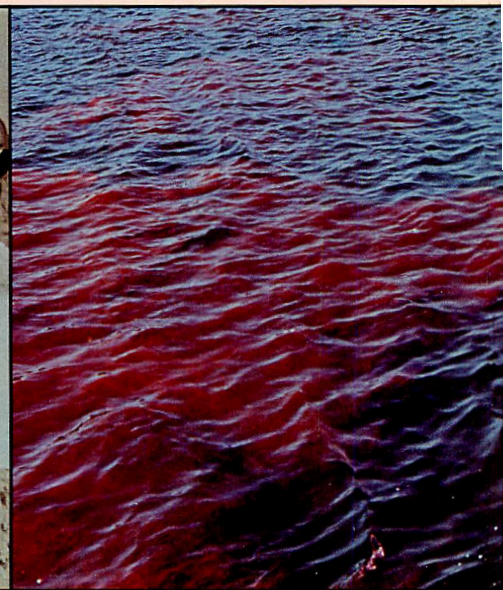
Quahog, a hardshell clam

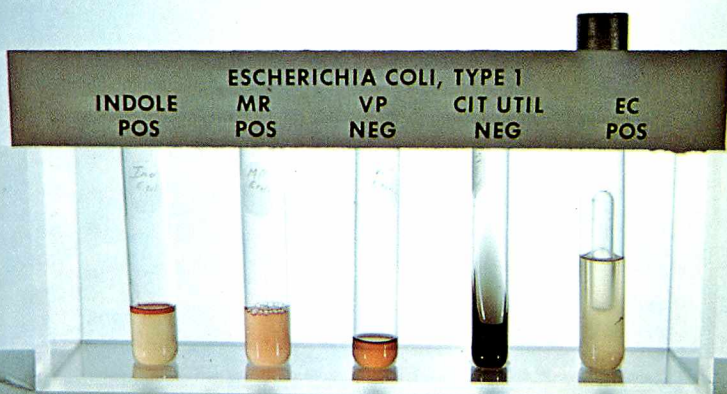


Soft shell clam

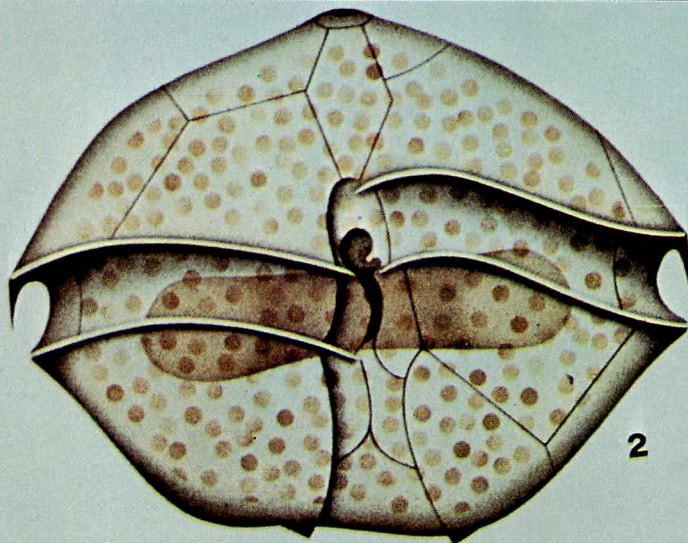


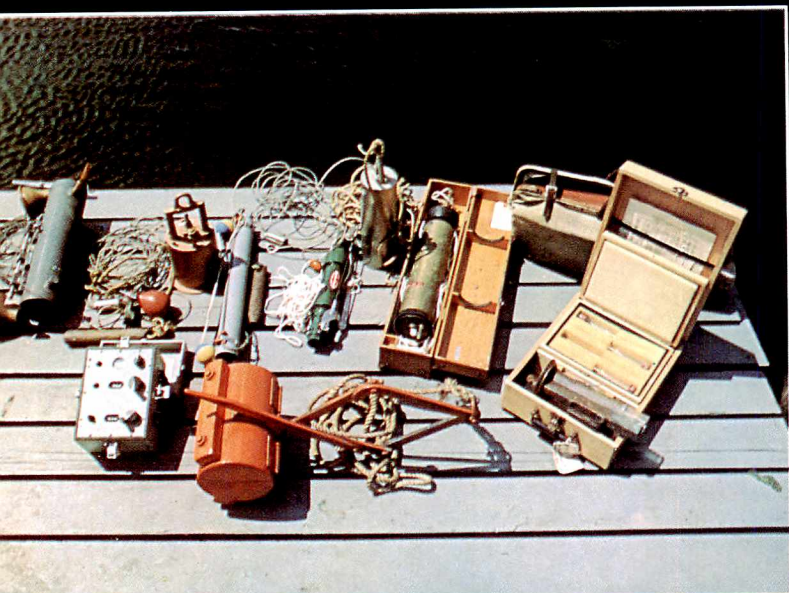
As part of a typical study by the Northeast TSU of the effects a new sewage treatment plant in a Maine community had on shellfish producing areas before and after construction, the unit made dye checks to determine the effects of chlorination of sewage. The first photo (left, top) shows the treatment plant; the second (left, second from top) shows dye in the contact chamber, the point where chlorine is added at the plant; the third (left, middle) shows dyed samples in bottles, taken at intervals to show the concentration of chlorine in the contact chamber after given times; and the fourth (right, middle) shows the dye representing chlorinated sewage at the outfall, where the sewage enters the water. Two marine biologists in a boat (left, bottom) deposit Rhodamine WT, a nontoxic fluorescent dye used to trace water masses, into the waters of Mobile Bay in a study of water flow. Later, one reads the concentration of dye in the water at a given point (right, bottom) with a fluorometer, which registers the concentration of dye flowing through a pump.





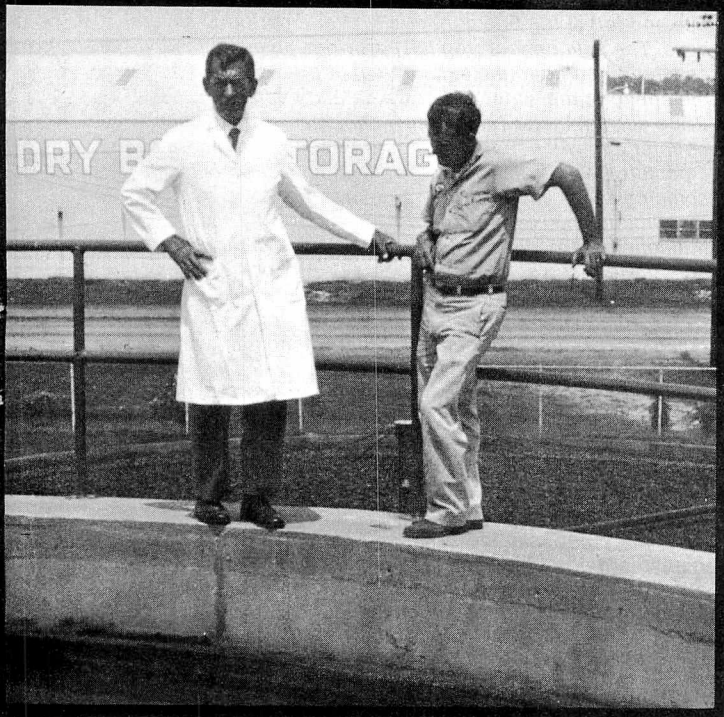
From the large flask, a bacteriologist (left, top) fills fermentation tubes, each also containing a smaller inverted tube, with brilliant green bile broth in a step of the liquid confirmatory procedure for determining the Most Probable Number of total coliforms. The tubes are then covered and sterilized and a loopful of culture from positive presumptive tests will be inoculated in each and incubated 24 to 48 hours. If gas from fermentation displaces the broth in the smaller tube, it confirms the presence of coliforms. The test tubes shown (right, top) represent the results of a series of four laboratory procedures (left to right) called the IMViC test, plus the E-C broth procedure, all used in identifying types of coliforms in samples. The results shown indicate the sample contained *Escherichia coli*, a fecal coliform. This is a typical sign (right, middle) erected by a State to indicate areas closed to shellfishing. Such posted signs may be erected on land or in water around the closed area. This scene of a small cove in Rhode Island (left, bottom) is blighted by an oil slick shown in the foreground. The hydrocarbon ingredients in petroleum oils are chemical contaminants that have been found in shellfish after spills. Oil contamination also can suffocate shellfish through interference with their breathing apparatus. The *Gonyaulax catenella* (right, bottom) produces a toxin that is responsible for paralytic shellfish poisoning, often fatal. If 80 micrograms of its toxin is found in a sample of 100 grams of shellfish from a given shellfish producing area, the State closes that area to shellfish harvesting. The drawing greatly enlarges the actual size of this flagellated protozoa.





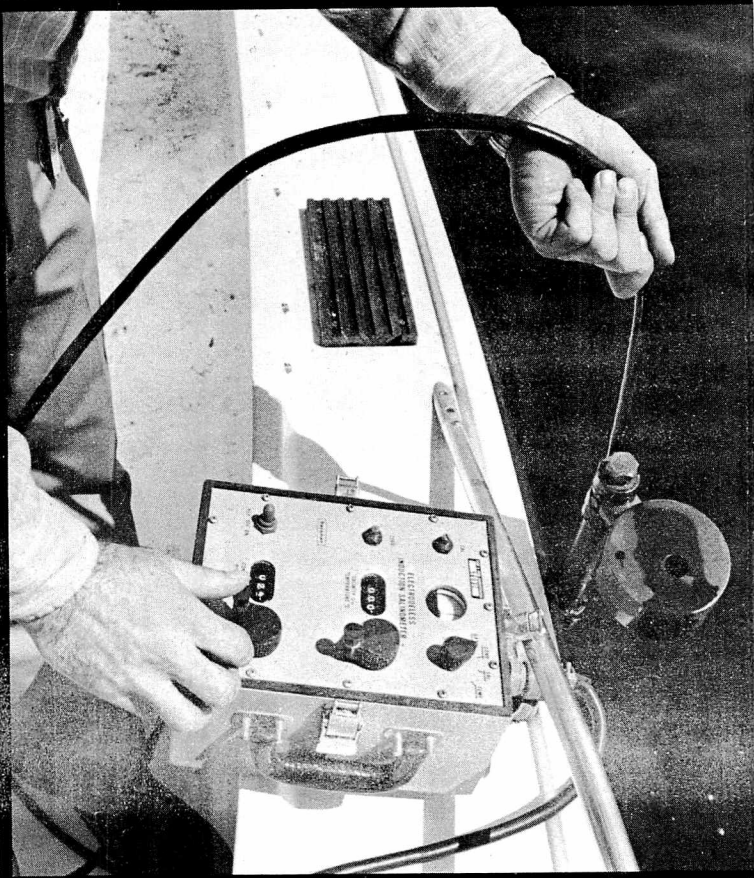
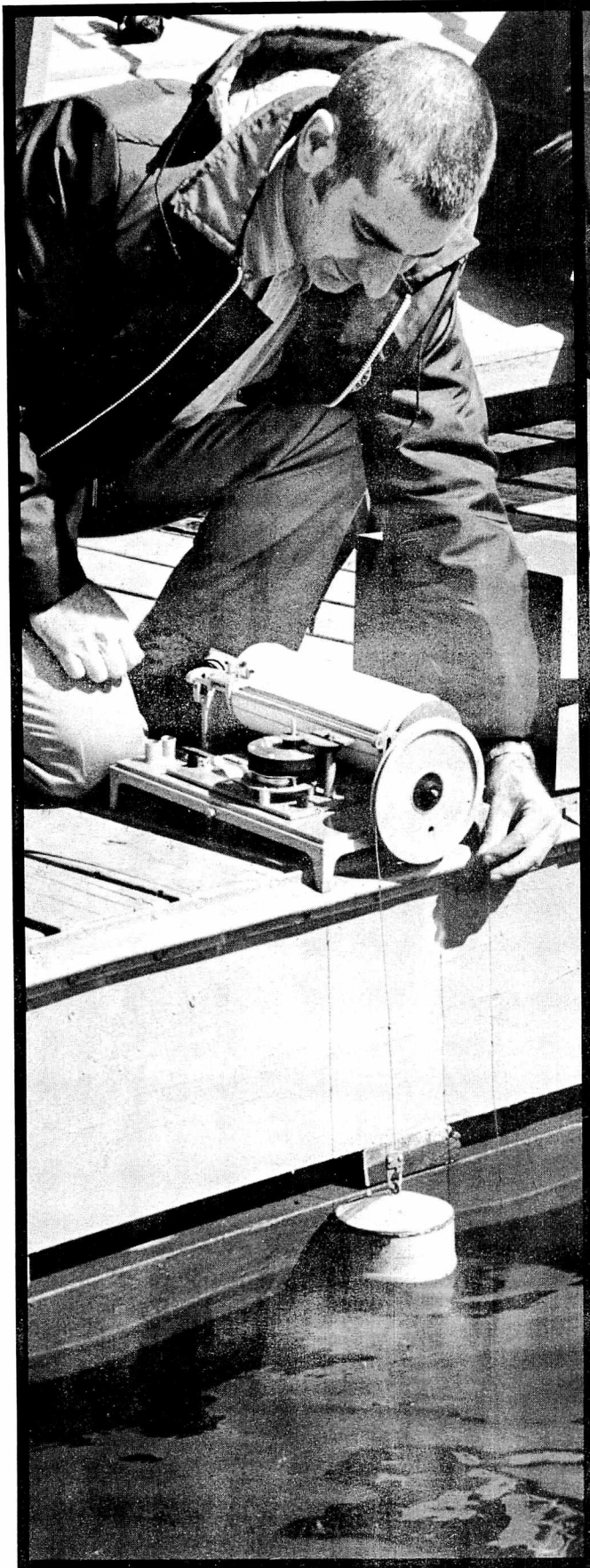
Some instruments used in water and sediment sampling (left) for various purposes are shown on the pier. At top left is a Van Dorn water sampler used to obtain samples at depths of 75 feet or more for chemical and physical analysis. Next to it is the small Zobell sampler, which breaks a glass tube at a given depth, creating a vacuum that draws water by the use of the rubber bulb to obtain bacteriological samples without further contamination. Successive samples are taken with additional glass tubes and rubber bulbs. Next, the somewhat bell-shaped Emery sampler for obtaining samples of bottom sediment without further contamination for bacteriological analysis. Next, the modified Kemmerer sampler (plastic with colored balls at each end) is used for water sampling for chemical and physical parameters, but if sterilized after each use, could be used for bacterial samples because the plastic is nontoxic. Next is a Suislaw water sampler, not yet put into use, as indicated by its new green paint and white draw cord. Next is a sampler (standing on end) that takes unaerated samples of water for laboratory measurement of the amount of dissolved oxygen, which is necessary for shellfish survival. The amount of dissolved oxygen is directly related to sewage pollution because micro-organisms in the sewage use up this oxygen. Next (in the narrow opened box) is a Kemmerer water sampler used to obtain samples for chemical analysis and such physical properties as temperature and turbidity. The toxicity of its brass construction precludes its use for bacterial sampling. Between the Kemmerer sampler and the opened chest is a bag of stream gauging equipment, including the Price current meter to measure the velocity of water flow. The opened chest (bottom right) contains a hydrometer to measure the density of water as affected by salts. The orange-colored Petersen dredge (bottom center) collects samples of bottom sediment that is usually analyzed for small organisms and sometimes for general chemical or microbiological content. The salinometer (lower left) has a long probe end and allows an instantaneous reading of water salinity at given depths.

Sewage Treatment Plant Studies

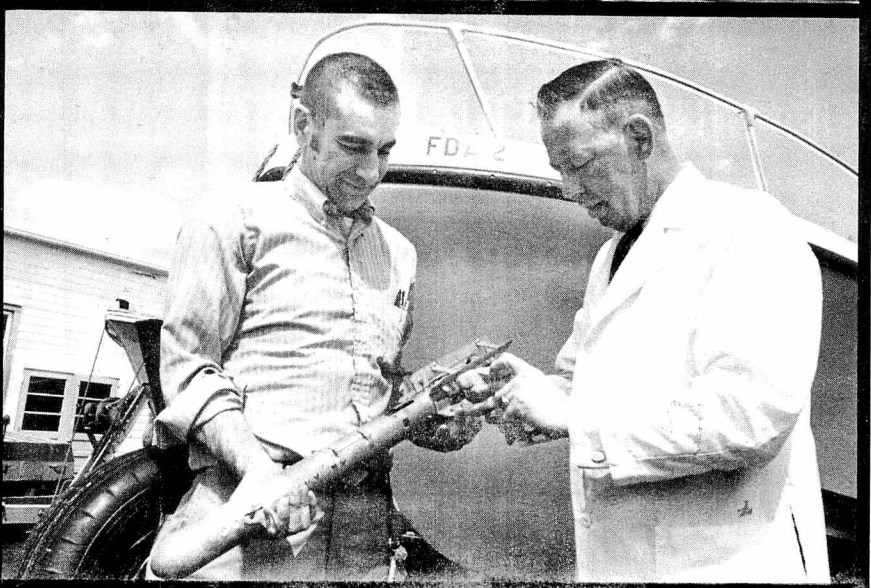


A major part of the Shellfish Sanitation Division's investigative and technological assistance to State control agencies is concerned with the existing or anticipated effects of sewage discharges on the quality of shellfish producing waters. Applications by municipalities for Federal financial assistance to construct or modify sewage treatment plants that may affect shellfish waters are reviewed before final approval by the appropriate TSU for the potential effect on harvest areas. Here a sanitary engineer examines engineering plans (top left) for such a plant. The TSU's also monitor the operation and efficacy of existing plants. Here a plant's chlorine analyzer (top right) is checked by a sanitary engineer. Those staff members who are commissioned officers in the Public Health Service wear PHS uniforms when on duty with the Northeast TSU because it is located on a U.S. Navy Seabees base at Davisville, Rhode Island. At a sewage outfall (middle) during low tide a sanitary engineer collects a sample of treated sewage effluent for later analysis. Atop the settling tank of a municipal sewage treatment plant (bottom), Albert H. Story (left), Ph.D., chief of the Gulf Coast TSU, discusses the operation with a plant employee.

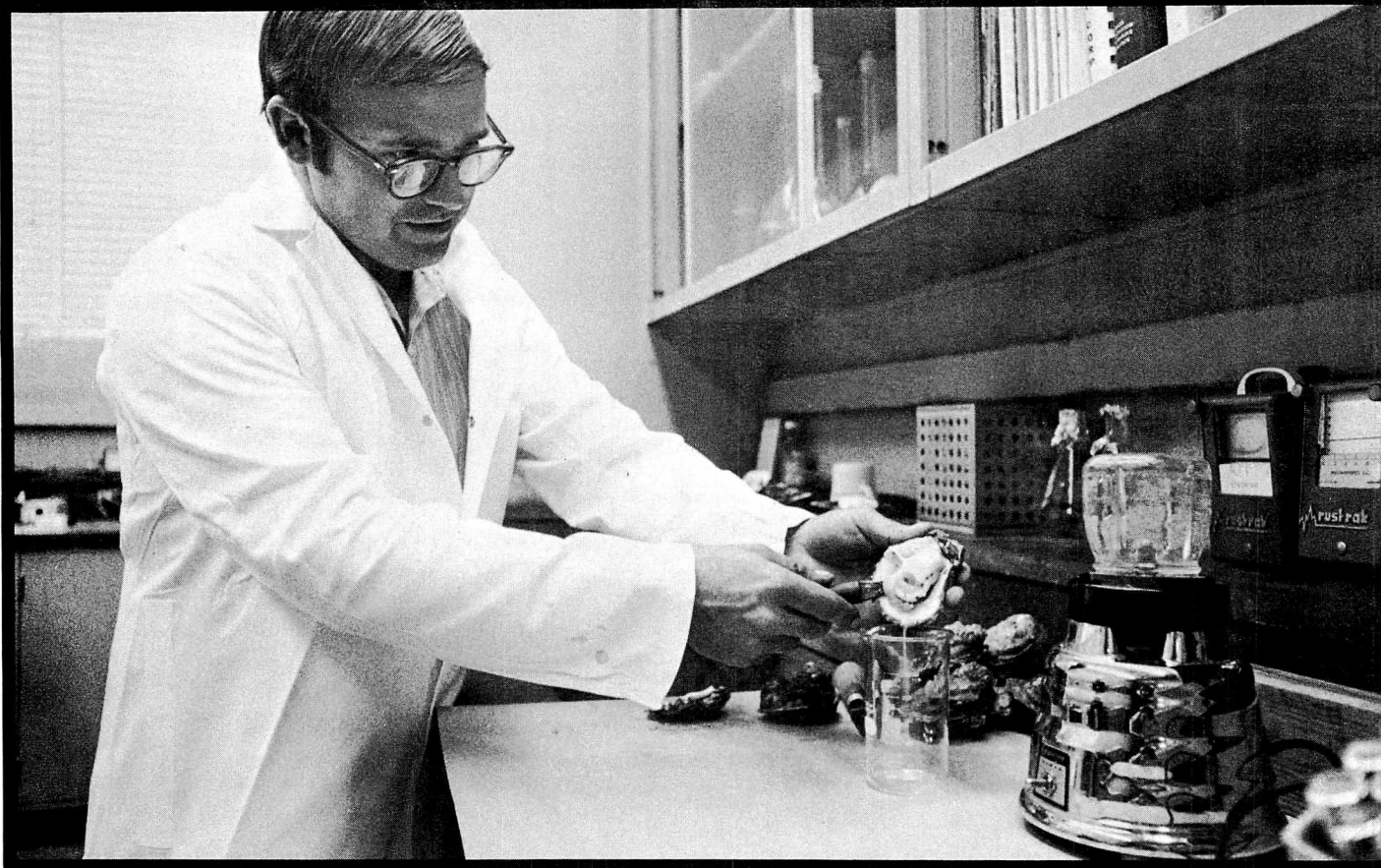
Oceanography and Hydrography



In determining the physical and chemical characteristics of the water in shellfish growing areas, the Shellfish Sanitation Division's technical service units use a number of oceanographic and hydrographic measuring or analytical instruments. The automatic tide recording device being installed on a pier (left) by a sanitary engineer will record the rise and fall of the tide continually over a period of several days. The salinometer (top left) provides an instantaneous and constant reading of the salt content of the water. To measure the speed of the water current, a sanitary engineer uses a Price current meter (top center) equipped with a "beep" counter and will time the number of beeps with his watch to calculate flow velocity. The drogue is an instrument with spinning vanes supported by a colored float and several thrown into an area of water can give an easily visible indication of the directions and patterns of water current and speed. Here two sanitary engineers (bottom center) toss a drogue overboard. The instrument being lowered into the water from a boat by a sanitary engineer (top right) is a dissolved oxygen water sampler that will collect water to be analyzed for content of dissolved oxygen, necessary to shellfish survival. Collecting a water sample (right, middle) for laboratory determination of its physical and chemical properties, a sanitary engineer (left) and a marine biologist use a modified Kemmerer sampler. The bomb-shaped instrument (bottom right) being shown to James Verber (right), senior oceanographer and chief of the Northeast TSU, by Santo Fufari, sanitary engineer and deputy chief, is a bathythermograph, which is heavy enough to drop through water to 200 feet at high speed and which records water temperature and depth as it descends.

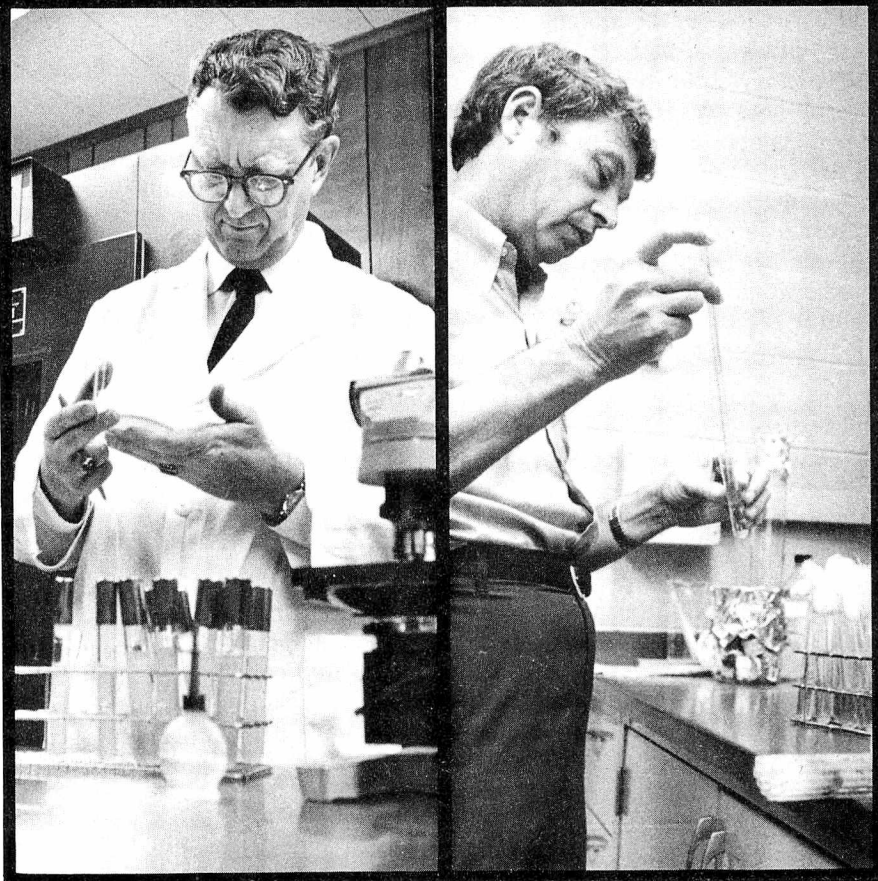


Microbiology





The microbiologists of the Division's TSU's must be familiar with the pathogens and indicator microorganisms that contaminate shellfish, know how to detect and enumerate them in the shellfish or in water or sediment, and know how to evaluate the threat to human health. Two marine biologists (top left) are using a bottom water sampling device designed by the Gulf Coast TSU for aseptic collection of samples. In the laboratory, a marine biologist prepares a sample from oysters (bottom left) collected for microbiological analysis. Oysters are washed in a depuration tank by a microbiologist (top right) prior to the depuration (purifying) process. In photos at bottom right, a microbiologist observes a Petri dish (left) following a plate count of bacterial colonies inoculated from a water sample, and a pipette is used by a microbiologist (right) to inoculate a water sample into a primary fermentation tube in a multiple tube fermentation test for enumerating coliform bacteria.



field reports

ATLANTA DISTRICT An entry of candy-filled bracelets from Hong Kong is being detained at Savannah, Georgia. The bracelets, each accompanied by two toy rings, are formed of transparent flexible tubing, the ends of which are joined by a removable rubber plug. Each bracelet is filled with multicolored candy beads, similar to those contained in the "Hippy Sippy," which was the subject of an FDA-initiated recall in mid-1969. In addition to the obvious hazard that pellets might be drawn through the tubing into the bronchial tube, laboratory examination showed that the articles also contained metal staples and wood splinters. FDA charged that the bracelets violate both the Child Protection Act and the Food, Drug, and Cosmetic Act. The 3,900-pound shipment is valued at \$2,300.

BALTIMORE DISTRICT A Norfolk, Virginia, importer rejected a toy shipment from Hong Kong because of conspicuous labeling reading, "Shoot the Cops." The product, packages containing a plastic gun, hand grenade, and knife, met the requirements of the Federal Hazardous Substances Act as well as all other current Federal laws and regulations; but because of the labeling, the importer brought the matter to the attention of the Baltimore District Compliance Branch. On his own initiative, the importer advised the District that he would immediately inform the foreign manufacturer that the toy was unacceptable as labeled. He added that he would suggest in strong language that the manufacturer refrain from using such provocative labels on products offered for future entry into this country.

A laundry detergent labeled as "***Ecolo-G Controlled Suds. Stops Pollution. No Phosphates! No Enzymes—No NTA (Nitrilotri-acetate) Laundry Detergent**" was seized at Landover, Maryland, on March 8, the charges being based on misbranding under the Hazardous Substances Act. The FDA charged that packages did not bear adequate labeling warning consumers of possible hazards if the product were accidentally misused. FDA's biological testing had shown the detergent to be toxic. Sodium metasilicate, a constituent of "Ecolo-G," is a caustic substance corrosive to intact skin, harmful if swallowed, and the cause of severe eye irritations.

The seizure of 146 cases was originally initiated at the request of FDA's Office of Product Safety, Newark Section, New York District, and with the cooperation

of the United States Attorney's Office, the U.S. Marshal's Office, and Baltimore District personnel, was accomplished immediately following the filing of the complaint for forfeiture by U.S. attorney, George Beall. A similar seizure was made in New York District and, subsequently, consent decrees were filed in both Districts providing for relabeling and bringing the product into compliance with the law.

BOSTON DISTRICT A U.S. marshal seized 68 34-pound cans of feta cheese valued at about \$1,850 on March 17 at Methuen, Massachusetts. The cheese, imported from Greece, was found adulterated. It contained the unsafe food additive, benzene hexachloride.

Judge D. J. Murray granted a temporary injunction against J. Fleishaman & Co., Inc., an egg processor at Roxbury, Massachusetts. The injunction requires that the firm perform a visual and organoleptic examination of all shell eggs after they are received. Prior to washing, those eggs which are fecal covered, have cracks in the membrane, have egg magma leaking from the shells, are decomposed, or are unfit for food must be segregated for nonfood use. After segregation all eggs must be washed prior to use, inspected again, and removed if unfit for food.

BUFFALO DISTRICT U.S. Customs agents arrested the driver of a hearse carrying two bodies and an undeclared quantity of drugs from Canada at the Peace Bridge in Buffalo on May 16. A total of 138 bottles of phenylbutazone tablets, 388 bottles of phenylbutazone injectables, and 72 bottles of chloramphenicol injectables was seized with the hearse. The tablets involved were labeled and the liquids unlabeled. Buffalo District analyzed and identified the products for Customs. The driver of the hearse has been charged with smuggling.

CHICAGO DISTRICT Chicago District consumer specialists, with the cooperation of the Region V product safety consultant, have developed a set of five transparencies for overhead projection concerning the requirements of the Hazardous Substances Act. They cover this act and its amendments, the Child Protection Act of 1966, the Child Protection and Toy Safety Act of 1969, and the Poison Prevention Act of 1970.

As a result of extensive epidemiological studies, two FDA inspections, and four recalls, a large candy manu-

facturer permanently closed one of its older physical plants after becoming convinced that the plant could not be operated satisfactorily in compliance with the law.

An initial FDA inspection about two years ago resulted in "an extremely aggressive" cleanup operation in which great quantities of water and steam were used. As a result, *Salmonella* was able to reproduce and live under the more favorable conditions created by the use of the water and steam. The obvious consequence was FDA's finding of more widespread *Salmonella* during a second inspection nine months later.

CINCINNATI DISTRICT Deputy Regional Food and Drug Director Clifford G. Shane appeared on the 90-minute program, "Community Forum," on Cincinnati's radio station WCKY on March 8. The program included an informal interview regarding FDA's activities, followed by an audience participation segment during which listeners telephoned in questions and statements. The station claims a 30-State listenership coverage.

The program was one of several consumer-oriented activities recently participated in by the Cincinnati District. Mr. Shane, District Veterinarian Homer R. Smith, and Consumer Specialist Catherine A. Knarr have made a number of appearances, including talks before the Ohio State Home Economics Meeting; the North Central Veterinary Medical Association; "You, the Consumer," a television program; an AFL-CIO counseling course on consumer protection; a professional workshop for the Hamilton County Educational Association; the Greater Cincinnati Consumers Conference; and professional supervisors and 40 presidents of various Senior Citizens Centers.

DALLAS DISTRICT Dr. Kearby Fugate, microbiologist with the Dallas District, has been invited to appear before the Second International Congress for Virology held in Budapest, Hungary, June 27 to July 3. "Food-borne Viruses" will be the topic of several seminars during a portion of the international meeting. Also to be discussed will be the "International Collection of Data on the Presence of Viruses in Foods," convened by Dr. J. Mensik, Brno, Czechoslovakia, and Dr. Dean Chiver, University of Wisconsin. Dr. Fugate will present a paper describing his work in isolating human enteroviruses from Gulf Coast oysters.

DENVER DISTRICT Four seizures were made in Cheyenne, Wyoming, of medicated animal feeds produced by John Ewing Company, La Salle, Colorado, in January. Charges included lack of an effective New Animal Drug Application, failure to comply with good manufacturing practices, false and misleading labeling, and inadequate warning statements on labels. The feeds totaled 38 tons and were valued at \$3,000.

In February, approximately 123 drums of Formula 707 Conditioner and 1,200 accompanying pamphlets

were seized in Salt Lake City, Utah, on charges that the lot was a new animal drug without an effective New Animal Drug Application, and was misbranded and ineffective. The drug was claimed to be effective to condition horses of all ages, to quiet nervous horses, and to enable horses to win races. It was also manufactured and shipped to Utah by John Ewing Company, La Salle, Colorado.

DETROIT DISTRICT Prosecution against Aster Nut Products, Inc., Evansville, Indiana, a manufacturer of granulated peanut products, was terminated May 21. FDA charged that the firm had introduced peanut granules adulterated with insects and insect fragments into interstate commerce. The defendant changed its previously entered pleas of "not guilty" to "guilty," and was fined a total of \$1,200 plus costs by U.S. District Judge Cole J. Holder.

A total of 77 persons representing 35 firms attended a workshop for the soft drink industry jointly sponsored by FDA's Detroit District and the Food Inspection Division, Michigan Department of Agriculture. Deputy Regional Food and Drug Director Alan L. Hoeting, Food and Drug Officer Carroll L. Dennis, Michigan Department of Agriculture officials, and industry personnel participated in the workshop, which was held at Michigan State University, East Lansing, Michigan, on March 31. The subject matter included microbial spoilage, fair packaging and labeling, and sanitation.

KANSAS CITY DISTRICT Leonard L. Blanton, chief inspector of the Kansas City District, was reelected secretary-treasurer of the Mid-Continental Association of Food and Drug Officials at its annual meeting on March 1-2. Other officers named were Ronald L. Spencer of the Oklahoma Department of Health, Oklahoma City, president, and Melvin Lynch of the Topeka-Shawnee County Health Department, Topeka, Kansas, vice president.

Dennis D. Manske, supervisory chemist of FDA's Kansas City District, was among the speakers at the gathering in Fort Smith, Arkansas. A total of 82 regulatory officials from Arkansas, Kansas, Missouri, Oklahoma, and Texas attended.

Presiding was Coy V. Dildy of Camden, Arkansas, president. The meeting featured speakers from industry and Government who discussed such issues as industry responsibilities to the consumer, food plant sanitation, and the national problems of pesticides and pollution. A panel of State program directors discussed drug control within each of the represented States at the meeting. The group also toured the American Can Company plant in Fort Smith.

Other speakers included John Dean, director, farm relations, Dean's Foods of Rockford, Illinois; Claude Todd, president, Stilwell Canning Company, Stilwell, Oklahoma; Dr. James Canada, Robert Price, and Rudy Winbern, Quality Control Division, Gerber Products

Company, Fort Smith, Arkansas; and George Purvis, Arkansas Game and Fish Commission.

The Association will meet in Tulsa, Oklahoma, in 1972 and in Kansas in 1973.

Complaints received by the Kansas City District that a locally bottled soft drink had an oily or kerosene taste precipitated a joint inspection of the bottler by State and FDA inspectors. Their inspection of the operation disclosed that a broken valve on a water line contaminated water used in beverages with oil from bottling machinery. An estimated 1,800 cases of bottled beverages was recalled from the retail market and the firm eventually destroyed approximately 4,500 cases.

LOS ANGELES DISTRICT Mercury found in frozen swordfish resulted in seizure of two lots, totaling 3,500 pounds, at Long Beach and Wilmington, California. The fish had been caught off the coast of California. The District has found 35 other lots of domestic swordfish to have excessive mercury content, and seizure actions for these are in process. The survey of swordfish in storage in southern California also uncovered 80 lots of imported fish high in mercury content. Importers are arranging to reexport these to the original Japanese shippers.

Prima Natura Night Veil Concentrate, a cosmetic made by Avon Products, Inc., at its plants in Pasadena, California, and on the East Coast, was recalled by the firm after its control laboratory found pseudomonas bacteria in the output from each plant.

MINNEAPOLIS DISTRICT Sue Hovik, news correspondent for the *Minneapolis Star* and zealous reporter of FDA activities, notified District officials of a stuffed Easter rabbit that contained straight pins. She had received a complaint from a man who had purchased one for his grandchild. Mrs. Hovik purchased a sample at a local drugstore affiliated with a Minneapolis chain and presented it to the Minneapolis District for evaluation. It was decided that the toy was dangerous, and the drug chain was requested to remove it from its shelves.

The president of the drug chain personally handled the removal action and immediately returned all rabbits to the source in New York City. The New York firm explained that the straight pin in the rabbit was a manufacturing error because the pin was to hold parts of the toy in place only until the glue dried.

Mrs. Hovik wrote an article including a picture which appeared in the *Minneapolis Star* on Monday, March 29, with the headline, "This Bunny is Not Funny for Little Honey," describing the dangerous toy.

NEW ORLEANS DISTRICT Import detentions for March prevented the distribution of \$2,800 worth of misbranded cheese, \$680 worth of misbranded frozen rock lobster tails, \$820 worth of misbranded canned tomatoes, \$660 worth of misbranded paprika, and \$4,900 worth of misbranded canned mushrooms. Products detained on adulteration charges included \$4,000 worth

of black pepper, \$2,500 worth of plaice, \$233 worth of cocoa powder, \$7,700 worth of coffee, and \$5,000 worth of blue poppyseed. In addition, \$625 worth of toys was detained as banned hazardous substances.

NEW YORK DISTRICT Newark Section Inspector Ronald E. Bernacki accompanied a deputy U.S. marshal during seizure of 3,752 10-pound boxes of Bohack's "No Phosphate Detergent" in Brooklyn, New York, on March 8. The product was misbranded within the meaning of the Hazardous Substances Act in that it contained the caustic ingredient sodium metasilicate without the necessary warning statement on the package.

The detergent is manufactured as "Ecolo-G Controlled Suds" by North American Chemical Corporation, Paterson, New Jersey. The firm packages the product for Bohack and, under private labels, for other supermarket chains. Samples were obtained in Brooklyn and Baltimore and seizures were made in both cities. Events leading to the seizure actions began February 24 when FDA's Bureau of Product Safety requested Newark Section, New York District, to obtain samples of "Ecolo-G" detergent.

During the subsequent Brooklyn seizure, the deputy marshal and inspector were joined by a camera crew from CBS Television, who attempted to film the entire sequence from presentation of identification and warrant to actual seizure of goods. Bohack management ordered its security guards not to allow newsmen into the warehouse, but the camera crew somehow gained entrance and filmed part of the seizure accomplishment before it was escorted from the premises.

The Bureau of Product Safety approved a cautionary label submitted by North American Chemical Corporation, and on March 15 the firm began recalling the product under all its brand names for relabeling. By court order and under the supervision of an inspector at FDA's Newark Section, the firm began relabeling the detergent taken in the Brooklyn seizure on April 5 and was to relabel the Baltimore-seized goods at a later date.

New York District's trial of Bronx Drug Company, Inc., and owner Isaac Zonana was successfully concluded in the Southern District of New York in March. The defendants were found guilty of storing drugs in a manner inconsistent with current good manufacturing practices and in violation of a permanent injunction imposed in November 1964. Inspection of the company's buildings in the Bronx and Mount Vernon, New York, by District officials in January 1968 revealed "haphazard" storing of drugs. A secret room was also discovered in which drugs were improperly stored and inaccurately labeled. The firm was fined \$1,000, as was Mr. Zonana.

Mr. Zonana's record includes a guilty plea to charges in Westchester County, New York, of possession of stolen drugs. Mr. Zonana surrendered his business license at a hearing of the New York State Board of Pharmacy on the charges of selling misbranded drugs, outdated and uncertified antibiotics, and narcotics without proper authorization. A 1970 inspection and Mr.

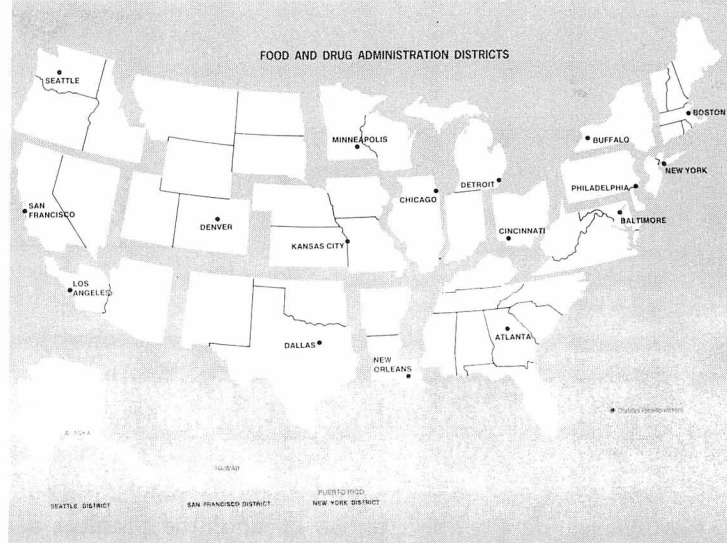
Zonana's testimony in court indicate that he no longer has any connection with the drug industry.

PHILADELPHIA DISTRICT Philadelphia has obtained its first seizure of drugs—based solely on charges of violation of good manufacturing practices with an accompanying misbranding charge—without analysis of samples. Seizure papers were filed on April 1 against two large lots of a prescription sedative and tonic preparations in possession of a drug manufacturer at Philadelphia. The lots were manufactured without company controls, including failure to identify and assay raw materials and to assay the finished product. The lots were discovered during an Intensified Drug Inspection of the firm.

Philadelphia District used its entire inspectional force, bolstered by ten members of its laboratory, to trace down cans of suspect Bon Vivant Vichyssoise soup distributed in the District. A total of 900 cans of the suspect code V141, in which *Clostridium botulinum* was found, was received by Trymore Foods, Philadelphia. About 80 percent of the cans have been accounted for and an investigation continues to recover the remaining cans. Three more Pennsylvania distributors of Bon Vivant Vichyssoise have been contacted in the search for the suspect cans, as well as a major New Jersey firm which distributes the product in Pennsylvania and Delaware.

A Berwyn, Pennsylvania, housewife who exhibited symptoms of bacterial poisoning after consuming portions of the soup has been released from the hospital upon recovering without developing the acute symptoms of botulism.

SAN FRANCISCO DISTRICT Cargill, Inc., a dealer in grain and vegetable oils, advised FDA's San Francisco



office on March 17 that a tanker of crude coconut oil it had purchased for import from Zamboanga, Philippines, was suspected of containing a human body. The suspect tank was sealed off and held separate from the other tanks of oil on the ship in Oakland, California. When the tank was drained, a human body was indeed found and was later identified as that of a Philippine dock security guard suspected to have jumped into the hold in an attempt to stow away on the ship. The lot of 1,000 liquid tons of coconut oil was detained and was to be released for nonfood use only.

SEATTLE DISTRICT The Seattle District held the fourth FDA-NCA Canned Salmon Workshop in Seattle on March 24. The workshop discussed good manufacturing practices as they apply to the salmon industry and was oriented to the production line employee. Attendance exceeded 200 persons and included all top level management personnel of the salmon-canning industry.

FDA 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. 5604/20th & 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. (at 30th St.)
Rm. 700/Brooklyn, N.Y. 11232

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

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

news highlights

Public Urged to Stop Eating Swordfish Because of Excessive Levels of Mercury

The FDA has recommended that the public discontinue eating swordfish unless or until the problem of excessive levels of mercury can be remedied. Commissioner of Food and Drugs Charles C. Edwards, M.D., announcing completion of a three-month program of testing swordfish for mercury on May 6, said an unacceptable percentage of the lots examined contains excessive levels of this metal.

The announcement came after test results showed only 42 of 853 swordfish samples to be within FDA's 0.5 parts per million mercury guideline and after review of the data by an Ad Hoc Committee of scientific and medical experts from this country and Canada. Meeting in Washington on April 28, the Committee expressed support (11 of 13 non-FDA members) for the 0.5 ppm guideline and said it was unable to suggest any basis on which swordfish consumption might be continued without a possible health hazard.

"Furthermore," said Dr. Edwards, "despite extensive recalls by major distribution chains, despite FDA seizures totaling 832,000 pounds, and despite overall cooperation of swordfish brokers in withholding up to four million pounds from the market, the Agency is still finding swordfish available to the public that are at or over the guideline.

"On this basis and in view of full evaluation of test data by FDA and by outside experts the FDA has no choice but to recommend at this time that the public not eat swordfish."

The warning is particularly important for children and for women of child-bearing age, Dr. Edwards said, adding that the Agency will continue to take all possible steps within its authority to keep swordfish with excessive mercury content off the market. He said FDA will continue to detain and to turn back at ports of entry all foreign swordfish over the 0.5 ppm guideline, and committed the Agency to continued use of its seizure authority wherever substantial lots of such fish can be located.

Through the National Fisheries Institute, the swordfish industry has indicated it already is trying to develop an effective program to certify for marketing the 5 to 8 percent of each catch likely to meet FDA mercury guidelines. Such a program would require FDA approval, including a labeling system for easy consumer identification of acceptable fish.

In thanking the advisory committee for responding to FDA's call on short notice, Dr. Edwards stressed

that "FDA took this extraordinary step for confirmatory consultation and out of a determination to exhaust all reasonable avenues of advice and scientific expertise."

Government agencies represented on the Committee in addition to FDA and the Center for Disease Control (Health Services and Mental Health Administration), were the National Oceanic and Atmospheric Administration and the Environmental Protection Agency. Non-government representatives from the United States included experts from three major universities, as well as from the Canadian Food and Drug Directorate and the Canadian Department of Fisheries and Forestry of Ottawa.

Canada, a major exporter of swordfish, previously has supported FDA actions and no longer exports the fish to this country.

Dr. Edwards said, "We are aware of the hardships being imposed by these actions on a legitimate industry which bears no blame for the existence of the methyl mercury hazard. At the same time under our obligation to consumer safety, we are compelled to take the actions announced today."

On May 1, FDA noted, the Small Business Administration (SBA) declared that the present swordfish situation constituted an economic disaster for swordfish ship owners, processors, and distributors. SBA said it would extend financial assistance where appropriate to alleviate economic losses suffered by individuals and small businesses in the industry.

The argument has been made that the FDA guideline as applied to swordfish is unnecessary, unrealistic, and should be raised.

"This argument is scientifically invalid," commented Dr. Edwards. "Furthermore, it is of no practical value when we consider that 89 to 95 percent of all swordfish tested not only is above the present guideline, but substantially so."

The average level of mercury in the swordfish tested exceeds one part per million, twice the FDA guideline. More than 8 percent of the samples showed mercury higher than 1.5 parts per million.

Dr. Edwards emphasized that with the exception of swordfish, the FDA at this time finds no substantial problem of mercury contamination in deepwater food fish. Inability to establish adequate control over swordfish is due in part to the fact that the swordfish industry largely consists of many small, scattered operators lacking both organization and finances to establish industry-wide controls.

Swordfish consumption in the United States is approximately 26 million pounds annually, of which 22 million pounds is imported from Japan and Canada.

The rest is caught seasonally in United States coastal waters, mainly off the Northeastern States and California.

FDA has been in contact with and will discuss further with other governments the scientific basis for its action.

Regional Warning to Consumers Notes High Lead Levels in Dinnerware Items

Consumers in Maryland, Virginia, the District of Columbia, and Harrisburg, Pennsylvania, have been warned by FDA to avoid using a brand of imported English dinnerware after analysis of the product revealed very high levels of leachable lead content.

The dinnerware, imported from England by Seymart Importing Company, Inc., New York, New York, and sold regionally by nearly a hundred Food Fair and Pantry Pride Food Chain Stores, is labeled on the back of each item: "Royal Blue Ironstone England" with a picture of a unicorn.

The source of the contamination is suspected by FDA to be a blue decal floral pattern used to decorate the product. Hollow ware pieces of the line, such as cups, coffee and tea pots, mugs, and casseroles which lack the design on interior surfaces have been found safe, the Agency said.

Lead amounts leached from samples of the dinnerware ranged from 18 parts per million to as high as 196 ppm in plates. A number of dishes averaged around 100 ppm. The FDA guideline for leached lead in pottery is 7 parts per million.

An investigation was begun after the Agency learned that a Baltimore County child became ill, apparently from eating a fruit preparation stored in a Blue Ironstone bowl. The Maryland State Department of Health and the Baltimore City Health Departments cooperated with and assisted FDA in its investigation.

More than 300,000 pieces of the dinnerware were sold only during the period of September to December 1970, FDA said, and are presumed to be in the hands of consumers.

Food Fair Stores, Inc., which has been cooperating with FDA in the matter, has informed FDA it will refund the purchase price of the items in question to consumers who return them to the Pantry Pride and Food Fair Stores from which they were purchased.

Label Programs on Fats and Nutrients Inaugurated to Keep Consumers Informed

The Food and Drug Administration is announcing major program initiatives to better inform consumers of the nutritional quality of processed foods.

The first initiative involves regulatory proposals requiring food manufacturers to disclose on product labels the name and source of all fat ingredients and allowing

label declarations on some foods to disclose the kinds of fatty acids present.

Under the mandatory provisions, all labels of processed foods would give the specific animal or vegetable source (such as beef fat, chicken fat, cottonseed oil, corn oil). This contrasts with present industry practice of broadly labeling oils and fats only as "shortening" or "vegetable oil." If the fat is hydrogenated, the labeling would disclose the fact. (Hydrogenation is a chemical technique to increase consistency and prolong shelf life). Where combinations of fats are used, all names would be listed in order of predominance.

Food products not labeled according to the proposed provisions would be subject to regulatory action by FDA one year after a final order is promulgated.

The FDA proposals also would allow foods offered for special dietary use to show on the label certain information about fat content and quality. If manufacturers choose to include such information, the label, in addition to disclosing hydrogenation, must bear an accurate listing of:

1. The percentage of polyunsaturated fatty acids, calculated as the glyceryl ester of the total *cis*, *cis*-methylene-interrupted polyunsaturated fatty acids and in equal prominence the percentage of saturated fatty acids, calculated as the glyceryl ester of the fatty acids, both being percentages of the fat as prepared for consumption according to directions.
2. The total fat content in terms of percentage of the food, as prepared for consumption according to directions.
3. The total fat content in terms of the percentage of the total calories in the food provided by fat.
4. The total number of calories provided by an average serving of the food.

All other labeling uses of these terms or suggestions that the food contains "no cholesterol" or "less cholesterol" would continue to be prohibited.

Charles C. Edwards, M.D., Commissioner of Food and Drugs, said: "The purpose of the proposed fat labeling regulations is to help consumers identify the amount, source, and type of fat in the foods they buy. We are not recommending changes in American dietary habits." The proposals are to be published in two separate documents in the June 15 *Federal Register*. Interested parties will have 90 days to comment.

The second major nutritional labeling initiative announced involves test programs being carried out to measure effectiveness and usefulness to consumers of various nutrient labeling. Under the plan, Giant Foods, Washington, D.C., and the Jewel Company, Melrose Park, Illinois, national retail food chains, each is conducting a nutrient labeling test on selected products. Other test plans are anticipated.

FDA previously reported that several types of experimental nutrient labels developed by the Agency are being studied by the Consumer Research Institute, using a consumer panel test.

In announcing the test programs, Commissioner Edwards emphasized a multiple approach.

"No one study is going to determine the best and most meaningful way to bring improvements in food labeling. We are, therefore, investigating a variety of approaches through a number of sources." The purpose of all the studies, he concluded, "is to gather information which FDA can use to evaluate consumer understanding, acceptance and use of nutrient labeling on food products." The Agency hopes to have final test results and make proposals for further actions affecting food labeling by early next year.

Citrus Growers, Orange Drink Processors Agree on Labeling for Juice Dilutions

Eastern and western citrus growers and processors of orange drinks have agreed on labeling changes to disclose the percentage of pure orange juice in diluted orange beverages, the FDA has announced. The agreement was reached unanimously June 3 among some 35 Florida, California, and Texas growers and orange drink processors at a meeting with FDA officials in Washington. The meeting was held at the request of the industry to achieve agreement on standards for diluted orange beverages.

The agreement means that the percentage of orange juice in any diluted orange beverage product will be stated as part of the product's name. For example:

XYZ (Brand) Orange-Juice Drink,
contains not less than 35 percent
orange juice.

General agreement was also reached in establishing categories of diluted orange drink according to orange juice content in the beverages. "Orange drink," "orange-juice drink," and "orangeade" were cited by FDA as examples of such categories. Label disclosure of ingredients other than orange juice, not fully resolved at the meeting, is expected to be settled in the near future, FDA said.

The Agency also said it would shortly publish in the *Federal Register* a proposed standard covering the beverages. Earlier standards, published as regulations in 1968, were stayed in July of that year while an industry compromise was pending.

Pure orange juice, orange concentrates, and frozen orange juice, covered by existing standards, will not be affected by a diluted orange beverage proposal.

New Regulation Restricts Train Dumping On Tracks of Sewage, Other Pollutants

A regulation restricting the discharge of human and other wastes from railroad conveyances becomes final June 8 as an amendment to the Interstate Quarantine

Regulations of the Public Health Service.

Under the revised regulations, "new railroad conveyances" (those placed in service for the first time after July 1, 1972), shall not discharge "human wastes, garbage, waste water or other polluting materials" except at servicing areas approved by the Commissioner of Food and Drugs. However, materials that have been suitably treated to prevent the spread of communicable diseases may be discharged at places other than stations.

Existing conveyances shall not discharge similar polluting materials after December 31, 1974, except at designated servicing areas. If justified, the Commissioner of Food and Drugs may extend this period but not beyond December 31, 1977. If suitably treated, such wastes may be discharged at places other than railroad stations.

The regulation is being published in the *Federal Register* of June 8. It should be noted that the terms "waste water or other polluting materials" do not include drainage of drinking water taps or lavatory facilities.

FDA first proposed changes in the regulation in a notice published in the *Federal Register* October 15, 1970.

Some Home Liquid Drain Cleaners Banned For High Content of Caustic Chemicals

The sale of household liquid drain cleaners containing more than 10 percent sodium or potassium hydroxide would be banned in 60 days under final regulations being announced June 9 by the Food and Drug Administration. The regulations are being issued under the provisions of the Federal Hazardous Substances Act.

Exemption is possible for products containing more than 10 percent sodium or potassium hydroxide only if packaged in compliance with requirements of the Poison Prevention Packaging Act of 1970. In its first meeting, the newly appointed Poison Prevention Packaging Act Technical Advisory Committee agreed to an interim testing protocol and will consider special packaging that will be suitable for these hazardous products.

Strong solutions of sodium and potassium hydroxide are highly corrosive and fast acting when ingested. No antidote is of value in preventing esophageal injury. FDA reports show 271 children accidentally ingested liquid drain cleaner in the past four years. Of these, 114 were hospitalized and three died.

The two major alkali liquid cleaner producers, which account for approximately 90 percent of the market, already have advised FDA that they have reformulated their products to contain less than 10 percent sodium and/or potassium hydroxide.

The regulation, scheduled to be published in the *Federal Register* of June 10, allows 30 days for the filing of objections by anyone who would be adversely affected by the final order.

state actions

Revised Testing Program Wheat stored on the farm instead of in public warehouses will not be included in the quality and protein testing program conducted by the Pacific Northwest Grain and Quality Committee on the 1971 wheat crop as originally planned (see FDA PAPERS, February 1971, State Actions).

Dale Stuart, marketing specialist with the Agricultural Development Division of the Oregon Department of Agriculture and coordinator of the program covering the testing, said representatives of the Pacific Northwest wheat industry reversed the original decision because they felt the time required for on-the-farm testing would result in too much delay in compiling test results. The time element is important in the survey, for information on test results must be disseminated as quickly as possible to potential buyers of wheat. Mr. Stuart added that the decision not to include that wheat stored on the farm in the testing program does not preclude producers from having their grain tested so the information on it can be made available to the trade. He recommended that the individual wheat producers storing wheat on the farm avail themselves of the testing services offered the industry by the grain testing laboratories of the three States cooperating in the program. He notes that by having these tests made to determine their crop's quality, producers should be able to facilitate the marketing of their wheat much more quickly and accurately.

Consumer Complaints When the Oregon Department of Agriculture's Consumer Advisory Council held its quarterly meeting in mid-May in Salem, two of the major consumer

complaints reviewed were that bacon with too much fat was being packaged so that the buyer cannot see all of the fat and that 2½-pound cans of whipped shortening were being placed on the grocer's shelf along with three-pound cans of shortening of the same size.

Hoping that regulations covering the packaging of bacon might help the consumer at the marketplace, the council supported a request for a hearing to discuss proposed packaging regulations for bacon and was informed by the department that a hearing was being considered. It was also advised that a hearing is set for the near future to consider regulations standardizing cottage cheese containers.

Council members also discussed and endorsed the Food and Drug Administration's proposal to require full ingredient labeling on food products. Not only did they plan as a group to send a support letter to the FDA but individual members also agreed to write supporting letters to the Agency. At present, label listing of all ingredients is not required for food products with standards of identity.

'Love Beads' Off Market Those candy "Love Beads" that contained enough of the heavy metal ingredient cadmium to make some children ill from eating them have been removed from retail shelves in Oregon, according to the Oregon Department of Agriculture, which had the responsibility for checking the retail market for the candy. The department said the candy had been generally distributed throughout the State and that the wholesaling companies had contacted retailers asking them to remove the candy from the shelves. The wholesalers are picking up all of the candy.

The action followed a warning the department, along with the Oregon State Board of Health, issued after the Food and Drug Administration alerted them to the candy, made in Hong Kong for the Ritz Plastic Co., Compton, California.

Certification E. A. Johnson, an inspector with the Iowa Department of Agriculture, has been certified as a food service sanitation survey officer for the State. Details of the certification, completed in March, were handled by the Special Programs Branch in the Kansas City Field Office of the Food and Drug Administration.

Mixed-Shipment Problem Officials from the Dairy and Food Division of the Nebraska Department of Agriculture embargoed and then supervised the destruction of almost three tons of bakery supplies because of the possibility that they had been contaminated by pesticides. The products consisted of flour, sugar, salt, and miscellaneous prepared mixes that had been included in a truck shipment of animal feeds and bagged pesticides from Sioux City, Iowa, to Nebraska points.

Education Conference Representatives from the Wyoming State and local health departments and the State Agriculture Department met at Casper April 1-2 to attend the first annual Education Conference of the Wyoming Environmental Health Association.

Nick Pohlit, executive director, National Environmental Health Association, was the keynote speaker at the two-day seminar, which covered such subjects as food sanitation, injury control, waste disposal, and water supplies. Election of local association officials followed.

Grain Diverted The Washington State Department of Agriculture removed two carloads of Montana wheat intended for human consumption from food channels in April. The 125 tons of grain, contaminated with a foreign odor, was diverted for animal feed use.

Legislative Hearing The State of Minnesota Legislative Committee met at a hearing March 24 to consider a bill that would establish an office of consumer affairs in the State. The bill is supported by the Minnesota Consumer's League, Joint Religious Legislative Council, the Farmers' Union, Model Cities representatives, and the Office of the Attorney General. It was the first time a hearing on this type of bill has been held in the State. Blanche Erkel, consumer specialist with the Food and Drug Administration's Minneapolis District Office, attended as an observer.

Pink Wheat The Minnesota Department of Agriculture issued a local press release in the spring warning against the use of pink (treated with a mercury fungicide) wheat purchased at a health food store in the Minneapolis area. Both department and FDA Minneapolis District officials had investigated a report in mid-March that the wheat was being sold at the store. They found that the store had purchased the wheat from a seed company along with various other seed to be sold either as seeds or as food. Since there was neither any interstate movement of the wheat to the dealer nor any interstate shipment of the contaminated wheat by him, the Minnesota Department of Agriculture assumed responsibility for correction of the problem. John M. Wefald, commissioner of the department, then issued the press release, for the investigation had revealed that 20 one-pound units had been made up and sold from the original 50-pound bag.

Contaminated Cheese Because it was found to be contaminated with the pesticide BHC, 44 barrels of

cheddar cheese is being returned by a large cheese processor in Missouri to a cheese consolidation center in Wisconsin. Norman Kirschbaum, Food Division administrator, Wisconsin State Department of Agriculture, explained that the residue problem appeared to have been caused by the inadvertent dusting of one dairy herd with BHC. The barrels of cheese, product of a single Wisconsin cheese factory, will be disposed of under supervision of the State department. Several samples of cheese produced by the plant were examined by FDA's Minneapolis District laboratory, supporting the analytical results obtained by the Wisconsin State department.

All the cheese produced during the period involved has been recovered and none was used in the production of processed cheese. In addition to the barrels being returned from Missouri, a number of barrels are under seizure by the Wisconsin State Department of Agriculture.

Taylor-Lube Ban The Florida Department of Agriculture and Consumer Services has banned the use of "Taylor-Lube" by Seven-Eleven stores in the State. The product, a lubricant manufactured in Chicago, is used on the gears of equipment dispensing frozen carbonated beverages. It was found being misused in excessive quantities by the service department of the Seven-Eleven chain, resulting in adulteration of the beverage. The ban was based on formulation information requested from FDA by Food Laboratory Chief Dr. W. D. Stallcup, Florida Department of Agriculture. The information was furnished by the Atlanta District with Chicago District's assistance.

Awarded Title Irwin L. Snyder, supervisor, Health Care Facilities Program of Baltimore County, Maryland, Department of Health, was selected as "Maryland Sanitarian of the Year." Among Mr. Snyder's accomplishments are his vigorous efforts toward cooperation between FDA and local officials.

Restrained Cannery Operator The State of California terminated a prosecution against George Noroian Cannery, Dinuba, California, and the owner and operator, George Noroian. The complaint charging six counts of violation of the California Health and Safety Code was filed with Tulare County by the California State Bureau of Food and Drugs, who inspected the firm. In the complaint the firm and its operator are charged with processing food in an unclean establishment under unhealthful and insanitary conditions. Mr. Noroian pleaded nolo contendere to two counts and the others were dismissed. He was sentenced to a one-year imprisonment, suspended for three years on condition that (1) he not hold the position of director or hold stock in any corporation engaged in any way in the packaging or canning of food, (2) that he not be employed in such business in any capacity, (3) that his wife not acquire any voting stock in any corporation engaged in food canning or packing, and (4) that he observe all laws of the State, city, and county in which he may reside. FDA Inspector Leon Rutledge, of the Fresno Resident Post inspected the firm separately but at the same time as the State, and testified on behalf of the State in the case.

Health Food Promoter The owner of a health food store in Garden Grove, California, was prosecuted by the State of California on charges of practicing medicine without a license and advising that certain health foods are beneficial in treating cancer, heart conditions, and stomach ulcers. The court ordered the defendant to make a \$2,000 restitution to the State's Bureau of Food and Drugs by July 30.

Device Restraint The State of California has obtained a permanent injunction against Dynatone, Inc., *et al*, to prohibit State-wide distribution of the electronic machines known as "Dynabelt," "Portable Body Exerciser," and "Facial Exerciser" until and if a new device application is approved by the State.

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 58 actions to remove from the consumer market products charged to be violative were reported in April. These included 44 seizures of foods: 24 involved charges concerning poisonous and deleterious substances, 14 involved charges concerning contamination, and 6 involved charges

concerning economic and labeling violations. Other seizures included 1 of food additives, 1 of vitamins—dietary food, 11 of drugs (including 3 of veterinary and medicated feed), and 1 of hazardous substances.

PRODUCT, PLACE & DATE SEIZED	MANUFACTURER (M), PACKER (P), SHIPPER (S), DEALER (D)	CHARGES
FOOD / Poisonous and Deleterious Substances		
Cottonseed/Hanford, Calif. 2/8/71	Shipped from Arizona to Hanford, Calif.	Contains aflatoxin, a poisonous substance, which may render it injurious to health.
San Marcos, Calif. 2/4/71	Hollandia Dairy/San Marcos, Calif. (D)	"
Santa Fe Springs, Calif. 12/30/70	United Dairymen's Association/Santa Fe Springs, Calif. (D)	"
Feathermeal/Jackson, Miss. 3/18/71 (2 actions)	Return shipments from Memphis, Tenn., and Palestine, Tex., to Jackson, Miss.	Contains Salmonella micro-organisms.
Feta cheese/Methuen, Mass. 3/17/71	Imported from Greece.	Contains benzene hexachloride, an unsafe food additive.
Seed corn, treated, intended for use as animal feed/Lancaster, S.C. 3/24/71	R. H. Collins Grain Co., Inc./Lancaster, S.C. (D)	Contains methoxychlor, dieldrin, and captan, pesticide chemicals not in conformity with regulations.
Lancaster, S.C. 3/24/71	Dwight E. Mungo/Lancaster, S.C. (D)	"
Lancaster, S.C. 3/24/71	Buford Milling Co., Inc./Lancaster, S.C. (D)	"
Lancaster, S.C. 3/24/71	Ralph J. Hunter/Lancaster, S.C. (D)	"
Swordfish/Bridgeport, Conn. 3/15/71	Imported from Japan (S)	Contains excessive mercury.
Raleigh, N.C. 3/31/71	Blue Water Seafoods/Cleveland, Ohio (S)	"
Raleigh, N.C. 4/2/71	Carnation Seafoods/Great Neck, N.Y. (S)	"
Memphis, Tenn. 2/16/71	Mogelberg Foods, Inc./Jersey City, N.J. (S)	"
Oxnard, Calif. 4/1/71	Caught in Pacific outside of Calif. limits	"
Panama City, Fla. 3/9/71	Cook Fish Co./Panama City, Fla. (S)	"
Somerville, Mass. 4/1/71	Imported from Japan and Taiwan (unknown S)	"
frozen/Seattle, Wash. 3/8/71	Washington Fish & Oyster Co. of Calif./San Francisco, Calif. (S)	"
Seattle, Wash. 3/8/71	Chas. P. Kearney & Co./Oakland, Calif. (S); Nozaki Associates/San Francisco, Calif. (S)	"
Long Beach, Calif. 3/31/71	Unknown (S)	"
Wilmington, Calif. 3/31/71	"	"
fillets/Somerville, Mass. 4/1/71	Imported from Japan and Taiwan (unknown S)	"
steaks/Cleveland, Ohio 2/26/71	L. N. White Co./New York, N.Y. (S); Southern Seafood Co./Baltimore, Md. (S); New England Fish Co./New York, N.Y. (S); John Howley, Boston, Mass. (S)	"
chunks/Mobile, Ala. 3/23/71	Mogelberg Foods, Inc./Jersey City, N.J. (S)	"

PRODUCT, PLACE & DATE SEIZED	MANUFACTURER (M), PACKER (P), SHIPPER (S), DEALER (D)	CHARGES
Contamination, Spoilage, Insanitary Handling		
Apple cider vinegar, crystal distilled vine- gar/Billings, Mont. 4/1/71	Speas Co./Denver, Colo. (M, S)	Cloudy and contains slimy masses.
Beans, baby lima/Americus, Ga. 3/6/71	Glover Wholesale Co./Americus, Ga. (D)	Held under insanitary conditions.
Great Northern, white marrow, baby lima, yellow split peas/Marcellus, N.Y. 3/31/71	Allen V. Smith/Marcellus, N.Y. (D)	Held under insanitary conditions in a rodent-infested warehouse.
Cake mix, coffee, rice/Selma, Ala. 3/15/71	Stewart, King & McKenzie/Selma, Ala. (D)	Held under insanitary conditions.
Cornmeal/Shreveport, La. 4/12/71	Alford Refrigerated Warehouse/Dallas, Tex. (S)	Rodent contaminated.
Dates, dried/Thermal, Calif. 3/31/71	Lyle Date Gardens/Yuma, Ariz. (S)	Insect contaminated.
Flour/New Orleans, La. 3/30/71	P. A. Menard, Inc./New Orleans, La. (D)	Held under insanitary conditions; rodent contaminated.
Grits/Columbia, S.C. 4/15/71	Merchants Wholesale Grocery/Columbia, S.C. (D)	"
Mexican oregano, Turkish sage leaves/ South San Francisco, Calif. 3/5/71	Presco Food Products, Inc./South San Francisco, Calif. (D)	"
Mustard seed/New Orleans, La. 4/13/71	Montana Mustard Seed Co., Inc./Great Falls, Mont. (M, S); New Orleans Import Co., Ltd./New Orleans, La. (D)	" ; label fails to bear place of business, quantity of contents, and common or usual name of food.
Peanuts/Shreveport, La. 4/1/71	Julius Gamm Co./Shreveport, La. (D)	Held under insanitary conditions; rodent contaminated; no quantity of content statement.
Memphis, Tenn. 4/16/71	McMurry's Warehouse/Memphis, Tenn. (D)	Held under insanitary conditions; rodent and bird contaminated.
Pecan pieces/Boston, Mass. 4/14/71	Nut Tree Pecan Co./Beaconton, Ga. (P, S)	Prepared and packed under insanitary conditions; E. coli.
Peruvian white corn/Seattle, Wash. 3/18/71	Jensen-McLean Co./Seattle, Wash. (S)	Contains insect-damaged corn kernels; improper la- beling.

Economic and Labeling Violations

Guava jelly/Hawthorne, N.Y. 2/25/71	Groveland Product Co., Inc./Hallendale, Fla. (M, S)	Fails to conform with standard of identity for jelly.
Haddock fillets, frozen/Somerville, Mass. 3/31/71	Mr. Boston Seafood Corp./Boston, Mass. (Repacker)	Cod was substituted for haddock.
Nopalitos al natural/San Antonio, Tex. 3/5/71	Productos Marpe, S.A./San Luis Potosi, Mexico (M)	Not in conformity with the Fair Packaging and Label- ing Act.
Pies, blueberry, apple, cherry/Denver, Colo. 3/23/71	Chef Pierre, Inc./Traverse City, Mich. (M, S)	"
Pimiento halves/Bronx, N.Y. 2/24/71	Perfect Packed Products Co., Inc./Hender- son, N.C. (M, S)	Bell peppers were substituted for pimientos.
Sugar wafer cookies/Fort Worth, Tex. 4/5/71	American Wafer Co./Joplin, Mo. (M, S)	Not in conformity with the Fair Packaging and Label- ing Act; net weight statement not of adequate size.

Food Additive

Aloe vera juice, aloe vera jel/Compton, Calif. 3/3/71	Aloe Products, Inc./Houston, Tex. (M, S)	Unsafe food additive not in conformity with regula- tions.
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Vitamins—Dietary Food

Supplement Extraordinary, bulk tablets: vitamin & mineral, vitamin E, C, protein hydrolysate, liver & yeast/Oklahoma City, Okla. 4/16/71	Century 21, Inc./Oklahoma City, Okla. (P)	False and misleading claims of significant benefit to health and well-being; have sexually stimulating effect. (Supplement Extraordinary is composed of the other five tablets from bulk and repackaged.)
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PRODUCT, PLACE & DATE SEIZED	MANUFACTURER (M), PACKER (P), SHIPPER (S), DEALER (D)	CHARGES
DRUGS / Human Use		
Digoxin tablets/Melville, N.Y. 2/22/71	Davis-Edwards Pharmacal Corp./Danbury, Conn. (S)	Fail to meet USP test for content uniformity.
USP 0.25 mg./Rio Piedras, P.R. 3/18/71	Halsey Drug Co., Inc./Brooklyn, N.Y. (M, S)	Below USP standard for quality and strength.
Estradiol valerate powder, injection/ Buena Park, Calif. 3/5/71	Tera Pharmaceuticals, Inc./Buena Park, Calif. (D) Raw materials imported from Italy.	Estradiol isovalerate and free estradiol have been substituted for estradiol valerate.
Neurobexin and neuralvitas, lot #70-9 injection vitamin preparation/Santurce, Hato Rey, San Juan, Rio Piedras, Caguas, all P.R. 2/24/71	Wiewall Drug Corp./Santurce, P.R. (D); J. M. Blanco, Inc./Hato Rey, P.R. (D); Drogueria Braulio Caballero/San Juan, P.R. (D); Drogueria Rio Piedras, Inc./Rio Piedras, P.R. (D); Drogueria Betances, Inc./Caguas, P.R. (D)	Below purported strength in vitamin B-12; lack of good manufacturing practice.
Rauwolfia serpentina/Melville, N.Y. 3/25/71	Richlyn Laboratories/Philadelphia, Pa. (M, S)	Differs from NF standard for strength.
T-E-E-V injection/Los Angeles, Calif. 3/2/71	Maurry Biological Co./Los Angeles, Calif. (D) Raw materials imported from Italy.	Estradiol isovalerate and free estradiol have been substituted for estradiol valerate.
Thyroxine in iodinated casein/Sioux City, Iowa 2/9/71	Austra Chemical, Inc./Fountain Valley, Calif. (M, S)	New drug not approved for safety and efficacy; inadequate directions for use.
Yellow Estrand-Gens (methyltestosterone)/ North Hollywood, Calif. 3/16/71	Richlyn Laboratories/Philadelphia, Pa. (M, S)	Below labeled strength in methyltestosterone.
Veterinary / Medicated Feed		
Dimethyl sulfoxide (DMSO)/Kingman, Kans. 3/22/71	Associated Veterinary Practitioners/Kingman, Kans. (D)	New animal drug not approved for safety and efficacy; false and misleading claims for treatment of certain veterinary conditions and diseases.
Formula 707 conditioner for horses/Fergus Falls, Minn. 3/2/71	John Ewing Co./La Salle, Colo. (M, S)	New animal drug not approved for safety and efficacy.
Ten-Sol/Hato Rey, P.R. 4/1/71	Thoroughbred Remedy Corp./Elmont, L.I., N.Y. (M, S)	”; false and misleading claims to be effective for treatment of horses' ailments.
Hazardous Substances		
Bostonian brown lightening shoe dye, Whittemore heel & sole enamel, Cadet enamel/Tampa, Fla. 3/17/71	Harri Hoffmann Co., Inc./Milwaukee, Wis. (M, S)	All articles are flammable and fail to state principal hazard on the main panel.

U.S. POSTAL SERVICE actions taken in medical cases under provisions of the Postal Fraud Statutes as reported by the Chief Postal Inspector.

False Representation Order Issued by Judicial Officer Under 39 U.S.C. 4005

March 30, 1971: False Representation Order issued against **Northland Drug**, P.O. Box 484, Morton Grove, Illinois. Advertising and sale by mail of "Devil Delight Tablets," represented as an aphrodisiac or sexual stimulant.

Complaint Filed by the General Counsel Under 39 U.S.C. 4005 (False Representation)

April 5, 1971: **Behavioral Science Laboratories**, 7100 Baltimore Ave., College Park, Maryland. Advertising and sale by mail of "Excite-X" liquid capsules, guaranteed in writing to induce sexual desire, and represented as a true, safe aphrodisiac.

notices of judgment

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

Coffee beans and granulated beet sugar, at Baltimore, Dist. Md.
Charged 7-6-70 and amended 8-6-70: while held by Chesapeake Operating Co., Baltimore, Md., the articles contained the added poisonous and deleterious substance, antimony dust, and the articles were held under insanitary conditions in bags contaminated with antimony ore dust; 402(a)(1), 402(a)(4). Consent decree authorized release of the coffee beans to International Produce, Inc., New York, N.Y., for reconditioning. Consent decree authorized release of the sugar to S. A. Wald & Co., Inc., Jersey City, N.J., for salvaging. (1)

Eggs, frozen, at Weedsport, N. Dist. N.Y.
Charged 11-18-70: when shipped by J. Fleishman & Co., Inc., Boston, Mass., the article contained the added poisonous and deleterious substance, *Salmonella* micro-organisms; 402(a)(1). Default decree ordered destruction. (2)

Pickle chips, cubes, slices, halves, relish, and juice, at Hurlock, Dist. Md.
Charged 7-27-70: while held by Hurlock Pickling Co., Inc., Hurlock, Md., who was manufacturing the articles with sugar which had been shipped from the Chesapeake Operating Co., Baltimore, Md., in bags contaminated with antimony ore dust, some pickle slices contained the added poisonous and deleterious substance, antimony ore dust, and all of the articles had been prepared under insanitary conditions from sugar in bags contaminated with antimony ore dust; 402(a)(1), 402(a)(4). Default decree ordered destruction. (3)

Wheat, at Clovis, Dist. N. Mex.
Charged 6-22-70: when returned to Curry County Grain & Elevator Co., Clovis, N. Mex., from Amarillo, Tex., the article contained a pesticide chemical, a mercurial compound, for which there was no tolerance or exemption; 402(a)(2)(B). Consent decree authorized release to Francis L. Decker, Broadview, N. Mex., for compliance operations. (4)

FOOD / Contamination, Spoilage, Insanitary Handling

Beans, kidney, dried, at Las Vegas, Dist. Nev.
Charged 10-21-70: while held by Madonna Italian Foods, Las Vegas, Nev., the article was held under insanitary conditions; 402(a)(4). Default decree ordered destruction. (5)

Beans, kidney, dried, and flour, at Hialeah, S. Dist. Fla.
Charged 7-22-70: while held for sale, the articles contained insects; 402(a)(3). Consent decree authorized release to Hammond Milling Co., Inc., Hialeah, Fla., for conversion to animal feed. (6)

Butter, at Kansas City, Dist. Kans.
Charged 10-14-70: while held for sale, the article contained moldy butter; 402(a)(3). Default decree ordered destruction. (7)

Candy jelly rings, at Columbus, S. Dist. Ohio.
Charged 11-4-70: when shipped by Farley Candy Co., Skokie, Ill., the article, labeled in part "Mel-O-Sweet Sugar Jells . . . Distributed by Topco Associates, Skokie, Illinois," contained wood chips; 402(a)(3). Default decree ordered destruction. (8)

Cashew nuts, at Portland, Dist. Oreg.
Charged 11-18-70: when shipped by Johnson Nut Co., Hopkins, Minn., the article contained insect filth and had been prepared and packed under insanitary conditions; 402(a)(3), 402(a)(4). Default decree ordered destruction. (9)

Cheese, stirred curd, for manufacturing, at Atlanta, N. Dist. Ga.
Charged 9-29-70: when shipped by Avalon Cheese Co., Leitchfield, Ky., the article contained insect filth and had been prepared and packed under insanitary conditions; 402(a)(3), 402(a)(4). Default decree ordered destruction. (10)

Cocoa cake, at Chicago, N. Dist. Ill.
Charged 7-1-70: while held for sale, the article contained rodent pellets, stones, wood fragments, and metal staples; 402(a)(3). Default decree ordered destruction. (11)

Cornhusks, at Tucson, Dist. Ariz.
Charged 9-8-70: when shipped by George Walcher, Weimar, Tex., the article contained insect filth and moldy cornhusks; 402(a)(3). Default decree ordered destruction. (12)

Cornmeal, 3 seizure actions at Fort Payne, Gadsden, and Scottsboro, N. Dist. Ala.
Charged 9-25-70 and 9-30-70: when shipped by Murphy Grain & Milling Co., Owensboro, Ky., the article contained rodent and insect filth and had been prepared and packed under insanitary conditions; 402(a)(3), 402(a)(4). Consent decree authorized release of the article to the shipper for conversion into animal feed. (13)

Flour, soybean flakes, and donut mix, at Atlanta, N. Dist. Ga.
Charged 9-28-70: while held by Anchor Warehouse Co., Inc., Atlanta, Ga., the articles contained rodent and insect filth and were held under insanitary conditions; 402(a)(3), 402(a)(4). Default decree ordered destruction. (14)

Nuts, mixed, at Denver, Dist. Colo.
Charged 11-12-70: when shipped by Johnson Nut Co., Div. of Fairmont

Foods Co., Hopkins, Minn., the article, labeled in part "Food Club Fancy Mixed Nuts . . . Dist. by Topco Assoc., Inc., Skokie, Ill.," contained insect filth and had been prepared and packed under insanitary conditions; 402(a)(3), 402(a)(4). Default decree ordered destruction. (15)

Nuts, mixed, Crest-pac, at Beaumont, E. Dist. Tex.
Charged 11-6-70: when shipped by Johnson Nut Co., Div. of Fairmont Foods Co., Hopkins, Minn., the article contained insect filth and had been prepared and packed under insanitary conditions; and the label vignette depicting the presence of pecans was false and misleading as applied to the article which contained no pecans; 402(a)(3), 402(a)(4), 403(a). Default decree ordered destruction. (16)

Peas, canned, Princella, at New Iberia, W. Dist. La.
Charged 8-21-70: when shipped by Princeville Canning Co., t/a Joan of Arc Canning Co., Princeville, Ill., the article contained a decomposed substance; 402(a)(3). Default decree ordered destruction. (17)

Pepper, black, at Houston, S. Dist. Tex.
Charged 8-10-70: while held for sale, the article contained rodent and insect filth; 402(a)(3). Default decree ordered destruction. (18)

Potato flakes and rice, at Columbia, Dist. S.C.
Charged 4-28-70: while held for sale, the rice contained rodent filth, and both articles were held under insanitary conditions; 402(a)(3), 402(a)(4). Default decree authorized destruction. (19)

Sausage links, at Oklahoma City, W. Dist. Okla.
Charged 11-23-70: while held for sale, the article contained decomposed and rancid sausage links; 402(a)(3). Default decree ordered destruction. (20)

Shrimp, breaded, frozen, at Detroit, E. Dist. Mich.
Charged 9-16-70: when shipped by Gulf City Fisheries, Inc., Pascagoula, Miss., the article contained coagulase positive staphylococci and had been prepared and packed under insanitary conditions; 402(a)(3), 402(a)(4). Default decree ordered destruction. (21)

Shrimp, breaded, frozen, at Port Lavaca, S. Dist. Tex.
Charged 6-8-70: while held by H. Morgan Daniel Seafoods, Inc., Port Lavaca, Tex., the article contained coagulase positive staphylococci and bacterial filth and had been prepared and packed under insanitary conditions; 402(a)(3), 402(a)(4). Consent decree authorized release to the dealer for salvaging. (22)

Shrimp meat, cooked, frozen, at Seattle, W. Dist. Wash.
Charged 11-5-70: when shipped by Winchester Bay Seafood Co., Winchester Bay, Oreg., the article contained coagulase positive staphylococci and had been prepared and packed under insanitary conditions; 402(a)(3), 402(a)(4). Consent decree authorized release to shipper for salvaging. (23)

Tomato paste, canned, at San Fernando, C. Dist. Calif.
Charged 11-2-70: while held for sale, the article contained a decomposed substance; 402(a)(3). Default decree ordered destruction. (24)

Walnut pieces, Fairmont Snacktime, at Sheboygan, E. Dist. Wis.
Charged 10-30-70: when shipped by Johnson Nut Co., Div. of Fairmont Foods Co., Hopkins, Minn., the article contained insect filth and had been prepared and packed under insanitary conditions; 402(a)(3), 402(a)(4). Default decree ordered destruction. (25)

Yams, cut, canned, Hopkins, Dist. Minn.
Charged 3-31-70: while held for sale, the article contained a decomposed substance; 402(a)(3). Default decree ordered destruction. (26)

FOOD / Economic and Labeling Violations

Pies, peach, pecan, pineapple, and strawberry, frozen, at Denver, Dist. Colo.
Charged 10-23-70: when shipped by Fasano Pie Co., Chicago, Ill., the articles were in violation of the Fair Packaging and Labeling Act in that the principal display panels of the packages of all pies, except the pecan pies, lacked a statement of identity of the articles, and lacked the name and place of business of the manufacturer, packer, or distributor, and the quantity of contents was stated as "Net Wt. 1 Lb. 12 Oz." instead of "Net Wt. 28 Oz. (1 Lb. 12 Oz.)"—15 U.S.C. 1453 (a)(1), 1453(a)(3)(A)(i); the quantity of contents declaration for the peach and strawberry pies was not separated from other printed label information appearing above the declaration—15 U.S.C. 1453(a)(2); and the quantity of contents of all pies was stated in a type size less than 3/16 inch high—15 U.S.C. 1453(c)(1). Consent decree authorized release to shipper for relabeling. (27)

Tomatoes, canned, at Fort Worth, N. Dist. Tex.
Charged 11-5-70: when shipped by Allen Canning Co., Siloam Springs, Ark., the article, labeled in part "Diamond Brand Tomatoes Net Wt. 16 Oz. . . . Distributed by Kimbell Grocery Company . . . Fort Worth, Texas," was short weight; 403(e)(2). Consent decree authorized release to shipper for reprocessing. (28)

VITAMINS / DIETARY FOODS

Multiple vitamin-mineral tablets, at Gardner, Dist. Kans.
Charged 9-22-70: while held for sale, the valuable constituent, vitamin B12, had been in part omitted or abstracted from the article, and the labeling contained false and misleading statements concerning the

article's content of vitamin B12; 402(b)(1), 403(a). Default decree ordered destruction. (29)

FOOD ADDITIVE

Kingfish, frozen, Fiesta Del Mar, at Wilmington, C. Dist. Calif.

Charged 12-4-70: while held for sale, after being packed by Del Mar Fish Co., Wilmington, Calif., the article contained the nonconforming food additives, DDE, DDT, TDE; 402(a)(2)(C). Default decree ordered destruction. (30)

DRUGS / Human Use

Amaze Aids antacid combination tablets, at Dallas, N. Dist. Tex.

Charged 11-4-70: while held by HLH Products, Dallas, Tex., after being repacked by that firm, the labeling contained false and misleading claims concerning the efficacy of the article as a treatment for hang-over, diarrhea, heartburn, and indigestion; 502(a). Consent decree authorized release to HLH Products for relabeling. (31)

Bariatric Formula tablets and capsules of various colors and formulations, at Coral Gables, S. Dist. Fla.

Charged 3-21-68 and amended on or about 7-16-68: when shipped by Libby, Edwards & Brown, Inc., Greenville, S.C., Don Hall Laboratories, Portland, Oreg., Milan Pharmaceuticals, Inc., Morgantown, W. Va., and while held by Bariatric Corp., Coral Gables, Fla., who was repacking the articles, the labeling of some thyroid tablets (Bariatric Formula Nos. 14, 14A) contained false and misleading representations that thyroid safely increases metabolism and that those articles were safely effective for the treatment of obesity; and the labeling of such tablets (Bariatric Formula Nos. 14, 14A) contained misleading representations that the articles were to be used in the treatment of myxedema, cretinism, and hypothyroidism with accompanying fatigue, obesity, menstrual disorders, infertility, sterility, or threatened abortion, and such labeling was misleading, since it failed to reveal the material fact that the overwhelming number of persons who suffer from such conditions are not afflicted with hypothyroidism, cretinism, or myxedema—502(a); thyroid-digitalis combination tablets (Bariatric Formula Nos. 19, 19A, 19B, 20, 21, 21A, 21B, 23, 23A, 23B, 24, 24A, 25, 25A, 26, 668) contained false and misleading representations that digitalis combined with thyroid was desirable and of value in offsetting tachycardia reactions brought about by the thyroid dosage levels recommended in their labeling, that the tablets were safe and effective in constitutional obesity, and that thyroid would safely increase metabolism—502(a); the labeling of some amphetamine-thyroid combination tablets and capsules (Bariatric Formula Nos. 108A, 108B, 108C, 108D, 108E, 108F, 108G, 108H, 108J) and amphetamine-thyroid-barbiturate combination tablets and capsules (Bariatric Formula Nos. 30, 31, 106, 107) contained false and misleading representation about the value of the articles in the dietary treatment of obesity—502(a); the labeling of the thyroid-amphetamine-phenobarbital sustained release tablets (Bariatric Formula No. 107) and the thyroid-amphetamine-amobarbital timed-disintegration capsules (Bariatric Formula No. 106) contained the statements which were ambiguous and inconsistent—502(a); the labeling of all of the articles lacked adequate directions for use, and they were not exempted therefrom as prescription drugs, since the labeling lacked adequate information for use by licensed practitioners for their intended purposes—502(f)(1); those articles (Bariatric Formula Nos. 21, 21A, 21B, 23, 25, 668, 108A, 108B, 108C, 108H, 108J, 107, 31, 106, 108D, 108G) packaged in 28-tablet unlabeled plastic bags lacked labels containing the name and place of business of the manufacturer, packer, or distributor, lacked labels bearing the established name of the drug and the established name and quantity of each active ingredient, and lacked labels bearing the Rx legend—502(b)(1&2), 502(e)(1)(A)(i & ii), 503(b)(4); and some of the thyroid-amphetamine-barbiturate combination capsules and tablets (Bariatric Formula Nos. 108A, 108B, 108C, 108H, 108J, 107, 30, 106, 108D, 108G) contained a barbituric acid derivative such as phenobarbital, or amobarbital, and their labeling lacked, in juxtaposition with the name and quantity or proportion of such derivative the warning that it may be habit forming—502(d); the thyroid-digitalis combination tablets and capsules (Bariatric Formula Nos. 19, 19A, 19B, 20, 21, 21A, 23, 23A, 23B, 24, 24A, 25, 25A, 26, 668) were new drugs without effective approved New Drug Applications—505(a); the 5 gr. and 6 gr. thyroid tablets (Bariatric Formula Nos. 15 & 16) and the thyroid-digitalis combination tablets (Bariatric Formula Nos. 19, 19A, 19B, 20, 21, 21A, 21B, 23, 23A, 23B, 24, 24A, 25, 25A, 26, 668) were dangerous to health when used in the dosage or with the frequency or duration prescribed, recommended, or suggested in their labeling—502(j). Consent decree ordered destruction of the thyroid-amphetamine-barbiturate combinations, and authorized release of some thyroid tablets (Bariatric Formula Nos. 14 and 14A) for relabeling. The consent decree also enjoined the claimant from distributing thyroid except for its labeling purposes as approved by FDA, and from representing or suggesting by any means that thyroid should be used for any other purpose than its approved label usage. Thereafter, the claimant having failed to repossess the thyroid tablets (Bariatric Formula Nos. 14 and 14A), the court ordered the destruction of these remaining drugs. (32)

Bar-O-Bex amphetamine-thyroid combination capsules, at Zionsville, S. Dist. Ind.

Charged 8-25-70: when shipped by Barrows Pharmacal, Inc., Inwood, Long Island, N.Y., the article was a new drug without an effective approved New Drug Application; 505(a). Default decree ordered destruction. (33)

Eye bath, at Dallas, N. Dist. Tex.

Charged 1-16-70: while held for sale after manufacture by Truett Labs., Dallas, Tex., from chlorobutanol shipped in interstate commerce, the article was deficient in chlorobutanol (approx. 24 percent), and its label failed to declare the presence of the active ingredient berberine; 501(c), 502(e)(1)(A)(ii). Default decree ordered destruction. (34)

Kolmet B manganese suspension injectable and Dexalith lithium salicylate com-

ination injectable, at Chicago Heights, N. Dist. Ill.

Charged 8-28-70: while held by Farnsworth Labs., Inc., Chicago Heights, Ill., after manufacture from raw materials shipped in interstate commerce, the labeling contained false and misleading claims concerning the efficacy of the Kolmet B in the treatment of conditions owing their origin to mixed bacterial infections and those resistant to the usual antibiotics and the efficacy of the Dexalith in the treatment of the larger types of varicose veins, and the label of the Kolmet B failed to declare the quantity of each active ingredient; 502(a), 502(e)(1)(A)(ii). Default decree ordered destruction. (35)

Niodolin sodium iodide and foreign protein injectable, at Bridge City, E. Dist. Tex.

Charged 8-7-70: when shipped by Lincoln Laboratories, Inc., Decatur, Ill., the accompanying package insert contained false and misleading claims that the therapeutic action of the article's iodide component was augmented by the foreign protein which induced leukocytosis and mobilization of the immune bodies; the labeling lacked adequate information for safe use by licensed practitioners; and the article was a new drug without an approved New Drug Application; 502(a), 502(f)(1), 505(a). Default decree ordered destruction. (36)

Obestat Ty-Med amphetamine-thyroid combination tablets and capsules, at Dayton S. Dist. Ohio.

Charged 11-2-70: when shipped by Lemmon Pharmacal Co., Sellersville, Pa., the article was a new drug without an effective approved New Drug Application; 505(a). Default decree ordered destruction. (37)

Oxytetracycline HCl capsules, at Bayshore, E. Dist. N.Y.

Charged 2-9-70: while held for sale, the article lacked an effective antibiotic certificate or release; 502(l). Default decree ordered destruction. (38)

Proplex suspension, at Detroit, E. Dist. Mich.

Charged 11-3-70: while held by Atlas Pharmaceutical Laboratories, Inc., Detroit, Mich., after manufacture from ingredients shipped in interstate commerce, the circumstances of the article's manufacture, packing, and holding lacked conformity with current good manufacturing practices; 501(a)(2)(B). Default decree ordered destruction. (39)

Proto-Jec foreign protein and iodide combination injectable, at Detroit, E. Dist. Mich.

Charged 8-13-70: when shipped by Taylor Pharmacal Co., Decatur, Ill., the labeling of the article contained false and misleading claims that the foreign protein content of the article causes leukocytosis and a mobilization of immune bodies and thereby augments therapeutic action of the iodide component, the labeling lacked adequate directions and did not comply with the Rx drug exemptions requirement for disclosure of information, and the article was a new drug without an effective approved New Drug Application; 502(a), 502(f)(1), 505(a). Default decree ordered destruction. (40)

MEDICAL DEVICES

Catheters, suction, at Nashville, M. Dist. Tenn.

Charged 2-26-70: when shipped by Ethylox Products, Inc., Buffalo, N.Y., the quality of the article, labeled in part "Flagg . . . Sterile Disposable Suction Catheter . . . Distributed by Flagg Enterprises, New York, New York," fell below what it purported to possess, since the packages in which each unit was sealed contained holes thereby compromising the integrity of sterile barrier between physician and patient, and the label statement "sterile" was false and misleading as applied to a product the package of which contained holes; 501(c), 502(a). Default decree ordered destruction. (41)

Gloves for examination, 2 seizures at Detroit, E. Dist. Mich.

Charged 4-16-70 and 9-14-70: when shipped by Oak Medical Supply Co., Ravenna, Ohio, the article, labeled in part "Sterile Veratex Disposable Hand-Y-Glove . . . Vertex Division . . . W. R. Grace & Co., Detroit, Michigan," was deficient in quality, since the gloves contained holes thereby compromising the integrity of the sterile barrier between the physician and the patient; 501(c).

The shipper claimed the articles and denied that the articles were adulterated. The actions were consolidated. The Government served interrogatories on the shipper. Thereafter, the shipper, without admitting any issue of law or fact, withdrew its claims and answers; and, upon consent of the parties, a consent decree ordered the articles destroyed. (42)

Gloves, latex, surgical, Perry, at Des Moines, S. Dist. Iowa.

Charged 9-11-70: when shipped by Affiliated Hospital Products, Inc., (Perry Division) Massillon, Ohio, the article's quality was deficient, since the article contained holes, thereby compromising the integrity of the sterile barrier between the physician and the patient; 501(c). Consent decree ordered destruction. (43)

Theramatic model A-6 DT40 electronic instrument, at St. Cloud, Dist. Minn.

Charged 3-30-70: 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 spasm, bursitis, arthritis, low back pain, sinusitis, urinary tract infections, prostatitis, and hepatitis; its labeling lacked adequate directions for such uses, and adequate directions could not be written, since the article was worthless for such uses; and the article was dangerous to health when used in the dosage and with the frequency and duration recommended in its labeling, since it was ineffective for the treatment of serious disease infections and, by reason of its ineffectiveness, it was unsafe for such use; 502(a), 502(f)(1), 502(j). Default decree authorized delivery of the device to the Food and Drug Administration. (44)

HAZARDOUS SUBSTANCES

Cherry bombs, M-80 firecrackers, aerial bombs, and repeater fireworks, at Charleston, E. Dist. Mo.

Charged 7-2-70: while held by Reeves Boomland, Charleston, Mo., the

articles were fireworks devices which were banned hazardous substances by regulations, since they were intended to produce audible effects by a charge of more than 2 gr. of pyrotechnic composition; 2(q)(1)(B). Default decree ordered destruction. (45)

Whittemore heel and sole enamel, at Philadelphia, E. Dist. Pa.
Charged 6-12-70: when shipped by Harri Hoffman Co., Inc., and Whittemore Polish Co., Milwaukee, Wis., the article was a flammable substance presenting a special hazard by reason of its methanol content, and it lacked a number of the required conspicuous label statements; 2(p)(1)(A,B,E,G,I,J), 3(b). Default decree ordered destruction. (46)

NOTICES OF JUDGMENT on Criminal Actions

FOOD

Tower Hill Bakery Corp. and Andrew J. Puglise, president and treasurer, Lawrence, Dist. Mass.

Charged on or about 9-3-70 by grand jury: when shipped, submarine rolls and Italian bread contained insect fragments and rodent and cat hair fragments, and had been prepared and packed under insanitary conditions; 402(a)(3), 402(a)(4). Guilty plea by corporation, fine suspended. Guilty plea by individual; imprisonment suspended on specified conditions. (47)

NOTICES OF JUDGMENT on Prosecution Actions

DRUGS

Stanack Sales Co., Inc., Howard Ackerman, secretary-treasurer, and **Stanley Ackerman**, employee, Englewood, Dist. N.J.

Charged 2-17-66: refusals to permit FDA inspection of all things relating to prescription drugs, as authorized by law, in a registered establishment in which prescription drugs were being held; 704(a). Not guilty pleas. Jury verdict of guilty on two counts. Upon appeal, the court said that there were additional issues presented other than the refusal by the appellants to allow the drug inspectors entry onto their premises: "First, is there a special exemption from the Fourth Amendment protection as to business records? . . . Second, assuming such a refusal to be lawful, did the appellants waive their rights to refuse inspection of their records by allowing Inspector Scharf to inspect their factory?" The court found that *See v. City of Seattle*, 387 U.S. 541, answered the first question; and that, in this case where the circumstances made it unclear whether the area searched was covered by the consent, the facts in *Karwicky (Karwicky v. U.S. 55 F.2d 225)* were most opposite and no waiver might be found. 387 F.2d 849 (1968). Accordingly, the convictions were vacated. (48)

NOTICES OF JUDGMENT on Injunction Actions

Harris & Katz Fish Co., Inc., Boris M. Katz, president, and **Samuel Harris**, vice president and treasurer, Baltimore, Dist. Md.

Charged 2-5-69: the defendants were engaged in receiving from outside the State of Maryland fish such as salmon, sable, herring, mackerel, and whitefish, and in processing and distributing, in interstate commerce and in the State of Maryland, such fish for human consumption, and until recently in processing chubs which had been received from interstate commerce; that, when distributed by the defendants, such fish had been prepared, packed, and held under insanitary conditions whereby such fish may have become contaminated with filth and whereby the chubs may have been rendered injurious to health; 402(a)(4).

Thereafter, a consent decree of permanent injunction was filed which enjoined the shipment in interstate commerce of chubs and other fish prepared, packed, or held under insanitary conditions whereby they may have become contaminated with filth or whereby the chubs may have been rendered injurious to health; which enjoined the doing of any act which resulted in chubs and other fish held for sale after shipment in interstate commerce being adulterated as above, and which also enjoined the shipment of chubs unless and until a number of conditions concerning the prevention of the outgrowth of *Clostridium botulinum* spores in smoked chubs were met. (49)

Moore's Seafood Products, Inc., Fort Atkinson, W. Dist. Wis.

Charged 11-24-69 in complaint for injunction: that the defendants were engaged in preparing, packing, holding, and distributing frozen breaded onion rings; that such article, when distributed, contained bacterial filth and had been prepared, packed, and held under insanitary conditions at the defendants' Fort Atkinson plant; 402(a)(1), 402(a)(4). A consent decree of injunction was entered which enjoined the defendant against the introduction into interstate commerce of frozen breaded onion rings that contained filth or had been prepared, packed, or held under insanitary conditions and which required the defendant before making further interstate shipment of such article to correct the insanitary conditions in its plant and to establish specified practices and procedures to prevent the contamination of the article with filth. (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.

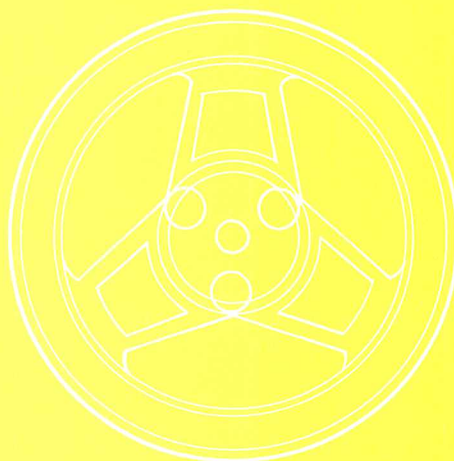
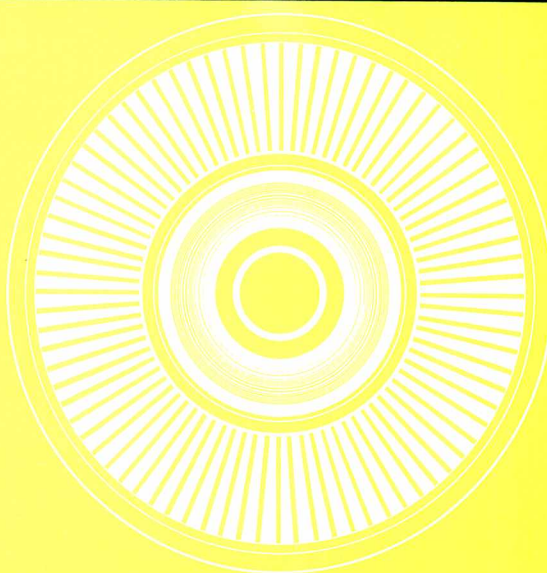
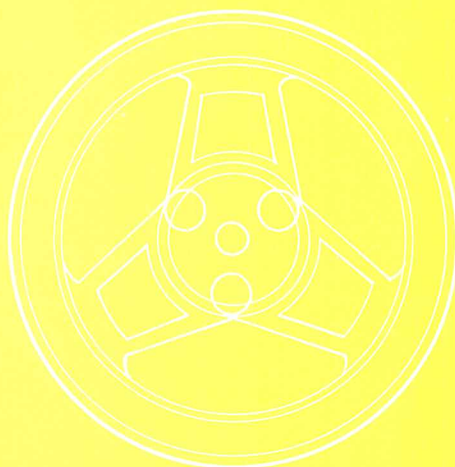
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Charles C. Edwards, M.D., *Commissioner of Food and Drugs*

Washington, D.C., June 1, 1971

“DRUGS & MICROBES”

“Drugs and Microbes” is a series of 62 color slides (2" x 2") with 15 minutes of taped narration. The presentation stresses nonsterile drugs and is designed primarily for in-plant training of employees, to make them aware that they have an important part to play in preventing microbial contamination. It deals with such matters as personnel hygiene, cleaning of equipment and facilities, and handling of the product during processing. It also gives the employee a simple introduction to some of the characteristics of micro-organisms. In-plant training of operating employees takes on added significance with the increased emphasis in the revised GMP's on employee understanding of microbiological and other factors. Available for purchase from the National Audiovisual Center, National Archives and Records Services, Washington, D.C. 20409. The cost of one set, with taped narration, is \$12.00.



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Announcements

AFDOUS HONORS BALASSONE The Association of Food and Drug Officials of the United States, holding its annual meeting in Columbus, Ohio, June 20-23, presented the association's Harvey W. Wiley Award to Francis S. Balassone, chief of the Division of Drug Control of the Maryland Department of Health. The award was presented in behalf of AFDOUS by Frank E. Fisher, director of the Bureau of Foods and Drugs, Indiana State Board of Health, and chairman of the Wiley Award Committee.

Officers elected by the association for 1972: president, Creo Jones, director, Food and Drug Division, Arkansas State Department of Health, Little Rock; vice president, Francis A. Timko, chief, Bureau of Foods and Dairies, New Jersey Department of Health, Trenton; secretary-treasurer, Evan Wright, director, Food and Drug Division, Kansas Department of Health, Topeka.

Mr. Balassone was cited "in recognition and appreciation of his personal attributes and his technical competence." Mr. Fisher noted that the honoree has served as president of the Central Atlantic States Association of Food and Drug Officials, is a past president of the National Association of Boards of Pharmacy and the Baltimore Branch of the American Pharmaceutical Association, and has served as a delegate to the U.S. Pharmacopeial Convention and on "many committees of these associations. He is a long-time member of AFDOUS and has served willingly and capably on many committees for us."

CASE STUDIES COMPILATION The Division of Industry Services has prepared a compilation of Case Studies of Drug Recalls in a single booklet.

This compilation, consisting of a variety of previously published case studies, categorized by specific problem areas, is available upon request from:

Food and Drug Administration
Bureau of Drugs, Office of Compliance
Division of Industry Services—BD-340
5600 Fishers Lane
Rockville, Maryland 20852

PHARMACEUTICAL PROTECTION URGED The National Formulary has asked FDA to consider pharmaceutical protection of contents as well as child protection in the latter's development of specifications for child-resistant (safety) closures for drugs. The National Formulary said it is planning a study to assess the capability of containers meeting FDA specifications to provide adequate pharmaceutical protection, too. In a letter to the FDA, John V. Bergen, NF director, offered the assistance of his organization in developing appropriate guidelines. Pertinent NF monographs now provide for specific container requirements, such as being well-closed, tight, and light-resistant, to insure protection from the environment, according to a news release by the American Pharmaceutical Association. Dr. Bergen said that providing pharmaceutical protection standards is a responsibility shared equally by both the NF and the United States Pharmacopeia and that steps are being taken to insure cooperation between the two in making the study.

NABP TRAINING GUIDE The National Association of Boards of Pharmacy announces the availability of a 60-page manual titled, "Pharmacy Preceptor's Guide—A Manual for Internship Training," recently published. It is intended for use by pharmacy preceptors training students to qualify for licenses, for students gaining experience, and for those interested in the general ethics and aesthetics of orienting future pharmacists to practice. Single copies are \$1, or 90 cents each for orders of 100 or more from National Association of Boards of Pharmacy, 77 West Washington St., Chicago 60602.

PHARMACEUTICAL SCIENCES CONGRESS The 31st International Congress of Pharmaceutical Sciences of the International Pharmaceutical Federation, scheduled in Washington September 7-12, will include a two-day symposium on "Optimizing Drug Activity" September 8-9, a full-day symposium on "Advances in Drug Metabolism Methodology" September 10, and an afternoon symposium on "International Trends in Pharmaceutical Patent Law" September 10.

The main symposium on "Optimizing Drug Activity" will be supplemented by two colloquia on September 10, in the morning on "Fundamental Properties of Powders and Compact Masses," and in the afternoon on "Optimizing Drug Activity Through Dosage Form Design." Among other colloquia will be one September 10 on "International Pharmaceutical Reference Standards, and the afternoon session will feature a talk on "Problems Involved with Antibiotic Reference Standards" by William W. Wright, deputy director, Office of Pharmaceutical Research and Testing, in FDA's Bureau of Drugs.

ISRAEL PHARMACY CONGRESS The second Congress of the World Alliance for Israel Pharmacy will take place in Jerusalem and Tel-Aviv in August 1972, Dr. J. Kohlberg, president, and Dr. E. Menczel, secretary general, have announced. There will be a scientific program including papers presented by leading pharmaceutical scientists, several panels discussing relations between pharmacy in general and practice of the profession in Israel, and a scientific exhibition emphasizing the industrial aspects of pharmacy. For further information: The Organizing Committee, Second Congress of the World Alliance for Israel Pharmacy, P.O.B. 16271, Tel-Aviv, Israel.