

FDA

CONSUMER

September 1982

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PUVA



Worms That Turn Good Food Into Bad

A number of diseases or ailments are caused by parasitic worms that sometimes find their way into food. These maladies range from mild to serious, and sometimes fatal. But in our modern society such troubles can usually be averted with a little caution.

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A Touch of Salt for Food Labels

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If misery loves company, this woeful gentleman should look for a friend who happens to have a non-prescription drug containing oil of cloves. That, says a panel of non-government experts, is the only ingredient safe and effective for relieving a toothache with "persistent throbbing" pain. What else the panel had to say on toothache remedies can be found in Some Medicine for Toothache Pain . . . But None for Bad Breath. The article begins on page 10.

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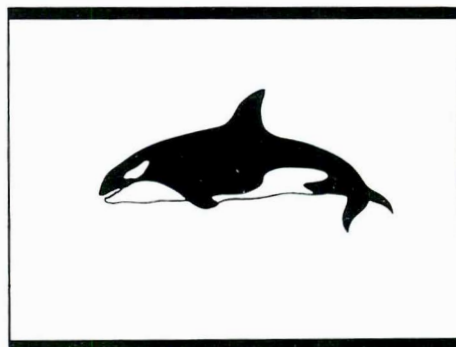
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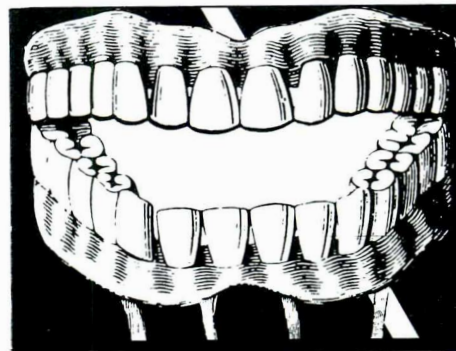
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Of Lice and Boils

A panel of experts studying the ingredients in non-prescription drugs has come up with good news for people suffering from lice but bad news for those with boils.

The good news is that a non-prescription combination of two pesticides, pyrethrins and piperonyl butoxide, was found safe and effective for treating lice infestations. Neither ingredient, however, was judged effective alone. The ingredients are poorly absorbed through the skin, making them generally safe to use externally. However, people who are allergic to ragweed may have problems with pyrethrins, which come from chrysanthemum flowers and can cause asthma and "hay fever" in allergic persons.

Three varieties of lice attack humans: the head louse, body louse and pubic or crab louse. How the little boogers do their dirty work was described in "All About Cooties and Such Critters" in the December 1980-January 1981 *FDA Consumer*.

The bad news is for boil sufferers. No ingredients in products sold without a doctor's prescription were found effective for treating these skin infections. Further, the panel said, boils should be treated by a doctor because of the risk of a serious blood infection known as septicemia. A boil is caused by an infection of a sweat gland or hair follicle.

These conclusions were made in two reports by the Advisory Review Panel on OTC Miscellaneous External Drug Products. FDA published the reports in the June 29 *Federal Register*, allowing 90 days for interested persons to comment. After the comments are evaluated, the agency will issue proposed standards for both types of products. Once final standards are issued, all non-prescription products for lice and boils must comply with them.

Starch Blockers Questioned

The Food and Drug Administration has asked more than 100 manufacturers and distributors of "starch blockers" to discontinue marketing them until scientific testing confirms the safety and efficacy of these weight management products.

Starch blockers are prepared from raw beans,



such as kidney and northern beans, and possibly other, unknown ingredients. The products have been advertised and sold nationwide with claims that they block or impede starch digestion and thus help in weight control and weight reduction by preventing absorption of carbohydrates.

Users of the products have complained to FDA of nausea, vomiting, diarrhea and stomach pains. Persons with diabetes should not depend on starch blockers in calculating their diets.

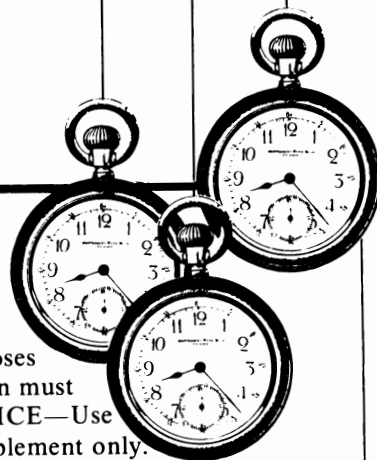
Manufacturers have refused to give FDA specific information about the exact chemical composition of starch blockers. Information supporting claims of safety or effectiveness in weight control or weight reduction has not been provided to FDA. The agency also is concerned about the safety of long-term use of starch blockers, because of the lack of adequate safety testing data.

Some manufacturers assert that starch blockers are special dietary foods. However, because these products claim to control or reduce weight by blocking or interfering with digestion, they may affect the body's normal metabolism function. Under the Food, Drug, and Cosmetic Act, a substance that is offered for a non-food purpose and that alters a function of the body is classified as a drug rather than a food, even if it is derived from a vegetable product.

Manufacturers were given 10 days to stop marketing starch blockers and to provide FDA with information about the manufacture and distribution of these products.

Home for an Orphan Drug?

The substance L-5HTP has been found "valuable" for the treatment of post-anoxic myoclonus, a neuromuscular disease, by the Pharmaceutical Manufacturers Association's Commission on Drugs for Rare Diseases. This was the commission's first evaluation of an "orphan drug"—a product that treats diseases with so few victims that it might go undeveloped without special attention. (Why some drugs are so neglected was explained in "Rx for Orphan Drugs" in the September 1980 issue of *FDA Consumer*.)



The PMA commission announced its findings in June in order to bring them to the attention of potential sponsors of L-5HTP. Such sponsors include pharmaceutical companies, the government, private health organizations and medical research institutions.

Evidence on the clinical use of L-5HTP in myoclonus victims was submitted to the commission by Dr. Melvin H. Van Woert, professor, departments of neurology and pharmacology, Mount Sinai Medical Center in New York City. L-5HTP is a non-patentable natural substance, presently available only for research purposes.

The commission also recommended development of triethylene tetramine for treatment of Wilson's disease, a condition associated with excessive amounts of copper in body tissues. An approved drug, penicillamine, is available for treatment of this condition, but some patients develop tolerance with prolonged use. Triethylene tetramine is currently under investigation by scientists in private institutions in the United States and the United Kingdom.

Liquid Protein Warnings

FDA has proposed labeling on certain protein diet products to warn that their misuse can be fatal.

The labeling would be required for very low-calorie "liquid protein" diet products such as those linked to a series of deaths in 1977 and 1978, and for other protein powders, capsules and tablets.

Under the proposal, food products deriving more than 50 percent of their calories from protein and promoted for weight reduction would have to carry the following label:

"WARNING: Very low calorie protein diets (below 400 calories per day) may cause serious illness or death. **Do not use for weight reduction without medical supervision.** Not for use by infants, children, or pregnant or nursing women."

Labels or labeling for protein products promoted as part of a nutritionally balanced diet plan providing 400 or more calories would have to declare: "NOTICE—Use only as directed in the diet plan described herewith. Do not use as the sole or primary source of calories for weight reduction."

Food products intended for dietary supplementa-

tion that derive more than 50 percent of their calories from protein for purposes other than weight reduction must state on their labels: "NOTICE—Use this product as a food supplement only. Do not use for weight reduction."

The proposed labeling regulation amends a rule that had been scheduled to go into effect in 1980, but was delayed when the U.S. District Court for the District of Columbia questioned certain scientific data related to one of the label statements.

FDA issued a public warning after a government investigation in 1978 found that the deaths of 16 women and one man were associated with the use of protein products in extremely low-calorie diets. Use of these products declined after the warning.

A specially formed U.S. Public Health Service "Protein Diet Task Force" concluded that protein products used as the principal or sole source of nourishment for rapid weight reduction may cause heart irregularities and death.

FDA published the proposed labeling requirements in the June 11 *Federal Register*, allowing 60 days for public comment. If a final rule is published it will become effective 90 days after it appears in the *Federal Register*.

Subscription Price Increased

Once again the Government Printing Office (GPO) has ordered a subscription price increase for *FDA Consumer*. The new price is \$21 a year domestic, and \$26.25 for foreign subscribers. GPO controls the subscription prices of government magazines such as *FDA Consumer*. GPO sets individual prices according to a formula based on its own expenses. In actuality, GPO provides minimal services to FDA on the magazine, those services being limited to setting up the printing contract for the magazine and handling subscription lists. The Food and Drug Administration pays all other expenses including costs of staff, special graphics, printing and postage. We regret that GPO has decided on this latest price increase—the third in less than 18 months for this magazine—and we hope that you the subscriber will be able to continue to afford the publication.

Worms That Turn Good Food Into Bad

by Marti Asner

Not all worms are found in bad apples. Other fruits and vegetables as well as fish and animals are hosts to such unwelcome guests. So are people.

Unlike the worms discovered in apples, those in many other foods are not often visible in the first bite, nor the last. Often concealed, they exist as microscopic eggs or larvae. If an animal or human eats the infested food, new generations may be produced in an unending cycle. The presence of worms in living hosts and foods may be unknown, subject to detection only by medical probing or laboratory analysis.

In the United States, the human worm burden remains a public health problem, although great strides have been made in sanitation, public education and medical treatment. Even legislation has helped, such as a requirement that garbage fed to pigs be cooked.

Trichinellosis (formerly called trichinosis), which comes mostly from infested pork, is probably the best-known food-borne parasitic disease. But others that cause major health problems around the world are diphylobothriasis, anisakiasis, heterophyiasis and chlonorchiasis from infested fish; taeniasis from infested beef and pork; and ascariasis and fascioliasis from infested fruits and vegetables (see Table 1).

Trichinellosis is not only the best-known but also one of the most serious of the parasitic worm diseases. The tiny roundworm that produces the disease is called *Trichinella spiralis*. Larval trichinellae infect rats and swine that dine on raw or undercooked meat in garbage. Bears and other wild animals (even the walrus) also may transmit the larvae. Humans can, in turn, become ill after eating undercooked meats from animals that harbor live larvae.

In the stomach the *T. spiralis* larvae

(in cysts or "sacs") are undaunted by potent gastric juices and proceed to the intestines. In about 48 hours the larvae mature into adults. Males and females mate and deposit a new generation of *T. spiralis* larvae. Then the moribund parents are evacuated from the body in the feces.

Baby *T. spiralis* larvae bore into the intestinal wall, then travel either to skeletal or heart muscles. Those that reach skeletal muscles dig into the muscle fiber. Life is good to them and they grow into "adolescents" that coil into spiral shapes (thus the specific name "*spiralis*"), develop a protective shell and remain for years. Larvae that enter the heart muscle die quickly; but the lining of this muscle can be seriously injured by even a short stay.

Trichinellosis symptoms vary with individual immunity and the intensity of the infection. During the intestinal phase, a person may experience minor diarrhea. After the *T. spiralis* larvae have invaded the muscle, the victim's symptoms become more severe and may include vomiting, muscular pain, fever, headache, facial swelling, small hemorrhages under the nails and difficulty in breathing. In the severest cases, death may come four to six weeks after onset of the disease.

The U.S. Centers for Disease Control in Atlanta receives about 150 reports a year of trichinellosis cases, of which about one is fatal. CDC suspects that another 100,000 to 300,000 mild cases go unreported. About 25 percent of trichinellosis cases result from eating the flesh of afflicted bears and other wild animals. In 1980 the greatest number of cases were reported in Louisiana (26), New Jersey (24) and Pennsylvania (12). Alaska had only 10 cases but had the dubious distinction of having the greatest rate of cases in proportion to population.

In 1981, an outbreak was reported

to CDC involving Asian refugees, many of whom prefer to eat pork lightly cooked. A total of 24 Cambodian and 13 Laotian refugees in Rhode Island contracted the disease after eating raw pork purchased from a local farm. All the patients recovered. In another incident, a 55-year-old woman in Greene County, N.Y., died 19 days after eating raw dried sausage.

Trichinellosis is one of the oldest of known human ills. The Egyptians are credited with developing the first recorded treatment in 1600 B.C. They believed that victims of the disease who ate the bark of the pomegranate tree would evacuate the worms and be cured. This may have worked during the very early stages of the disease. A more modern medication is thiabendazole, used in combination with corticosteroids, to alleviate some of the symptoms.

Prevention is the best safeguard against trichinellosis. To be on the safe side, the U.S. Department of Agriculture advises consumers to cook all pork to a uniform internal temperature of 170 F. Recently the department warned users of microwave ovens that the heat may not be evenly distributed and *Trichinella* organisms may survive in "cold spots." Both USDA and the National Pork Producers Council recommend the following procedures for cooking pork in microwave ovens:

- Choose evenly shaped cuts weighing five pounds or less.
- Cook at low or medium power settings (300 to 350 watts).
- Use a meat thermometer several times to be sure the product is 170 F throughout.
- Rotate the dish several times during cooking.
- Allow meat to set at least 10 minutes after cooking under a tent of aluminum foil. This allows even heat distribution.

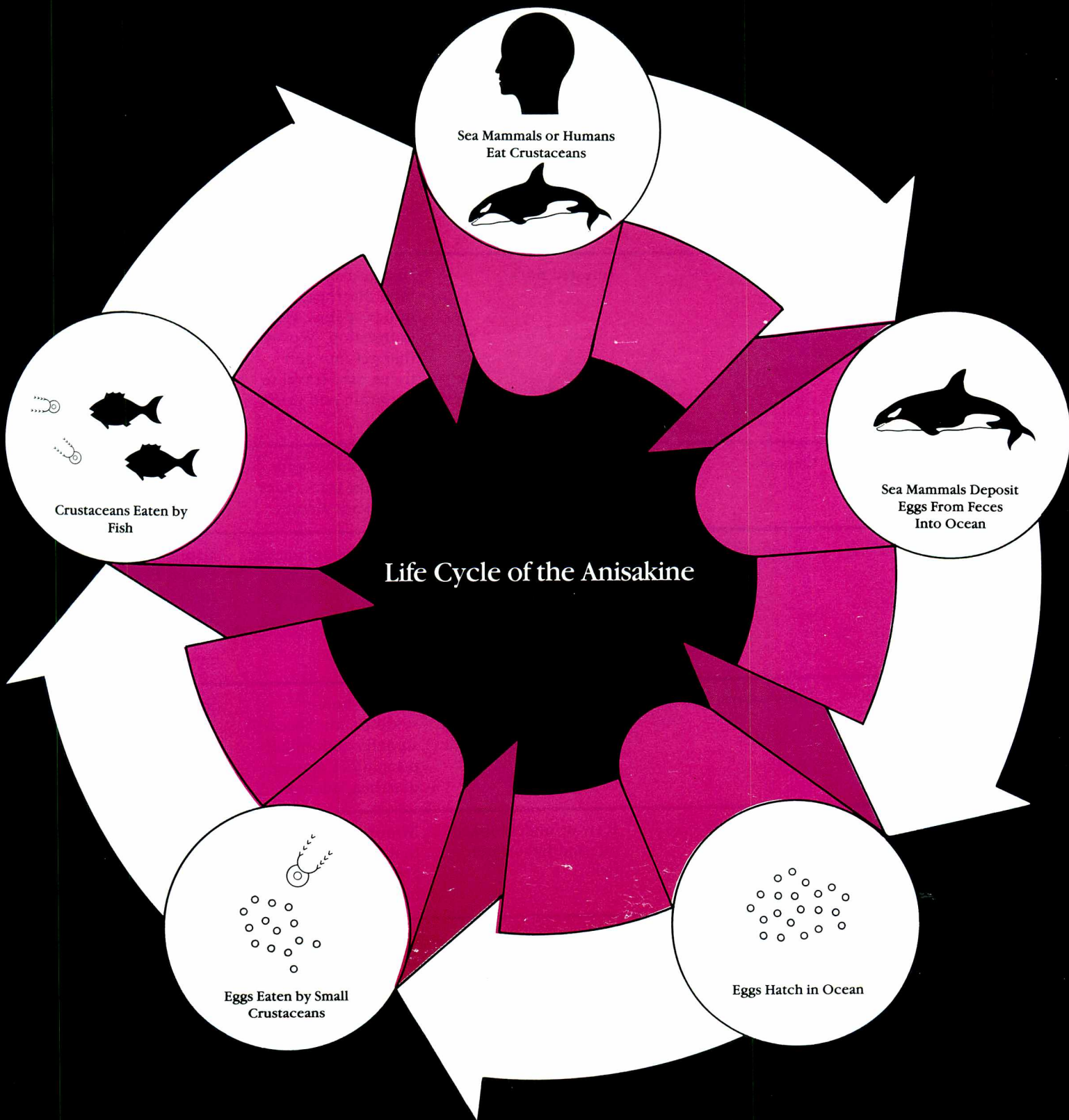


Figure 1.

Table 1. Examples of Common Food Worm Diseases

Name of Worm	Disease	Source of Illness	Symptoms	Prevention
<i>Trichinella spiralis</i>	trichinellosis	Raw or undercooked meat of infested animals. Found primarily in pork and bear meat.	Vomiting, muscle pain, fever, headache, facial swelling, trouble breathing, small hemorrhages.	Cook all pork and game to a uniform internal temperature of 170 F.
<i>Taenia solium</i>	taeniasis	Infested pork.	In digestive tract: mild diarrhea, false hunger pangs, chronic indigestion. Worms that get into soft tissue may travel to the brain and cause death.	Same as above.
<i>Taenia saginata</i>	taeniasis	Infested beef.	Same as above for digestive tract; does not invade tissues.	Cook beef to an internal temperature of 160 F.
<i>Anisakis</i> species	anisakiasis	Infested marine fish that are raw or undercooked.	Ulcers, hemorrhages, nausea, stomach cramps, granulomas.	Freezing: -4 F for 72 hours. Frying: 140 F for 5 minutes. Baking and broiling: cook until meat flakes easily.
<i>Diphyllobothrium latum</i>	diphyllobothriasis	Infested marine fish that are raw or undercooked.	Usually non-symptomatic; occasionally abdominal discomfort, nausea, diarrhea, anemia.	Same as above.
<i>Chlonorchis sinensis</i>	chlonorchiasis	Raw or undercooked infested freshwater fish.	Minor liver ailment that may progress to gross liver enlargement, toxic edema.	Same as above.
<i>Heterophyes heterophyes</i>	heterophyiasis	Raw or undercooked infested fish in fresh or brackish waters.	Colicky pains with mucous diarrhea.	Same as above.
<i>Ascaris lumbricoides</i>	ascariasis	Infested fruits and vegetables.	Asthma-like condition, intestinal blockage; can be fatal in children.	Thoroughly wash all fruits and scrub vegetables; canning and long-term freezing.
<i>Fasciola hepatica</i>	fascioliasis	Contaminated watercress.	Fever, abdominal pain, vomiting, jaundice, diarrhea.	If infected sheep are in the area, avoid watercress.

Also potentially life-threatening to humans is the tapeworm called *Taenia solium*, which occurs in countries where people eat undercooked pork. It is rarely encountered in the United States, but it is quite prevalent in certain parts of Mexico and Central Europe. The larvae develop into adults in the small intestine. Some symptoms of the associated illness include hunger pangs, diarrhea and chronic indigestion. Some eggs, which may be consumed in vegetables, hatch in the intestine and the larvae penetrate the digestive tract. If the larvae invade certain areas of the brain, infections can be fatal.

A more common tapeworm in the United States is *Taenia saginata*. The larvae grow in the flesh of cattle and are transmitted to humans in insufficiently cooked or raw beef. Illness symptoms are similar to those caused by *T. solium*, but milder.

Fish lovers also should be cautious when preparing their meals. At least six varieties of worms that can make humans ill are known to infest fish. Most of the fish worm problems in the United States are caused by a group of related roundworms called anisakines. They need three types of hosts to complete their life cycle (see Figure 1). The eggs may occur in the feces of seals, sea lions, whales and other marine mammals. They hatch in the water, and the larvae are eaten by marine invertebrates (small crustaceans), which are then consumed by fish that, in turn, are consumed by marine mammals or humans.

The larvae anchor themselves in the stomach or intestinal lining of the human host, where they can cause ulcers and bleeding. Nausea and stomach cramps are common complaints.

If the worms get restless and start to wander throughout the body, granulomas, or tumors, can appear in the tissues. Such masses are often misdiagnosed as cancerous tumors. Truly adventurous anisakines have been known to roam from the stomach up the esophagus to the throat.

Anisakiasis, like other human worm diseases, is preventable and infestation by this worm is usually not life

threatening. Freezing fish at -4 F for 72 hours kills the larvae. Frying temperatures for foods should be at least 140 F for five minutes. There is no specific formula for baking and broiling, but experts recommend cooking the fish until the meat separates easily. There are no drugs currently approved for treatment of this illness.

Diphyllobothriasis, other than a mouthful of syllables, is also a dangerous disease caused by the tapeworm *Diphyllobothrium latum*. The worm behaves in much the same way as the anisakines and may attain lengths to 100 feet in humans. In some cases these tapeworms cause a pernicious anemia in humans. Two years ago this worm caused a rash of human cases on the West Coast, attributed to eating salmon. The type of salmon dish eaten varied. Of the people who became ill, 26 percent had eaten the salmon raw; 41 percent ate only cooked salmon; 7 percent ate it pickled, marinated or salted; and 26 percent ate it prepared in a combination of the previously mentioned methods. (Only one individual ate the salmon at a sushi bar, a Japanese eatery serving raw fish. Sushi chefs, it should be noted, are generally experts in detecting and removing the sac-like larvae and carefully choose deep water fish, which are less apt to be contaminated.) The drug niclosamide has been recently approved by FDA for treating *D. latum* infections.

Another fish worm, the liver fluke, *Clonorchis sinensis*, is found primarily in the Orient. The worm is transmitted by undercooked, brined or marinated and dried fish. Travelers to the Middle East and Near East should also be aware of a tiny intestinal fluke called *Heterophyes heterophyes*, transmitted in fish, particularly the mullet.

A worm that may infest fruits and vegetables to the detriment of human health is *Ascaris lumbricoides*. *Ascaris* eggs can be found on fresh fruits and vegetables grown in contaminated soil or fertilized with sewage sludge. The worm's eggs survive wherever sanitation is poor and in city sewage systems.

When full size, the *Ascaris* worm resembles the common earthworm.

Females can be as thick as a pencil and produce about 200,000 eggs a day. Males are slenderer and are distinguished by an incurved tail. Both sexes are creamy-white with a pinkish hue.

Pesticides, dry weather spells and high humidity do not affect the hard-shelled *Ascaris* eggs. Once swallowed, the eggs hatch in the intestines and the larvae begin a complicated migration through the tissues that lasts up to 10 days.

Symptoms first appear when the larvae reach the lungs. The victim may develop an allergic condition similar to asthma. The larvae then migrate to the small intestine where they mature and remain as adults. An illness caused by a small number of worms may go unnoticed in an adult. Children are especially vulnerable and may suffer intestinal blockage from the worm. In infants, the disease can be fatal. Medication given during the intestinal phase can cause the worm to become more active and to penetrate the intestinal wall, appendix, gall bladder and liver. Eventually, after about two weeks to two months, the worm is expelled in the feces. Drugs used to treat ascariasis include mebendazole, pyrantel pamoate and piperazine citrate.

The best way to prevent ascariasis is to thoroughly wash all fruits in water before eating them and to scrub all vegetables. Canning and long-term freezing also kill the worms.

Not eating watercress in certain areas where sheep are infected is recommended to eliminate the threat of infection by *Fasciola hepatica*, a sheep liver fluke. These organisms are common in contaminated watercress. Infections are more prevalent in Hawaii than in the continental U.S.

No doubt we live in what the eminent worm expert, the late Norman R. Stoll, called "this wormy world." But consumers can protect themselves and their families by taking the necessary precautions when preparing food. After all, what you can't see can sometimes hurt you.

Marti Asner is a member of FDA's public affairs staff.

A Touch Of Salt For Food Labels

by Chris Lecos

Scanning food labels may never be as popular as reading the newspaper funnies. Likewise, the labels on cans of peas and packages of frozen pizza may never be read as thoroughly as the *Daily Racing Form*. However, reading food labels is a lot more popular than reading the old love letters of Attila the Hun.

In fact, since nutrition information was added to food labels nine years ago, it is not uncommon to round a supermarket corner and find a consumer immersed in the facts and figures found on the paper that surrounds a container of food. Since FDA published regulations in 1973 calling on the food industry to start providing consumers with more complete nutrition information, shoppers are able to note the number of calories and the amount of protein, carbohydrate and fat in a specified serving of food. Also available is a listing of the percentages of the U.S. Recommended Daily Allowance (U.S. RDA) of protein and seven vitamins and minerals in a serving.

Nutrition labeling is not used on all food products regulated by FDA and is mandatory only if a food manufacturer adds one or more vitamins, minerals or protein to a product or the labeling makes some kind of nutritional claim about it. But FDA has encouraged the industry to supply nutrition information voluntarily, and many food products today bear this information because the manufacturer is willing to provide it. (Some food

products under U.S. Department of Agriculture jurisdiction, such as packaged processed meats, also may carry nutrition labeling.)

Now, through new regulations proposed in the *Federal Register* on June 18, 1982, FDA is urging the food industry to take another major step, primarily on a voluntary basis, to give the American consumer more important labeling information—on the sodium content of food products.

Sodium can be found in measurable amounts in almost every food. There are at least 70 sodium compounds that may be used in food today. FDA's proposed regulations follow a year-long, nationwide campaign of encouraging Americans to reduce their sodium intake and urging the food industry to cut down on the sodium used in food processing. FDA marketing studies indicate that more than three-fourths of the food brands surveyed listed one or more sodium-containing substances in their ingredient lists, attesting to sodium's widespread use in food.

As early as 1904, scientists noticed an association between excessive dietary intake of sodium and high blood pressure, or hypertension. However, it cannot be said with certainty that excess consumption of sodium is what causes high blood pressure.

"Although many epidemiological studies indicate a relationship between sodium intake and the prevalence of hypertension, the evidence that sodium consumption is a major factor

in causing hypertension is not fully conclusive," FDA noted. "Nevertheless, the evidence is strong enough for most members of the medical and scientific community to conclude that a substantial portion of the U.S. population which is predisposed to hypertension would benefit from a reduction in dietary sodium."

Hypertension is a leading cause of strokes, and is viewed as a major contributor to heart attacks and heart and kidney failure. It is, said FDA, a "major health concern in the United States today." An estimated 23 to 60 million Americans are believed to be hypertensive.

The main intent of FDA's proposal is to get food manufacturers to identify the sodium content of their products and to establish definitions for the terms "sodium free," "low sodium," "moderately low sodium" and "reduced sodium" used on food labels. Because of possible confusion between the terms "salt" and "sodium," FDA's proposal explains what would be acceptable use of terms such as "no salt added," "salt free" or "unsalted" on the label. Salt and sodium are not synonymous terms. Chemically, salt is sodium chloride. It is about 40 percent sodium and is the largest single contributor of sodium to the human diet.

When the nutrition labeling regulations went into effect in 1973, food producers were not required to include sodium as one of the nutrients on a nutrition label. They were given the option of doing so. By special exemption, a manufacturer also could show the sodium content of a product without having to provide the rest of the required nutrition information. The only mandatory requirement for listing sodium content has been when a food is used or sold for controlling one's sodium intake.

Under the proposed amendments, a food company would have to give sodium content on the label if nutrition labeling is used. It would be listed along with the other required nutrition information. Companies also would be permitted to identify the sodium content without having to use nutrition labeling.

Manufacturers producing foods for special dietary use who want to emphasize lower sodium content would have to follow the criteria set

forth in the proposed regulations. They could use these terms on a label, provided certain limits were met:

- The term "sodium free" would refer to any food with 5 milligrams of sodium or less in a specified serving. This would include sodium added to a food and any naturally present. It's possible to detect even minute amounts of sodium in almost any food, but 5 milligrams is considered trivial enough to satisfy the "sodium free" definition. A consumer on an extremely stringent sodium diet could consume 20 servings of "sodium free" food daily with no more than 100 milligrams of sodium.
- The term "low sodium" would apply to foods with 35 milligrams or less sodium in a serving. The National Academy of Sciences National Research Council has estimated that a "safe and adequate intake" of sodium for adults ranges from 1,100 to 3,300 milligrams a day when there is no heavy physical activity or other body demands for more sodium. Thus, 20 servings of "low sodium" foods in a day would keep a person below "normal" levels.
- The term "moderately low sodium" could appear on a label for foods that contain 140 milligrams or less sodium in a serving. Twenty servings at this level would contribute 2,800 milligrams a day.
- The term "reduced sodium" could be used if sodium content is reduced at least 75 percent below that of the regular food item. The label on a reduced sodium product "must bear information comparing the product's sodium content per serving with that of the food it replaces."

In its published comments, FDA acknowledged there is some consumer interest in requiring labeling on certain products indicating they are high in sodium. However, FDA said that imposing such a requirement is not justified at this time because there is "no general scientific agreement on what 'high in sodium' is."

The proposed regulations also would allow foods to be marketed as being "unsalted" or having "no salt added" or some other equivalent phrase provided (1) no salt is added during processing, (2) the food it resembles and for which it is a substitute is normally processed with salt, and (3) the sodium content is stated. A

food produced without salt (or sodium chloride) is not necessarily sodium free.

A "salt free" food would be viewed as having false and misleading labeling unless it contained no more than 5 milligrams of sodium in a serving. In effect, it would have to meet the same sodium levels as a "sodium free" product.

After the proposed regulations were published, the food industry, citizen groups and the general public were given 60 days or until Aug. 17, 1982, to submit any comments or reactions to the proposals. A final regulation probably could go into effect sometime in 1983. In publishing the proposals, FDA reiterated its longstanding position that it is relying on voluntary participation by and support from the food industry to achieve the goals of providing consumers not only with more foods in which sodium content is listed but also more processed foods in which the amount of sodium, especially salt, has been cut down. As the agency put it:

"This proposal is the only element in the agency's program that requires a regulation and is not meant to supersede or overshadow the emphasis that FDA places on the voluntary efforts of the food industry." To date, the agency said, FDA has been encouraged by the efforts and interest of the food industry. "Many of the major food companies have advised FDA that they are providing or intend to provide sodium information on their product labels," FDA said. In addition, many food companies are working on ways to reduce the sodium content of their products where feasible. FDA Commissioner Arthur Hull Hayes Jr. has praised the cooperation from industry and has noted that FDA plans to carefully monitor the effectiveness of the present sodium information effort.

Marketing data compiled by FDA gives some indication of the impact the program could have. Based on surveys in 1979 of food brands, 44 percent of packaged food sales in the United States were foods that had full nutrition labeling. Half of the food represented by this sales figure bore nutrition labeling because it was a mandatory requirement; the other half had such labeling because it was voluntary on the part of the manufacturers.

The degree of potential impact can be viewed another way than by sales figures. The 1979 marketing survey involved 1,044 food brands. Of these, nearly 33 percent had nutrition labeling. Fifteen percent of the 1,044 brands bore nutrition labeling because it was mandatory. Thus, under the proposed amendments, at least that number would have to show sodium content if the proposed regulations are approved. Another 17.5 percent of the brands were nutritionally labeled on a voluntary basis, and it is FDA's hope that these, and other products as well, continue to use nutrition labeling including sodium content information.

FDA's 1979 marketing survey also revealed that 1,031 of the food brands listed ingredients on their labels, and of that total, 76 percent included sodium-containing ingredients. Less than 6 percent of these actually gave the amount of sodium. This figure is expected to rise substantially, based on the responses of many food companies to date.

In an evaluation of the economic implications of its proposed regulation changes, FDA concluded that approximately 3,500 food manufacturing firms would incur a first-year cost totaling up to \$14.7 million and recurring annual costs of \$500,000 to comply with the proposed regulations—costs that would be passed on to consumers. The agency estimated that the first-year cost represented about "one one-hundredth of one percent of consumer expenditures for FDA regulated food products or about three one-hundredths of one percent of consumer expenditures" for all the foods that are nutritionally labeled.

In announcing its proposed sodium labeling regulations, FDA also said it would defer action on the current regulatory status of salt (sodium chloride). Salt is currently considered "generally recognized as safe" as an ingredient in food. Although there are considerable health concerns about the present levels of salt use in the food supply today, the agency said it is "not now proposing any change in the regulatory status of salt . . . because the agency believes that the proposed sodium labeling regulations . . . will respond to those concerns."

Chris Lecos is a member of FDA's public affairs staff.

Some Medicine For Toothache

Drugs Take The Bite Out of Toothache

by Annabel Hecht

A few people sometimes have throbbing toothaches. Others wake up in the morning with bad breath. Those with toothaches can get some temporary relief with non-prescription drugs containing oil of cloves (or eugenol). But for those who want to freshen their breath, medical ingredients in mouthwashes may not provide any health benefits and indeed may do some harm.

These are the conclusions reached by two expert advisory panels reviewing the ingredients in toothache remedies and oral health-care products respectively as part of FDA's massive study of the safety and effectiveness of non-prescription, or over-the-counter (OTC), drugs. The reports of the Advisory Review Panel on OTC Dentifrice and Dental Care Drug Products and of the panel on OTC Oral Cavity Drug Products were published by FDA in the May 25, 1982, *Federal Register* to elicit public comment. The recommendations are those of the panel members and are not binding on the agency. After the public comments have been reviewed, FDA will propose standards covering products promoted for non-prescription use for toothaches and for oral health care.

Here is more detail on what the two panels had to say.

There is a consumer population with occasional needs for non-prescription products to treat minor trauma or irritation of the teeth and gums, according to the expert panel on dentifrices and dental care products. Despite the need, the panel found only a few ingredients on the market that are safe and effective for use as (1) agents for the relief of toothache; (2) oral mucosal analgesics (pain-killers); (3) oral mucosal protectants; and (4) tooth desensitizers.

Of the 12 active ingredients in common toothache remedies, only clove oil, or a similar oil containing 85 to 87 percent eugenol (a derivative of cloves), is safe and effective for toothache. But, said the panel, this ingredient should be used only on a tooth with "persistent throbbing" pain. This kind of pain indicates the tooth pulp is already irreversibly damaged, so topical pain-killing products can't cause additional injury, the group reasoned. But if the pain is occasional or intermittent, a characteristic of reversible damage, such products could injure the pulp, perhaps causing irreversible damage, and should not be used.

Three of the 12 ingredients reviewed were not considered safe and effective toothache remedies. They are capsaicin (from hot pods of pepper) when used on an open cavity, menthol and methyl salicylate. Further study is needed to determine the safety and effectiveness of nine ingredients, including benzocaine, creosote, phenol and thymol preparations and capsaicin as a counterirritant in a poultice that's applied to the gum near the toothache.

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But None For Bad Breath

Medicated Mouthwashes Wash Out

Those couples on television who discuss the relative merits of their favorite mouthwash could solve their early morning bad breath problems just as easily by rinsing their mouths with water, brushing their teeth, flossing, or just by eating breakfast, said a panel of experts studying ingredients in oral health-care products.

As for adding germ killers to such non-prescription drugs, the panel vetoed the idea. Bad breath in the morning, something nine out of 10 people have, is not evidence of a systemic or oral disease, the panel said. No health benefits result from the long-term use of antimicrobial agents on a daily basis, and there is evidence that they may be harmful in some instances, the panel said. For these reasons, the panel felt obliged to discourage the use of antimicrobial agents in oral health-care products.

A minority of panel members felt the final report should have included the anti-plaque activity of mouthwashes, which the full panel had considered earlier in its deliberations. In recent years some consumers have used antimicrobial mouthwashes to prevent cavities and periodontal disease by reducing plaque (material that is deposited on the teeth). There have been a number of reports in the dental literature on the clinical effectiveness of three antimicrobial agents in reducing dental plaque, the minority noted.

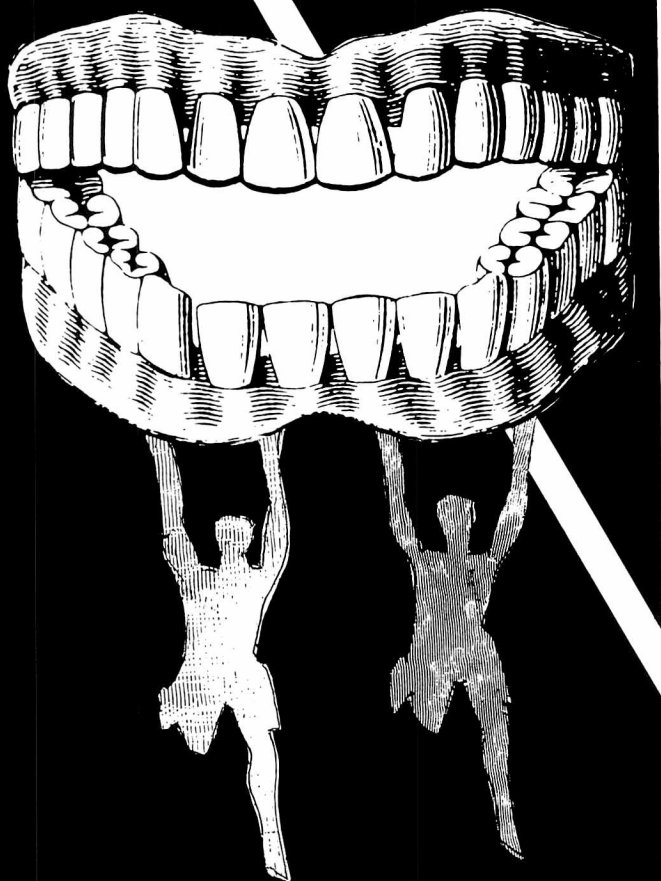
Nonetheless, the group did classify some 34 active ingredients found in mouthwashes. None, they said, is safe and effective. Ten—including boric acid, ferric chloride, potassium chlorate, sodium dichromate, phenol and cetylpyridinium—should not be used in mouthwashes. Twenty-four ingredients, among them benzoic acid, chlorophyll, eucalyptol, iodine, menthol and tolu balsam, require further tests to determine their safety and effectiveness.

The panel not only discouraged the use of antimicrobial ingredients in mouthwashes but said their labeling should not claim the product kills germs by the millions or in minutes, or inhibits odor-forming bacteria.

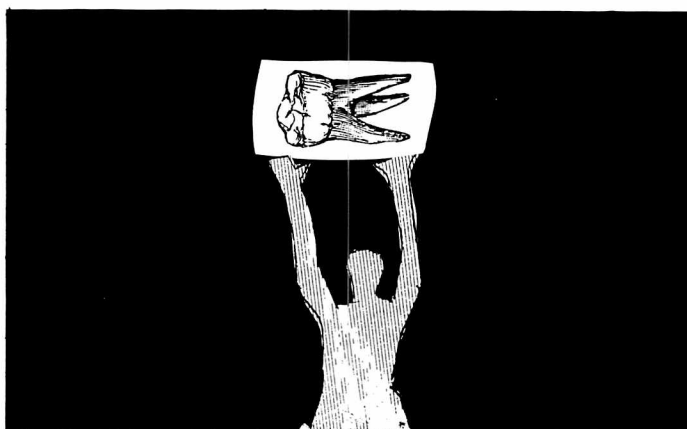
The panel also reported on six other categories of oral health-care products: anesthetics/analgesics, astringents, debriding agents, decongestants, demulcents and expectorants.

In the category of anesthetics and analgesics, marketed for the temporary relief of the pain of sore throat, the panel found the following ingredients safe and effective: aspirin, benzocaine, benzyl alcohol, dyclonine hydrochloride, hexylresorcinol, menthol, phenol, phenolate sodium and salicyl alcohol. Dyclonine hydrochloride at present is available by prescription only. A minority of the panel members felt aspirin should not be included.

(continued on page 12)



(continued from page 10)



Labeling for toothache remedies should warn that the product is only for persistent, throbbing tooth pain. The user should see a dentist as soon as possible and not use the product for more than seven days, the panel recommended. Toothache products should not be promoted for rapid and effective relief of sore gums or for sore gums following tooth extractions, they said.

Benzocaine, butacaine sulfate and phenol preparations (phenol and phenolate sodium) are all safe and effective as oral mucosal pain-killers, but camphor and methyl salicylate are not, according to the expert panel. Benzyl alcohol and cresol should be further tested.

Oral mucosal pain-killers can be labeled for the temporary relief of pain from minor irritation or injury of soft tissues of the mouth, minor dental work or canker sores already diagnosed by the dentist, the panel said. Labels for products containing benzocaine or phenol can also claim to ease the discomfort of teething in infants and children 4 months of age and older. But, said the panel, these products cannot be labeled as quick acting or especially soothing after extractions or for temporary relief of pain from tooth cavities.

Only two ingredients were reviewed as oral mucosal protectants (substances that help protect irritated areas of the mouth from further irritation from chewing and swallowing). One of them, benzoin preparations (benzoin tincture and compound benzoin tincture), was found safe and effective by the panel, while the other, fluid extract of myrrh, was recommended for further study.

Approved labeling for protectants includes such claims as "forms a coating over a wound" and "protects against further irritation." Labels should warn consumers not to use the product for more than seven days. Unacceptable to the panel are claims such as "especially soothing after extractions or for minor gum boils" or "gives quick relief that lasts for hours."

As for desensitizers, the panel found no ingredients it considered safe and effective to treat hypersensitive teeth, that is, teeth that are extra sensitive to heat and cold. The combination of sodium fluoride, strontium chloride and edetate disodium should not be marketed. Five ingredients, including fluoride preparations, formaldehyde solution and potassium nitrate, should be subjected to additional testing to establish whether they are effective as tooth desensitizers.

(continued from page 11)

Another 10 ingredients were deemed not safe and effective, including antipyrine, camphor, and a number of "caine"-type anesthetics (lidocaine, dibucaine, tetracaine). In addition, eucalyptol, methyl salicylate and thymol should be further tested, according to the panel recommendations.

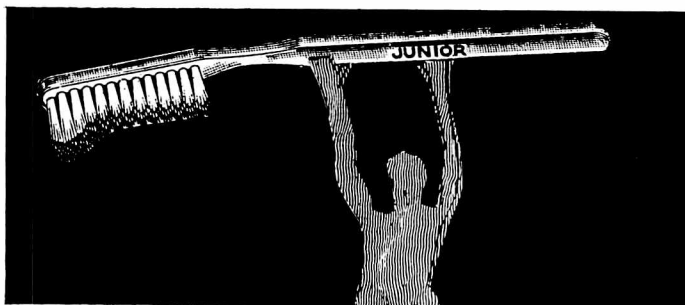
Oral astringents are drugs that form a thin protective film on the cells of the mouth to lessen their sensitivity to external stimuli. Alum and zinc chloride will do this job, said the expert panel, but tincture of myrrh will not.

Among the ingredients considered as debriding agents (substances that mechanically wash secretions from the surface of the mouth), the panel said carbamide peroxide in anhydrous glycerin, hydrogen peroxide and sodium bicarbonate (baking soda) are safe and effective. Sodium perborate did not measure up as a debrider.

The panel found no ingredients that were safe and effective as decongestants, to aid in the temporary relief of occasional discomfort due to congestion in the mouth and throat. Phenylephrine hydrochloride and phenylpropanolamine hydrochloride might make the grade but first must be subjected to additional testing.

Elm bark, gelatin, glycerin and pectin would be acceptable ingredients in demulcents, according to the panel. Demulcents aid in the temporary relief of minor discomfort and protect irritated areas of the mouth and throat.

Finally, the oral health-care panel said there are no ingredients safe and effective as expectorants to help remove thick secretions from the mouth and throat. They said potassium iodide is not safe and effective and ammonium chloride, horehound and tolu balsam need further testing.



Labeling for all oral health-care products should include a warning that severe or persistent sore throat or sore throat accompanied by high fever, headache, nausea and vomiting may be serious. Such products should not be used for more than two days and should not be given to children under 3 years of age unless directed by a physician. Consumers also should be warned not to swallow these products and to discontinue their use and consult a physician if irritation persists or increases, or a rash appears on the skin.

Among the claims the panel said should not be made are suggestions that the product works quickly, relieves pain from canker sores, helps kill mouth germs, or is soothing and cleansing to the mouth.

Annabel Hecht is a member of FDA's public affairs staff.

Removing The Dread From EPILEPSY

by John M. Couric

People suffering from epilepsy have been freed from much of the fear and stigma experienced by earlier victims, thanks to anti-convulsant drugs now available. There still is no cure for this nervous system disorder, which is characterized by a variety of symptoms including muscle spasms, mental confusion and loss of consciousness. However, an array of anti-convulsant drugs is available, and proper use of the appropriate medication can help make possible an active and fulfilling life for most with only a small chance of suffering an epileptic seizure.

Therapy for epilepsy is intended to prevent seizures in which brain cells, or neurons, create abnormal electrical discharges that cause temporary loss of certain body functions. These seizures can range from mild to severe and usually last only a short time. Epilepsy is not contagious, is not a mental illness, and is not indicative of a low intelligence level.

Anti-convulsant or anti-epileptic drugs are chemicals that may be prescribed singly or with other drugs. Some people who have epilepsy are subject to more than one kind of seizure, and treatment may require more than one anti-convulsant drug. When

possible, physicians try to find a single drug that is effective and whose benefits can be balanced against possible side effects or other adverse reactions.

It's estimated that 2.1 million Americans suffer from epilepsy. The three main types of seizures are classified by the Epilepsy Foundation of America as generalized tonic-clonic (or grand mal), generalized non-convulsive (also known as petit mal or absence), and partial. Tonic-clonic is the most dramatic form of epilepsy. As nerve cells discharge throughout the brain the entire body stiffens and shakes, the arms and legs jerk violently, and the victim falls, loses consciousness, becomes rigid and begins breathing irregularly.

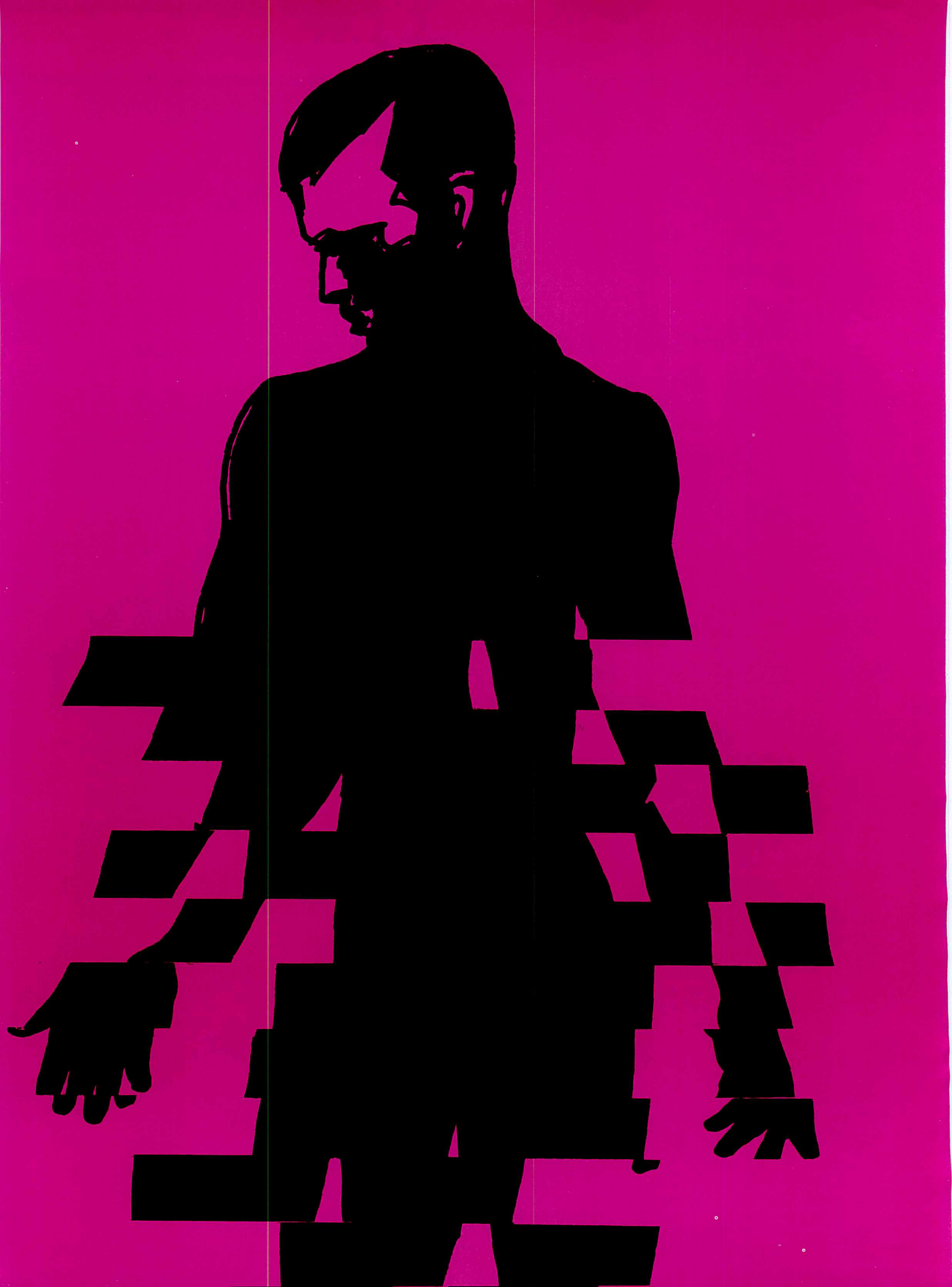
Tonic-clonic attacks last one to several minutes. A period of rigidity in the tonic phase is followed by the clonic aspect in which the major muscles alternately contract and relax. As the seizure subsides, a period of deep relaxation follows. Non-convulsive attacks last only a few seconds and consist of blank spells in which the victim loses awareness, twitches slightly, stares and blinks. Unlike tonic-clonic attacks, which are rarely continuous, generalized non-convulsive attacks may occur dozens or

even hundreds of times a day and may even be mistaken for daydreaming or inattentiveness. Partial epilepsy results when nerve cells discharge in a part of the brain, causing a period of mental confusion followed by pointless movements such as pacing and hand rubbing, pain, dizziness and irritability. These seizures can last up to 20 minutes.

There are many less common types, including one in which abnormal electrical activity in a given area of the brain causes spasms in a specific part of the body while the ill person remains conscious. Another less common type causes infantile convulsions in which babies lose consciousness or muscle control for a short while.

Scientists still do not know why neurons build up and discharge in the brain, but epilepsy has been related to birth defects, prenatal damage or injury at birth to the central nervous system, head injuries, poisons, diseases such as measles, circulatory disorders, brain tumors and poor nutrition. In some cases, it is impossible to identify the cause. Those that can be traced to a specific cause are classified as symptomatic; those that cannot are called idiopathic.

Researchers really don't know



exactly how medication helps sufferers, but the drugs may work in one or more ways. Some may interrupt the spread of excess energy in the brain while others may increase the amount of a natural seizure inhibitor which turns brain cells on and off like a light bulb. Up to now, therapy has been largely based on experience, but researchers are trying to find better scientific answers that could lead to even more effective treatment.

The physician's skill is especially important in prescribing drugs for the treatment of epilepsy because patients react individually. The right dose needed to gain control of the disease may be determined quickly for some; in others, considerably more experience is necessary before a seizure-preventing level of the drug is reached in the patient's blood. In addition, individuals suffer different side effects from anti-convulsants.

With the development of a technique called anti-epileptic drug level testing, physicians can tell sooner what happens when medication enters a patient's body. This monitoring is carried out by analysis of a blood sample to find the amount of the medication present in the bloodstream, the route by which anti-convulsants reach the areas of the brain where the seizures begin. Levels too low can result in inadequate seizure protection. Levels too high can cause undesirable side effects, including drowsiness or confusion.

Generally, side effects are mild and usually occur at the beginning of therapy. Besides drowsiness or confusion, side effects can include irritability, nausea, rash, some thickening of facial features, increased growth of body hair, some physical clumsiness, overgrowth of gum tissue, and hyperactivity in children. Some individuals undergo emotional changes caused by the drug they are taking. Careful monitoring by the physician is required to customize the proper drug and dosage.

Interaction with other drugs, including non-prescription products, must be watched for and patients are urged to tell their physicians about the other medications they are taking.

Drugs used for treating epilepsy include quinacrine, methsuximide, clonazepam, valproic acid, methamphetamine, dextroamphetamine, acetazolamide, phenytoin, metharbital, chlorthalidoxepoxide, mephobarbital,

mephénytoin, primidone, paramethadione, ethotoin, phenobarbital, phenacemide, methylphenidate, carbamazepine, clorazepate, trimethadione, diazepam, and ethosuximide.

The Epilepsy Foundation says that anti-convulsant drugs are successful in preventing seizures in the majority of people who take them regularly and as prescribed. According to the foundation, at least 50 percent of all patients with epilepsy gain complete control of their seizures for substantial periods. For many of this group there may be no seizures for years, while for another 30 percent seizures may be as infrequent as once or twice a month or even once or twice a year, the foundation says.

A recent study published in *The New England Journal of Medicine* reported that certain epileptic children who remain free of seizures during four years of treatment probably can stop taking drugs without suffering relapses. These are children who do not fall into four high-risk categories: (1) those who had epilepsy for a long time before treatment was started, (2) those with mental retardation or physical disability caused by neurological disturbances, (3) patients with certain types of unusual seizures, or (4) those with a combination of seizures.

The study, conducted at Washington University in St. Louis, involved 148 children whose treatment was stopped after four years without a seizure. For up to 23 years afterward only 41, or 28 percent, suffered relapses and these were in at least one of the four risk categories.

Any discontinuance of medication must be carefully monitored by the patient's physician, however, because of the danger of non-stop seizures, which could cause brain damage.

Some patients at all ages continue to experience seizures regularly, even when they take medication, because the right chemical combination has not been found to control their epilepsy. Because of this, researchers are still seeking to produce new drugs and find new ways to use them.

Women who have epilepsy and are also pregnant face a vexing choice between risk and benefit. Without medication there is a risk of having a seizure that could lead to a fall. This might damage the developing child more than a possible fetal defect caused by anti-convulsant medication.

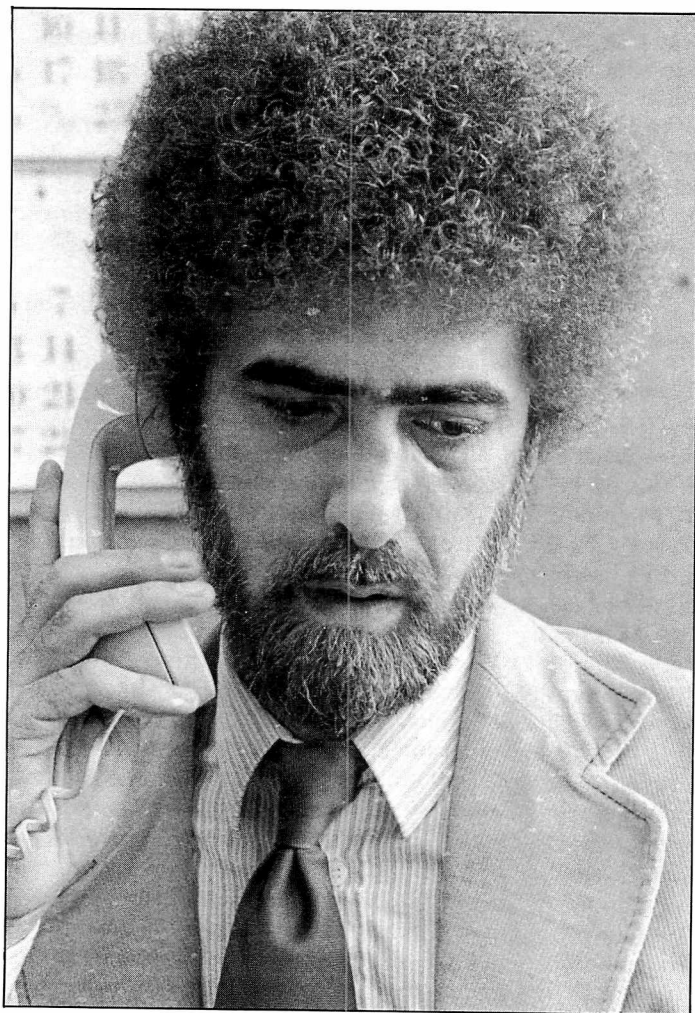
There is not enough knowledge for an easy solution to this problem. However, sudden withdrawal of anti-convulsants could cause non-stop, severe seizures that might be injurious to the mother and to the unborn child. The Epilepsy Foundation says that 92 percent of mothers on anti-convulsant medication give birth to normal, healthy babies.

As in other regimens, the patient is a key member of the therapy team. To assist him or her, the Epilepsy Foundation has a publication, *Medication for Epilepsy*, which offers these suggestions for taking medications:

- Don't take less than prescribed. You may have a seizure.
- Don't ever stop your medication abruptly. If you do, you risk a medical emergency in the shape of non-stop seizures that can threaten your life.
- Don't try other people's pills. Even if a friend says he or she has better control with a different medication, check with your doctor instead.
- Don't mix large amounts of alcohol with your medication. This can be a deadly combination. Both anti-convulsants and alcohol act as depressants, and one may intensify the effect of the other.
- Don't drive when starting a new medication until you know how it affects you. You may be able to function perfectly, or it may make you drowsy at first. Find out before you get behind that wheel.
- Don't assume that if you've missed a few doses of your medication you can then make them up safely by taking them all at once. It doesn't work that way. What you need is a certain amount of medication, taken at regular intervals.
- If you have trouble remembering to take your medication in sequence (this may be necessary if you are taking more than one type of anti-convulsant drug), give your memory some help by counting out each day's supply of pills and storing them in special containers, which you can buy at the drugstore.
- Don't let yourself run out of medication. Set up a schedule for re-ordering so that it becomes automatic.
- Keep all medication locked up and away from children.

John M. Couric is a writer/editor with FDA's National Center for Drugs and Biologics.

The Story Of An Epilepsy Victim



(Contrary to popular belief, most epileptic victims were not born with the problem. Brain damage, often from a blow on the head, is a more likely cause. Here's the story of how one person became epileptic and learned, at long last, to live with it.)

by Gerald Farber

When I was 13 years old, I played a game that started a nightmare which may never go away.

It all began after baseball practice on Easter Sunday in 1959. Eleven of us got together in the woods behind the elementary school where we could sneak a smoke. That was when one of the boys introduced me to a game called "blackout."

The rules were simple: You squatted down, put your head between your legs, breathed through your mouth quickly and deeply about twenty times, and then stood up and blew on your thumb until you passed out. After a few seconds you regained consciousness.

I watched as one after another of my friends played the game. Everyone regained consciousness within a matter of seconds, although some temporarily lost their coordination and others couldn't move at all for a time. I, too, revived in a matter of seconds. Although I was groggy, I felt fine. However, later that evening I developed a headache that grew more severe with the passing hours. When the headache persisted, I was taken to our doctor for a check-up, but she could find nothing wrong with me.

The following afternoon I had a dizzy spell and fell to the floor. My speech became slurred. Then I was taken to the hospital for tests and observation.

Fluid was removed from my spinal column to determine if there was any abnormality of the brain. In another test, objects were placed in my hands, and I was asked to tell what they were without looking at them. At first I had no trouble doing this, but after a few days the sense of feeling on my left side gradually deteriorated. By the fifth day in the hospital, I could no longer identify objects in my left hand. Within a couple of weeks I lost the feeling in both hands.

The doctor then decided to do a right cerebral arteriogram (a brain X-ray) to determine if my condition was due to any swelling of brain tissue caused by accumulation of blood on the surface of my brain. The arteriogram left me in a coma for five days with fevers exceeding 106 F. Neurologists who were consulted said the game "blackout" had caused small hemorrhages in my brain. Dye from the arteriogram had seeped through these hemorrhages and caused more damage to the surface of the brain and the tissue beneath.

After I regained consciousness, my left side was temporarily paralyzed. In the next four weeks I had convulsive spells, during which I had no bladder control. My speech was extremely slurred and incoherent. This lasted for several months. I also suffered a total memory loss and had to relearn everything, right back to the preschool level.

Some months after coming home from the hospital I began having petit mal seizures, a form of epilepsy characterized by frequent, transient lapses of consciousness and occasional falling. Months later I had Asian flu, which brought on my first grand mal seizure, the type of epilepsy that results in a loss of consciousness. My eyes opened and pulled to the left and I suffered convulsions of the arms and legs. I was put on drug therapy. The barbiturates reduced the seizures but left me in a heavily sedated state.

In the summer of 1961 I was admitted to the National Institutes of Health. I was taken off all medication and given a room equipped with a closed-circuit TV so the doctors could monitor my seizures. More tests were done. In the end the doctors said the brain damage was too deep and nothing could be done.

Getting an education was another nightmare. After I recovered sufficiently from the first onset of seizures I returned to school, but I had to repeat the eighth grade. Now 14, I was over six feet tall and towered over the other stu-

dents. I was considered the "big dumb kid." I can still hear their laughter and taunts after my first seizure in class. Ninth grade in another school was no better. I was expelled as a result of an incident involving some homework I was trying to finish in a different class. The teacher took the paper and I grabbed it back. She thought I was going to hit her.

I never had a discipline problem before the onset of seizures, but now I resented authority of any kind. I was always rebelling against something.

In the summer of 1962 I was sent to a rehabilitation school in Leesburg, Va. The school was truly beautiful, and I wish I could say that I was a model student, but I wasn't. My hostilities arose from the first day I was there. I would occasionally break the rules and go into town to get away. One day I hitched a ride with a trucker who took me as far as Charlotte, N.C. A state patrolman found me wandering the streets at 3 a.m. and I had to wait in jail until someone from the school came to pick me up. The next morning I ate my last breakfast at the school.

My seizures were so bad at this time that I missed a year of school.

In September 1962, I enrolled in high school. Hardly a week went by without an ambulance being called because I had had a seizure in class, even though I told the staff it would not be necessary if I could just be allowed to rest after the seizure.

I was 21 when I graduated from high school in 1967. I had always looked forward to graduation and the feeling of succeeding in something nobody thought I could do. I also felt that now a whole new world would open up to me, a grown-up world where people would understand and accept me for what I was and not for what they felt I should be. I was wrong. People were still the same, trying to pretend that I didn't exist or pushing me off into a corner.

After high school I twice went to another rehabilitation school in Fishersville, Va. I started taking a course in general business but couldn't keep up due to my heavy medication.

Job hunting proved to be another nightmare. At interviews I would be told I was just the right man for the job, but when I revealed I was an epileptic there always seemed to be another candidate with better qualifications. I could get work if I didn't mention epilepsy. But this usually lasted only until I had a seizure. Within two weeks I would be fired.

At 22 I started learning various job skills at Goodwill Industries. One day a rehabilitation counselor asked if I would like to work for the federal government. I thought this would be a chance of a lifetime. Shortly after I turned 23, I started working for the Food and Drug Administration. That was in 1969. As a GS-2 clerk, my job wasn't the best in the world, but it was a job.

I had several seizures during my first month there, but nothing was said. Then one day it happened. I had a severe seizure and as I lay on the floor in convulsions, my supervi-



Every day Gerald Farber must take this medicine to control his epilepsy. But thanks to these tablets, he can lead a normal, productive life.

sor said, "I'm going to have to put you out of this office before you hurt yourself." This time I did not walk away. I asked him if he was going to pay my welfare personally or let me try to make a living by working there, even if I did occasionally fall. I asked him not to take away my dignity by telling me I was to be fired because of a seizure.

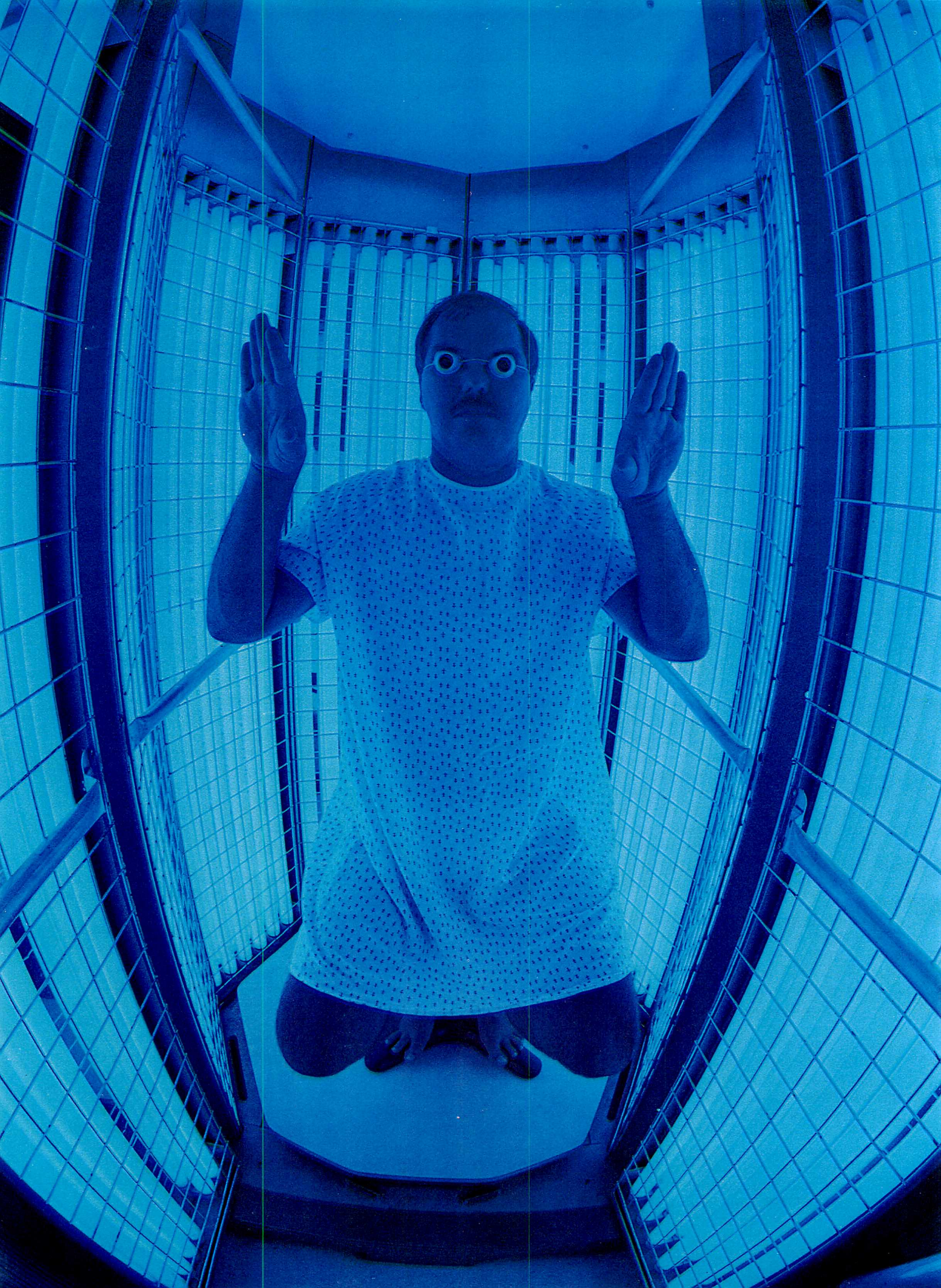
I stayed on at FDA and eventually was transferred to the press office in the agency's Washington, D.C., offices. Here I am a file clerk and messenger with light typing and other clerical duties. I am pleased to say that I now answer the telephones, something I was not permitted to do at first because my speech was too slow and too slurred due to my medications.

Five years ago I was given a new medication that has left me virtually seizure-free and more alert than I have been at any time since the "accident."

I am now 36 years of age, married and the father of a normal, healthy 6-year-old son and the stepfather of an 18-year-old daughter. Thanks to my medications I am able to lead a reasonably normal life, something I didn't think would ever be possible. Epilepsy is not only a greatly misunderstood condition. It is also a terribly lonely one that imposes isolation, ostracism and rejection on its victims.

My nightmare has subsided now, but it will never end. My seizures are under control, but that does not mean I will never have another one. If the blood tests I must have periodically show deterioration of the bone marrow my medication will have to be changed, with the possibility of more seizures.

I live for the present and future now, but I will never forget my past and how a simple game could so change my life.



PUVA's Double Whammy On Psoriasis

by Larry Bockstahler

PUVA is the acronymal name referring to a fairly new medical treatment intended for severe, stubborn cases of a relatively common skin disorder called psoriasis. The treatment consists of an oral dose of methoxsalen, which makes the skin sensitive to light, and exposure to longwave ultraviolet radiation (so-called UV light).

PUVA gets its name from **P** (for psoralen, the class of drug used) plus **UV-A** (an abbreviation for a type of longwave ultraviolet radiation). PUVA therapy was developed by a Harvard Medical School group and was first reported in 1974. Since then it has been tested in cooperative clinical trials at numerous medical centers in the United States and Europe.

The therapy is not a cure for psoriasis; however, it is highly effective in controlling the disease. PUVA was recently approved by FDA on the basis of effectiveness and safety.

Psoriasis is a chronic, recurring skin disease that affects several million people in the United States and 1 to 5 percent of the world's population. Psoriasis comes from the Greek word so spelled, meaning "to have the itch." Psoriasis victims experience an abnormal outer skin layer growth, resulting in red, scaly patches that can occur anywhere on the body. In most cases they occur on the elbows, knees, back, chest, buttocks and scalp. The reddish spots don't hurt and often don't itch. However, they are topped with silvery-white scales of dead skin that are constantly flaking off. The disease is not contagious, but a severe case can be a disfiguring cosmetic problem. The patches and the flaking scales of untreated, severe psoriasis

can be embarrassing to victims. Novelist John Updike described what it is like to cope with psoriasis in a short story for the *New Yorker* magazine and in his novel *The Centaur*. Fortunately, most cases are mild, and patients generally are in reasonably good health.

The tendency to psoriasis is inherited but anyone can have it. It is a lifetime disease that may begin at any age, but usually starts early in life. Its cause is unknown.

Everyone sheds some dead skin cells daily, and they are replaced by skin cells that migrate to the surface from deeper layers. Apparently this orderly process is disrupted in people who have psoriasis. The new skin cells multiply too rapidly and form the abnormal patches on the skin's outer layer.

Although psoriasis can't be cured, it is treatable by dermatologists (physicians who specialize in skin problems). A number of conventional treatments exist to remove the symptoms of psoriasis and bring temporary remission. One consists of coal-tar treatment plus exposure to ultraviolet radiation. Millions of dollars a year are spent on these treatments. However, they tend to be messy, inconvenient, time-consuming and expensive.

In PUVA therapy, a patient with severe psoriasis that fails to respond well to conventional treatments might experience something like this:

First comes a discussion of the patient's medical history. Then PUVA therapy would be reviewed, including benefits and potential risks. This may involve a physician who has special competence and training in photochemotherapy, the branch of medicine involving the use of both light and

chemicals as "drugs." Once a decision has been made to give PUVA a try, the physician would request that the patient avoid sunbathing for 24 hours before the treatment begins. On the day treatment starts, the drug methoxsalen, also known as oxsoralen or 8-methoxypsoralen, would be given. Methoxsalen belongs to a group of drugs known as psoralens, which are naturally occurring substances found in carrots, celery, parsnips and other vegetables. When eaten, psoralens cause the skin to become much more sensitive to light—especially longwave ultraviolet light. UV light is energy moving through space as invisible waves or particles. It represents that part of the sun's electromagnetic spectrum that lies between visible light and X-rays.

The dose of methoxsalen depends on the patient's weight, among other things. Once the methoxsalen is swallowed (usually with milk or food), it binds to the genetic material (DNA) of the body's cells.

About two or three hours after taking methoxsalen, the patient is exposed to a carefully measured amount of the longwave ultraviolet radiation known as ultraviolet-A, or UV-A. The exposure usually takes place in a specially designed exposure chamber, called a light box or irradiator, with banks of UV-A fluorescent lamps. The patient is asked to remove most or all clothing so as not to inhibit the radiation from reaching the skin. Special goggles must be worn to protect the eyes from damage by the invisible rays. The dosage of UV-A administered depends on several factors such as skin type, previous treatment history and recent exposure to



Psoriasis patients take three to six tablets of the drug methoxsalen for each PUVA treatment. Patients are also required to use special goggles for eye protection during the controlled ultraviolet exposure and must wear special glasses before and after treatment to protect against ultraviolet radiation from the sun.

The Curse Of Psoriasis

Had the world been watching, it would have been startled, for my belly, as if pecked by a great bird, was dotted with red scabs the size of coins. Psoriasis. The very name of the allergy, so foreign, so twisty in the mouth, so apt to prompt stammering, intensified the humiliation. "Humiliation," "allergy"—I never knew what to call it. It was not a disease, because I generated it out of myself. As an allergy, it was sensitive to almost everything: chocolate, potato chips, starch, sugar, frying grease, nervous excitement, dryness, darkness, pressure, enclosure, the temperate climate—allergic, in fact to life itself. My mother, from whom I had inherited it, sometimes called it a "handicap." . . .

. . . I had come to this conclusion about my psoriasis: it was a curse. God, to make me a man, had blessed me with a rhythmic curse that breathed in and out with His seasons. The summer sun melted my scabs; by September my chest and legs were clear but for a very faint dappling, invisibly pale seeds which the long dry

shadow of the fall and winter would bring again to bloom. The curse reached its climax of flower in the spring; but then the strengthening sun promised cure. January was a hopeless time. My elbows and knees, pressure areas of skin, were capped with crust; on my ankles, where the embrace of my socks encouraged the scabs, they angrily ran together in a kind of pink park. My forearms were mottled enough so that I could not turn my shirt cuffs back, in two natty folds, like other boys. Otherwise, when I was in clothes, my disguise as a normal human being was good. On my face, God had relented; except for traces along the hairline which I let my hair fall forward to cover, my face was clear. Also my hands, except for an unnoticeable stippling of the fingernails. Whereas some of my mother's fingernails were eaten down to the quick by what looked like yellow rot.

(From The Centaur by John Updike, published by Alfred A. Knopf, New York.)



Typical psoriasis patient, before and after successful PUVA treatments.

(Photos courtesy of Dr. John Parrish, Harvard Medical School.)

sunlight. The first UV-A exposure is usually short, lasting only several minutes. The light penetrates several layers of the methoxsalen-sensitized skin cells. If the treatments are successful, the spread of the disease is halted by inhibition of the growth of new cells in the patches of psoriasis. How and why this happens is unknown. Researchers believe that binding the drug to cellular DNA, followed by UV-A exposure, produces photochemical reactions that somehow inhibit the abnormal growth of new skin cells.

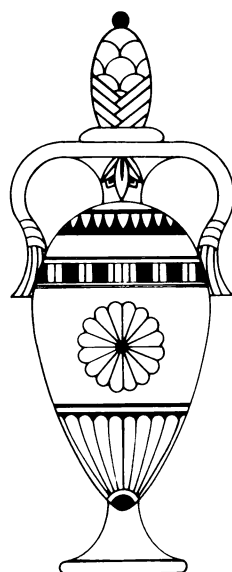
After the UV-A treatment, the patient is given special protective glasses (ordinary sunglasses are inadequate) and asked to avoid sunlight as much as possible over the next 24 hours. More than one PUVA treatment is required, and a regulated schedule is developed for each patient. Usually patients receive two or three treatments a week for a total of 10 to 30 treatments until the psoriasis is cleared. A pinkness of the skin resembling a light sunburn may be noticed after treatment. A tan may even develop.

Periodic PUVA treatments normally are required afterward to keep the psoriasis under control. Many patients must continue the treatments indefinitely to remain cleared.

According to dermatologists, the advantages of PUVA include relative ease of administration, speed of achieving remission and frequent disappearance of psoriasis patches without a trace.

The most common short-term side effects of PUVA therapy that may occur include itching, nausea and skin redness. Painful burns and blistering of the skin can occur if the doses of the drug or the UV-A radiation are excessive or if treatments are too frequent. The margin of safety between effective and toxic exposures of UV-A is narrow.

The most serious potential long-term risk is skin cancer—a risk that



PUVA Not So Modern

Sometimes it turns out that the basis of a modern medical treatment is an ancient folk remedy. PUVA therapy is a good example of this. The *Ammi majus* plant, a weed that grows along the Nile River, has been used as a medicinal plant by Egyptian and Indian peoples for centuries. Oil from this plant contains the drug methoxsalen, a compound that makes the skin of humans sensitive to longwave ultraviolet radiation. These ancient peoples found that application of the oil plus exposure to sunlight was successful in treating vitiligo, a skin disorder characterized by white patches of skin cells that lack pigment. This treatment was probably one of the first medical therapies in which light was used as a drug. Nowadays we call such a therapy phototherapy. Therapy such as PUVA, employing the use of both light and a drug, is called photochemotherapy.

sunbathers or sunlamp bathers also take. Follow-up studies made of PUVA patients in U.S. clinical trials at medical centers indicate several times more skin cancer among this group than has been observed in the general U.S. population. The risk was especially greater for patients previously exposed to known potential carcinogens, such as therapeutic X-rays, or those who had had skin cancer.

That PUVA treatments can cause skin cancer is not surprising. It has been shown that methoxsalen can produce skin cancers when applied to the skin of certain laboratory animals and this is followed by exposure to UV-A radiation.

Needless to say, the skin cancer potential is greater for patients who receive maintenance PUVA treatments for many years. Because of the skin cancer threat, PUVA should be avoided altogether by psoriasis patients who have skin tan burns instead of tanning, or those who are

sensitive to sunlight, have a history of skin cancer, or have received treatment with therapeutic X-rays or arsenic.

Serious eye problems are another potential hazard of PUVA, especially if recommended protective glasses are not used. UV-A radiation penetrates the cornea (outer transparent coat of the eye) and the eye's lens. Exposure to large doses of UV-A causes cataracts to occur in the unprotected eyes of laboratory animals, and the effect is greater if the animals are pretreated with methoxsalen (i.e., PUVA treatment). That's why patients are required to wear protective glasses during and after PUVA treatments. Eye examinations are recommended before therapy starts and every one or two years thereafter.

Premature aging of the skin can also result from PUVA treatment, especially in people who tan poorly.

Larry Bockstahler is a biochemist with FDA's Bureau of Radiological Health.

The Notebook: a potpourri of items gathered from FDA news releases, the Federal Register and other sources. The Federal Register (designated FR, with date of publication) is available in many large public libraries.

■ FDA's newly combined bureaus of drugs and biologics will be called the **National Center for Drugs and Biologics**. The center will have four major offices: new drug evaluation, drugs, biologics, and management.

■ **Drug labeling** regulations may be amended to allow a firm to claim to have made a product actually made by a corporately related firm under common ownership and control. The change was proposed because of concerns that the present rule requiring the corporate name on labels poses problems for certain diversified corporate structures (FR June 8).

■ The first **bifocal soft contact lens** to get FDA approval is called Bi-Soft Hydrophilic Contact Bifocal Lens and is a product of the Ciba Vision Care Division of Ciba-Geigy Corp., Atlanta, Ga. The lens is circular with a focus for distance in the center and for close-up vision around the outside.

■ FDA is withdrawing a proposal to halt sales of the antibiotic **erythromycin estolate** (brand name Ilosone) on the recommendation of a special advisory committee. The ban had been proposed because of reports of more incidents of liver damage with its use than with other forms of erythromycin (FR May 25).

■ Newport Pharmaceuticals International has withdrawn its request for a hearing on FDA's refusal to approve **Isoprinosine**, used for the treatment of subacute sclerosing panencephalitis (FR June 8).

■ Florida residents who received the **snake venom product PROven** in the past may get it on a limited, experimental basis under a license granted to the Miami Serpentarium and the Immunological Research Institute, a new firm, by the Florida Department of Health and Rehabilitative Services. In March, FDA won a court injunction blocking the serpentarium from making PROven and distributing it outside the state because it had not met agency requirements.

■ The administrative record for OTC anti-microbial drug products has been re-opened to allow consideration of an advisory panel's recommendation that **ethyl alcohol and isopropyl alcohol** be classed as safe and effective ingredients in first-aid products to treat minor cuts and scrapes. FDA published a tentative final

monograph establishing standards for OTC topical anti-microbial drug products in 1978 (FR May 21).

■ **COLOR UPDATE:** After July 1, 1982, all foods containing **FD&C Yellow No. 5**, the most widely used color additive, will have to identify the color by name on the label. Drugs were required to list Yellow No. 5 after June 26, 1980, and cosmetics have been required to identify this and all other colors by name on the label since May 1976. Some people suffer reactions to the color. . . . FDA is permanently listing **D&C Red No. 30** and **D&C Green No. 5** for use in drugs and cosmetics except those used in the area of the eye (FR May 25 and June 4).

■ The use of **formaldehyde** in products FDA regulates is not a threat to public health, the agency says. After receiving a report of a two-year inhalation study on laboratory animals FDA concluded that no regulatory action against use of the substance is necessary at this time. Formaldehyde solution (formalin) is used in various biologicals, human and veterinary drugs, and cosmetics as an inactivating agent, anti-bacterial preservative, or sterilant. It also occurs as an indirect food additive liberated from packaging materials in trace amounts.

■ **NOTES FROM THE MARKET BASKET:** A National Cancer Institute study has found that **cinnamyl anthranilate** causes cancer in laboratory animals, and FDA has proposed banning its use in foods. The flavoring agent has been used as an imitation grape or cherry flavor in a wide variety of foods, including beverages, ice cream, candy, baked goods, gelatins, puddings and chewing gum. It also has been used as a fragrance ingredient. Since release of the NCI study, industry has informed FDA it has stopped using the agent (FR May 25). . . . The food additive regulations are being amended to allow for the safe use of **natamycin (pimaricin)** as a mold-inhibiting agent on surfaces of cuts and slices of cheese where such use is provided for by specific standards of identity (FR June 22). . . . FDA is proposing to amend the standard of identity for **canned mushrooms** based on international standards and to amend the standard of fill of container and the drained weight requirements for certain sizes of cans (FR June 22). . . . Japan has decided to restrict the use of **potassium bromate**, an additive used in baking, and **butylated hydroxyanisole**, an anti-oxidant known as BHA, according to an international news source. An advisory council called for the ban because animal tests indicated the additives cause cancer. Neither substance has been banned in other countries.



by Richard C. Thompson

Willard's Withdrawal Symptoms

"As the manufacturer and bottler of Dr. Willard's Water, CAW Industries, Inc. of Rapid City, S.D., does not endorse any claims that its Catalyst Altered Water products are effective in the cure, mitigation, treatment or prevention of any diseases in man or animals. Dr. Willard's Water has not been approved as a 'drug' by the Food and Drug Administration, and CAW Industries, Inc. does not have available scientific proof that its Catalyst Altered Water products are effective in the cure, mitigation, treatment or prevention of any disease in man or animals."

In this short statement, signed April 20, 1982, William J. Willard, president of CAW Industries (and son of the founder), acknowledges that there is no scientific basis for medical claims made over the past 20 years for Willard's Water.

The statement was sent with a cover letter to all distributors of Willard's Water, cautioning them to make no such claims for the product.

Like most products whose sales are based on testimonials, Willard's Water has had a curious history. It was developed by John Wesley Willard, Ph.D., professor of chemistry at the South Dakota School of Mines and Technology at Rapid City, S.D. In the 1930s, he had patented an industrial cleaner for passenger train use that he called "Carbonaceous Activated Water" or "Catalyst Altered Water" (CAW). This basic formulation was reworked over the years and claims for it changed from a simple cleaner to a product that apparently had almost endless uses.

Dr. Willard's Water became widely known in that part of South Dakota among ranchers and townspeople, who were taking it for almost any condition found in man and beast. In 1971 he wrote to FDA, asking about an investigational new drug exemption for Willard's Water that would permit human studies. The agency replied that it needed some additional information, but there is nothing in FDA files to show that Willard followed up on this.

Two years later, Willard formed CAW Industries in Rapid City to manufacture and distribute a second product. That was "Dr. Willard's Water XXX" with lignite, advertised as an aid for plant health and growth. It was to be this product that brought him national attention.

In late 1980, the CBS television program "60 Minutes" featured Willard and his water, showing fruits and plants that were many times their usual size, allegedly because of Willard's Water treatment. In his enthusiasm, Willard told of all the other remarkable qualities of his product and how beneficial it had been to those who had used it. A national sales system quickly formed, with regional and local distributors holding franchises.

Some of these distributors expanded on the virtues of Willard's Water, even

going beyond the claims made by Willard in his public appearances, and these exaggerations came to the attention of FDA. The agency, in just a few months, found Willard's Water being promoted as a treatment for arthritis, acne, anxiety, nervous stomach, high blood pressure, ulcers, digestive problems, colds, strep throat infections, psoriasis, burns, sore muscles and stress. According to the claims, it was useful for growing hair and preserving foods, for the care of goldfish and for houseplant ailments, for improved cooking and facial beauty, for doing the laundry, and for treating cancer in cows and leukemia in cats.

It is the medical claims that concern FDA. Products that are sold for such uses are considered drugs under the law. Before they can be marketed, the manufacturer must show that they

WILLARD'S WATER

As Seen On CBS "60 Minutes"

Has Been Tested On Plants, Heals Burns,
Psoriasis, Acne, Colds, Strep Throat,
Reduces Anxiety, Nervous Stomachs,
Cleans, Shampoos, Bathes, Enhances
Cooking, and More.

\$13.50 Per Bottle
Postage Paid

Mail To:
SOLVENT, INC.
P.O. Box 12510
K.C., KS.
299-9511

or

FINE ARTS & SOLVENT STORE
6000 Leavenworth Rd.
K.C., KS.
299-6827

HOURS: MON-SAT. 9:30-5:30

DONALD R. HENDRICKSON, PRES.
EXCLUSIVE K.C. DISTRIBUTOR

are safe and effective for the uses intended. There is no such evidence available for Willard's Water, by the firm's own admission.

The success of Willard's Water has brought other firms into the market with their own versions of catalyst altered water. One is Donino Chemical Co. of New York, which has met with FDA officials to discuss marketing requirements of its "Biowater" as a cosmetic, food additive, or human and veterinary drug. However, Donino has not yet filed any data or made applications to FDA for this.

Both FDA and other laboratories have analyzed the Willard's Water

products and found that they contain various combinations of rock salt, lignite, sodium metasilicate, sulfated castor oil, calcium chloride and magnesium sulfate. No tannic or humic acid, substances that may cause liver damage, have been found in Willard's Water or similar products as some competitors have claimed. And FDA has not received reports of adverse reactions from catalyst altered waters.

The medical benefits claimed for Willard's Water and similar products are illegal under the Food, Drug, and Cosmetic Act. The statement by William J. Willard disavowing medical claims for the water came after the

law's provisions were pointed out. Willard also included the following in his statement:

- When notified by FDA that a CAW Industries distributor is making such new drug claims, the firm will take action to stop them.
- Dr. John Wesley Willard, no longer a company officer or employee, will make no claims in his public appearances that CAW Industries' products are effective in the cure, treatment, mitigation or prevention of any disease in man or animals.

Richard C. Thompson is a member of FDA's public affairs staff.

Unwelcome Pesticide

When the ground is frozen and snowbanks are high, Americans still want fresh produce. To satisfy this demand, foreign exporters ship millions of pounds of fresh fruit and vegetables into the United States each year. It is the job of FDA's field personnel to assure that imported produce is safe and wholesome and free of such contaminants as insects, mold and illegal pesticide residues.

Last winter FDA's **Orlando** district office collected routine samples of fresh snow peas offered for import from Guatemala. Analysis by the Atlanta regional laboratory revealed a problem: Some of the samples contained residues of the pesticide chlorothalonil. Pesticide residues are allowable only when the Environmental Protection Agency sets a tolerance, or acceptable level of residue. Otherwise, the fruits or vegetables containing the residues are in violation of the Food, Drug, and Cosmetic Act. There is no EPA tolerance for chlorothalonil in snow peas.

Orlando investigators took additional samples from eight shippers offering snow peas from Guatemala, and analysis revealed the residue problem in seven. The district recommended that FDA automatically detain all lots of snow peas from Guatemala. Headquarters approval resulted in an automatic detention and an import alert to every field office warning about the problem.

Under automatic detention, all lots

of the product offered for import from the specified sources are rejected unless the shipper can prove that the product does not violate the law. This step may be taken when examination of shipments from a particular source shows such a repeated or flagrant history of violations that a strong possibility exists that any given shipment from that source will be in violation.

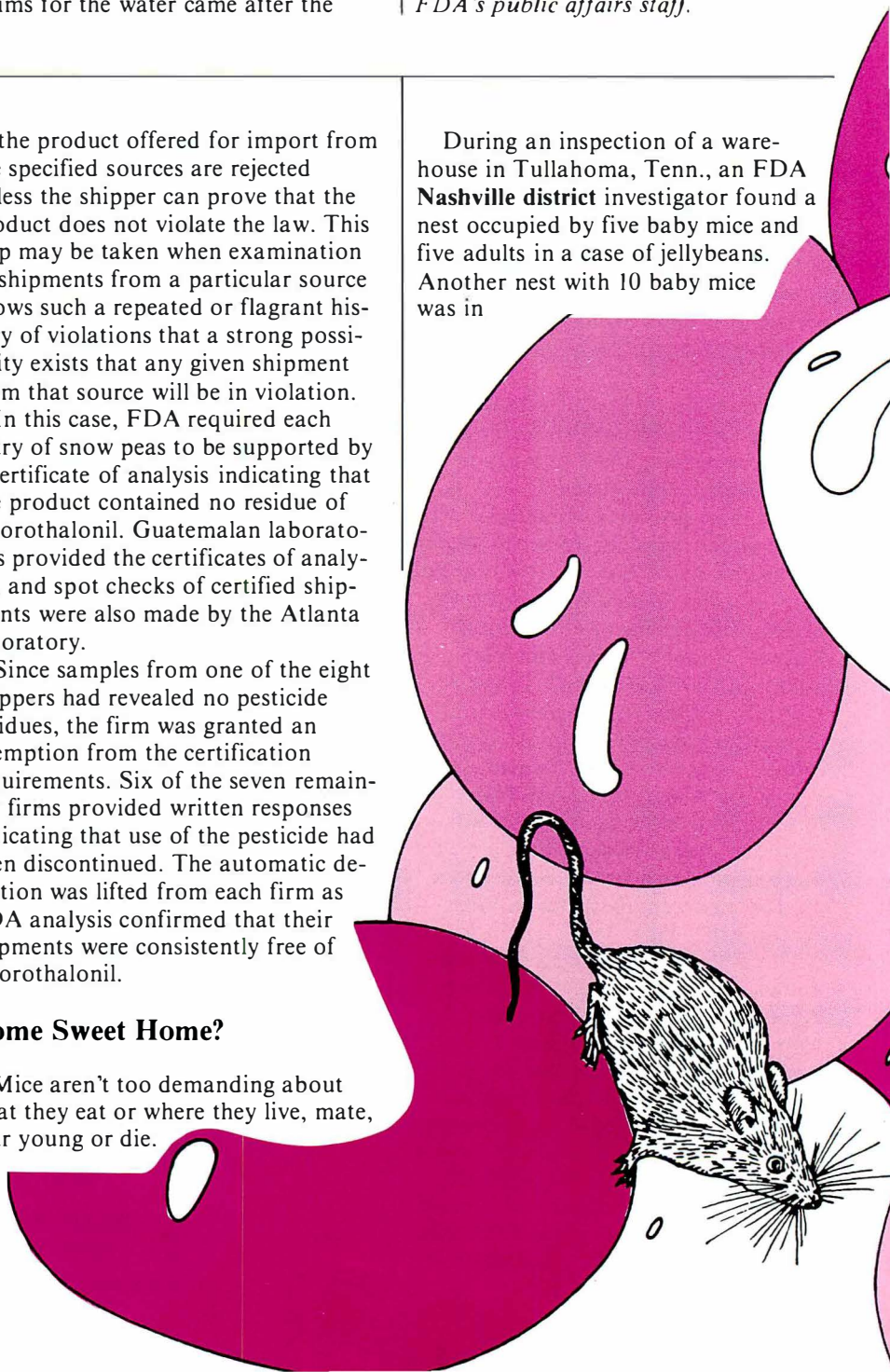
In this case, FDA required each entry of snow peas to be supported by a certificate of analysis indicating that the product contained no residue of chlorothalonil. Guatemalan laboratories provided the certificates of analysis, and spot checks of certified shipments were also made by the Atlanta laboratory.

Since samples from one of the eight shippers had revealed no pesticide residues, the firm was granted an exemption from the certification requirements. Six of the seven remaining firms provided written responses indicating that use of the pesticide had been discontinued. The automatic detention was lifted from each firm as FDA analysis confirmed that their shipments were consistently free of chlorothalonil.

Home Sweet Home?

Mice aren't too demanding about what they eat or where they live, mate, bear young or die.

During an inspection of a warehouse in Tullahoma, Tenn., an FDA **Nashville** district investigator found a nest occupied by five baby mice and five adults in a case of jellybeans. Another nest with 10 baby mice was in



a bag of dogfood. Nearby, three mice were nibbling at table salt. There were 19 dead mice, as well as gnawing marks, excreta and urine stains to show they'd been living in or on at least 25 lots of food. There were also live insects in rice, oatmeal and flour mix.

The warehouse owner, Smith and Son Wholesale Co. Inc., asked for 30 to 60 days to correct the trouble before FDA reinspected. But there was not much change five weeks later when the investigator returned and saw four live and nine dead mice, rodent signs in over 70 lots of food, and hundreds of rodent pellets throughout the warehouse.

Based on FDA's evidence, the District Court for the Eastern District of Tennessee ordered a U.S. marshal to seize all food in the warehouse that was susceptible to rodent or insect contamination. Value of the seized goods was \$900,000. Afterward, the firm fumigated the warehouse and completed structural repairs to discourage further infestation. Non-food items and salvageable food were cleaned or otherwise reconditioned.

Destruction was required for only \$1,700 worth of the goods.

Natural Poison

Aflatoxins are natural poisons (toxins) produced by two common molds that can grow on corn, peanuts, some varieties of seeds and tree nuts, and certain other food crops.

The molds—*Aspergillus flavus* and *Aspergillus parasiticus*—do not always produce the toxins. But if aflatoxins are found at any level above 20 parts per billion in foods or in animal feed, FDA must take regulatory action.

For a recent shipment of dried melon seeds being imported as snack food from Sudan, that action was detention at the port of entry. FDA's **New York Regional Laboratory** had found aflatoxin in the seeds ranging from 114 to 175 parts per billion, many times the permitted levels. These findings have prompted the agency to keep close watch over such imports.

Aflatoxins as natural poisons were identified only 20 years ago, although they have always been around. They

are much more toxic than some man-made chemicals and are known to cause cancer, liver damage and other illnesses.

At first it was thought that the molds would grow and the toxins be formed only when the peanuts, corn and other crops were stored under faulty conditions. Now it has been discovered that crops are susceptible to the mold while still in the field, even before harvesting. This has been a problem to farmers in recent years, especially those who grow corn in the Southeastern states, caught in cycles of drought, insect damage and other conditions that encourage growth of the mold. (See "Aflatoxins: Hazards From Nature," *FDA Consumer*, May 1978.)

Quarantine

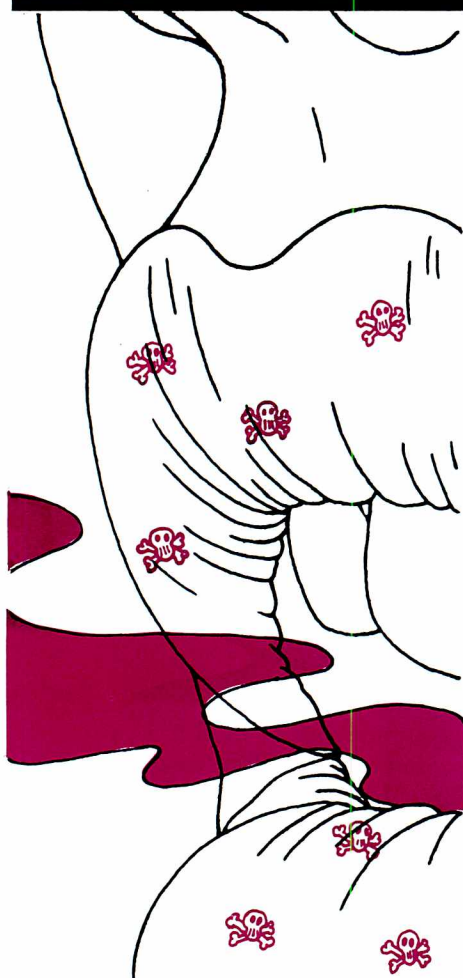
An investigator from FDA's **Newark district** office was looking at the stocks and records of Pharmadyne Laboratories, a drug manufacturer in Elmwood Park, N.J., that had just gone out of business. He noted that Pharmadyne had made shipments to Bioline Labs, a distributor in Brooklyn, and that information on some of the shipments, including a recalled product, seemed incomplete. He asked the **New York district** to check this.

Visiting Bioline, the New York inspector found four lots of tablets labeled dihydroergotoxine mesylate, a drug for treatment of senility, that Bioline had received from Pharmadyne. At the time, Bioline had doubts about the tablets and had them analyzed by a private laboratory.

The tests showed the tablets were placebos with no active ingredients and were not at all the drug they were claimed to be. Bioline then recalled the tablets it had distributed, for return to the manufacturer.

But there was no longer a manufacturer, since Pharmadyne had gone out of business. With no place to send the mislabeled drugs, Bioline placed them in a quarantine area under lock and key, which is where the FDA investigator found them.

The agency's New York Regional Laboratory tested the tablets and confirmed that they were placebos, not a senility drug. With that confirmation, Bioline destroyed the entire four lots, valued at \$58,700.



Hot Pop

One sip apiece, and two Dayton, Ohio, residents wound up in an emergency room last April for treatment of caustic burns of the mouth and throat.

Both individuals became ill after drinking Mountain Dew, a soft drink in 16-ounce bottles, which contained a 3.8 percent solution of sodium hydroxide, a potent bottle-washing detergent used in the soft drink industry to sterilize bottles.

FDA's Cincinnati district office was notified by the Montgomery County (Ohio) Health Department. Samples from the contents of the two bottles were analyzed by FDA's Cincinnati laboratory and the caustic fluid discovered.

Pepsi-Cola Bottlers manufactures the citrus-flavored, carbonated soft drink. The Dayton franchise, owned by GCC Beverages Inc., recalled about 866,000 of the 16-ounce bottles of Mountain Dew that had been distributed in eight west-central Ohio counties.

The cause of the problem was not definitely determined.

FDA Upheld on Shrimp

The headless, deveined and frozen shrimp had traveled halfway around the world to reach the Port of New York, but the shipment, which originated in India, was doomed from the start.

When the shrimp arrived in New York in April 1979, FDA investigators from the New York district office in Brooklyn found evidence of *Salmonella* contamination in all three lots offered for import. *Salmonella* bacteria in the digestive tract cause salmonellosis, a contagious disease characterized by diarrhea, fever and kidney problems. The *Salmonella* in the shrimp resulted from improper handling and insanitary processing in India. FDA refused to permit importation of the shrimp to this country, saying the product was adulterated. A hearing was held and after reviewing the evidence, FDA issued a "Notice of Refusal of Admission."

FDA representatives and Indian trade officials had met several times in February 1979 in efforts to forestall automatic detention of shrimp from India. An automatic detention is an administrative action by which the agency detains a particular product from a particular source without laboratory analysis because of a history of violations involving the product and source.

A month after the three lots of contaminated shrimp arrived at the Port of New York, an FDA delegation was invited to India to inspect shrimp processing plants. Numerous insanitary conditions were observed, any one of which could have contributed to the shrimp contamination.

Some processing areas were fly infested; inadequate icing resulted in the temperature of the stored product rising to 90 F; pitted and cracked work surfaces were covered with fecal matter from previously processed frog legs; and shrimp were held in bamboo baskets, which are almost impos-

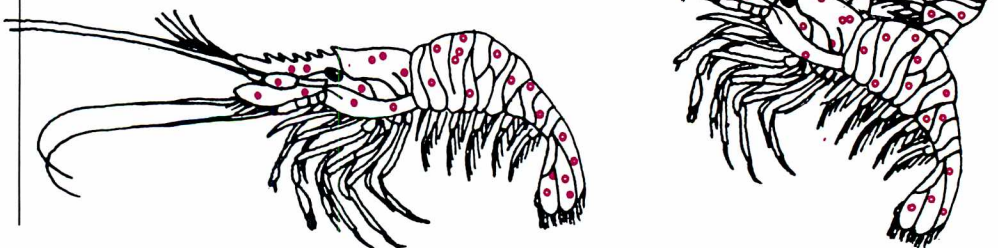
sible to sterilize.

When the FDA delegation returned to the United States, the agency imposed automatic detention on all shrimp from India. This action was taken based on the observations of the delegation, as well as on a large number of import shipments from India over the previous several months that had been found contaminated with *Salmonella*. The three lots detained in New York were re-exported to other countries.

Continental Seafoods Inc., importers of the shrimp, filed suit in the U.S. District Court, which sustained FDA's decision. In March 1982 the U.S. Court of Appeals for the District of Columbia upheld FDA's decision.

Since then, "It appears that the Indians have made great strides in improving overall shrimp processing conditions," reports Gary J. Dykstra, chief of the regulatory operations section of FDA's Office of Regulatory Affairs. The Indian government has instituted a certification program in which only those firms participating in the program can export to the United States. Negotiations continue between FDA and the Indian government in efforts to remove automatic detention requirements.

—This small sample of reports from the field was compiled and written by Marti Asner, Louise Fenner and Richard Thompson.



Seizures

FILED SEIZURE ACTIONS

charge violations of the Federal Food, Drug, and Cosmetic Act and are initiated based upon FDA recommendations. A seizure action is commenced by the filing in the U.S. district court where the goods are located. A U.S. marshal is then directed by the court to take possession of the goods, removing the product from commerce, until the matter is resolved.

A total of 12 actions to remove from the consumer market products charged to be violative was reported in May and June. These actions included 10 of foods: 1 involved charges concerning poisonous and deleterious substances, 7 involved charges concerning contamination, spoilage or insanitary handling, 1 involved economic and labeling violations, and 1 involved food additives. Others included 1 of cosmetics and 1 of medical devices.

PRODUCT, DISTRICT & DATE FILED	FIRM & PLACE OF BUSINESS	CHARGES
FOOD/Poisonous and Deleterious Substances		
Fish fillets, frozen/U.S. District Court for the District of New Jersey 5/22/82	Imported from Panama.	Articles contain the deleterious substance histamine in such quantities as to ordinarily render them injurious to health; articles contain decomposed fish; the labeling of the articles falsely and misleadingly represents the articles as being red snapper.
FOOD/Contamination, Spoilage, Insanitary Handling		
Flour, macaroni products, sugar, and other food stocks/U.S. District Court for the Northern District of New York 6/2/82	R. Pusatere Inc./Troy, N.Y.	Products were held under insanitary conditions, and certain of the articles contain rodent filth.
Macaroni products/U.S. District Court for the District of Puerto Rico 5/10/82	Freiria & Co. Inc./Puerto Nuevo, Puerto Rico	Products contain insects, and were held under insanitary conditions.
Mole, a seasoning paste/U.S. District Court for the District of Illinois 4/16/82	Imported from Mexico.	Product contains insect, bird, rodent and other filth; also, the label was not in the English language.
Pinto beans/U.S. District Court for the Eastern District of Washington 4/30/82	Northwest Produce Co. Inc./ Yakima, Wash.	Product was held under insanitary conditions.
Rice, Sello Rojo/U.S. District Court for the District of Puerto Rico 4/8/82	Rice Growers Association of California (Puerto Rico) Inc./Guaynabo, Puerto Rico	Product contains insect filth and was held under insanitary conditions.
Rice/U.S. District Court for the District of Puerto Rico 5/24/82	Farmers Rice Co. of Puerto Rico Inc./Guaynabo, Puerto Rico	Product contains insect and rodent filth and was held under insanitary conditions.
Sunflower seeds/U.S. District Court for the Eastern District of Missouri 4/19/82	Shipped from Fargo, N.D.	Product contains insect filth and was held under insanitary conditions.
FOOD/Economic and Labeling Violations		
Syrup/U.S. District Court for the Southern District of Mississippi 5/7/82	Norris Brothers/West Monroe, La.	Corn syrup has been substituted in part for the company's "Sorghum Syrup, Cane Molasses & Sugar Syrup"; labeling false and misleading in that it represents that the food is a sorghum syrup, cane molasses, and cane sugar mixture, when the food contains corn syrup; the article fails to bear the name of the food and the name of each optional ingredient, as specified in the definition and standard of identity for table syrup.
FOOD ADDITIVES		
Cake decorating wafers/U.S. District Court for the Northern District of Illinois 4/5/82	Imported from Italy and West Germany.	Product contains the non-conforming food color additives FD&C Red #2 and Cochineal Red A.
COSMETICS		
Tablets of canthaxanthin and beta-carotene for all-over tan without the sun/U.S. District Court for the District of New Jersey 5/4/82	Cosmetest Corp./E. Rutherford, N.J.	Product contains the non-conforming color additives canthaxanthin and beta-carotene.
MEDICAL DEVICES		
Bandages and bandage components/U.S. District Court for the Western District of New York 6/1/82	Medex Products Corp./Buffalo, N.Y.	Products were prepared, packed and held under insanitary conditions; the circumstances used for the products' manufacture, packing and storage are not in conformity with regulations.

Notices of Judgment



NOTICES OF JUDGMENT on Seizure Actions

FOOD/Contamination, Spoilage, Insanitary Handling

Beans, green, canned, at Sand Springs, N. Dist. Okla.

Charged 9-16-80: while held for sale, the article was held in swollen cans and contained decomposed green beans; 402(a)(3). Default decree ordered destruction. (F.D.C. No. 63168; S. No. 80-266-114; N.J. No. 1)

Grapefruit sections, canned, at St. Louis, E. Dist. Mo.

Charged 1-21-82: when shipped by Morris Canning Co., Winter Haven, Fla., the article had been held in cans which were too small and leaking; 402(a)(3). Default decree ordered destruction. (F.D.C. No. 63633; S. No. 82-257-597; N.J. No. 2)

Lupini beans, oregano leaves, and flour, at Chicago, N. Dist. Ill.

Charged 11-25-81: while held by Joseph Antognoli & Co., Chicago, Ill., the articles had been held under insanitary conditions; 402(a)(4). Consent decree authorized release to the dealer for salvaging. (F.D.C. No. 63605; S. No. 82-177-368; N.J. No. 3)

Peanut butter candy cups, chocolate bars, caramel bars, crackers, gum, and other confectionary stocks, at Buffalo, W. Dist. N.Y.

Charged 4-1-82: while held by Shosho Brothers Inc., Buffalo, N.Y., the candy cups and caramel bars contained rodent filth, and all of the articles had been held under insanitary conditions; 402(a)(3), 402(a)(4). Consent decree authorized release to the dealer for salvaging. (F.D.C. No. 63695; S. No. 82-285-572; N.J. No. 4)

Peanuts, shelled, at San Francisco, N. Dist. Calif.

Charged 3-15-82: while held by Art's Trading Co., San Francisco, Calif., the article contained rodent filth and had been held under insanitary conditions; 402(a)(3), 402(a)(4). Consent decree authorized release to the dealer for salvaging. (F.D.C. No. 63679; S. No. 82-390-846; N.J. No. 5)

Pecan pieces, at Albany, M. Dist. Ga.

Charged 2-11-82: when shipped by Pippin Pecan Co. Inc., Albany, Ga., the article had been prepared, packed or held under insanitary conditions; 402(a)(4). Consent decree authorized release to the shipper for salvaging. (F.D.C. No. 63644; S. No. 82-260-321; N.J. No. 6)

Rice flour, at St. Louis, E. Dist. Mo.

Charged 1-12-82: while in transit and when shipped from Memphis, Tenn., the article had been held under insanitary conditions; 402(a)(4). Default decree ordered destruction. (F.D.C. No. 63615; S. No. 82-256-959; N.J. No. 7)

Sauces, chili and bean, at Chicago, N. Dist. Ill.

Charged 11-25-81: while held for sale, the articles contained mold and were contained in leaking jars; 402(a)(3). Default decree ordered destruction. (F.D.C. No. 63600; S. No. 81-291-926 et al.; N.J. No. 8)

Sugar, and other food stocks, at Tullahoma, E. Dist. Tenn.

Charged 3-2-82: while held by Smith & Son Wholesale Co. Inc., Tullahoma, Tenn., the articles had been held under insanitary conditions; 402(a)(4). Consent decree authorized release to the dealer for salvaging. (F.D.C. No. 63660; S. No. 82-276-329; N.J. No. 9)

Walnuts, pecans, brazil nuts, and mixed nuts (all unshelled), at Oklahoma City, W. Dist. Okla.

Charged 11-19-81: while held by Frank's Tomato and Banana House, (Tanaka Produce Inc.), Oklahoma City, Okla., the articles had been held under insanitary conditions; 402(a)(3). Consent decree authorized release to the dealer for salvaging. (F.D.C. No. 63586; S. No. 81-209-898; N.J. No. 10)

Whiting fish, headless, frozen, at Columbus, M. Dist. Ga.

Charged 12-22-81: when shipped from Massachusetts, the article, labeled in part (case) "H&G Whiting . . . Boothbay Fisheries, Inc., Boston, Mass" and (box) "Eastern seas . . . Quick Frozen Fillets Product of Canada . . . Headless Whiting . . . Distributed By . . . Eastern Point Seafoods, Inc. . . . Gloucester, Ma.," contained decomposed headless whiting fish; and the article's label contained the false and misleading label statement "fillets"; 402(a)(3), 403(a)(1). Default decree ordered destruction. (F.D.C. No. 63604; S. No. 82-289-419; N.J. No. 11)

FOOD/Economic and Labeling Violations

"Concentrated orange juice for manufacturing," at San Jose, N. Dist. Calif.

Charged 2-24-82: when shipped by Fresh Pak Foods Inc., McAllen, Texas, the color turmeric had been added to make the article appear better or of greater value than it was—402(b)(4); the article contained the non-conforming color additive turmeric—402(c); the article's name "Concentrated Orange Juice for Manufacturing" on the label was false and misleading because the article was not concentrated orange juice for manufacturing, since it contained the artificial color turmeric—403(a)(1); the article failed to conform to the definition and standard of identity for concentrated orange juice for manufacturing because it contained the added color turmeric—403(g)(1); and the article contained an artificial color (turmeric) and the label failed to reveal that fact—403(k). Default decree authorized donation to a charitable organization. (F.D.C. No. 63641; S. No. 82-345-781; N.J. No. 12)

"Orange juice from concentrate," at San Jose, N. Dist. Calif.

Charged 3-5-82: while held by Beech-Nut California Corp., San Jose, Calif., who had manufactured the article using "concentrated orange juice for manufacturing" shipped by Fresh Pak Foods Inc., McAllen, Texas (see N.J. No. 12 of this issue), the article contained the color turmeric so as to make it appear better or of greater value—402(b)(4); the article contained the non-conforming color additive turmeric—402(c); the article's name "Orange Juice From Concentrate" on the label was false and misleading, since the article did not meet the definition and standard of identity for orange juice from concentrate because it contained turmeric—403(a)(1); the article failed to conform to the definition and standard of identity for orange juice from concentrate since it contained the added color turmeric—403(g)(1); and the article contained the artificial color turmeric and the label failed to reveal that fact—403(k). Default decree ordered destruction. (F.D.C. No. 63664; S. No. 82-345-790; N.J. No. 13)

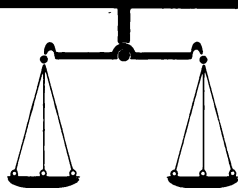
"Sole" fillets, at St. Louis, E. Dist. Mo.

Charged 10-31-78: when shipped by New York Sea Food Exchange, New York, N.Y., the article, labeled in part "IQF Sole Fillet Product of Holland," had had Greenland turbot substituted for sole—402(b)(2); the article's label was false and misleading in representing that the only fish in the article was sole—403(a)(1); Greenland turbot was offered for sale under the name of another food, "sole"—403(b); and the labels of the article lacked the common or usual name of the food because "sole" was not the common or usual name for Greenland turbot—403(i)(1). Consent decree authorized release to the shipper for relabeling. (F.D.C. No. 61941; S. No. 78-123-749; N.J. No. 14)

DRUGS/Human Use

Betamethasone valerate cream, at City of Industry, C. Dist. Calif.

Charged 3-6-81: when shipped by Premo Pharmaceutical Laboratories Inc., South Hackensack, N.J., the article was a new drug without



an effective approved New Drug Application—503(a); and its labeling lacked adequate directions for use and was not exempted due to its new drug status—502(f)(1). Default decree ordered destruction. (F.D.C. No. 63383; S. No. 81-258-705; N.J. No. 15)

Chlorothiazide tablets, two seizure actions, at Hollywood and Fort Lauderdale, S. Dist. Fla.

Charged 6-5-80 and 6-5-80: when shipped by Camall Co., Detroit, Mich., the article, labeled in part "Chlorothiazide . . . Manufactured . . . by Camall Co., Detroit," was a new drug without an effective approved New Drug Application; 505(a). Default decrees ordered destruction. (F.D.C. Nos. 62891, 62923; S. Nos. 80-197-875 & 80-193-660; N.J. No. 16)

Chlorthalidone tablets, at Hollywood, S. Dist. Fla.

Charged 12-11-80: when shipped by Zenith Laboratories Inc., Northvale, N.J., the article was a new drug without an effective approved New Drug Application; 505(a). Default decree ordered destruction. (F.D.C. No. 63217; S. No. 80-239-255; N.J. No. 17)

Chlorthalidone with reserpine tablets, at City of Industry, C. Dist. Calif.

Charged 3-6-81: when shipped by Premo Pharmaceutical Laboratories Inc., South Hackensack, N.J., the article was a new drug without an effective approved New Drug Application—505(a); and the article's labeling lacked adequate directions for use and was not exempted due to its new drug status—502(f)(1). Default decree ordered destruction. (F.D.C. No. 63381; S. No. 81-258-705; N.J. No. 18)

Cough syrup, and other drug stocks, at Cleveland, N. Dist. Ohio.

Charged 7-30-79: when shipped by C. M. Bundy Co., Erlanger, Ky., the circumstances used for the articles' manufacture, processing, packing or holding failed to conform with current good manufacturing practice; 501(a)(2)(B). The article was claimed by Reese Chemical Co., Cleveland, Ohio. A consent decree authorized release to the claimant for salvaging. Subsequently, salvaging not being financially feasible, the parties jointly moved that the articles be destroyed, and the court ordered the articles destroyed. (F.D.C. No. 62327; S. No. 79-114-023; N.J. No. 19)

Diethylpropion HCl tablets, at San Mateo, N. Dist. Calif.

Charged 8-6-81: when shipped by Premo Pharmaceutical Laboratories Inc., South Hackensack, N.J., the article was a new drug without an effective approved New Drug Application; 505(a). Default decree ordered destruction. (F.D.C. No. 63522; S. No. 81-247-776; N.J. No. 20)

Renacidin 10% solution, at Milwaukee, E. Dist. Wis.

Charged 3-3-81: when shipped by K-N Enterprises Inc., t/a Iota Corp., Skokie, Ill., the article was a new drug without an effective approved New Drug Application; 505(a). Default decree ordered destruction. (F.D.C. No. 63334; S. No. 81-201-713; N.J. No. 21)

Triamterene-hydrochlorothiazide capsules, doxylamine succinate with pyridoxine HCl tablets, hydroxyzine HCl tablets, Hydergot sublingual tablets, hydroxyzine pamoate capsules, betamethasone valerate cream, allopurinol tablets, trifluoperazine HCl tablets, and chlorthalidone tablets, at New Britain, Dist. Conn.

Charged 5-12-80: when shipped by Premo Pharmaceutical Laboratories Inc., South Hackensack, N.J., the articles were new drugs without effective approved New Drug Applications; 505(a). The articles were claimed by the shipper who denied the charge. Subsequently, the action was transferred to the district of New Jersey. Ultimately, upon joint motion of the parties, the articles were ordered destroyed. (F.D.C. No. 62863; S. Nos. 80-191-134/5; N.J. No. 22)

DRUGS/Veterinary

Expectorant for horses and dogs, at Cleveland, N. Dist. Ohio.

Charged 7-30-79: when shipped by C. M. Bundy Co., Erlanger, Ky., the circumstances used for the manufacture, processing, packing or holding of the article failed to conform with current good manufacturing practice; 501(a)(2)(B). Consent decree authorized release to Williams Drug Distributors Inc., Cleveland, Ohio, for salvaging. Subsequently, it became apparent that salvaging of the article was not financially feasible. Upon joint motion of the parties to destroy the article and cancel and discharge the claimant's bond, the court ordered the article destroyed, ordered payment by the claimant of the costs of destruction, and, upon such payment, ordered the claimant's bond discharged. (F.D.C. No. 62328; S. No. 79-114-027 et al.; N.J. No. 23)

Oxytetracycline HCl preparations for veterinary uses, at Kansas City, W. Dist. Mo.

Charged 4-25-77: while held by I. D. Russell Co. Laboratory, Kansas City, Mo., who had manufactured the articles using interstate oxytetracycline HCl, the articles were new animal drugs and no approvals of New Animal Drug Applications were in effect with respect to their use and intended uses—501(a)(5); and certain preparations (coded "51093," "51094" and "12353") differed from their purported strength because the articles contained less oxytetracycline hydrochloride than was declared on their labels—501(c).

The articles were claimed by the manufacturer who denied the charges. The parties served written interrogatories on each other. After discovery in the action had been closed, the government moved to compel the defendant to comply with the district's standard pre-trial order for filing lists of witnesses and exhibits. The court granted the government's motion. The claimant filed the required lists of witnesses and exhibits and also moved for an order granting permission to take a deposition.

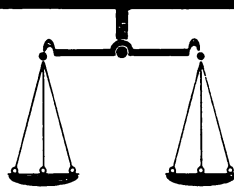
Subsequently, the court issued a show cause order against the claimant concerning failure to comply with a deadline. The claimant responded that the delay was unintentional and inadvertent and requested permission to file its response forthwith. The government subsequently moved to amend its witness list to include two additional experts. The court granted the motion. Meanwhile, the articles were substantially damaged and destroyed by a fire at the manufacturer's plant.

Pursuant to stipulation, the parties jointly moved to dismiss the action, without prejudice, as *moot* on the following grounds: the oxytetracycline HCl product "RV-VI-OXY" was no longer in production or distribution, and the manufacturer would not produce or distribute "RV-VI-OXY" without the prior written permission and approval of FDA; and the articles recited in the complaint had been destroyed by a fire, so the *res* no longer existed. The court ordered the action dismissed without prejudice and ordered that each side bear its own costs. (F.D.C. No. 61173; S. No. 77-24-342 et al.; N.J. No. 24)

"Skin Medicine" for horses and dogs, at Jupiter, S. Dist. Fla.

Charged 7-25-80: while held by Jupiter Veterinary Products, Jupiter, Fla., who manufactured the article using interstate camphor, the article was a new animal drug and no approval of a New Animal Drug Application was in effect with respect to its use or intended use—501(a)(5); and the article had been manufactured, prepared, compounded and processed in an unregistered establishment—502(o). Default decree ordered destruction. (F.D.C. No. 63117; S. No. 80-166-721; N.J. No. 25)

Various drug stocks for veterinary use and various syringes and other



devices for veterinary use, at Peoria, C. Dist. Ill.

Charged 9-30-80: while held by Miller Chemical Co., Peoria, Ill., the circumstances used for the holding of the drugs failed to conform with current good manufacturing practice, and the facilities and controls used for the storage of the devices failed to conform with prescribed regulations, since both the drugs and devices had been exposed to exploding chemicals, intense heat, smoke, soot and water damage as a result of a fire at the dealer's distribution center; 501(a)(2)(B), 501(h). Default decree ordered destruction. (F.D.C. No. 63156; S. No. 80-248-245; N.J. No. 26)

MEDICAL DEVICES

Adhesive patch with magnet, Acu-Dot, at Fort Lauderdale, S. Dist. Fla.

Charged 1-18-80: the article, which had been distributed by Acu-Dot International Pharmaceutical Co. Ltd., Akron, Ohio, and which was labeled in part "Acu-Dot Magnetic Analgesic Patch . . . Mfg. For temporary relief of occasional minor aches and pains of muscles and joints Mfg. for Acu-Dot International Pharmaceutical Co., Ltd. . . . Akron, Ohio," had false and misleading labeling since the article had not been shown to be adequate or effective for such intended use—502(a); the article's labeling lacked adequate directions for its intended purposes—502(f)(1). Default decree ordered destruction. (F.D.C. No. 62711; S. No. 80-193-640; N.J. No. 27)

Slendertone muscle stimulators, at Great Neck, E. Dist. N.Y.

Charged 2-13-81: the article, which was held by Passive Fitness Inc., Great Neck, N.Y., was accompanied by promotional materials (news-paper and magazine article reprints) which contained false and misleading claims for the article concerning losing inches and flab without physical exercise, revitalizing muscles without physical exercise, and breaking down toxic wastes and deposits trapped between layers of connective tissue with resulting loss of weight and inches—502(a); the article's labeling lacked adequate directions for lay use, since the article was ineffective for its promoted uses, was potentially harmful and was offered for use without a prescription—502(f)(1); the article's labeling lacked adequate warnings against unsafe use (e.g., use in pregnant women and individuals with cardiac conditions or vascular disorders)—502(f)(2). Default decree ordered destruction. (F.D.C. No. 63096; S. No. 80-194-208; N.J. No. 28)

X-ray system, Traceray III, at Redford, E. Dist. Mich.

Charged 10-5-79: the article, which had been manufactured by Western States Supply Ltd., Pueblo, Colo., was dangerous to health when used as directed because the article would emit radiation beyond the pre-set exposure time—502(j); the accompanying labeling was false and misleading in claiming compliance with the regulation's standards, and in claiming that the devices would deliver the radiation exposure stated in the instruction manual—502(a); and the article's quality fell below its purported quality—501(c). Default decree ordered destruction. Consent decree authorized release to the possessor for reconditioning. (F.D.C. No. 62505; S. No. 79-120-714; N.J. No. 29)

NOTICES OF JUDGMENT on Criminal Actions

Morton-Norwich Products Inc., t/a Norwich Pharmacal Co., and James J. Mahoney, operations vice president, Norwich, N. Dist. N.Y.

Charged 9-30-75 by grand jury: when Furacin nitrofurazone-impregnated gauze pads (counts 1-3) were shipped, the circumstances used for the article's manufacture, processing, packing and holding failed to conform with current good manufacturing practice, and the purity of the article differed from its purported purity (i.e., "sterile"), since the article was contaminated with mold; 501(a)(2)(B), 501(c). The defendants pleaded not guilty. The defendants requested that the

government produce for inspection and copying a number of specified documents. (See N.J. No. 33 of this issue of *FDA Consumer*.)

The court denied a motion by the defendants to dismiss the "current" good manufacturing practice charges, saying:

"The defendants, above-named, have moved to dismiss a portion of each of the three counts in the above numbered indictment each of which charges them with a violation of 21 U.S.C. §351(a)(2)(B) on the grounds that they are being denied their Fifth and Sixth Amendment rights, (1) because Section 351(a)(2)(B) is unconstitutionally vague as enacted, (2) because the regulations promulgated in connection with Section 351(a)(2)(B) are unconstitutionally vague, (3) because the application to the defendants of Section 351(a)(2)(B) and of the regulations is unconstitutional, and (4) because the indictment, which in the part challenged, only tracks the language of the statute and is unconstitutionally vague.

"Defendant, Morton-Norwich Products, Inc. (Norwich), is a pharmaceutical company which manufactures, among other things, a sterile gauze pad impregnated with Furacin. These dressings are applied to wounds, burns, etc. The gauze pad is automatically enclosed and sealed in a paper foil container under sterile conditions. The packages thus prepared are 100 percent inspected before packing to assure the integrity of the package and therefore presumably the continued sterile condition of the medicated pad. Defendant, James J. Mahoney (Mahoney), is the operations vice president of Norwich.

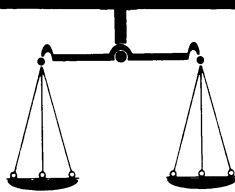
"The first paragraph of each of the counts in this indictment which was filed on Sept. 30, 1975, recites that between particular dates or on certain dates Norwich introduced into interstate commerce certain shipments of Furacin gauze pads with specific destinations. The first charge in each count which defendants find objectionable provides: 'That said drug, when caused to be introduced and delivered for introduction into interstate commerce, as aforesaid was adulterated within the meaning of 21 U.S.C. 351(a)(2)(B) in that the methods used for the manufacture, processing, packing and holding of said drug did not conform to and were not operated and administered in conformity with current good manufacturing practice to assure that said drug would meet the requirements of the Federal Food, Drug, and Cosmetic Act as to safety and would have the identity and strength and would meet the quality and purity characteristics which it purported and was represented to possess.'

"No definition of 'current good manufacturing practice' (CGMP) is contained in either the statute or the rules and regulations issued under it.

"It is clear from reading the affidavits of the experts employed by both parties that the term current good manufacturing practice is and of necessity must be flexible in its application to the manufacture of particular drugs. Furthermore, considering the end to be accomplished, i.e., the identity, strength, quality and purity of the drugs being introduced into commerce for the purpose of use by human beings, improvements and consequent change in what is CGMP is always to be anticipated as well as a desired end. The ultimate test of CGMP therefore is whether it results in a product which possesses the characteristics which the manufacturer represents it to have and whether the methods used to produce it are designed to assure that result.

"A review of the legislative history of this section as contained in the affidavits and memoranda supplied and an examination of the cases which have been cited which have upheld the constitutionality of the statute leads me to the conclusion that there is not only a sufficient standard but also that the statute is not void for vagueness.

"The considerations inevitably leading to this conclusion are that the manufacturers participated in the legislative hearings which resulted in the legislation and regulations, that there are many publications which discuss CGMP, college courses dealing with the subject,



Food and Drug Administration (FDA) seminars and courses and various trade associations which concern themselves with this subject as well as other matters coming under the jurisdiction of the FDA.

"It is undoubtedly true that the manufacturer of drugs must assume hazards which may be different from those which others bear but that is not unfair.

"Similarly, and for the reasons stated I do not find the regulations promulgated under 21 U.S.C. §351(a)(2)(B) void for vagueness nor do I find their application to these defendants unconstitutional either for vagueness or because they fail to satisfy due process requirements.

"An examination of the regulations provide a sufficient standard with respect to basic essentials as evidenced by Part 133 'Drugs: Current Good Manufacturing Practice in Manufacture, Processing, Packing or Holding.' The fact that proposed new regulations have been prepared to supersede those in effect in 1973 and that FDA has recognized the need for more specificity does not affect the validity of the regulations applicable here. I see no reason why this claim for more specificity does not fall within the ambit of those cases which have held that although a statute might have been drawn more precisely does not make it unconstitutional. . . .

"I adopt the language of the Court in *United States v. Bel-Mar Laboratories, Inc.*, 284 F. Supp. 875, 883 (E.D.N.Y. 1968) which explicitly approved the CGMP regulations. . . .

"Finally it should be noted that we are dealing here with an established manufacturer. It is incredible that they now claim that they do not know what CGMP is in view of the in-house memoranda to make sure that they were in compliance with CGMP and their certification to FDA when approval of the Furacin products were sought that the product was to be manufactured in accordance with current good manufacturing practice.

"It is the rule in this Circuit that an indictment which tracks the language of the statute is sufficient to withstand an attack based upon the requirements of the Fifth and Sixth Amendments and Rule 7(c)(1) of the *Federal Rules of Criminal Procedure*. The language is sufficient if it tracks the language of the statute and provides enough information to assure against double jeopardy. . . .

"I do not find the requisite prejudice demonstrated here. The defendants obviously have recourse to a bill of particulars and discovery to ascertain in what areas the government will prove beyond a reasonable doubt their operation was not in compliance with CGMP.

"The motion with respect to each count is denied."

After additional litigation, the defendants waived jury trial and, with the government's consent, the case was tried by the court. Trial commenced on Jan. 13, 1977, and this case was taken under submission on March 18, 1977. On Aug. 18, 1978, the court returned a general verdict finding the individual not guilty on all counts, finding the corporation not guilty on Count 3, not guilty of the current good manufacturing practice charges, and finding the corporation guilty on Counts 1 & 2. Following the verdict, the corporation moved to have the verdict set aside and moved for acquittal on the following grounds: (1) that the government's post-shipment testing of pads (in which mold was detected) was prejudicial and irrelevant in view of the defendant's testing prior to shipment; (2) that the government was estopped due to reliance by the defendant on an FDA assurance in 1973 that its test methods were adequate; (3) that the court erred in not striking the testimony of Dr. Philip Mislivic because the cultures upon which he based his testimony had been destroyed and his testimony had not been properly connected; (4) that the testimony of FDA inspector Donald Howard before the grand jury was so prejudicial that the grand jury had been unable to render a proper verdict; and (5) that the time delay between the submission of the case and the verdict

violated the corporation's rights to due process and to a speedy trial.

The court denied the firm's motion, saying:

"This is a criminal action involving three alleged violations of the Federal Food, Drug, and Cosmetic Act, Title 21 U.S.C. §§301, et seq. Named as defendants in the Indictment are Morton-Norwich Products, Inc., a corporation doing business as Norwich Pharmacal Company, and James J. Mahoney, Vice-President of Operations for Morton-Norwich Products, Inc.

"Indictment Number 75-CR-114, which was handed up on or about Sept. 30, 1975, alleges three violations by both defendants of the Food, Drug, and Cosmetic Act, all of which violations involve the interstate shipment of adulterated drugs, in contravention of sections 301(a) and 303 of the Act, 21 U.S.C. §§331(a) and 333 respectively. Each count, in turn, alleges adulteration in two separate and distinct senses, one falling within section 501(c), 21 U.S.C. §351(c), in that the purity of the drugs involved differed from that purported, the other coming under section 501(a)(2)(B), 21 U.S.C. §351(a)(2)(B), contending that the drugs were not manufactured, processed, packaged or held in conformity with current good manufacturing practice so as to assure that they would conform to the Food, Drug, and Cosmetic Act requirements as to safety, and would have the strength and identity and meet the quality and purity characteristics which they purported to possess (the (a)(2)(B) violation will be referred to simply as CGMP).

"The products involved in the three counts of the Indictment are two lots, numbered 705553 (Counts I and II) and 710749 (Count III), of individually packaged gauze pads impregnated with Furacin (trade name for nitrofurazone), an antibacterial dressing. All of the products involved were manufactured at the defendants' sterile fill facility located in Norwich, New York.

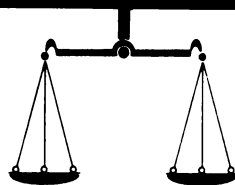
"The gravamen of the charge of adulteration under 21 U.S.C. §351(c) is that the pads, purported to be sterile according to the labeling found on the foil envelopes in which the pads were to be marketed, were not, in fact, sterile. The charge under 21 U.S.C. §351(a)(2)(B) relates to several alleged violations of CGMPs, based heavily upon observations made during Food and Drug Administration (FDA) inspections of the defendants' sterile fill facility at Norwich, as well as the actual evidence of product contamination.

"This Court conducted a rather lengthy non-jury trial of this action, commencing on Jan. 13, 1977, and ending on March 18, 1977. Following the trial, the Court reserved decision on the verdict. Since none of the parties requested that the Court make special findings, the general verdict was announced to the parties in open court. See *Fed. R. Crim. P. Rule 23(c)*. To recapitulate, the Court found defendant Morton-Norwich guilty on Counts I and II and not guilty on Count III, and acquitted defendant Mahoney on all three charges.

"Prior to, during, and after the trial, the parties made numerous motions, upon many of which the Court reserved decision. This supplemental Opinion is being rendered in order to deal with those motions, and to hopefully clarify the verdict somewhat for the benefit of the parties.

I. Motion To Strike Government's Test Results

"Throughout this proceeding, the defendants have attacked, on three grounds, the introduction into evidence of the results of tests performed by FDA analysts on post-shipment specimens of product taken from the two lots in issue. First, they claim that owing to the fact that a sterility test such as involved in this case is necessarily destructive of the product unit tested, and because sterility in a manufacturing situation cannot be guaranteed on an absolute basis, sterility is necessarily a probabilistic concept. The defendants have insisted that their representation of sterility was proper in this case as long as pre-shipment tests, validly conducted by them in accordance with the



methods prescribed by the United States Pharmacopoeia (U.S.P.), indicated sterility, despite the fact that later tests revealed the presence of contamination in one or more samples of previously untested product. Secondly, the defendants attack the relevance of post-shipment tests with respect to the issue of sterility at the time of shipment. Finally, the defendants have sought to impeach the results of the Government's tests, pointing to several deviations of the methods used from that prescribed by the U.S.P.

A. Defendants' Representation of Sterility

"In support of their position on this score, the defendants, through various expert witnesses, have proffered definitions of the term 'sterility' or 'sterile,' all of which reject the notion of sterility as being an absolute concept in favor of a definition dependent upon results of probabilistic testing performed upon random samples of the product in accordance with U.S.P. testing methods. Thus, the argument goes, an article is properly labeled as 'sterile' if it has passed pre-shipment sterility tests performed pursuant to the U.S.P. method, notwithstanding the fact that some untested product units are in fact contaminated.

"The Court rejects the notion that the term 'sterile,' as contained within the labeling which accompanies the defendants' product, is susceptible of such a narrow interpretation. This Court is of the opinion that the meaning to be ascribed to labeling which accompanies a product is, like beauty, properly in the eyes of the beholder, rather than the manufacturer. Cf. *United States v. Article . . . Consist. of 216 Carton. Bot.*, 409 F.2d 734 (2d Cir. 1969). A customer who utilizes defendants' Furacin gauze or batiste pads, whether he be a doctor, a nurse, or a layman, in this Court's estimation, will interpret the representation of sterility to mean the total lack of contamination of the product. To allow the defendants to avoid liability under the Act merely by testing samples of the product, which samples prove negative for contamination, would be to obliterate the standard of absolute liability imposed by the Food, Drug, and Cosmetic Act, see *United States v. Park*, 421 U.S. 658 (1975); *United States v. Dotterweich*, 320 U.S. 277 (1943), and subtly inject into the statute an element of scienter, or conscious awareness of guilt. The Court believes that the relevant inquiry under 21 U.S.C. §351(c) is whether or not the gauze and batiste pads contained in Lots 705553 and 710749 were, in fact, sterile when shipped, utilizing an absolute definition of sterility.

"The defendants' motion to exclude the Government's test results upon this basis is accordingly denied.

B. Relevance of Post-Shipment Testing

"The clear import of 21 U.S.C. §331(a) is that in order to prove a violation of that provision, adulteration *at the time the product entered, or was delivered for introduction into, interstate commerce* must be proven beyond a reasonable doubt. *Penobscot Poultry Co. v. United States*, 244 F.2d 94 (1st Cir. 1957). Adulteration, of course, may be demonstrated by any logical and convincing means. *United States v. Lesser*, 66 F.2d 612 (2d Cir. 1933); cf. *Fed. Rules of Ev. Rules* 402, 702. One manner of proving pre-shipment adulteration is by showing adulteration after receipt at some point in time subsequent to travel in interstate commerce, together with proof that the adulteration necessarily occurred prior to shipment, rather than some later time. *Pasadena Research Laboratories v. United States*, 169 F.2d 375 (9th Cir. 1948), cert. den. 335 U.S. 853 (1948).

"The Court believes that the Government has sufficiently demonstrated that the post-shipment tests performed upon samples of their product are highly probative with regard to the issue of pre-shipment sterility. The defendants' motion to exclude those test results upon this basis is therefore denied.

C. Reliability of FDA Tests

"The defendants have drawn into issue the reliability of the FDA analysts' test results, pointing to various deviations of the methodology utilized from that prescribed by the U.S.P.

"In proving adulteration under 21 U.S.C. §351(c), the Government is not limited to any particular manner of proof, and is especially not limited to use of tests conducted in accordance with the U.S.P. *Woodward Laboratories v. United States*, 198 F.2d 995 (9th Cir. 1952). This Court has had ample opportunity to hear testimony from FDA analysts who performed the various post-shipment tests upon the products in issue. The Court was similarly able to view those analysts' test worksheets and to listen to numerous expert witnesses' opinions with regard to the validity of those tests. As must be obvious from the verdict, the Court has concluded that the tests conducted upon samples from Lot 705553 were valid, especially with regard to demonstrating pre-shipment contamination, and that the Government has proven pre-shipment adulteration of that lot beyond a reasonable doubt.

"A separate but related motion was made by the defendants to exclude certain of the Government's sterility test results (Government Exhibits 63, 64, and 78), based upon the Government's failure to preserve and produce records relating to the preparation and sterilization, by autoclaving, of the culture media utilized in the testing. . . .

"The Court is of the opinion that this deficiency relates not to the admissibility *vel non* of those test results, but merely to the weight to be accorded to them. In light of the use by the FDA analysts of both positive and negative controls, all of which produced results indicative of satisfactory testing conditions, the Court determines that the results of the tests are accurate and relevant and therefore should not be excluded.

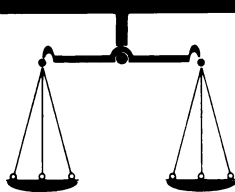
"The defendants have also challenged the testimony of Leonard Mastrandrea, the FDA laboratory supervisor for the Brooklyn facility, as a portion of their attack upon the Government's test results. In particular, they contend that Mr. Mastrandrea's testimony as to lack of positive results in open controls on tests in which fleakers were used was hearsay, and should therefore be stricken (T. 3261-3264). The Court is of the opinion that, with proof that all instances of positive results in those open controls would be reported to Mr. Mastrandrea, evidence of the absence of such reports is not hearsay, is highly relevant, and should therefore be admitted. See *McCormick on Evidence* §250 (2d Ed. 1972).

II. Motion To Strike Testimony Relating to Speciation of the Mold

"The defendants have moved to exclude testimony of Dr. Mislivic, an FDA mycologist who testified on behalf of the Government concerning his speciation of the molds cultured by the several FDA analysts during their testing of samples from defendants' Lot 705553 (T. 2412-2417; 2495; 3424). The defendants have also moved to strike testimony of Government expert witnesses, which testimony was based in part upon the speciations performed by Dr. Mislivic. The basis of their objection in this regard is Dr. Mislivic's failure to preserve the specimens from which he identified the presence of the mold *paecilomyces varioti*, which they claim effectively deprived them of their right to confront and cross-examine Dr. Mislivic, one of the Government's crucial witnesses.

"While the Court believes that the better practice would have been for Dr. Mislivic to preserve, in some manner, the samples actually speciated, whether by photograph or by maintaining the sample itself, especially since litigation was, at that point, virtually inevitable, the Court does not believe that his failure to do so rendered the results of those speciations inadmissible. Rather, it should merely affect the weight to be accorded to the results of his speciations. The defendants' motion in this regard is accordingly denied.

III. Motion To Dismiss Based Upon Allegedly False Grand Jury



Testimony

"The allegations set forth by the defendants in support of their motion to dismiss, based upon the prosecution's purported knowing use of perjured testimony before the Grand Jury in order to secure the instant Indictment, center around the testimony of Donald Howard. Mr. Howard was the FDA inspector whose observations during an inspection of defendant's Norwich sterile fill facility during June of 1973 form the core of the FDA's case concerning CGMP violations (T. 1935-1938; 1966-1987; 1990-2022; 3423). During his testimony before the Grand Jury, Mr. Howard characterized defendants' Norwich sterile fill facility as being in substantial violation of the CGMPs in June of 1973. He failed to mention to the Grand Jury, however, that he had inspected that same facility in February of 1973, and reported no major CGMP violations at that time. In fact, his testimony was such that the Grand Jury could reasonably have believed that the June inspection was Howard's first visit to the defendants' Norwich plant.

"This Court is indeed somewhat troubled with this aspect of Mr. Howard's testimony before the Grand Jury. That witness's characterizations of the Norwich facility as being in substantial violation of CGMPs are somewhat misleading when taken in context with the fact of his previous visit during which he failed to report any substantial violations.

"This Court has read the Grand Jury minutes of this case *in camera*, however, and is convinced that the Indictment is not vitiated by Mr. Howard's testimony. As should be obvious by now, the Court's verdict in this case with respect to Counts I and II was primarily the result of a finding of adulteration as defined in 21 U.S.C. §351(c), rather than any CGMP violation under 21 U.S.C. §351(a)(2)(B). On this score, there was ample evidence before the Grand Jury, quite independent of Mr. Howard's testimony, to support the charges lodged in the Indictment. As such, the defendants' motion to dismiss based upon this ground is denied. *United States v. DeLeo*, 422 F.2d 487 (1st Cir. 1970), cert. den. 397 U.S. 1037 (1970); *Coppedge v. United States*, 311 F.2d 128 (D.C. Cir. 1962) (Burger, J.).

IV. Motion To Exclude Certain Observations

"The defendants challenge the introduction, as evidence of CGMP violations, of various observations made at the Norwich sterile facility outside of the time frame during which the lots in issue were manufactured (e.g., T. 1603-1605; 2395; 2396-2400). While the Court has indicated that its verdict rests upon finding actual contamination, in violation of 21 U.S.C. §351(c), rather than a CGMP violation under 21 U.S.C. §351(a)(2)(B), it nevertheless feels compelled to briefly address this point.

"The Court is in agreement that, with respect to CGMP violations, the evidence must relate to conditions as they existed at the time applicable to the Indictment; that is, the time of manufacture of the lots in question. In proving its case, however, the Government should not be limited to use of testimony of observations actually made during the critical time period. Rather, it is proper to consider proof of conditions existing at times reasonably close to those in issue, providing that the Government can demonstrate that, by virtue of the nature of the conditions and the closeness in time, it is reasonable to infer that the same conditions occurred during the critical time period. *United States v. 1,200 Cans, Pasteurized Whole Eggs, Etc.* 339 F. Supp. 131 (N.D. Ga. 1972). For example, while it is reasonable to assume that the physical layout of defendants' sterile facility was, for the most part, the same in June of 1973 as it was earlier that year, it is not necessarily proper to infer, without more, that because a wooden-handled tool was present in the sterile fill area in June, that it was also there in February. Likewise, while observations of many insects present in the fill room in June might be relevant as indicative of a continuing CGMP violation for improper insect-proofing, the mere

presence of a single fly on one or more occasions cannot be used to infer the presence of insects at other times.

"Because the verdict as to Counts I and II was based upon actual adulteration rather than CGMP violations, and because the Court finds insufficient evidence of CGMP violations even considering all of the evidence now under challenge, it is unnecessary to rule upon the defendants' various objections falling within this category.

V. Conclusion

"In closing, the Court would like to express its deep appreciation to all of the lawyers who worked so diligently in preparing and presenting this case. The amount of time and effort which went into preparation of the case on both sides was apparent to this Court. The parties' efforts succeeded in enlightening the Court with regard to a rather complex and technical subject matter.

"The verdict stands as previously announced in court. The various motions upon which the Court reserved decision at different stages in the proceedings are resolved in accordance with the foregoing Opinion."

Thereafter, the corporation was fined \$1,500.00. (F.D.C. No. 60004; S. No. 25-167G et al.; N.J. No. 30)

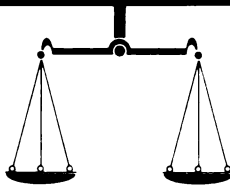
Penn Central Transportation Co. (a carrier with headquarters in Philadelphia, Pa.) and **CPC International** (a producer of bulk corn products with headquarters in Englewood Cliffs, N.J., and with a manufacturing plant at Pekin, Ill.), acting at Pekin, S. Dist. Ill.

Charged 2-17-78 by grand jury: when bulk corn gluten meal (Count 1) was shipped from Pekin, Ill., for delivery to Meadville, Pa., via the assigned railroad hopper car PR254567, and when bulk corn gluten feed (Count 2) was subsequently shipped for delivery to Augusta, Maine, via the same assigned railroad hopper car PR254567, the meal and the feed both contained the poisonous and deleterious substance lead oxide [which contrary to the car assignment had previously comprised an earlier cargo of that hopper car]; both the meal and the feed were unfit for food because of such substance, and both had been packed and held under insanitary conditions whereby they may have been rendered injurious to health; 402(a)(1), 402(a)(3), 402(a)(4). The carrier attempted to enter a plea of nolo contendere. Such a plea was rejected by the court. Both defendants pleaded not guilty.

The carrier moved to dismiss the complaint on the grounds that 21 U.S.C. 373 of FDA's statute (The Federal Food, Drug, and Cosmetic Act) excluded carriers, in the usual course of business, from 21 U.S.C. §§331, 333 and 342, because FDA's statute provided that "carriers shall not be subject to other provisions of this chapter by reason of their receipt, carriage, holding, or delivery of food . . . in the usual course of business as carriers"; that the carrier was subject to the Interstate Commerce Act and FDA's statute was intended to work in conjunction with the Interstate Commerce Act which already regulated carriers; that a compliance program had been established in 1975 to inspect food transport vehicles; that, in the 11 percent of cases where contamination was shown, it was not possible to tell how it originated; that generally, therefore, compliance by carriers should fall within the specialized knowledge of the Interstate Commerce Commission and not FDA. The carrier also moved to suppress from use at trial certain evidence obtained from the carrier. The government opposed both such motions by the carrier.

The case came on for trial by court and jury. CPC International was found to be not guilty as to both counts. Penn Central Transportation Co. was found guilty on Count 1 and found not guilty on Count 2. At sentencing, Penn Central Transportation Co. was fined \$1,000 and was assessed costs.

Meanwhile, the carrier moved for a new trial, claiming, in part, that the jury's verdict was contrary to the weight of the evidence and



was not supported by substantial evidence; that the court erred in not sustaining objections to questions in regard to an "assigned car" for lack of a foundation that the car in question was an "assigned car" on the date of the occurrence; and that the court erred concerning various jury charges. Similarly, the carrier moved for an acquittal and for an arrest of judgment, claiming, in part, that the court lacked jurisdiction because of the exemption of 21 U.S.C. §373, and that to hold the carrier and other carriers liable in view of the provisions in Title 21, Title 15, and Title 7 would make the exemption and suppression of evidence complete nullities and would be similar to a type of "entrapment." The court denied the carrier's motions (which appeared to the court to be on the grounds previously asserted, argued and decided adversely to the defendant).

After the court had assessed \$6,865.86 costs against the carrier, the carrier moved to vacate such assessment. After a hearing, the court excluded various FDA expert witness fees and reduced the assessed costs to \$2,493.16. (F.D.C. Nos. 60272, 60436; S. Nos. 26-137G, 96-447H; N.J. No. 31)

NOTICE OF JUDGMENT on Injunction Action

The Twin City Hospital, and the Twin City Hospital Corp. of Dennison & Uhrichsville, Ohio, and James Z. Scott, M.D., president & medical director, Eddie P. Sutkin, administrator, Charles W. Grandison, laboratory director, and Frank J. Wanosik, assistant laboratory director, Dennison, N. Dist. Ohio.

Charged 7-23-75 in a complaint for injunction: that the defendants had been engaged at their hospital in Dennison, Ohio, in collecting, manufacturing, processing, testing, packing, labeling, storing and issuing bags of human whole blood and human red blood cells with anticoagulant (which had been shipped in interstate commerce), intended for transfusion; that FDA inspections revealed that the circumstances used for the collection, manufacturing, testing, packing, labeling, storage and disposition of human whole blood and human red blood cells were inadequate in a number of specified respects, and accordingly failed to conform with current good manufacturing practice; that the bagged blood and blood cells fell below the U.S.P. standards for quality and purity because they had not been manufactured in accordance with the biological products regulations; that the articles' labeling was false and misleading since it represented that complete Rh negative (CDE and Du) testing had been performed and the labeled results were final and conclusive, but in fact certain aspects of such testing (CE and Du) had not been performed at the time of labeling; and that the defendants were well aware that their activities were in violation of the law; 501(a)(2)(B), 501(b), 502(a).

A consent decree of permanent injunction enjoined the complained of violations and enjoined the continued storage and testing of such blood products at the defendants' blood bank except in a life saving emergency, unless and until a number of specific current good manufacturing practice methods, facilities and controls were found to have been established, operated and administered at the defendants' blood bank, and all the human whole blood and human red blood cells on hand were brought into compliance. A reinspection of the blood bank found it to be in compliance. (Inj. No. 706; S. No. 94-040H; N.J. No. 32)

NOTICE OF JUDGMENT on Miscellaneous Action

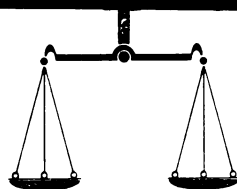
Sterility tests by FDA and information pertaining to laboratory controls, contamination, and design charges involving such tests, Washington, Dist. Columbia.

Charged 1-21-76 by Morton-Norwich Products Inc. (Norwich Pharmaceutical Co. Div.), Chicago, Ill., against HEW Secretary David Mathews and FDA Commissioner Alexander M. Schmidt: that the plaintiff had filed 39 requests for documents from FDA; that five of the requests (which were the subject of the plaintiff's action) sought copies of each FDA memorandum, record or document prepared between Jan. 1, 1965, and Oct. 15, 1975, pertaining to laboratory controls, contamination, and design charges involving FDA sterility tests; that FDA notified Norwich on Nov. 14, 1975, that additional time was required to determine its response to the plaintiff's requests; that on Dec. 3, 1975, FDA denied all documents requested by the above five requests; that Norwich filed an appeal with the assistant secretary for health requesting a review of each of the five denials; that, although Norwich had inquired concerning review of its five requests for information and had been advised by telephone that the bulk of the requested records would be denied, no decision in writing, as required by statute, had been received by Norwich within the specified 20 days; that the plaintiff was deemed to have exhausted its administrative remedies and had accordingly filed this action; that plaintiff prayed that defendants be enjoined from withholding the contested agency records which had been improperly withheld; that the defendants be ordered to produce such records; and that the court issue written findings determining that FDA's denials raised questions whether the agency personnel acted arbitrarily and capriciously. The government generally denied most of the plaintiff's charges. The plaintiff moved for summary judgment, as did the defendants. The court granted in part the defendants' motion for summary judgment authorizing any deliberative or policy material contained in the approximately 40 documents (which are the subject of the five requests in issue) to be withheld as exempt from compelled disclosure. The plaintiff's motion was also granted in part to the extent that within 10 days the agency had to reveal the fact later in the documents. In rendering such order, the court said:

"This is another Freedom of Information Act case. Following its now-settled practice, the Court requested the Government agency to submit samples of the documents for which exemption from disclosure is claimed in order to focus the issues in an adversary context. This was done, aided by some discrete excerpting, and the controversy was briefed and argued.

"At stake are some 49 documents out of hundreds requested and disclosed following an elaborate file search and administrative clarification of what was sought. The documents still in controversy are claimed to be exempt under (b)(2) and (b)(5), 5 U.S.C. §552. The claim of exemption is supported by an affidavit from a responsible, informed official. Appropriate indices were furnished, together with the sample documents. The parties cross-moved for summary judgment. There is no factual dispute. The Court must accordingly attempt to interpret what the Freedom of Information Act means when applied to the circumstances of this case.

"Three requests of plaintiff are still opposed by the agency and form the basis of this litigation. The first contested request seeks: 'a copy of each memorandum or other record or document relevant to the controls and procedures utilized between Jan. 1, 1965, and Oct. 15, 1975, to eliminate possible laboratory contamination in the facilities operated by or on behalf of the Food and Drug Administration for the performance of sterility tests.' Two categories of documents within this request have been withheld: (1) worksheets showing quality assurance sterility sample results of analyses conducted in 1972 and 1974 on 'audit' samples, and (2) inter-agency memoranda containing selective portions of the results of the samples, analyses of the results, and recommendations for changes in laboratory operation, analytical



procedures and/or additional training.

"Plaintiff's second request seeks to obtain a copy of each memorandum or other record or document prepared between Jan. 1, 1965, and Oct. 15, 1975, pertaining to the need or desirability of changes in the design, construction materials, structure, or equipment in facilities operated by or on behalf of the Food and Drug Administration for performing sterility tests. Included in these documents are specific cost estimates supporting the budget needed to make proposed changes. A sample was again provided.

"The final dispute concerns plaintiff's request for: 'a copy of each memorandum or other record prepared between Jan. 1, 1965, and Oct. 15, 1975, pertaining to the need or desirability of changes in the sampling and laboratory procedure in use by each laboratory of the Food and Drug Administration for testing (a) sterile impregnated gauze pack and/or (b) other sterile products.' Three classes of documents are within this request. First, there are 23 intra-agency memoranda reflecting the on-going pre-decisional deliberations of, summaries of meetings by, and correspondence between the members of, an internal FDA working group known as the Task Force on Sterility. No representative sample is provided, but the memoranda have been clearly indexed. Also withheld are memoranda containing discussions of possible modifications of analytical procedures and controls utilized in performing sterility testing. A sample document has been made available. Finally, the agency refused to reveal two interagency memoranda containing recommendations of personnel from the Center for Disease Control of the Public Health Service and the Food and Drug Administration concerning a draft set of Good Manufacturing Practice regulations (GMPs) for large volume parenteral products.

"The defendants claim exemption under (b)(2) and (b)(5) for the first category and again invoke a (b)(5) exemption as to all the other requests in dispute as summarized above.

"Certain benchmarks, well established by prior decisions, serve as initial guides in interpreting and applying the statute. A person requesting information is not required to show a need or a reason, and an agency must disclose wholly useless, meaningless and misleading information unless it is exempted. Where exemption is claimed, as here, the exemption must be narrowly construed, and the burden of proof is on the agency, *e. g.*, *Washington Research Project, Inc. v. Department of Health, Education & Welfare*, 164 U.S.App. D.C. 169, 504 F.2d 238, 244 (1974), *cert. denied*, 421 U.S. 963, 95 S.Ct. 1951, 44 L.Ed.2d 450 (1975). Against this background, the Court turns to the specific requirements of the exemption.

"The Court finds that (b)(2) does not support the agency's refusal to release documents in the first category. The material relates neither to minor or 'housekeeping' matters nor predominantly to internal personnel rules and practices of the agency, but rather to the substantive performance, and competence of the FDA in this area. Moreover, plaintiff has agreed to the deletion of the names of both the employees tested and the employees' supervisors, and therefore the aspects of the documents which might otherwise relate to personnel practices have been eliminated. Accordingly, under the opinion of either Judge Wilkey or Judge Leventhal in *Vaughn v. Rosen*, D.C.Cir., 523 F.2d 1136 (1975), the (b)(2) exemption is not available.

"It remains to consider the (b)(5) claims as to all of the materials in controversy.

"The Court has before it here primarily documents that recommend or are, as in the case of the Task Force papers, clearly developed in aid of a recommendation. Thus the papers are unquestionably an integral part of the agency's deliberative processes. All of the documents fall directly under the (b)(5) exemption, and the agency may refuse to produce any material that contains opinions, advice, evaluations, deliberations, policy formulations, proposals, conclusions or recom-

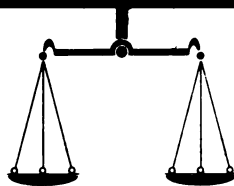
mendations. The issue is whether factual statements found in these deliberative documents must be disclosed or also treated as exempt along with the rest of the text. If this proposition were presented as a matter of first impression, the Court would favor a rule of thumb to the effect that any document containing an explicit recommendation and legitimately prepared in the regular course of the agency's business to further its deliberative process is exempt in its entirety. It appears that Congress could rationally have so intended, recognizing the overriding need to encourage the free exchange of ideas within the Government during deliberations and policymaking.

"The United States Court of Appeals for this Circuit has, however, taken a different approach. It has narrowed the exemption and required that even purely deliberative documents be excerpted under certain conditions to disclose facts stated within the four corners of the documents. . . . The task presented here therefore is to specify what statements of fact must be disclosed as outside the exemption after censoring the deliberative document of its policymaking features. In the present state of the law the Court of Appeals has understandably given only the most general indication of its point of view. In view of the infinite variety of documents that the Freedom of Information Act covers and the equally great variety of procedures followed by Government agencies in formulating policy, the case-by-case development of the meaning and effect of exemption (b)(5) has left many unanswered questions and much uncertainty. The Court of Appeals has suggested certain general tests: Is the fact 'easily severable'? Is the fact 'inextricably intertwined'? Is the fact contained in a 'summary' that has become part of the deliberative process? Is the fact already in the 'public domain'? Is the fact purely 'investigative'?

"It is necessary in this case to give these tests a clearer definition so that disclosure, where appropriate, may proceed. It appears to this Court that the rules stated immediately below must be followed in separating fact statements from their deliberative context in the case of the documents here in controversy.

"A fact is 'easily severable' if it is in a separate sentence and is deemed 'inextricably intertwined' only if it is stated along with non-factual material in a single sentence. Since almost all statements of fact are summary in the sense of being incomplete and the inclusion or emphasis of a particular fact is necessarily a matter of judgment, a statement of fact contained in a separate sentence or sentences may be withheld as exempt even if a part of the deliberative process only (1) when it appears from the face of the document that the writer is intentionally purporting to summarize facts, and (2) the facts have already been made public by the agency or may be elsewhere ascertained from other documents available from the agency by operation of the Act.

"The Court is aware that this places a heavy burden on the responding agency but the difficulty is largely of the agency's own making. There is nothing in the Freedom of Information Act which requires an agency to claim an exemption. It is also obvious from the experience under the Act that much material for which exemptions are now being claimed has no current value or significance whatsoever. Demands are being made for disclosure of documents that go far back in time and which truly have lost any practical consequence. Indeed, it is difficult to understand why the Government has preserved many of these papers. If an agency takes a more liberal attitude about its relations to the public it can proceed by disclosing much of the exempted material without damage to the public interest or creating precedent which will injure its interests. A more enlightened policy would be one that asserted exemption only when genuinely important. This would greatly reduce the ever-growing burden on the Federal Courts and would also reduce the expense of attorneys' fees assessed in these cases against the Government. Most importantly, such an approach would



promote the purposes underlying the Act and bring about a far healthier understanding of governmental process. Thus the agency has it within its own hands to minimize greatly the need for excerpting and reviewing sentence-by-sentence papers that intermingle fact and policy.

"One issue remains. Counsel for plaintiff urges that the Court examine each disputed document *in camera* and make the determinations as to what is fact and what is not. . . . This Court has elsewhere expressed some of the considerations which have led it to reject *in camera* proceedings. . . . In the present instance, these same reasons, plus other considerations, again prompt the Court in its discretion to reject *in camera* review of the designated documents.

"The principal reason advanced by plaintiff in urging *in camera* consideration is that courts are to be trusted to be impartial and that a third-party review by a court is more comforting than review by representatives of the agency resisting disclosure. This is superficially enticing if one overlooks the experience of history that indicates how arbitrary judges as well as others in authority become if they conduct their business in secrecy. But apart from this danger, which plaintiff recognizes, it is necessary to point out two countervailing considerations. First, if the Government wished wrongfully to withhold, it need not have ever indicated that the documents existed in the first place. Second, sanctions now exist under the amended Act against those who improperly conceal, 5 U.S.C. §552(a)(4)(F). The FDA processes thousands of Freedom of Information Act requests a year. It has a specialized staff which proceeds with legal advice. The U.S. Attorney in contested cases reviews that advice. There is nothing in this case to suggest that the agency has not been forthright or responsible. The Freedom of Information Act must proceed in an atmosphere of confidence in government. If the agency cannot be trusted, the Act will never work. It is a profound mistake to transfer administrative responsibility to judges on the theory that persons employed by the Executive branch are not honest or lack judgment. The effort to do this through the *in camera* process is misplaced.

"Defendants' motion for summary judgment is granted in part and any deliberative or policy material contained in the documents may be

withheld as exempt from compelled disclosure. Plaintiff's motion is granted in part to the extent that within ten days the agency must reveal the fact data in the documents as directed in this opinion."

Thereafter, the defendant moved for clarification or to amend the court's order, so as to delete the identity and location of the FDA laboratories from the laboratory work sheets showing quality assurance sterility sample results of 1972 and 1974 "audit" analyses. Upon consideration of such motions, it appeared to the court that in conformity with the Freedom of Information Act, the identity and location of the FDA laboratory could and should be disclosed, and the court denied the defendant's motions and ordered that its previous order should stand without amendment. Meanwhile, the plaintiff made various objections concerning the documents that the defendants produced. Ultimately, however, in a Northern District of New York criminal action, in response to a motion by Morton-Norwich to compel discovery and inspection of the documents covered by the court's order in this case, complete copies of all the documents were released to the defendants. (Misc. No. 328; N.J. No. 33)

Notices of Judgment are given pursuant to section 705 of the Federal Food, Drug, and Cosmetic 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, or cosmetics 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 and Drug Division, Office of the General Counsel, HHS.

Published by direction of the Secretary of Health and Human Services.

Arthur Hull Hayes Jr., M.D., *Commissioner of Food and Drugs*
Washington, D.C., Sept. 1, 1982

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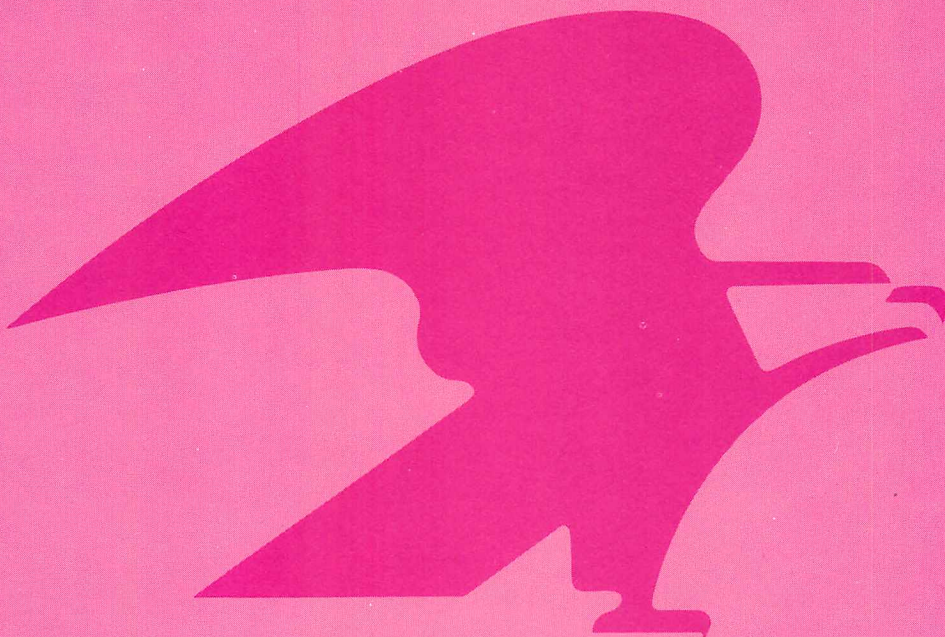
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Section 705[375] of the Food, Drug, and Cosmetic Act: (a) The Secretary shall cause to be published from time to time reports summarizing all judgments, decrees, and court orders which have been rendered under this Act, including the nature of charge 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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