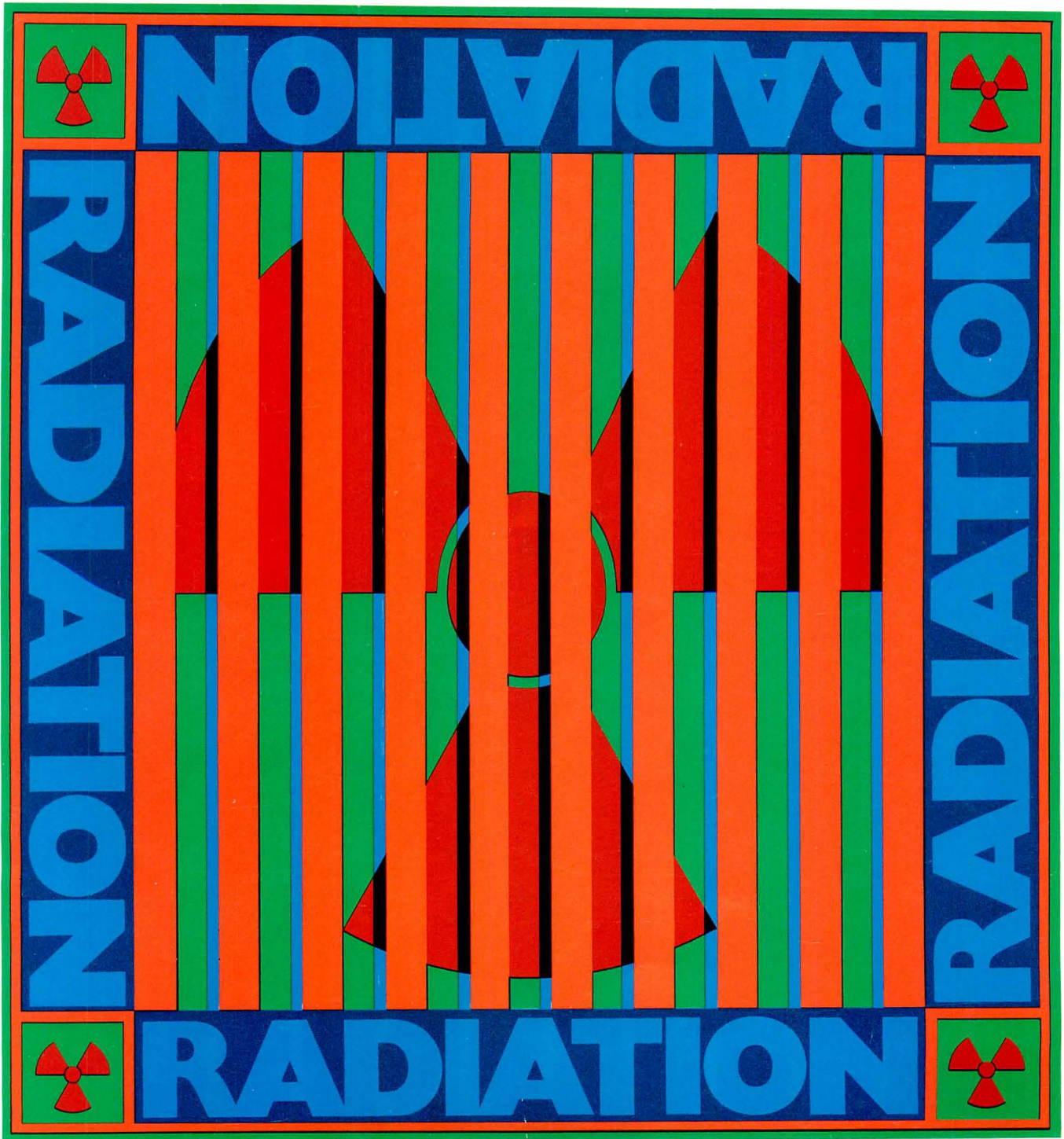


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July-August 1979









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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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**Inside Front Cover:** Tiny laboratory animals, like these white mice, play a big role in the testing of substances that might be hazardous to man. More than 24,000 of them were part of a long range study recently completed at FDA's National Center for Toxicological Research. Preliminary findings and the logistics of carrying out the largest animal study ever undertaken are the subject of the article 24,000 Mice Tell Us Much About Cancer Risks.

## Hearing on Sweetener

*Articles on artificial sweeteners have appeared on the pages of FDA CONSUMER for years. Most recent was the April issue, which featured Focus on Food Safety and a rundown of the saccharin controversy. With saccharin use likely to be limited in the future, the search is on for another artificial sweetener. In the running is Aspartame. But some questions have been raised about its safety. Here's an update.*

The Food and Drug Administration will convene a scientific Board of Inquiry later this year to recommend to the Commissioner whether to approve the artificial sweetener Aspartame.

Aspartame, a combination of amino acids, is about two hundred times sweeter than sugar. Manufactured by G. D. Searle Co., Skokie, Illinois, Aspartame has never been marketed. Its use as an artificial sweetener would be as a "table-top" sweetener and as an ingredient in dry beverage mixes to which water is added. The marketing application now before FDA is not for Aspartame use in diet sodas.

This will be the first Board of Inquiry ever convened by the Agency. The Board of Inquiry system was established as a means for helping the Commissioner resolve scientific issues; it is an alternative to a formal evidentiary hearing before an administrative law judge. It is intended to provide a forum in which scientific issues can be considered by scientists without the legal formalities of an evidentiary hearing. The procedure is experimental and FDA will evaluate its success after the Aspartame hearing has been completed.

FDA approved Aspartame in July 1974 but questions were raised by objectors about whether it induces brain tumors in rats or contributes to mental retardation, brain damage, or other undesirable effects. The objectors were Dr. John Olney, professor of psychiatry at the Washington University Medical School in St. Louis, and James

Turner of the Washington, D.C., law firm of Swankin and Turner.

FDA decided then to convene a Board of Inquiry but postponed it when an investigation of Searle studies on some drugs raised questions about the reliability of the Aspartame studies. In December 1975 FDA stayed approval of Aspartame pending a comprehensive review of the studies and put in abeyance its intention to convene the Board of Inquiry.

The Universities Associated for Research and Education in Pathology (UAREP), a scientific group, contracted with Searle to review the studies. That review was completed in December 1978. FDA has concluded, based on UAREP's review, that there were no significant discrepancies in the data originally submitted by Searle.

The status of Aspartame now has returned to where it was in 1975, and FDA will proceed with the Board of Inquiry.

The board will consist of three members. Olney and Turner, G. D. Searle, and FDA's Bureau of Foods will submit to the Commissioner a list of five nominees. The Commissioner will select one nominee from the list submitted by Olney and Turner and one from the lists provided by Searle and the Bureau. The third member will be selected by the Commissioner.

It is expected that the board will be selected and will begin its deliberations by late summer or early fall. The board will hear oral presentations from anyone it believes can contribute valuable information. After evaluating the information, the board will render an "initial decision." The participants will be given time to file "exceptions" or objections to the Commissioner, after which time he will decide whether to approve or permanently withdraw approval for Aspartame.

## GLP Regulations Become Effective

New Standards for Test Laboratories was the title of a March 1977 FDA CONSUMER article that



told of Good Laboratory Practice (GLP) regulations proposed by FDA. Those regulations have passed from the proposal stage to the CODE OF FEDERAL REGULATIONS. Here's an update.

FDA's Good Laboratory Practice (GLP) regulations to assure more reliable safety information on products subject to the Agency's regulation went into effect June 20.

The regulations affect those laboratories that supply information from nonclinical studies offered in support of research on products regulated by the Agency. They provide for FDA inspection of the laboratories and establish standards for personnel, operation, and maintenance of the establishments involved.

The GLP regulations are intended to assure the quality and integrity of safety data from nonclinical laboratory studies submitted to FDA in behalf of food additives, color additives, prescription and nonprescription drugs, biological products, electronic products, medical devices, and other articles subject to regulation under the Food, Drug, and Cosmetic Act and those parts of the Public Health Service Act administered by the Agency.

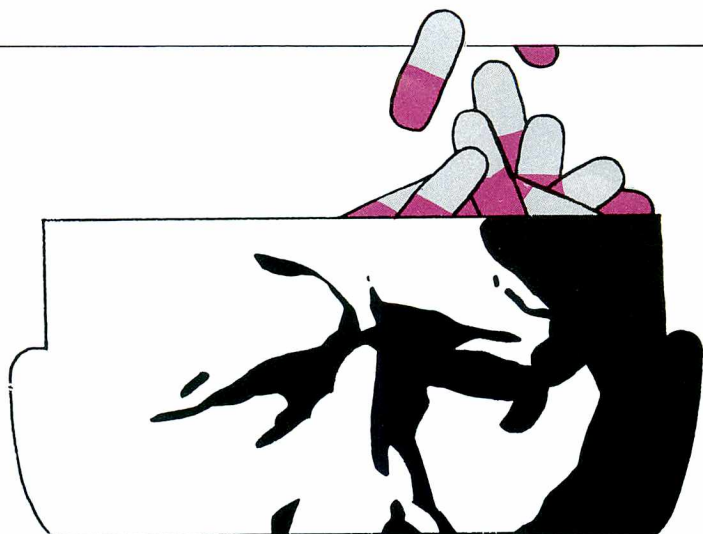
The GLP regulations were proposed by FDA in November 1976 after the Agency's investigations showed that the conduct of some studies submitted in support of the safety of regulated products did not measure up to acceptable practice, and the results therefore were not enough to assure product safety.

The events that resulted in FDA's GLP proposals involved mainly laboratories conducting tests on drugs before ultimate testing in humans. But the critical nature of laboratory data obtained from animal and other studies, and intended to be correlated to the safety of humans, can apply to any product regulated by FDA and the Agency thus determined to make its GLP regulations for nonclinical laboratory studies effective across the board—for all classes of products it regulates.

The regulations provide for disqualification of studies from a facility that does not comply with them in all respects.

## Darvon Study Continues

Caution: Darvon Subject to Misuse was the title of a March 1979 article in FDA CONSUMER about the painkiller Darvon and other propoxyphene drugs. The article told of 1,000 to 2,000 deaths a year associated with propoxyphene when taken alone or with other drugs. The possibility of physical and psychological dependence was also pointed out. The article noted that stricter controls were being considered for the drug. Here's an update.



Monthly research and monitoring reports on the painkiller propoxyphene—better known by the brand name Darvon—have been called for by Health, Education, and Welfare Secretary Joseph A. Califano, Jr.

Secretary Califano was responding to a petition from the Health Research Group, an organization affiliated with Ralph Nader. The group had asked for tighter controls over the drug because of reported abuses in prescribing and usage.

Califano directed the Surgeon General to make monthly reports on the efforts of three HEW agencies that are to research and study the "factors bearing on scheduling of Darvon." The agencies are FDA, the National Institutes of Health (NIH), and the Alcohol, Drug Abuse, and Mental Health Administration (ADAMHA). In addition, the Surgeon General is to report each month on FDA's monitoring of propoxyphene-related incidents gleaned from the Drug Abuse Warning Network. The reporting is to continue to June 1980.

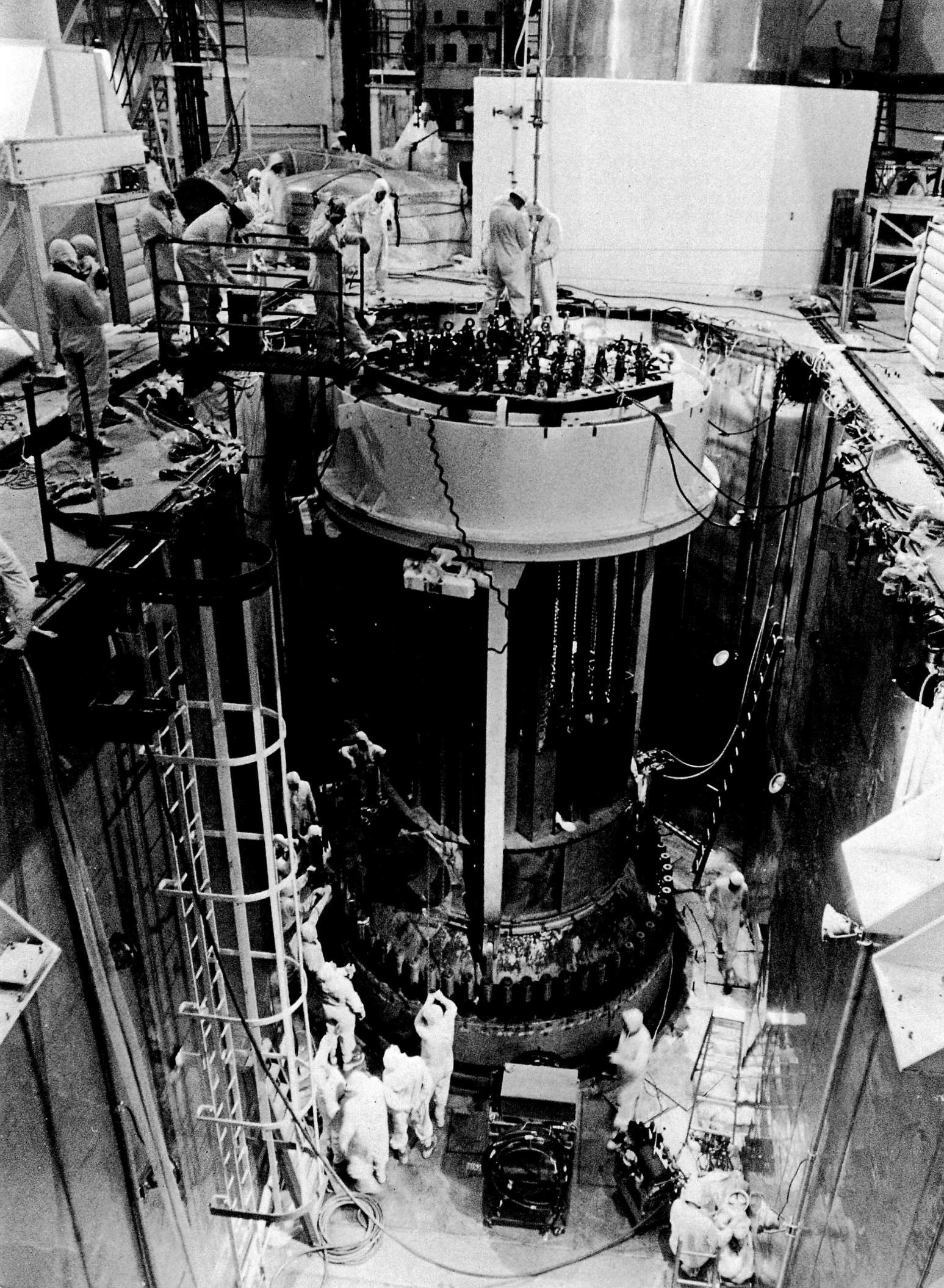
As a Schedule IV drug, Darvon would be limited in production, could not be prescribed over the telephone, and prescriptions of it could not be refilled.

Califano noted that since February FDA has sent a warning on Darvon to one million doctors, pharmacists, and other health professionals through its DRUG BULLETIN, and had publicized the problems with the drug through FDA CONSUMER and other media. Publicity included 650,000 reprints of the March 1979 FDA CONSUMER article. Four thousand supermarkets were among the distribution outlets.

In calling for additional research and monitoring, the HEW Secretary also issued these cautions:

- Never use Darvon and other propoxyphene products unless there really is no alternative, and then only with care.
- Pharmacists should warn patients of the dangers of using Darvon along with tranquilizers, sedatives, or alcohol.
- Patients should not ask for Darvon.







# Primer On Radiation

*The recent nuclear powerplant accident in Pennsylvania left many people wondering just what radiation is and why it can be dangerous. Bombs and nuclear accidents aside, the facts as unfolded here are that radiation is virtually everywhere and that man has lived with it, and will continue to do so.*

by Bill Rados

**T**True or false: (1) Man-made sources of radiation, such as atomic weapons and x rays, have caused new diseases never before encountered by medical science. (2) You can reduce the amount of radiation to which you are naturally exposed by living in a house made of brick, rather than wood. (3) The first nuclear reactor began operating within the last 50 years.

Oddly enough, all the foregoing statements are false:

Radiation, man-made or natural, does not cause unique diseases. The same kind of harmful effects that radiation produces can be brought on by other causes, such as carcinogenic chemicals. (That's one reason scientists find it difficult to measure the biological effects of radiation, particularly from low-level exposures.)

Bricks not only provide no more protection from natural radiation than wood or other building materials—they actually increase it. Like certain other common materials, such as granite and some types of shale, bricks contain minute, though measurable, amounts of natural radioactive substances that constantly emit low-level radiation.

Although the first nuclear reactors for commercial production of electricity did not come into being until after World War II, Mother Nature was in the nuclear powerplant business about 1.7 billion years ago. Eric Hall, in his book *RADIATION AND LIFE*, explains that eons ago in Africa natural deposits of uranium ore occurred in rock structures through which water flowed. The peculiar arrangement sparked a process quite similar to that of today's nuclear powerplants: heat from the radioactive uranium turned the water to steam, generating the equivalent of several kilowatts of energy for hundreds of thousands of years. (Since those primeval times, however, uranium ore has lost so

much of its radioactivity through millions of years of decay that such spontaneous nuclear reactors are no longer found in nature.)

Radiation is not a modern creation of man's curiosity in tinkering with the atom. Radiation has permeated the universe since time began. Even today, with widespread medical and other technological applications, natural, non-man-made radiation accounts for more than half of the exposure we receive. Cosmic rays from the sun and stars bombard us constantly. (Airline passengers receive a little extra dose because they fly above the protective screen of the atmosphere.) Our own Mother Earth subjects us to still more radiation from such widely distributed materials as granite, natural gas, and phosphates. In one area of intense radioactivity in India, the population is exposed to a natural background radiation of some 1,300 millirems a year, more than ten times the U.S. average. ("Rem" is a unit for measuring the biological effects on a person from a dose of radiation. One rem equals 1,000 millirems.)

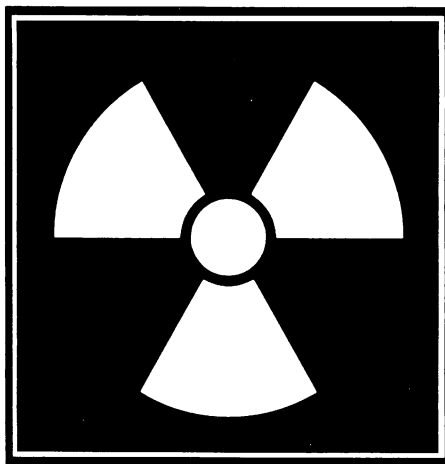
Even our bodies contain minute traces of radiation from radioactive materials in our food. Altogether, natural background sources expose Americans to an average of about 100 millirems a year.

The biggest man-made contribution to radiation exposure of individuals results from the medical and dental use of x rays and of radioactive materials to diagnose and treat disease. These applications account for about 90 percent of all man-made radiation exposure to the general public—an average of about 90 millirems per person yearly. When these medical procedures are needed, the benefits far outweigh the risks, but studies indicate that a significant percentage of the 240 million x-ray examinations conducted annually may not be necessary. FDA, through its Bureau of Radiological Health, has an active program to reduce such unnecessary exposures—and to reduce, as much as possible, the amount of radiation used in these examinations that are needed.

The remaining 10 percent of man-made exposure comes from nuclear weapons testing, nuclear-powered electric plants, industrial uses of radioactive materials, and even minute emissions from certain consumer products, such as color television sets. These sources combined expose each of us to about 10 millirems a year, on the average.

These exposure figures are for the general public. Patients who get large numbers of x rays or undergo radiation

*Workers refuel the uranium core of a nuclear reactor at Turkey Point, Florida. (Photo courtesy Atomic Industrial Forum.)*



“Radiation is not a modern creation of man’s curiosity in tinkering with the atom. Radiation has permeated the universe since time began.”

therapy and workers in a number of occupations, including uranium and phosphate miners, researchers, nuclear powerplant employees, radiologists, and others who work with medical radiation may be exposed to radiation levels well above that normally received by the general public.

Radiation deliberately used to provide numerous benefits to modern society is classified as man-made radiation. The most obvious, of course, is medical use of radiation. X rays help physicians diagnose illnesses that might otherwise remain hidden or obscure. In what is known as nuclear medicine, radioactive substances administered to patients permit detection of diseases, including tumors. These “tracers” emit radiation that can be detected from outside the body by instruments that identify the organ and the quantity of the tracer present.

This technique is often used to diagnose thyroid disorders. The thyroid gland normally absorbs iodine from the bloodstream, using it to manufacture thyroid hormone. When a patient suspected of having a thyroid disorder is given a small amount of radioactive iodine, the tracer, like ordinary iodine, accumulates in the thyroid. From measurement of the radiation coming from the thyroid, hyperthyroidism (thyroid overactivity) or hypothyroidism (underactivity) can be detected and appropriate treatment begun.

Interestingly, one of the accepted treatments for hyperthyroidism is radioactive iodine, but in a much larger dose than that used for diagnosis. Typically, the diagnostic dose exposes the thyroid to about one-half of a rad, while the therapeutic dose may be as much as 10,000 rads. (“Rad” is a unit for measuring a dose of radiation.) The risk from this high dose of radiation is offset by the benefit of the treatment, considered by many to be more successful than surgery (which, of course, also entails risk).

Radiation therapy is also used to treat cancer. Here again, the risks from exposure are offset by the tangible benefits a cancer patient may receive from the treatment.

Nonmedical radiation also provides benefits, but weighing these benefits against the risks is more difficult. Unlike

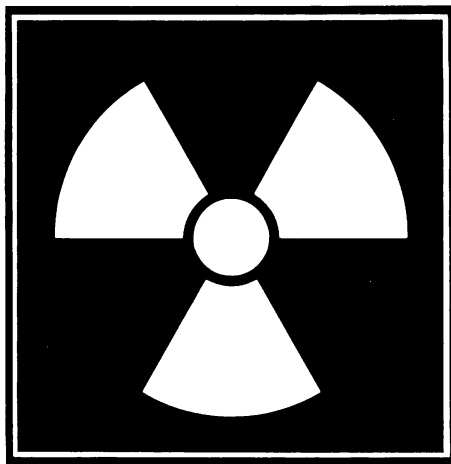
medical applications, the benefits of other man-made uses of radiation do not accrue to just one individual but to society as a whole. And those who sustain the greatest risks from these sources of radiation do not receive a proportionately large share of the benefits. Miners who dig the uranium to fuel nuclear powerplants may be subject to an increased risk of lung cancer but their share of the benefits—the electricity generated by nuclear reactors—is no greater than anyone else’s.

This situation is not unique to radiation. The same perplexing problem of weighing individual risks vs. societal benefits arises with coal-fired powerplants, for instance. Coal miners are subjected to a high risk of lung disease, but use no more electricity than those who don’t share the health risk. As researchers learn more and more about the health hazards of our technologically advanced society, it becomes increasingly clear that none of the “miracles of modern science” is without its risks. This is true of drugs, pesticides, automobiles, air travel, and countless other “advances,” including man-made sources of radiation.

What exactly are these radiological health hazards? As the true-false quiz pointed out, radiation has no unique biological effects. Burns from exposure to high levels of radiation appear virtually the same as burns from a hot stove. Radiation-induced leukemia is indistinguishable from that caused by certain viruses or chemicals. This, of course, makes it next to impossible to pinpoint radiation as “the cause” of, say, a particular case of cancer. What is possible is to roughly estimate the number of “extra” cancers that might occur in a population of people because of radiation exposure. A recent National Academy of Sciences (NAS) report on the effect of low-level radiation, while admitting the uncertainty of the task, does attempt such estimates. According to the report, a single exposure of 1 rad (a level of radiation roughly comparable to 35 to 40 simultaneous chest x rays) to 1 million people would cause 268 to 1,031 of them to have cancer. About one in three of these cases would be fatal.

With these figures as a basis, scientists from FDA’s Bu-





“ . . . no ‘threshold’ level of exposure . . . is completely safe; some degree of risk is assumed when people are exposed to even very small amounts of radiation.”

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reau of Radiological Health, the Environmental Protection Agency, and the Nuclear Regulatory Commission estimated the probable effects of the nuclear reactor accident at Three Mile Island last spring. According to these figures, one additional fatal cancer, plus one additional nonfatal effect, such as cancer or a genetic defect, might be expected among the 2 million people living within 50 miles of the nuclear plant from the additional radiation they received between March 28 and April 7, 1979. (Out of a population of this size, about 325,000 fatal cancers would be expected to occur normally.) While inexact, such estimates are useful in weighing the risks of low-level radiation against its benefits.

Direct evidence of human health risks from radiation has been obtained almost entirely from study of people exposed to high levels. The information is mainly from studies of Japanese survivors of the atomic bombs dropped on Hiroshima and Nagasaki during World War II, of patients undergoing radiation therapy, and of workers chronically exposed to radioactive substances in the days before the hazards of such high exposure were realized. These early victims of a new and largely unknown technology included women employed to paint radium watch dials who wet their brushes on their tongues, unknowingly ingesting minute amounts of radium that years later proved deadly to many of them. Others were the pioneering radiologists of the 1920's, 30's, and 40's who suffered exposure to radiation levels many times greater than today's health professionals. They learned too late of the dangers of their profession in high incidences of leukemia and other cancers.

High level doses of radiation (generally doses of more than 100 rads), if received all at once, cause short-term effects that appear within hours, days, or weeks of the irradiation. These effects are collectively known as acute radiation syndrome (sometimes called radiation sickness). The first symptoms are nausea, vomiting, and malaise. After a latent period, during which these symptoms subside, more serious problems can arise: infections, fever, hemorrhage, loss of hair, diarrhea, loss of body fluid, and effects

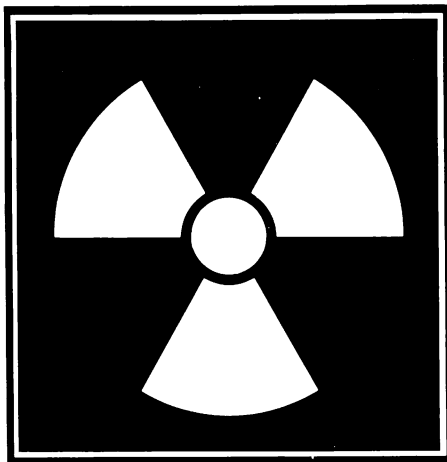
on the central nervous system. If the exposure is more than 600 rads, death is almost certain to follow.

When the dose is not great enough to cause death, long-term damage can occur, becoming apparent years, decades, or even generations after exposure. Acute radiation syndrome has been observed mainly during experiments on laboratory animals; human cases have been limited to the Japanese A-bomb victims and a handful of people irradiated in peacetime radiation accidents.

The long-term effects of radiation may appear in those who survive a large, acute dose of radiation, or in persons who have received smaller, recurring doses over a long period. Experts are not in agreement about the precise nature and extent of risk from exposure to low-level radiation. Recent studies, however, support the view that there is no “threshold” level of exposure below which a person is completely safe; some degree of risk is assumed when people are exposed to even very small amounts of radiation. Thus, some risk must be accepted by society in exchange for the benefits of man-made radiation.

The recent NAS report acknowledges the uncertainty of forming conclusions about low-dose effects from data involving high-level exposure. But, the report adds, to assume that risk is directly proportional to dose is an acceptably convenient way to estimate health effects from low exposures.

All types of ionizing radiation induce similar effects, although some types—alpha particles, for example—can be more potent than others. The damage done by radiation results from the way it affects molecules essential to the normal function of body cells. Four things may happen when radiation strikes a cell: (1) It may pass through the cell without doing any damage. (2) It may damage the cell, but the cell partially repairs the damage. (The ability of a cell to repair some of the damage wrought by radiation explains why a given dose of radiation delivered in small amounts over a long period of time is less damaging than the same total dose given all at once.) (3) It may damage the cell so that the cell not only fails to repair itself but



“The developing embryo in the mother’s womb is thought to be the most vulnerable of all. . . .”

reproduces in damaged form over a period of years. (4) It may kill the cell. The death of a single cell may not be harmful, but serious problems occur if so many cells are killed in a particular organ that the organ no longer can function properly. Incompletely or incorrectly repaired cells may, over time, produce delayed health effects such as cancer, genetic mutations, or birth defects.

The amount of radiation absorbed is the most important factor in determining biological effects. But the same amount of radiation is generally more harmful to children than to adults. The developing embryo in the mother’s womb is thought to be the most vulnerable of all because of the damage that can be done to the unborn child. (That was why Pennsylvania Governor Richard Thornburgh advised that pregnant women and children leave the area around Three Mile Island during the nuclear emergency last spring.)

In general, the greater the body area exposed, the greater the overall damage from radiation. But radiation does harm some body tissues more than others. It has its greatest effect on tissues made of cells that divide rapidly and that are not specialized. For instance, bone marrow cells are highly sensitive to radiation; since bone marrow helps produce blood cells, victims of acute radiation syndrome who have received high-level radiation exposure often suffer from anemia, hemorrhage, and infection—all related to problems with the blood. Muscle and nerve cells, on the other hand, are less sensitive to radiation.

This variation in cell sensitivity accounts partly for the success of radiation therapy in treating cancer. Cancer cells are primitive instead of specialized and divide rapidly, and thus may be more susceptible to radiation than nearby normal cells. It also explains the extra sensitivity of children and developing embryos, with their large proportion of rapidly dividing cells.

Certain radioactive materials can affect specific organs more than others. Radioactive iodine, for example, will do its greatest harm to the thyroid gland because that is where iodine tends to accumulate. Radium, on the other hand, resembles calcium and, like calcium, will accumulate in bones and do the most damage there.

The most common adverse effects from radiation are cancer, birth defects, cataracts, and a shortening of lifespan. In addition, if the reproductive organs are irradiated, genetic mutations may occur in sperm or egg cells, bequeathing the ill effects to future generations.

Data from a number of studies indicate that lung, thyroid, and breast cancer, and leukemia (so-called “cancer of the blood”) are the most common radiation-induced malignancies. As with the other ill effects of radiation, virtually all the evidence of its carcinogenicity comes from studies of individuals exposed to very high doses, such as the World War II A-bomb survivors. It is extremely difficult to assess the risk from low levels of exposure based on evidence gathered from cases of high-level radiation.

Even harder to gauge than the incidence of cancer is the increase in genetic damage that will take its toll on the descendants of those exposed to radiation. Such effects come about when radiation damages the genes or chromosomes in sperm or egg cells that subsequently take part in conception. All the cells of the developing individual (including his sperm or her eggs) will carry the distorted genetic information and the effects will be passed on to succeeding generations as well. The consequences are varied: The damage may cause no ill effect at all. Or it may subtly alter the body’s metabolism, causing a slightly greater predisposition to a certain disease, for example. Or it may bring about mutations so lethal that the fetus dies in the womb. It should be noted that direct evidence of genetic mutation caused by radiation comes only from animal studies. Radiation-induced genetic mutation has not been demonstrated conclusively in humans, not even among the descendants of the survivors of the atomic explosion at Hiroshima and Nagasaki.

Radiation also can take its biological toll on the developing embryo or fetus when the mother’s abdomen is exposed, even to low doses. The effects of radiation on an unborn child vary with the stage of its development. Exposure during the first few weeks of pregnancy may cause a spontaneous abortion or, particularly between the second and seventh weeks (when pregnancy may still be unsuspected), an increased risk of major malformations in the



child. During this period, major body organs are forming and their rapidly dividing cells are particularly sensitive to radiation. Scientists generally agree, however, that malformations are unlikely to occur in unborn children as a result of exposure to ordinary diagnostic x rays. Only exposure of more than 50 rems (50,000 millirems) are thought to produce an increased incidence of skeletal, nervous system, and other birth defects. The risk of childhood cancer, however, may be increased by exposures in the womb of only 200 to 2,000 millirems. The results of several studies indicate that the possibility of a child developing cancer before age 15 as a result of radiation could be as great as one in a thousand, assuming a typical two- or three-film x-ray examination of the mother's abdomen.

Calculating the health risks from radiation is a very inexact science, riddled with uncertainty. It can be said, however, that any risk from low-level exposure is small. Apart from the effects on developing fetuses through exposure of the mother's abdomen, there is no direct evidence of human harm from low doses of radiation. Scientists can only surmise such risk exists and make "educated guesses" as to its degree.

While these risks are by no means negligible, they appear to be small compared with other hazards that most people face and accept every day. Eric Hall, in the earlier noted book, *RADIATION AND LIFE*, estimates that a typical chest x ray involves a risk of developing leukemia of about 3 people in 10 million; radiation thyroid treatment, a risk of 3 people in 10,000. Comparing these with risks commonly faced in everyday life, a single chest x ray is as potentially dangerous as smoking two cigarettes or driving on the high-

way for 5 miles. The treatment of thyroid disease with radioactive iodine is as risky as smoking 100 packs of cigarettes or driving 5,000 miles on the highway.

The important point, of course, is that any radiation exposure should be avoided if possible. It is up to society to decide what is possible; what price it is willing to pay to enjoy the benefits of radiation, and what price it will pay for safety. The price of the benefits from radiation—nuclear power, medical diagnosis and treatment, research, etc.—is clearly some degree of risk to the public health, particularly to workers employed in these fields but, to a lesser degree, to the public in general.

The price of safety depends on the degree of protection that society demands. Absolute safety from man-made sources of radiation is only possible by entirely eliminating those sources. Relative safety entails relative costs. Trade-offs are a part of modern civilized life. Even shutting down every nuclear powerplant would not eliminate the health hazards of generating electricity: Coal- and oil-fired plants present health risks of their own from air pollution and other causes.

If we are to weigh the risks and benefits of man-made radiation more accurately, more studies must be done on radiological health hazards, especially from low doses of radiation. The Department of Health, Education, and Welfare is currently engaged in conducting several such studies. The results will make it easier to know the health costs society must pay for the benefits of man-made radiation.

*Bill Rados is a member of FDA's Public Affairs staff.*

## A, B, C, and X of Radiation

With the advent of atomic weapons, nuclear powerplants, x-ray machines, and other such technological marvels, "radiation" has become a household word. But though we talk about it, read about it, and even worry about it, few of us understand what radiation is or how it "works."

First of all, there are two main types of radiation. *Ionizing* radiation comes from x-ray machines, nuclear reactors, and radioactive materials. It gets its name from its ability to knock electrons out of atoms, creating electrically charged *ions*. In the human body, these ionized atoms can affect normal biological functions. *Nonionizing* radiation, such as microwaves, sound waves, and light, damages living tissue by other means. For our purposes here, only ionizing radiation will be discussed.

In the vernacular of the '70's, *radioactivity* is nature's way of "building a stable relationship." When a nucleus of an atom has a ratio of protons to neutrons that is outside an optimum range, the atom is unstable, or radioactive. Such a radioactive element (or radionuclide) can achieve stability by changing the proton-neutron ratio. To do this, radiation is released from the nucleus.

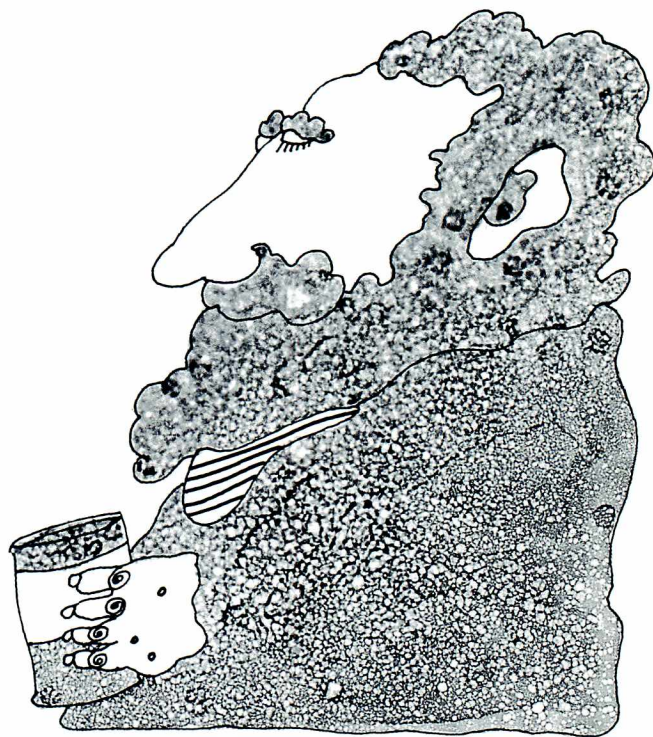
Some radionuclides occur in nature. For example, radium-226, used in medical therapy, comes from uranium ore. On the other hand, cobalt-60,

also used in medicine, does not exist in nature and must be artificially produced by means of sophisticated nuclear technology.

Radioactive substances emit radiation in several forms. Some, like alpha and beta radiation, are particles of matter. Others—gamma rays and x rays—are pure energy, possessing no mass. (Gamma rays and x rays are identical in their physical properties and biological effects. The only difference is that gamma rays are natural products of radioactive atoms while x rays are produced in man-made machines.) Particulate radiation does not penetrate body tissue as deeply as gamma or x rays. It mainly damages the skin and surface organs, although it can harm the surfaces of internal organs if it is inhaled or ingested. Gamma and x rays penetrate more deeply into the body and can do their damage throughout any internal organs that are exposed. Ionizing radiation gradually uses up its energy as it collides with the atoms of the material through which it travels. The material—for example, living tissue—absorbs the energy, mainly through the ionization of its atoms. It is this transfer of energy that can cause tissue damage and adverse health effects. The damage can be done by external radiation, such as gamma rays from an atomic bomb explosion, or internally, for example, from drinking milk contaminated with radioactive iodine that is giving off beta particles.

# Food Labels Get High Readership

*Most people read food labels at one time or another. But they read them for differing reasons. Some people would also like to see different information on the labels. Those are some results of a public opinion survey done by FDA as part of its long-range program to make food labels more relevant to consumers.*



A young man unconcernedly tosses this canned food product and that packaged food item into his supermarket cart. Across the aisle, a woman picks through the products, carefully reading the labels to make sure none of the items she puts in her basket contains sugar. Another shopper checks the ingredient labeling with a pleased expression on his face, assured that there's no monosodium glutamate (MSG) in the food he's buying, since he's allergic to MSG. A fourth person intently reads the labels on one can and then another, occasionally shaking her head in dismay.

Such scenes occur daily in supermarkets across the country. Some people read labels, others don't. Some scan them intently for what seems to be trivial information. Others find the information confusing, bewildering, uninteresting.

Just how often consumers read food labels and why were the subjects of a 1978 survey conducted by FDA. The results show that three out of four consumers pay attention to what's written on the package—especially ingredient and dating information.

But the overall results also showed that most people—about 75 percent, or 3 out of 4—are satisfied with the information provided on food labels.

The other 25 percent would like to see some changes in food labeling and some are quite vocal about it. Most of

this 25 percent—about 15 percent of all consumers—do not feel strongly about changing the food label, but do have some suggestions. The rest, amounting to 10 percent of American consumers, are strongly critical of present food labeling and see a serious need for revision.

These consumers appear to be motivated mainly by some degree of apprehension about what may be in the packaged, processed, and canned foods they are buying. Relatively few question the nutritional value.

Many are concerned with what they see as a proliferation in foods of substances that may have long- or short-term adverse health effects, including additives that may cause cancer. The FDA survey suggests that the desire for more information stems from this fear, instead of from a desire for a more nutritious diet, from economic concerns, or from feeling they have a "right to know."

Of those who said they pay attention to ingredients listing, three out of four said they use the information to avoid one or more specific ingredients. The most frequently mentioned ingredient to be avoided was sugar. Others included salt, fats and oils, preservatives, artificial colors and flavors, artificial sweeteners, starches, seasonings, cholesterol, and monosodium glutamate.

The reason most people gave for wanting to avoid these substances was

the harmful or hazardous quality of the ingredient, although a considerable number also mentioned dietary reasons such as weight control, personal tastes, and religious beliefs.

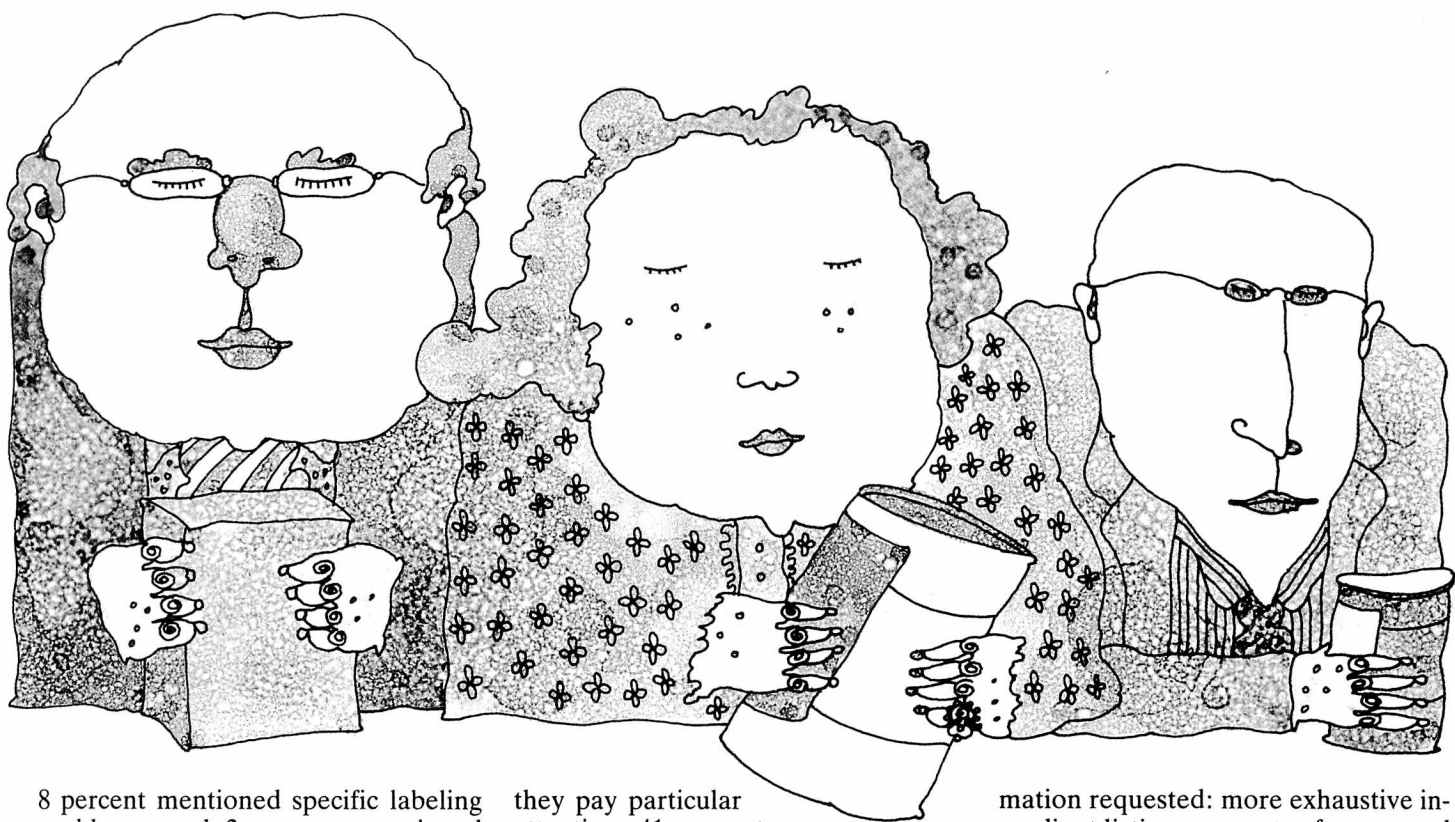
The Consumer Food Labeling Survey, part of FDA's Multipurpose Food and Cosmetics Survey, was designed and directed by the staff of the Division of Consumer Studies of the Bureau of Foods. Response Analysis Corp., of Princeton, N.J., did the shopper interviews. Part of a long range label review project, the survey will help determine new label regulation proposals.

During October and November 1978 surveyors interviewed 1,374 "primary food shoppers"—the persons in the household who do most of the food shopping. The 1,374 were selected on a statistical basis to represent a genuine cross-section of the shopping public.

The first question surveyors asked: "Aside from prices, please tell me about any particular problems, difficulties, or concerns which you have with food these days."

In response, 49 percent said they were concerned only with price. One or more problems, usually with food itself, was mentioned by 47 percent; 14 percent were concerned with general product quality, another 14 percent worried about adverse health implications, and 8 percent were concerned about freshness of food. An additional





8 percent mentioned specific labeling problems, and 3 percent mentioned problems with damaged containers, insufficient stock, and similar shopping concerns.

Of the one in seven persons concerned with the health implications of food, 35 percent worried about preservatives, 29 percent about "additives" or "chemicals" in general, 20 percent about sugar content, 8 percent about artificial colors, 7 percent about salt content, and 4 percent about artificial flavors.

When asked directly and specifically if they were satisfied with the amount of information on food packages and cans, 59 percent said they were fully satisfied. However, one person in three saw some need for improvement, the most frequently mentioned part of the label needing improvement being the ingredient list. The most commonly expressed needs were for manufacturers: to list *all* ingredients, to simplify the language, to extend the ingredient list to all products, to use larger print, and to list quantities in percentages rather than giving only the order of dominance.

Other areas consumers said are in need of improvement include the nutrition label (8 percent), open dating of more products (3 percent), and inclusion of drained or fill weight on canned goods (2 percent).

Asked to which label information

they pay particular attention, 41 percent mentioned the ingredient list, 22 percent—the nutrition label, 18 percent—quantity information, and 11 percent—open dates.

Most shoppers are able to understand the information on food packages and cans. However, 27 percent admitted that they are sometimes confused, most frequently by the use of technical and chemical names in the ingredient list. Other causes of confusion were lack of quantity information on the ingredient list, use of the metric system, U.S. Recommended Daily Allowances (RDA's) and other nutrition information, date codes, and use of small print.

Another 23 percent of consumers pay no attention to the ingredient listing and 36 percent ignore the nutrition label. The surveyors suggest that it would not be unreasonable to conclude that many find the information too difficult to understand and use.

Queried directly about whether they would like more or less information on the label, only 2 percent responded that the label had too much information. One-quarter of the shoppers would like additional label information, usually about ingredients. Most commonly requested was a statement of quantity of the ingredients, followed by simplification of the ingredient list, and calorie information. Other infor-

mation requested: more exhaustive ingredient listing, amounts of sugar, and open dating on more products.

From this recent FDA survey it is clear that food labeling has caught the eye of most American shoppers and that many have suggestions on ways to make labeling more useful to them.

## Summary of Suggestions From 1978 Consumer Food Label Survey

### Ingredient List

- Simplify the list
- Add quantitative ingredient list—preferably in percentages
- List all ingredients
- Give amount of sugar
- Extend ingredient information to all products

### Nutrition Label

- Give calorie information on all products
- Simplify overall format

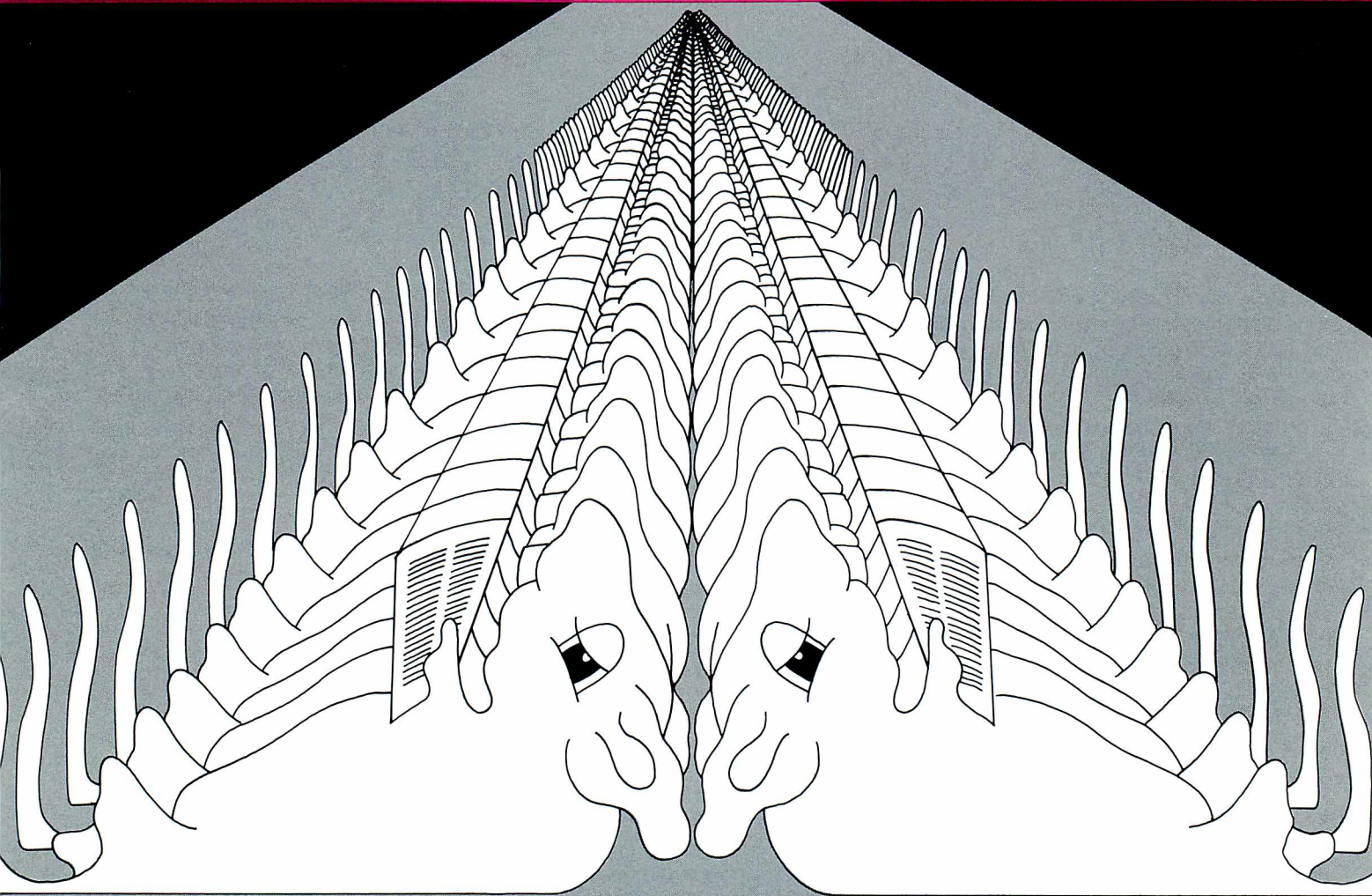
### Open Dating

- Extend to more products
- Use expiration date for perishables

*(Contributing analysis and technical assistance for this article was Dr. James T. Heimbach, chief of the consumer research staff, FDA Bureau of Foods.)*



ED<sub>01</sub> Study  
NCTR





# 24,000 Mice Tell Us Much About Cancer Risks

*More than 24,000 mice were the “subjects” in the largest animal study ever undertaken. Analysis of data from the study, just completed at FDA’s National Center for Toxicological Research, produced unexpected findings that may change the way cancer risk is determined.*

by Annabel Hecht

**E**D<sub>01</sub>, most science fiction buffs will be disappointed to learn, is not the latest model of a computerized robot. It is the official designation for a study whose size and complexity makes the walk on the moon seem almost like a trip to the corner grocery. ED<sub>01</sub> stands for “Effective Dose needed to cause 1 percent incidence of cancer.” Utilizing more than 24,000 mice, the study was the largest animal experiment ever undertaken or likely to be.

The ED<sub>01</sub> study was conducted at the National Center for Toxicological Research (NCTR), in Jefferson, Arkansas, a unique facility run by the Food and Drug Administration with support from the Environmental Protection Agency. The mission of NCTR is to study the long range health effects of exposure to chemicals such as food additives, pesticides, drugs, or pollutants.

The major purpose of the ED<sub>01</sub> study was to take a substance known to produce bladder cancer in experimental animals—in this case 2-acetylaminofluorene (2-AAF)—and feed it to groups of animals in successively lower doses to find the dose that would cause an increase in tumors 1 percent above that of a control group, that is, a group not fed this chemical. Seven dosage levels of 2-AAF were used, ranging from 150 parts per million (ppm) to 30 ppm, plus a zero level for the control groups. As the dose level was reduced, the number of animals was increased to assure that an effect would be detectable. Some 5,000 mice received the lowest dose level.

Originally, the plan was to sacrifice all animals by 18 months of age for examination of their organs and tissues, since previous work had indicated tumors would have developed by that time. NCTR mice, however, were different, perhaps because of the unusual environmental conditions maintained at that FDA center. At 18 months, 90 percent of the animals were still alive and well, and the cancer-causing agent wasn’t producing tumors at the low doses.

The NCTR researchers then decided to extend the study to 24 months for some of the mice and allow another group to live out their lifespans. Some reached the ripe old age of 33 months. By extending the study, NCTR scientists learned some important and unexpected things.

They found that liver tumors developed after 18 months of life, which was not anticipated. The seeds of these tumors were planted in the first 9 months of feeding with 2-AAF. It didn’t matter whether 2-AAF was stopped after that time, the tumors kept on developing.

Bladder tumors, on the other hand, developed earlier and their incidence depended on continuous feeding of the cancer-causing substance. When 2-AAF was discontinued, the incidence of bladder tumors dropped off. This suggests that if the tumor had not been induced by the time the feeding with 2-AAF was stopped, its development was radically curtailed.

Time of exposure proved important. As animals were examined at 18, 24, and 33 months, tumors were detected at successively lower doses for the longer periods. This finding has implications for development of regulations governing the risk assessment of hazardous substances. Until now, there has been little evidence that much would be gained by conducting bioassay studies beyond 18 months. If the ED<sub>01</sub> study had been stopped at 18 months, the potential of 2-AAF to cause liver tumors might have been overlooked or the substance might have been dismissed as a “weak” carcinogen.

These findings indicate there is no threshold, or dose level, below which this carcinogenic substance would be safe. The findings also provide additional evidence that high dose feedings of small numbers of animals is a valid way to assess risk.

Accurate risk assessment is possible even in short-term studies by the addition of 3 dosage levels to the 2 normally used, according to the ED<sub>01</sub> study results.

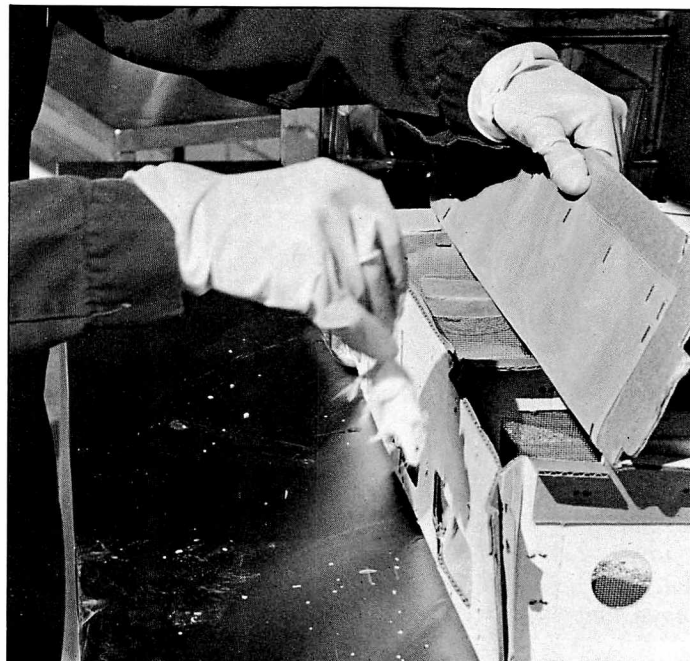
Preliminary results of the ED<sub>01</sub> study were reported June 15 at a symposium co-sponsored by NCTR and the American College of Toxicology, in Washington, D.C. In addition, a number of papers presented described the logistics of conducting this unusual, large-scale project.

Certain basic elements are required in any research project: getting the raw materials (namely, experimental animals, the chemical to be tested, feed, and housing material), maintaining the study, having the right materials on hand at the right time, and collecting the data. Putting it all together presents problems enough for a short-term study. When more than 24,000 experimental animals are involved, the task can only be described as mind-boggling.

Nearly 2 years of preparation were required before the study could begin. ED<sub>01</sub> was one of the first studies to be initiated at NCTR, and plans for the project were started soon after FDA took over the facility from the U.S. Army’s

*The heritage of the mice used in the ED<sub>01</sub> study could be traced to breeding stock purchased from commercial sources. New arrivals in the breeding facility at the National Center for Toxicological Research (NCTR) are first placed in quarantine where they are checked for signs of disease and the presence of bacteria, viruses, and parasites. (Photo, left)*

*Water for experimental animals at NCTR is prepared in an enclosed cabinet system to ensure absolute sterility. (Photo, right)*



Pine Bluff Arsenal in May 1972. In that month, pilot studies with 2-AAF were conducted. In June, work was begun on the derivation of the breeding stock that would provide animals for the vast experiment.

During the next year, chemistry and microbiology laboratories were readied. In 1974 the Experimental Data Collection System was completed and the first of a series of automated data processing systems was ready for use. Early the next year the Computer Center was completed and processing equipment installed. The Diet Preparation Facility was finished in February and work was begun to "shake down" the operation in preparation for supplying sterile feed dosed at various levels for the ED<sub>01</sub> study.

The twelfth of April 1974 was a big day for NCTR. Construction was complete on "A" Barrier, the environmentally controlled area where the study would be conducted. Such "barriers" are physically designed and maintained to protect or isolate the animals completely from random exposure to any biological conditions not controlled by the researchers. The first animals were transported to the experimental barrier from the breeding barrier in special isolators. Allocation of the mice to ED<sub>01</sub> was completed in 42 weeks.

All the mice used in the study were raised in NCTR's breeding colony. Started with commercial stock, the colony eventually was bred in its own environmentally controlled barrier. A total of 576 female mice were put on experiment each week. Beginning in 1974, breeding colony records and genetic histories of the animals were fed into an automated Breeding Information System, which made it possible to trace the origins of any one animal. Once inside the experimental barrier the mice were randomly assigned four to a cage. Ear clipping was used for individual mouse identification within the experimental cage.

The experimental area is called, technically, an SPF/DF barrier. The initials translate to "specific pathogen free/defined flora." Every precautionary measure possible is built in to assure an absolutely clean environment. Air, filtered to remove airborne bacteria, viruses, and dust particles,

passes in a oneway stream through the barrier to exit, unfiltered, on the opposite side of the building. Temperature and humidity are stringently controlled and continuously monitored. Lights are timed to go off and on at specific periods of the day. Alarms and backup power systems assure that nothing disturbs the delicate environmental balance.

Closed circuit television monitors and an intercom system provides communication between the barrier and the outside world.

All equipment and feed that went into the barrier during the experiment was sterilized. Personnel entering the area followed a routine to guard against the intrusion of unwanted elements. They were required to brush their teeth, gargle, scrub hands and arms the way a doctor does before surgery, shower, and wash their hair. Finally they donned sterilized work clothes, including disposable masks and gloves. Disposable items of protective clothing were collected after use and incinerated to destroy any traces of the test chemical.

Once in the barrier, personnel were on a one-way street. The only way out was via a return corridor on the opposite side of the area from the entrance. There was no passage from one animal room to another. To get back in meant another complete shower and change.

Before they were allowed to work inside the barrier, animal caretakers were given a general physical examination by a physician, a TB skin test, various inoculations, tests to detect color blindness, and a microbiological survey to detect carriers of germs. Every 3 months, urine specimens from each person potentially exposed to the test compound were checked.

To detect specific microorganisms such as bacteria, fungi, parasites, and viruses, which could affect the study, a continuous comprehensive surveillance program was carried out on the microbiological condition of the test animals and their environment. Absolutely everything involved in any way in the study was checked for contamination: the animals, their feed, bedding, cages, the air, walls and floors





of the barrier rooms, and all persons authorized to enter the area. This was undoubtedly the cleanest collection of mice in history.

Feeding animals in a toxicity study presents a double challenge, for what shouldn't get into the feed is almost as important as what is put there by design. ED<sub>01</sub> operations concerned with diet preparation, mixing, and bulk packaging were conducted in a glovebox cabinet system that guaranteed the material would be untouched by human hands. Individual cardboard feed boxes were filled by workers wearing protective clothing to prevent exposure to the test chemical.

Filled feed boxes, coded as to dose level, were then transported to the experimental barrier in air-tight stainless steel carrying cases. Cards on the outside of the case identified which feed box was intended for which cage. The cardboard boxes were weighed before being put into specially designed stainless steel feeders and again when they were replaced after a week's time. At every step of the way, from the time the feed was delivered, during storage and diet preparation, tests were made to certify that the food was free of pathogens. The same was true of the water supply. Every object that touched the feed was sterilized. Material remaining in the feeder boxes was destroyed under exacting conditions to eliminate traces of the test chemical. Water used throughout the study was similarly decontaminated.

Changing of feed, water, and bedding material was done weekly, but checks on the animals' condition were made twice a day. Because small animals deteriorate quickly after death, it was important to remove dead and sick animals as soon as possible so important pathological data would not be lost.

Complete necropsies were performed on each animal and a total of 50 organs and various tissues were collected from each animal for study. As many as 3,000 individual observations were recorded per mouse.

Pathology work for the study was done by the University of Arkansas Pathology Service Project, through a contract between NCTR and the University.

To manage the staggering amount of data generated by the ED<sub>01</sub> study the center developed a complex automated data collection, storage, and retrieval system. Everything that could be known about each animal was recorded, from before birth to after death. Even before the study began, the Experimental Start-Up System developed a "model" of the experiment, defining how facilities and resources would be used. The Breeding Information System monitored and controlled the NCTR breeding colony, kept heredity information, and automatically allocated the animals to their experimental cages.

Through computer terminals located in the animal rooms, the Experimental Information System kept track of daily events: weighing of mice and feed, observations on the animals' conditions, microbiological surveillance, as well as routine management chores. When animals were removed from the study by design or because of death, each received a Carcass Identification number and the Post Experiment Information System took over. By the time the animal reached the pathology lab, prelabeled materials carrying the correct ID number were ready for the post mortem examination.

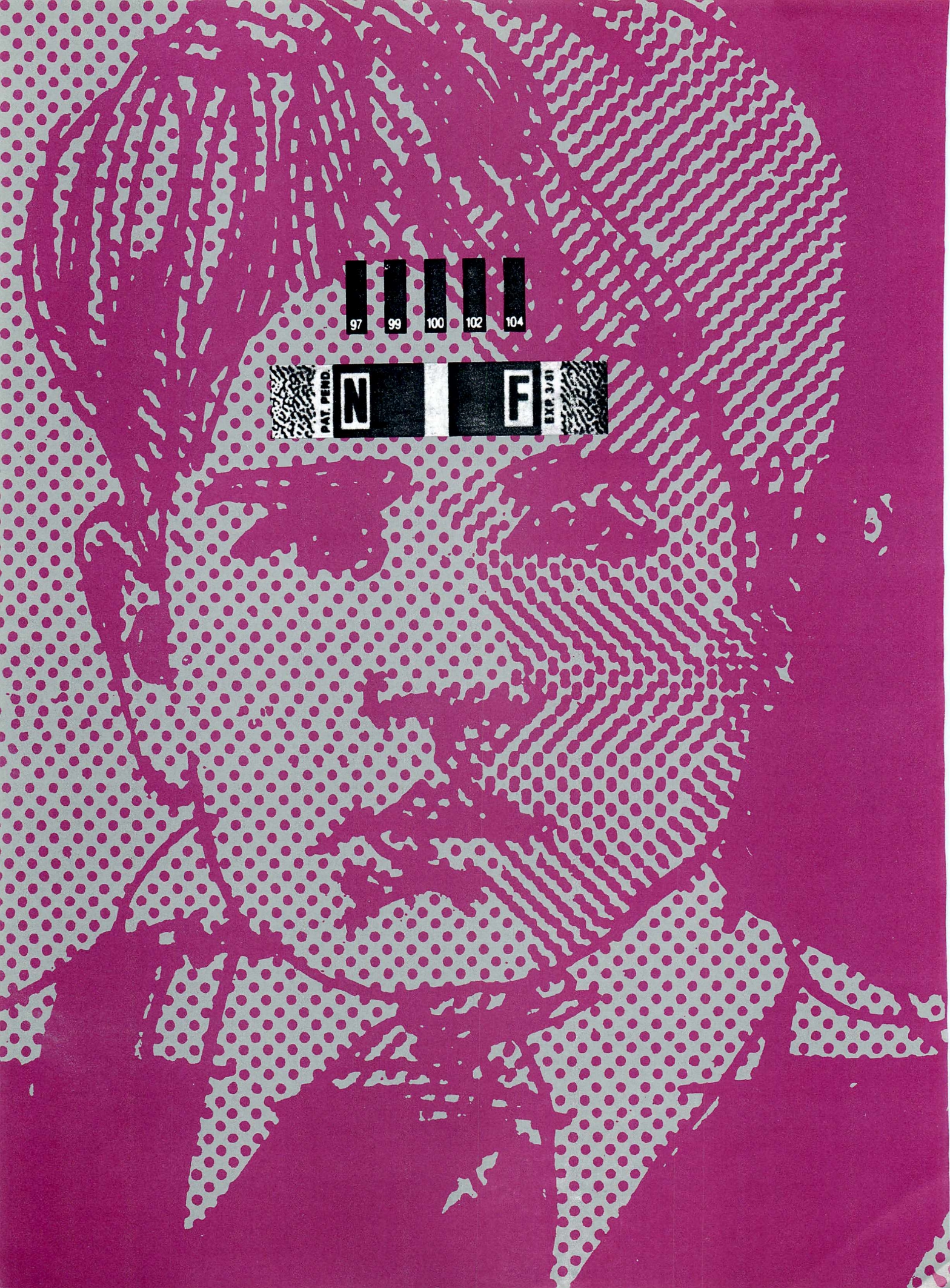
The NCTR computer system offers many advantages, including capability for making corrections at the time information is put into the system, for rapid transfer of updated information to a centralized data base, and for retrieval of selected information from any of the major data systems quickly and easily. The center has been assisted by two contractors: Beckman Instruments, Inc., and Program Resources, Inc.

The scientific report at the June symposium was just the "tip of the iceberg." ED<sub>01</sub> was not a single experiment, but encompassed about 80 different treatment groups. It is expected that analysis of the large quantity of data from the 4-year study will take many more years.

That's a lot to learn from a live-in rodent.

*Annabel Hecht is a member of FDA's Public Affairs staff.*





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# Fever Strips: Get A Second Opinion

*A fever is a symptom of something wrong in the body. It is most often caused by bacterial or viral infections, which generally produce a 3 or 4 degree increase in temperature from the normal level of 98.6 degrees Fahrenheit. An accurate reading of body temperature is a must if a fever exists. Some consumers now are using plastic "fever strips" instead of clinical mercury thermometers to check for fevers. FDA has a word of caution about these new fever indicators.*

by James Greene

**“W**hen you're hot you're hot,” the saying goes. It's a saying used often by gamblers and athletes. However, “when you're hot” you may also be sick, for excessive body heat has always been a telltale sign, for people of all ages, of a fever. The sooner a fever is detected the quicker treatment can begin to bring about recovery and the less likely there will be complications. The back of the hand on the forehead followed by a glass thermometer in the mouth is the everyday method used by most people to detect a fever.

Now, however, some people are substituting strips of blackened plastic in which liquid crystals are embedded. These products, generally labeled as fever indicators or detectors, are pressed against the forehead and 15 to 60 seconds later register a letter or number to indicate if there is a rise in the skin surface temperature. Most manufacturers use the letter “N” (for normal) and “F” (for fever) or numeral markings to indicate the skin temperature (the higher the number the higher the skin temperature). Other companies, however, use a letter/number combination.

In addition, the indicators turn one of three colors: tan (warm), green (warmer), or blue (warmest). Any shade in the “N” category is considered a normal temperature, while any shade of color with a numerical reading such as 1, 2, or 3 is considered to indicate an elevated temperature. Generally, doctors consider a temperature of 100 or above as cause for concern.

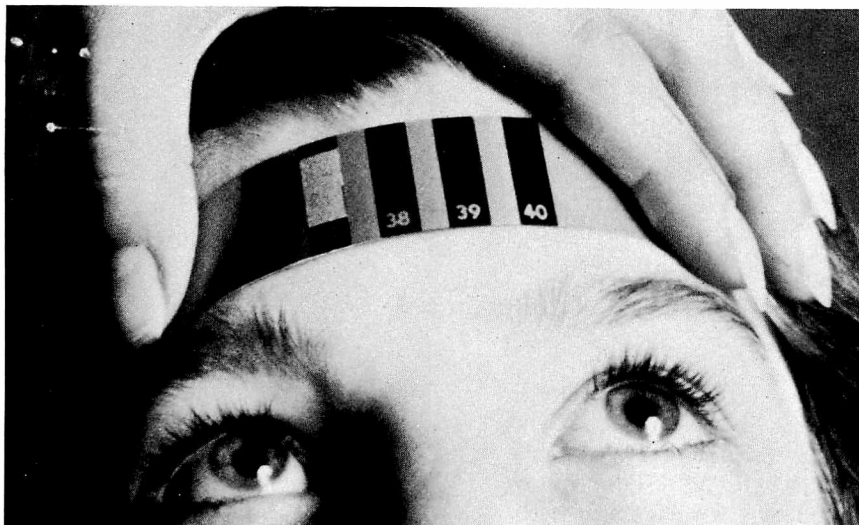
Manufacturers of these fever detectors claim they are reliable enough to tell whether a person has a fever. FDA, however, strongly recommends that consumers read the product's directions for use carefully, and that they use a clinical mercury thermometer to double check any high reading indicated by a fever strip, or anytime a fever is suspected even though the strip registers normal. Most of the labeling with these products recommend that a mercury thermometer be used to confirm any high reading. One manufacturer, in fact, sells a glass thermometer with its fever detector product.

One of FDA's concerns with these fever detectors is that they give a reading of surface skin temperature, when placed on the forehead, while the mercury thermometer gives a more accurate body (core) temperature when placed in the mouth or the rectum.

Forehead surface temperatures can vary 2 to 8 degrees between individuals. Body (core) temperature generally remains constant (98.6 degrees Fahrenheit) in the absence of disease for the overwhelming majority of people. In addition, external and internal physical factors can raise an individual's forehead temperature. These factors include air temperature, direct sunlight or artificial light on the forehead, and physical exercise or even flushing of the face caused by an emotional state.

The heat-sensitive chemicals in these liquid crystals do react to temperature changes and clinical tests conducted under ideal conditions—





*Plastic strips that adhere to the skin and that contain heat-sensitive chemicals are being sold as fever indicators or detectors. The heat-sensitive liquid crystals in the strips light up a letter or number to indicate surface skin temperatures. Strip (top photo) is marked in Celsius readings with the number 37 aglow. The Celsius scale included with the product translates the readers to Fahrenheit degrees, with 37 being the normal 98.6° F. Though manufacturers may claim that their products are accurate enough to detect a fever, confirmation from a conventional mercury thermometer (bottom photo) is recommended on any high reading.*

that is, without other factors interfering—do show that these products may be useful as indicators of elevated temperature.

Although these fever strips have been marketed in this country since about 1975 it has only been recently that manufacturers and distributors have made a concentrated effort to sell them in retail outlets. With this increased marketing effort has come a number of consumer complaints to FDA about the reliability of these products in detecting a fever.

As a result, FDA's Bureau of Medical Devices is conducting an investigation to assure that the labeling of these devices, including the instructions for use, is adequate. The investigation included inspections at the known manufacturers and distributors in Massachusetts, New Jersey, Ohio, Indiana, Missouri, and California.

During these inspections FDA investigators were instructed to obtain samples of each firm's products and a list of all distributors and other firms that repack the products under private labels. The investigators also were to obtain copies of any clinical studies, which the firms relied on to establish the reliability of these products.

Some of this scientific data will be used by the American Society for Testing and Materials (ASTM) to develop at FDA's request a voluntary performance standard for these medical devices. This standard will help ensure that these fever indicators are manufactured according to strict specifications and are effective for their intended use as required under the Medical Device Amendments of 1976. These amendments gave FDA the authority to regulate all medical devices, and to take legal action against any firm that manufactures, distributes, or sells medical devices that are mislabeled or found to be unsafe or ineffective.

*James Greene is a member of FDA's Public Affairs staff.*

# Dialog In Dallas



*One way FDA is keeping a finger on the pulse of the consumer is through Consumer Exchange Meetings, held by District offices throughout the country. Recently, it was Dallas District's turn to find out what people want to know about additives, saccharin testing, food and drug labeling, etc.*

“Everyone should attend one of these meetings at least once a year.” This ebullient praise came from a high school student at the end of an FDA-sponsored Consumer Exchange Forum.

Advertised with the intriguing title “What in Health is Happening,” the Forum took place in Dallas, in May. It was one of many such consumer exchange programs held every year by FDA’s District Offices throughout the country.

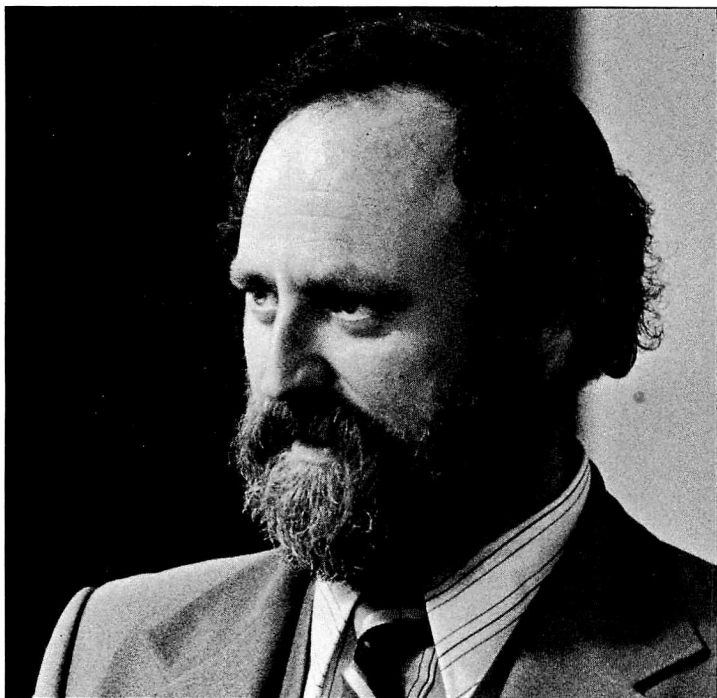
The 2-hour session in Dallas was different from many other exchange programs because the occasion was

both an educational experience and an opportunity for the public to express its views and concerns. Students from two residential home-making programs in the Dallas school system were among the nearly 90 people who filled the conference room.

The main theme was food additives—what they are, what they are used for, and why FDA permits them in food. The questions that consumers in Dallas asked and the concerns they voiced were much the same as those expressed by consumers in other parts of the country.

They wanted to know about artificial sweeteners: Why can’t cyclamates be put back on the market? What happened to aspartame? How was the saccharin administered to the mice—orally or injected—and, if injected, wouldn’t the great number of injections in itself cause problems?

One woman, whose husband is a diabetic, felt that the people who



*That Dallas consumers are very much concerned about what goes into their food supply was evident from questions about additives that were raised during the Consumer Exchange Forum. FDA's Jerry Henderson (left) and Hazel Wallace (right) had ready answers to these and other concerns that came out during the 2-hour meeting at the Lange Community Center.*





need saccharin should have the final say about whether it should be banned. And there was the inevitable query: If FDA can ban saccharin why can't it ban cigarettes?

Questions and comments ranged far beyond the Nation's sweet tooth. One mother, whose child is on the Feingold additives-free diet, described the problem of adjusting to it. It can be done, she said, but it is not easy. Urging that the case be made against additives, this mother said that if it were not for the Feingold diet her son would be in a special education class and on drugs. Instead, he is in the first grade reading on a fourth grade level.

BHT and BHA, additives used to prevent spoilage, also came under fire. One participant said that several countries have totally outlawed them, while England carefully regulates their use. Another mother expressed concern about the total effect of combinations of BHT, BHA, and other additives on children. Such combinations promote degenerative and metabolic diseases, she said.

One question perhaps not heard too frequently was "How can we pre-

vent premature press releases about additives?" Possibly referring to the number of conflicting reports that came out regarding the cancer-causing potential of saccharin, the consumer who posed this one wanted to know if FDA could withhold information until it is a "sure thing."

Age had its say. One consumer asked why ingredients listed on food labels and warnings on drug labels can't be written large enough "for us old folks to see?" Apparently unaware that she could request and get regular closures on her drug containers, this consumer also asked why prescription bottles had caps that kids can open, but oldsters can't.

These questions and many others on food labeling, use of fertilizers, and natural versus artificial foods were fielded by James E. Anderson, director of FDA's Dallas District Office; Hazel Wallace, consumer affairs officer for the Dallas District; and Jerry Henderson, program manager for foods for FDA's Region VI. Gwen Gilbreath, one of the District's compliance officers, was on hand to describe the food labeling hearings held nationwide last year. Presiding over both the planning committee, which did the preliminary groundwork, and the Consumer Exchange Forum, was Charlotte Gibson, energy conservation specialist with the Dallas Power and Light Company.

The need for consumers to have a say in the way decisions are made by their Government has long been recognized by FDA. As far back as 1952 the Citizens Advisory Committee Report to the Commissioner prompted the first consumer programs. Establishment of the Consumer Affairs Officers program in 1963 called for exchanges between the public and the Agency. Only since 1971, however, have meetings

between the two been held on a regular basis.

Each of the 22 FDA districts holds 3 or 4 meetings each year, 2 of which are usually in the vicinity of the district office. Other informal meetings also can be scheduled to provide opportunity for exchange of ideas and viewpoints. Food labeling, nitrites, generic versus brand name drugs, and even veterinary medicine are typical of the subjects discussed.

Would the citizens of Dallas like more consumer exchange meetings? A good number of the participants queried after the meeting said "yes." They felt the meeting was about the right length and the way the program was set up made it easy to exchange views and learn from the FDA staff. Not everyone agreed that they got what they came for. Several were frank enough to say that the topics discussed did not fulfill their expectations.

Despite fears only moments before the Forum began that there wouldn't be enough chairs and the coffee wouldn't be ready, the Consumer Exchange Committee was pleased with the way it all turned out.

# Biggest Recall Of All Hits Sleep-aid Products

*Methapyrilene, a key ingredient in over-the-counter sleep aids, has been found to be a potent carcinogen. As a result of the findings, a massive recall of all sleep-aid products containing the compound was ordered at the retail level. It was massive because more than 600 products are involved in this \$28 million-a-year business.*

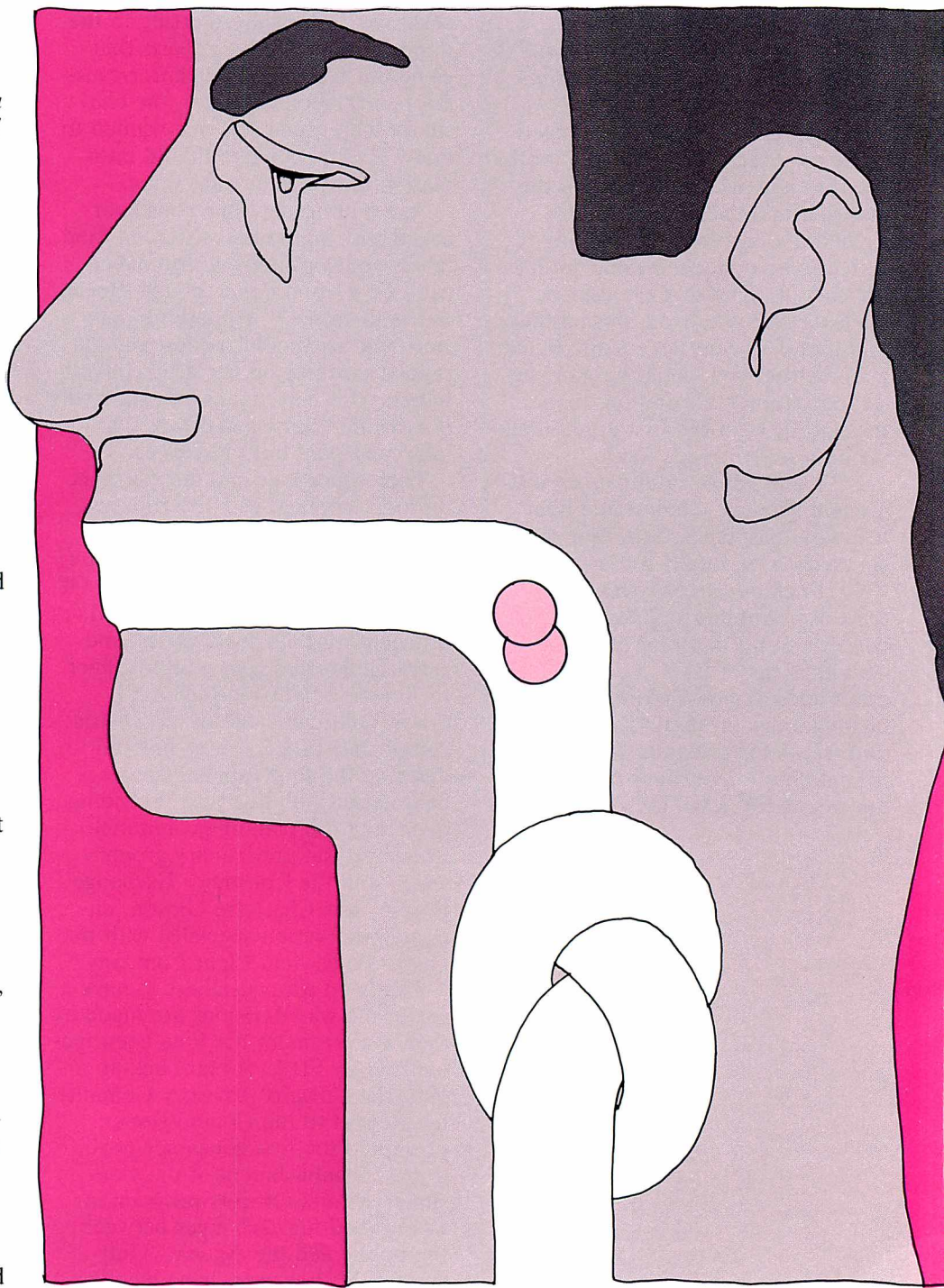
by Judith Willis

Compelling scientific evidence forced a trade association and FDA to reach into the marketplace for the biggest product recall in the Agency's history recently.

The recall involved the compound methapyrilene, identified as a potent carcinogen. It is found in over-the-counter (OTC) sleep aids, cough-cold remedies, and other oral medications. In all, more than 600 products were involved in the recall, which was carried out by FDA together with the Proprietary Association, an organization of OTC drug manufacturers.

Most extensively affected were sleep aids, on which Americans spent \$28 million last year. Some of the brand names of the more than 300 OTC sleep aids/sedatives which contained methapyrilene include: Nytol, Sominex, Sleep-Eze, Quiet World, Compoz, Cope, Sleepinal, Tranquim, and Nervine.

Because many of the manufacturers had already begun reformulation of their products at the time of the recall, most people were able to continue buying OTC sleep aids without interruption. However, consumers should note that scientists have raised questions about the possible carcinogenicity of pyrilamine, the drug now most commonly substituted



for methapyrilene in OTC sleep aids.

The story behind the recall started when methapyrilene was selected as one of several drugs and food additives to be tested in combination with sodium nitrate to determine if the combinations formed nitrosamines, known to be carcinogenic. Methapyrilene itself was not a suspected carcinogen because it does not resemble in chemical structure any known cancer-causing agent. The drug had been used in OTC products for 25 years.

In the nitrosamine experiment, carried out at the Oak Ridge National Laboratory, 50 percent of the rats fed methapyrilene and sodium nitrate showed degenerative liver changes of the type that often accompany or precede cancer. Indeed, nine of the rats (30 percent of the total 29), developed liver tumors.

These results raised the question: Is methapyrilene carcinogenic only in combination with sodium nitrate, or is it also carcinogenic by itself?

To find the answer, National Cancer Institute (NCI) scientists undertook two further studies. In the first, rats were divided into three groups: one group was fed methapyrilene combined with sodium nitrate; another was given methapyrilene alone; and a control group was given neither. At the 69th week, the death rate from liver cancer was 18 percent in the methapyrilene-dosed group and 17 percent in the combination group, while no control rats had died. Therefore, NCI scientists concluded that not only is methapyrilene carcinogenic when combined with sodium nitrate, but it is also a carcinogen in its own right.

In the final study, NCI scientists fed rats five different dose levels of methapyrilene, ranging to 2,000 parts

per million (ppm). They found the incidence and extent of liver tumors directly related to the dose level, and all rats exposed to 2,000 ppm methapyrilene developed liver lesions.

The data from these three studies were passed on to the Data Evaluation/Risk Assessment Subgroup of the NCI Clearinghouse on Environmental Carcinogens. On May 1, 1979, the Subgroup concluded that methapyrilene is "a potent hepatocarcinogen in rats, and, as such, of potential human hazard."

When NCI announced its conclusions, FDA appointed a Task Group to evaluate the data and to recommend what action, if any, the Agency should take. After reviewing the studies, the Task Group concluded that methapyrilene is "a potent carcinogen in animals and a potential human carcinogen." The group, therefore, recommended that methapyrilene products be removed from the market as soon as possible.

When weighing the benefits and risks to consumers of continued methapyrilene use, FDA had to balance the potential carcinogenicity of the drug with its health benefits and the possibility of substitution. On the market at the time were more than 300 OTC sedatives/sleep aids and more than 200 OTC cough-cold medications containing methapyrilene.

Since a large number of Americans who suffer from insomnia turn to OTC sleep aids for help, FDA scientists knew that the number of people affected by the recall would be considerable. Yet they also were acquainted with medical doubts about the value of OTC sleep medications and of other opinions that taking a couple of aspirins or an antihistamine is as helpful in attaining sleep as tak-

ing one of the OTC medications. In addition to this controversy over the medical value of OTC sleep aids, the Task Group also took into account that by the time of the recall several sleep aid manufacturers had begun reformulation of their products, substituting pyrilamine for methapyrilene.

However, because pyrilamine is structurally related to methapyrilene, there is some speculation that it, too, may possess cancer-causing properties. There are no conclusive studies regarding the carcinogenicity of pyrilamine and, therefore, the FDA Task Group did not recommend either for or against the substitution. FDA did, however, urge NCI to begin carcinogenicity studies on pyrilamine as soon as possible.

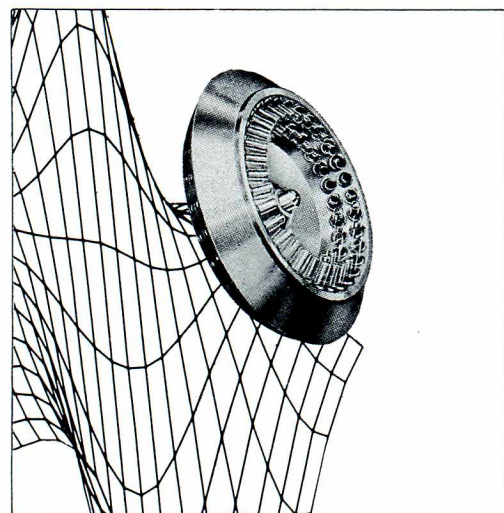
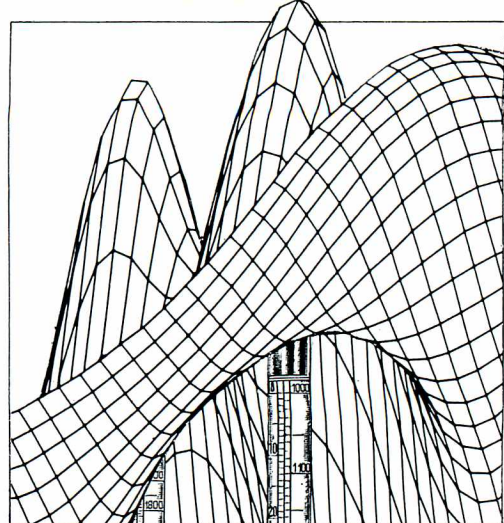
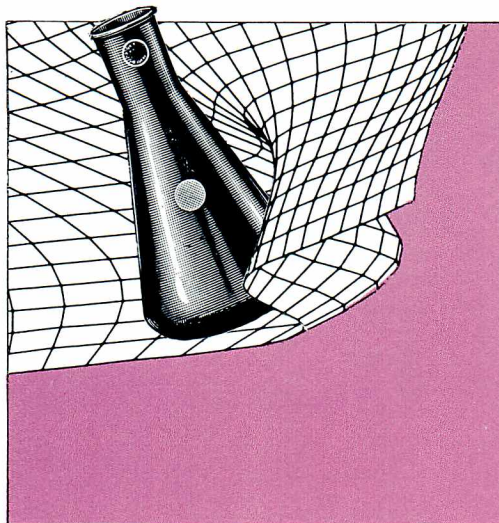
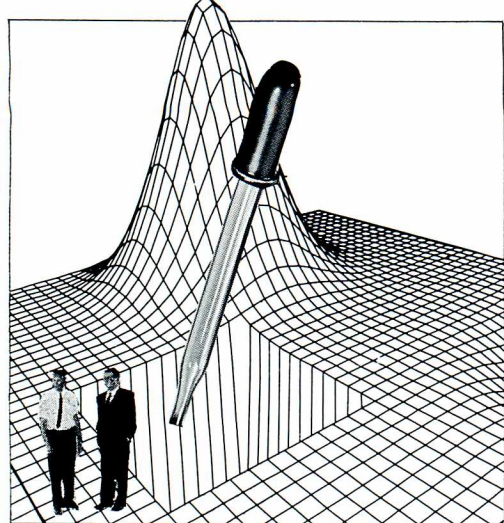
In addition to pyrilamine, there are three other antihistamines that may be usable in sleep aids in the future: diphenhydramine, phenyltoloxamine, and doxylamine. These drugs are not yet approved for marketing, but due to the recall of methapyrilene, they have been earmarked by FDA for expedited review.

Antihistamines in the cough-cold preparations that contained methapyrilene was somewhat easier because adequate safe and effective substitutes, such as chlorpheniramine, were already readily available.

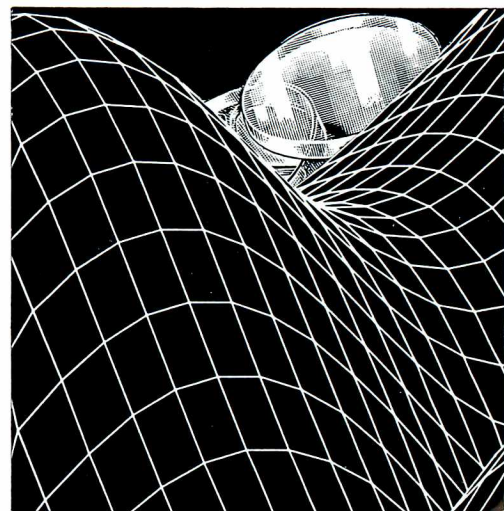
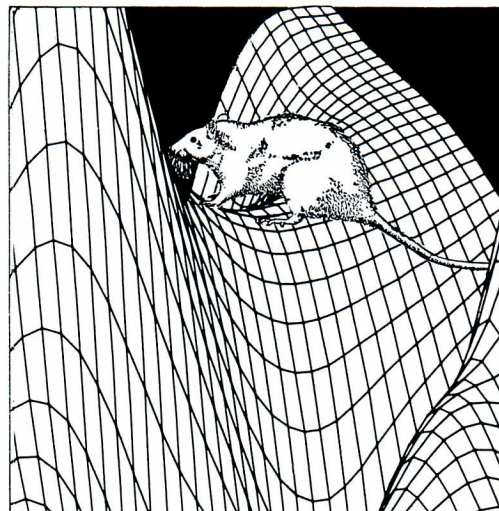
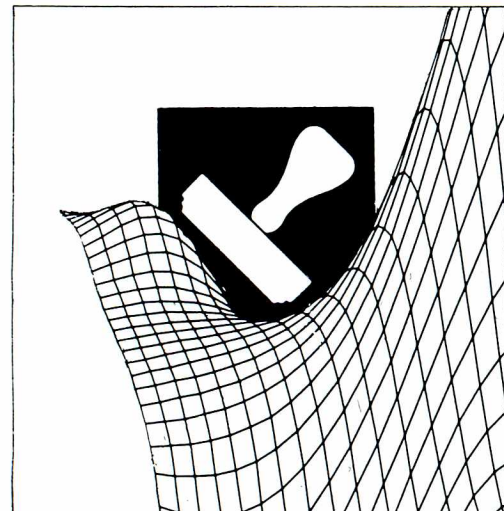
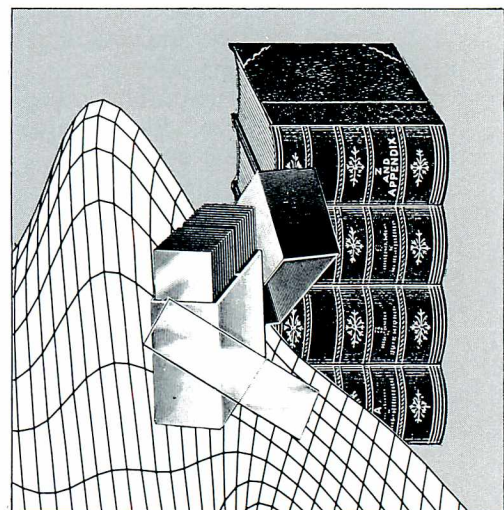
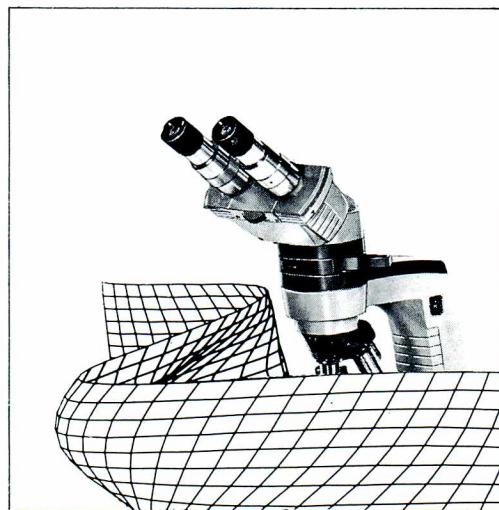
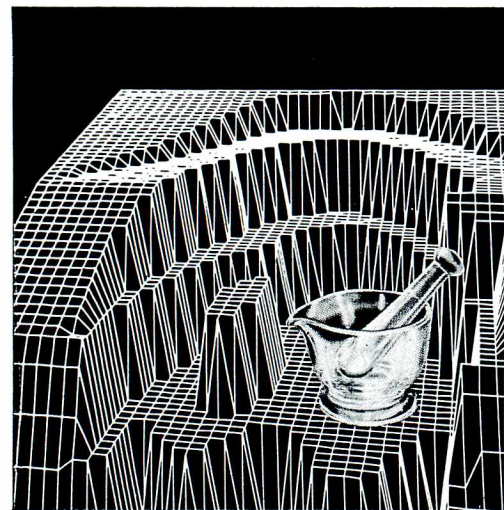
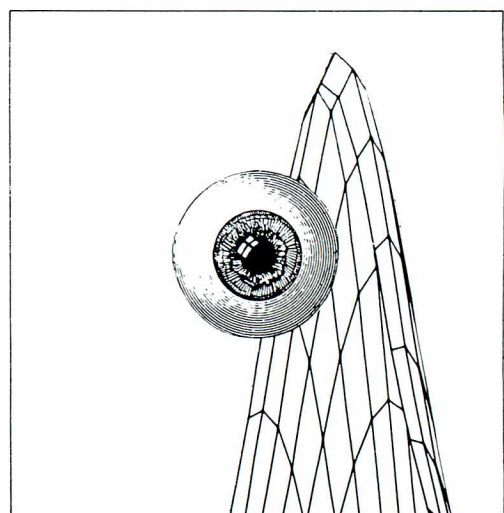
The recall also included OTC asthma/bronchodilators, appetite suppressants, smoking deterrents, as well as prescription medications in all groups. It did not include topical products, such as salves, rubs, and nasal sprays, because the risk associated with them is lower.

*Judith Willis is a member of FDA's Public Affairs staff.*





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11 22.9898 892 97.8 0.97 1 Na [Ne]3s <sup>1</sup> Sodium	12 24.305 1107 650 1.74 2 Mg [Ne]3s <sup>2</sup> Magnesium	13 26.98 1149 690 1.72 3 Al [Ne]3s <sup>2</sup> 3p <sup>1</sup> Aluminum	14 28.09 1401 754 1.58 4 Si [Ne]3s <sup>2</sup> 3p <sup>2</sup> Silicon
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37 85.47 1329 79.9 2.6 1 Rb [Kr]5s <sup>1</sup> Rubidium	38 87.62 1370 768 2.6 2 Sr [Kr]5s <sup>2</sup> Strontium	39 88.91 1471 833 1.37 3 Y [Kr]4d <sup>1</sup> 5s <sup>2</sup> Yttrium	40 91.22 1573 893 1.33 4 Zr [Kr]4d <sup>2</sup> 5s <sup>2</sup> Zirconium
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87 226.03 8762 208.98 2.23 3 Fr [Rn]7s <sup>1</sup> Francium	88 226.03 8762 208.98 2.23 4 Ra [Rn]7s <sup>2</sup> Radium	103 258.11 9691 289.05 2.23 5 Lr [Xe]4f <sup>14</sup> 5d <sup>1</sup> 6s <sup>2</sup> Lutetium	104 258.11 9691 289.05 2.23 6 Hf [Xe]4f <sup>14</sup> 5d <sup>2</sup> 6s <sup>2</sup> Hafnium





# Providing A Breakthrough For Drugs With Promise

*FDA is often criticized for taking too long to approve new drugs, thereby contributing to a "drug lag" in this country. Since 1974, however, the Agency has used a unique classification system to identify and put on a fast track, for in-house review, those new drugs that offer significant or modest advantages over products already on the market.*

**"T**he desire to take medicine is perhaps the greatest feature which distinguishes man from the animals," said a noted Canadian physician, Sir William Osler. Undoubtedly spoken in jest, Osler's comments have an element of truth; the search to find new and better ways to treat man's afflictions has been going on as long as man has been afflicted.

Today there are thousands of prescription drug products on the market, plus hundreds of thousands of products consumers can get over the counter. Some of the ingredients in these products were "discovered" centuries ago by ancient physicians whose concoctions of seeds, bark, animal organs (and occasionally precious gems and metals) were compounded largely by trial and error. Drug approval in those days came from the testimonials of satisfied and surviving patients.

Science, not guesswork or personal opinions, is the basis of modern drug development. Today the Food and Drug Administration evaluates the detailed information about new drugs provided by the manufacturer. The intent of the evidence is to demonstrate that the drug is safe and that it works.

There has been criticism in recent years from people in the drug industry and elsewhere that FDA's approval process moves at a snail's pace; that,

as a result, valuable new drugs are not getting into the marketplace as quickly as they do in other countries. A recent analysis by FDA's Bureau of Drugs indicates that the average number of months from the time a New Drug Application is received until it is approved has increased overall (in 1978 the average time for such approval was 32 months, compared to 24.5 in 1974).

But the same analysis shows that the approval time for drugs that offer some therapeutic advantage over products currently marketed has been relatively constant (approximately 22 months). No ground was lost on these drugs because FDA has expedited the approval process by classifying new drugs by chemical type and therapeutic potential. Drugs that offer potentially important new therapies get priority treatment or get put on a "fast track," while those of lesser importance must wait their turn for review.

FDA's approval process begins while new drugs are still in the developmental stage. When a drug company develops a chemical entity that shows potential drug activity, the company first must put the drug through a series of animal tests to measure its safety. If the chemical passes these first tests, the company may submit a Notice of Claimed Investigational Exemption for a New Drug (IND). After an initial safety review of the IND, the company may proceed with clinical studies in human volunteers.

Not all prospective new drugs survive the early experimental stages. Many fall by the wayside because they do not work or because they provide unacceptable side effects. When a manufacturer has completed the studies necessary to show that the drug is safe and effective for its claimed use,

he may submit a New Drug Application (NDA) to request approval for marketing. This contains the results of the studies conducted to demonstrate the drug's safety and effectiveness, the details of its chemical and manufacturing characteristics, and its pharmacologic and toxic properties.

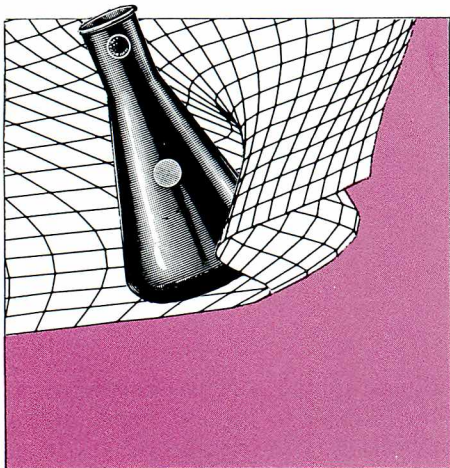
An NDA is truly a formidable document. The summary alone may be as long as 4,000 to 5,000 pages, while the total package—including case reports on each of the subjects in the clinical studies—may run 50,000 to 100,000 pages. The NDA review is carried out by a three-member team, including a chemist, a pharmacologist, and a medical reviewer. They get support from other experts such as biostatisticians, biopharmaceutists, and microbiologists when necessary.

This immense compilation of material is evaluated to determine whether drug quality is assured, if appropriate studies have been conducted to define its potential toxicity, if clinical studies demonstrate effectiveness, and whether the drug is truthfully and thoroughly labeled. If the NDA provides the evidence, and if FDA determines that the benefits from the drug's use will outweigh any potential risks or adverse effects, the Agency approves the drug and the company may begin marketing.

The increase in the average length of time it takes to review and approve drug applications is the result of a number of factors. Regulatory requirements are responsible for only some of the delays. FDA needs to know more about stability, toxicity, manufacturing processes, clinical studies, statistics, bioavailability, and bioequivalency than it has in the past.

Processing time often is increased





because of delays by drug sponsors in providing additional data, correcting deficiencies, or clarifying certain aspects of the application as requested by the Agency. One application approved in 1978 was in the pipeline almost 10 years because the sponsor decided not to move ahead to correct deficiencies in his application after he was notified by FDA. He later decided to conduct the required studies and resubmit the application.

Under FDA's priority classification system, in effect since 1974, new drugs are classified according to chemical type (using a number) and therapeutic potential (using a letter). A new molecular entity (in this case a drug not yet marketed in the United States) is in class 1 on the chemical scale. A new salt, ester, or derivative of an existing drug is in class 2, while a new formulation of an existing drug is in class 3. Classes 4, 5, and 6 are assigned to new combinations of ingredients, duplicates of drugs already on the market, and currently marketed products for which a firm proposes new uses.

On the therapeutic scale, a new drug offering the potential of an important gain over existing products is rated "A." A "B" rating is assigned to drugs that offer only moderate gains. Drugs that provide little or no therapeutic gain over drugs already on the market are rated "C."

Chemical and therapeutic ratings are assigned to drugs by FDA reviewers at the time the drug is first submitted to the Agency, either during the IND or NDA stage of development.

The classification may change during review with evidence of its therapeutic value or upon comparison with other drugs in the approval process. A final classification is assigned at the time the NDA is approved.

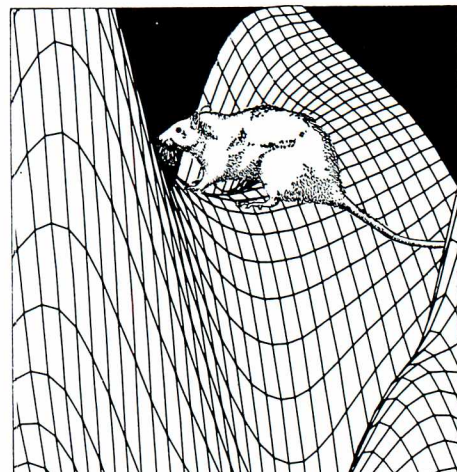
As a result of the way the Agency is implementing the classification system, important new drugs are reaching the market as much as a year earlier than those which offer no health gains. In 1978, for example, FDA approved 87 New Drug Applications of which 21 were classified as totally new molecular entities. While the average time for approval was 32 months, average approval time for the 21 new molecular entities was 21 months.

Thirteen of these newly approved drugs are uniquely useful for treating specific diseases. Among these are calcitriol, an analog of vitamin D<sub>3</sub> used in the treatment of hypocalcemia (low blood calcium) in patients undergoing chronic kidney dialysis, and timolol maleate, for the treatment of glaucoma. Other important new drugs approved last year were natamycin, for the treatment of a rare eye infection; valproic acid, for some forms of epilepsy; bretylium tosylate, used in the management of life-threatening heart irregularities; and vidarabine, the first injectable drug for a life-threatening viral infection.

The classification system has done more than speed up the processing of certain drug applications. High priority applications also mean that FDA gets together with manufacturers early in the IND review process. If a manufacturer doesn't get such a call, he can assume his application won't get priority handling. As a result, companies are working on insuring that sufficient documentation goes along with the application to get the highest rating.

New molecular entities have been growing. Between 1974 and 1978, 103 new drug entities were approved, almost twice as many as in the 5 years preceding and half again as many as 10 years ago. This tends to dispel the oft repeated myth that FDA's requirements for proof of effectiveness have stifled innovation in the drug industry.

Over the period 1974-1978 new molecular entities represented just over



25 percent of all new drugs approved by FDA. Those classed 1A and 1B, that is, new entities that offer some therapeutic gain, constituted 15.6 percent of the total. Nearly half of the drugs approved represented copies of already marketed drugs with little or no therapeutic gain (Class 5C).

Initiation of the "fast track" classification system is not the only step FDA has taken to move new drugs to the marketplace more quickly. In addition, the Department of Health, Education, and Welfare's Management Initiatives Tracking System (MITS) has set a goal and specific timetable for reducing the time for processing applications. Under this program FDA has pledged to reduce its processing time for all New Drug Applications at least 15 percent by 1982; processing time on important drugs will be reduced 25 percent. FDA is working to streamline its administrative procedures and is preparing a revision of the IND/NDA regulations.

The Drug Regulation Reform Act, recently introduced in Congress for the second time, would, if enacted, provide additional avenues for speeding up new drug approval. Features such as post approval surveillance, reduction of regulation in the early stages of drug research, provisions for an even faster track for breakthrough drugs, and FDA authority to permit restricted distribution of valuable drugs that otherwise could not be approved—all are designed to speed up the transfer of new technology without sacrificing safety.





## Drugs Can Skew Clinical Tests

*Many people may not realize that drugs, as well as food, can alter the outcome of clinical laboratory tests. Patients should tell their doctors what drugs they are taking at the time lab tests are ordered.*

**G**o to the doctor for a checkup and it is likely you will be asked to supply a small bottle of urine and what seems to be more blood than necessary for a variety of clinical laboratory tests. To add to the indignity, it's usually done on an empty stomach. Fasting

before undergoing lab tests is important, because what you eat could affect the results of these tests.

Food is not the only substance that can interfere with clinical tests. Most commonly prescribed drugs and many over-the-counter drug products can skew the results of certain tests performed to aid in determining the state of a person's health. Antibiotics, tranquilizers, aspirin, laxatives, cough and cold remedies, oral contraceptives, and vitamins are among the many drug products reported to cause variations in clinical lab tests.

Since 1974 FDA has required that labeling for *in vitro* diagnostic products—that is, products used in clinical lab tests—include information on substances that are known to interfere with the results. For this information to be useful, however, it is important that the lab technician know what drugs the patient is taking.

In some instances a drug may cause a “false positive” (abnormally high) response to a specific test; in others there may be a “false negative” (abnormally low) reaction. In either case an inaccurate lab test can lead to a di-



agnosis of a disease the patient doesn't have or cover up the existence of a serious condition, and result in incorrect prescribing and inappropriate treatment. Not the least of the consequences of inaccurate tests is the possibility of prolonged hospital stays and additional, often expensive laboratory work.

Drugs interfere with lab tests in a number of ways. One is the result of a physical change produced by the drug. For instance, some prescription and nonprescription drugs can color the patient's urine, thus confounding the colorimetric, photometric, and fluorometric analysis of the sample. Some laxatives purchased over the counter contain an ingredient that can color the urine red to purple-red. The antidepressant amitriptyline may impart a blue-green color, while the "major" tranquilizer, phenothiazine, makes the urine pink to red brown. The tetracyclines and vitamin B<sub>2</sub> (riboflavin) turn the urine a brighter yellow which could cause misreading of a test for jaundice. The antihypertensive drug methyldopa, fluoresces at the same wave length as catecholamines, hormones secreted by the adrenal gland. Picked up in a lab test, the drug's fluorescence might be mistaken for an excess of catecholamines, suggesting that the patient has a tumor.

Another way in which drugs alter lab tests is through biological changes they cause in the body. As an example, diuretics, the so-called water pills, can alter the concentration of electrolytes in the blood and urine. Electrolytes are inorganic ions present in body fluids in just the right proportion to aid in maintaining metabolic processes. A suspected electrolyte imbalance might lead to a diagnosis of a kidney malfunction that didn't exist.

Drugs that alter the metabolism, such as central nervous system depressants or stimulants, may cause faulty readings on tests of thyroid function. Such tests also may be skewed by a number of other drugs including oral contraceptives, antihistamines, and large doses of aspirin.

Certain tests to determine levels of bilirubin in the blood—an indicator of liver disease—may be affected if the patient has been taking epinephrine,

isoproterenol (an asthma medication), or chlorpromazine. Chlorpromazine also can produce a laboratory picture similar to that of systemic lupus erythematosus, a degenerative disease.

Everyday drug products such as aspirin, glyceryl guaiacolate (an ingredient in cough medicine), and caffeine are among those known to interfere with several methods of detecting a substance in urine which indicates the presence of a tumor linked with hypertension. Penicillin can cause a false positive result on tests to measure protein in the urine, a sign of kidney disease.

A number of widely used drugs are known to interfere with several different laboratory tests. Tetracycline, for example, may play havoc with values for albumin, amino acids, bilirubin, catecholamines, glucose, and estrogen in the urine, plus values for a number of substances tested in the blood. Vitamin C, widely used as a home remedy for the prevention and treatment of the common cold, may interfere with measurements of acetaminophen in the urine and with tests for liver disease, and heart and blood vessel diseases. This vitamin, along with a number of tranquilizers, antibiotics, and reserpine, may affect urinary steroid determinations, and tests made to detect hormonal problems and adrenal tumors.

One drug-lab test interaction that can have surprising, if not embarrassing, results involves antidepressant drugs and tests for pregnancy. One Washington, D.C., teenager found out about this test interference the hard way. Her physician insisted, on the basis of lab tests, that she was pregnant despite her denials and those of her parents. When it was learned that she was taking an antidepressant, prescribed by another physician, her "pregnancy" was reversed and a potential lawsuit aborted.

Still another source of error in clinical tests comes from chemical interference. Often unsuspected as a cause of false lab test results are chelating agents such as ethylenediaminetetraacetate (EDTA). These agents are sometimes used to treat lead poisoning, but they also are used in many drug products to prevent discoloration

and oxidation. EDTA will cause decreased values in tests to determine the amount of calcium in the blood.

Some drugs produce false results by canceling out certain reactions in clinical tests. Penicillin, streptomycin, and ascorbic acid (vitamin C) are known to react with copper sulfate in one test using that chemical to measure sugar in the urine, thus producing false positive results. Strangely enough, when the oxidase method is used to measure urinary sugar, a false negative reading results.

Because many people take vitamin C without medical supervision, a panel of experts set up by FDA to evaluate vitamin and mineral drug products, recently recommended that products containing vitamin C be labeled with the warning, "Diabetics taking more than 500 mg vitamin C daily may obtain false readings in their urinary glucose test."

Some drugs may interfere with clinical lab tests almost as soon as they are taken; others may not cause problems for years. The iodine content of a dye, used to measure thyroid function, has been found to alter iodine determinations 30 years or more after the first tests were made.

This is but a sampling of thousands of possible ways drugs may cross up diagnostic tests. Researchers at the National Institutes of Health, the research arm of the Department of Health, Education, and Welfare, have compiled a file of some 9,000 drug-lab test interferences. The computerized file has been used by the clinical chemistry laboratories at NIH and a number of medical centers to assist in the interpretation of unusual test results.

Consumers can help avoid inaccurate lab test results by telling their physician, at the time tests are ordered, what drugs they are taking. This applies to over-the-counter as well as prescription drugs. The physician can then see that this information gets to the technician who will do the tests. In some cases, it may be wise to stop all medication for a few days to assure that there will be no interference with a specific test. However, this is a decision that should be made by the physician, not by the patient acting on his own.

# News Highlights

## FDA Seeking Advisory Committee Members

FDA is looking for qualified people to serve as voting members on certain public advisory committees of the Bureau of Medical Devices. The Agency is particularly interested in nominations of women and minority candidates. The term of office is 3 years.

Advisory committees review the safety and effectiveness of devices currently in use and advise the Commissioner of Food and Drugs on classification of devices for regulatory purposes. Persons nominated must have experience appropriate to the work of the committee in such fields as clinical and administrative medicine, engineering, and biological and physical science. Advisory committee members are paid \$128.80 per day salary plus a per diem of \$50. Travel expenses are also paid.

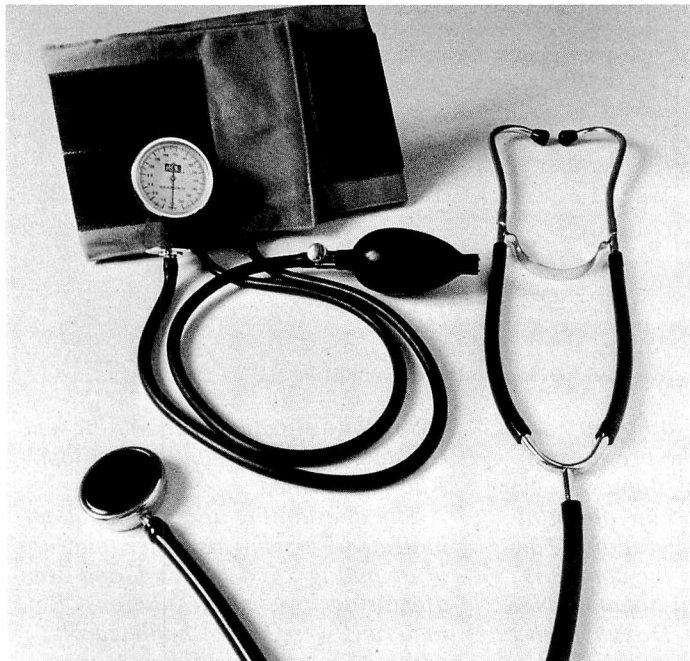
Nominations are being sought for members of the following committees:

Circulatory Devices Panel

Gastroenterology and Urology Section of the General Medical Devices Panel

Ophthalmic; Ear, Nose and Throat; and Dental Devices Panel

Respiratory and Nervous System Devices Panel



Surgical and Rehabilitation Devices Panel

Clinical Chemistry and Hematology Devices Panel

Radiologic Section of the Obstetrics-Gynecology and Radiologic Devices Panel

In addition, FDA is seeking nominations for nonvoting

consultants on the above panels as well as the following:  
General Hospital and Personal Use Section of the General Medical Devices Panel

Obstetrics-Gynecology Section of the Obstetrics-Gynecology and Radiologic Devices Panel

Hematology Section of the Clinical Chemistry and Hematology Devices Panel

Immunology and Microbiology Devices Panel

Scheduled vacancies occur at various times during the year; nominations, however, should be received 6 months before a vacancy occurs. A notice published in the May 11 FEDERAL REGISTER indicates the dates of scheduled vacancies. Nominations should be sent to Kay A. Levin, Bureau of Medical Devices (HFK-50), Food and Drug Administration, 8757 Georgia Ave., Silver Spring, Md. 20910. For further information contact Robert S. Kennedy, Bureau of Medical Devices (HFK-410) at the same address.

## Radiation Reduction Studied

With more than 100 hospitals participating, FDA's Bureau of Radiological Health has begun a program to find how effective its radiation reduction programs are. The hospitals, which are a representative sample from around the country by geography and numbers of beds, are participating in the Radiation Experience Data (RED) program begun July 1 which collects information on use of diagnostic x rays, nuclear medicine, and ultrasound.

The facilities will transmit to the Bureau basic data on each type of procedure performed, the age and sex of the patient, and a patient identification number. The identification number will be used by the hospital to trace the record of the patient if needed.

The Bureau will use the information to evaluate the effectiveness of its various radiation reduction programs. The RED program will also help identify emerging trends and new methods of radiation examinations. Each participating hospital will benefit by receiving summaries of its own data, comparative data for similar institutions, and national estimates. The hospitals will be reimbursed by FDA for the cost of collecting and submitting data.

The program, as currently planned, is limited to hospitals since most of the procedures are done there, and because an accurate list of these facilities is available for such a study.

The Bureau plans to continue the program on a 3-year rotating basis. Each year one-third of the hospitals would be replaced by a similar number of new hospitals. The RED program was reviewed by the American Hospital Association, the American College of Radiology, the Society of Nuclear Medicine, and the American Institute of Ultrasound in Medicine.



## Regional Reports

### Hokum On Yoakum Boulevard

"Celestial Discovery Astounds World!" the ads read. "Scientific International Inc. of Texas, a company devoted to health, has discovered an incredible link to pain and disease. The remarkable new formula DOXYHYDREN is a unique type of celestial energy . . ."

According to ads in the HOUSTON CHRONICLE and other newspapers around the country, the product ("Pure Doxyhydren 100% fast 200% effective") was capable of relieving pain, stiffness, swelling, numbness, infection, inflammation, and itching when applied externally. The ads even hinted that Doxyhydren might "reduce" the "causes" of symptoms produced by such diseases—arthritis, muscular disorders, psoriasis, acne, and dermatitis. Eight ounces of the product cost \$110.75.

A number of consumers were suspicious. The ads stated that Doxyhydren has been approved by the Consumer Product Safety Commission (CPSC). But CPSC has no jurisdiction over drugs. Some consumers called CPSC; some called FDA; and some called Texas State Health Department offices. The three official groups talked it over and an investigation of Scientific International Inc. followed.

On January 18, three men went to the firm's headquarters to find out about Doxyhydren: Richard Aleman, investigator from FDA's Houston Section; G. Brent Bradford, CPSC investigator; and James Allen, chief of the Drug Control Division, Food and Drug Division, Texas Department of Health.

Scientific International Inc., incorporated in 1977, was a small concern on the first floor of a two-story building on Yoakum Boulevard in Houston. One room was used as an office and a second, smaller room for manufacturing of finished products and storage of bulk products and raw materials. Some raw materials were also stored in the firm's washroom and in

## CELESTIAL DISCOVERY ASTOUNDS WORLD! WHEN PAIN AND DISEASE DISAPPEAR

Do you constantly suffer from a severe ailment or skin condition? This could make life very miserable, effecting work, play, personalities and sometimes our loved ones. The thought of getting through each day, wondering when the pain will strike again or a skin condition that could make us self-conscious, these problems can simply destroy our emotions.

Scientific International Inc. of Texas, a company devoted to health, has discovered an incredible link to pain and disease. The remarkable new formula DOXYHYDREN is a unique type of celestial energy that is so advanced medical science found DOXYHYDRENS' type of energy to be by far the most effective for reducing pain, stiffness, swelling, numbness, infection, inflammation and itch. These symptoms are almost always associated with Crippling Arthritis, Back Pain, Muscular Disorder, Psoriasis, Acne, Dermatitis and other conditions. Most important, DOXYHYDREN is external and regardless of how severe or how long the condition has existed dramatic relief can be immediate. Finally you can look forward to relief, just rub the problem away.

DOXYHYDREN is not the magic cure all it appears to be. DOXYHYDREN performs only one extremely important function and that's very fortunate for our civilization, because it's the one that counts!! Man has dreamed of a formula like DOXYHYDREN and even though it may stagger the imagination, and be incomprehensible, the dream has come true, and many will agree with that in just minutes—the longer you doubt and wait, the longer you suffer!

DOXYHYDREN is laboratory tested and complies with regulations of the United States Consumer Products Safety Commission. DOXYHYDREN is available without prescription. Because of the tremendous need and demand for DOXYHYDREN, the decision was made to make it available the fastest possible way.



Mr. James Farrish  
President, chairman of the board,  
Scientific International Inc.  
"We are pleased to have developed  
DOXYHYDREN and for all the good  
it can do mankind. We thank God."

#### GUARANTEE

DOXYHYDREN™ is 100% guaranteed to immediately start reducing the very causes and discomforts of your ailment or skin condition, eliminate visits to Chiropractors, Acupuncture, Skin Centers and other inconveniences, help you feel more alive and look better fast, and to satisfy you in every way or it cost you absolutely nothing! Simply return the unused portion within 15 days for a courteous and prompt full refund.

#### LIMITED OFFER. PURE DOXYHYDREN 100% FAST 200% EFFECTIVE EACH BOTTLE OF DOXYHYDREN IS REGISTERED

Circle Your Order: 4 oz. \$65.50 8 oz. \$110.75 16 oz. \$179.00 **NO POSTAGE HANDLING**  
✓ Please Rush Airmail Special Delivery \$2.75 Extra ✓ C.O.D. Texas Residents Add 5% Sales Tax  
Airmail Special Delivery Send \$19.90. Pay Postman Balance and C.O.D. Charges.

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P.O. BOX 25245 5215  
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the president's garage at home.

An interview with the president of Scientific International, James H. Farrish, quickly pointed to the doubtful legality of the firm's operations. Farrish had not registered the company with FDA and had not obtained New Drug Applications for Doxyhydren or any of the other products the firm manufactured. He told Aleman he considered his products to be cosmetics. When Aleman read him the definitions of "drug" and "cosmetic" from the Food, Drug, and Cosmetic Act, Farrish seemed to have trouble

seeing the distinction. He said he had registered with the State, a fact that Allen confirmed.

The questioning and investigation indicated Farrish was either unaware of or had ignored FDA's Good Manufacturing Practice Regulations. Raw materials were stored haphazardly without proper identification; there were virtually no written records (Farrish said he had memorized the formula for his products); and there was no evidence that the products were ever tested, either in bulk or finished form, for safety, effectiveness, stabil-



ity, or potency. There was simply no evidence the products were safe or that the medical claims made for them were true.

Farrish claimed sole responsibility for the firm's operations and products. Two other employees included the office manager and the typist, the latter of whom had a host of duties, including mixing bulk products, putting finished products into containers, and labeling and distributing the products. According to Farrish, the firm's secretary-treasurer was "inactive" in the firm's operations, and the vice president had left the previous year.

To questioning, Farrish said he had no medical degree from any recognized university and that his employees had no training in the manufacture of drug products.

The investigators discovered that two other products were being manufactured: Drex-Odyne—claimed in newspaper advertising to be "the most successful scalp treatment in the world . . . guaranteed to immediately start reducing hair loss . . . [and] promote growth of new hair . . ."; and Derma Clear, claimed to reduce acne and make the skin smooth, clear, and attractive. Four ounces of either product sold for \$19.90.

All three products were made by mixing different amounts of water with the same active ingredient, so-

dium dihydroxyethylglycinate, trade name "Hampshire DEG." Allen, who is a registered pharmacist, said it was the first time he had ever seen one active ingredient combined with water to manufacture three products with different labeling and promotional claims.

Aleman took samples of finished and bulk products, but was informed by Farrish that stocks of the active ingredient were stored in his garage at home. The investigators examined the products stored there and took samples of "Hampshire DEG."

The identity of Hampshire DEG was not shown in the U.S. Pharmacopeia, the National Formulary, the U.S. Homeopathic Pharmacopeia, or any other accepted source.

The investigators had seen enough. Farrish had already signed an affidavit stating that the ads were misleading because CPSC had not approved, and had no jurisdiction to approve Doxyhydren. Farrish swore in the affidavit to make no such statements in the future.

Allen and Aleman conferred with the FDA Houston Section's director, Anthony Whitehead, and supervisory investigator, Boland Shepherd. Allen talked by phone with Spencer Gardner, attorney in the Consumer Fraud Division of the Harris County District Attorney's Office. All felt it was imperative to stop Scientific Interna-

tional from manufacturing and distributing untested and possibly unsafe products. The State, which has the power of immediate embargo, agreed to handle the matter. In late evening on January 19 a Harris County justice of the peace signed a warrant for Farrish's arrest and the embargo of all products. The next morning he was arrested.

The mystery of Hampshire DEG was cleared up by Allen, who called the New Hampshire manufacturer and found that the active ingredient in Farrish's miracle drugs was a soap used to remove calcium, iron, and phosphorous from the inside of industrial boilers. In other words, the company was charging over \$100 for 8 ounces of soap and water.

Farrish pleaded nolo contendere to a charge of deceptive business practices on March 15 in a case whose evidence was provided largely by Aleman, Allen, and Bradford. In the Harris County District Court Farrish was fined \$2,000 and sentenced to 6 months in jail, both penalties suspended for 1 year; and Farrish was ordered to stop manufacturing and marketing drug products unless they complied with both State and Federal regulations. The embargoed stocks of Hampshire DEG, Doxyhydren, Drex-Odyne, and Derma Clear, estimated to be worth about \$4,000, were ordered by the court to be destroyed.

*Regional Reports consists of important information on inspections, product seizures, court proceedings, and other regulatory and administrative actions initiated by FDA's regional and district field offices across the country to provide protection to consumers under Federal laws.*

## REGION I

Connecticut, Maine, Massachusetts, New Hampshire, Rhode Island, Vermont

A routine inspection by FDA's **Boston District** turned up problems at Musolino Loconte Co., an oil repacker and

warehouse in Cambridge, Massachusetts. Cartons of cheese fluoresced under the investigator's black light, indicating that they were stained with urine. Gnawed holes in product packaging and tiny pellets on the floor provided additional evidence that the warehouse was infested with rodents. Approximately \$3,000 worth of food was seized at the District's recommendation. The firm then agreed in the U.S. District Court of Massachusetts to recondition the products and, under FDA supervision, salvaged most of the food.

A U.S. marshal seized over 5,500

pounds of nuts at Eaton & Eustis Co., Inc., a warehouse in Chelsea, Massachusetts, after a routine inspection by the Boston District revealed that the warehouse was rodent infested. Approximately \$5,000 worth of walnuts and mixed nuts were seized.

## REGION II

New Jersey, New York, Puerto Rico, Virgin Islands

Bennett X-Ray Corp., Freeport, New York, and three of the firm's top officials were fined a total of \$1,000 for violating the Radiation Con-



trol for Health and Safety Act. The firm's president, Bennett Kleinman; vice president, Calvin Kleinman; and general manager, Donald Reilly, were each assessed \$250 by the U.S. District Court for the Eastern District of New York. FDA's **New York District** filed a complaint for injunction and civil penalties after a District investigator found that the firm had certified a diagnostic x-ray system that was assembled from both certified and uncertified components. Under Federal regulations, all components used in the assembly of x-ray systems must be certified as meeting FDA standards. The court also enjoined the firm from assembling or selling falsely certified x-ray systems.

The U.S. Board of Tea Appeals supported FDA tea examiner Anthony Daly's determination that a shipment of "Old Man Tea"—believed by many consumers to have rejuvenating properties—was substandard. The tea, entered at the Port of San Francisco, was rejected by Daly because of a musty flavor. The importer, a restaurant in Mountain View, California, then petitioned the Board to overturn the tea examiner's ruling. However, the Board ordered that the 477-pound shipment, valued at over \$800, be returned to the exporter in China.

The Board of Tea Appeals, estab-

lished under the provisions of the Tea Act of 1897, meets regularly in New York District to review appeals on tea that has been refused entry by one of FDA's four tea examiners. Standards for tea are set by a seven-member U.S. Board of Tea Experts, whose members, like the tea examiners, rely solely on organoleptic (sensory) testing to evaluate the quality of tea samples.

Investigators from FDA's **Newark District** collected samples from bags of whole cloves at Marlo Transport Corp., South Kearney, New Jersey, after finding evidence that workers may have dragged the burlap bags across an oil-stained, greasy floor. When laboratory analysis confirmed the bags were stained with hydraulic oil, the District filed for seizure. Fifty bags, valued at about \$24,000, were seized.

A labeling mixup led to the recall of 4,600 diaphragm kits by Holland Rantos Co., Inc., a New Jersey firm that manufactures and distributes the devices. An investigator from the Newark District checked out the distributor in Piscataway after the District received a report from the U.S. Pharmacopeia that some of the firm's size 65 Koro-Flex Arcing Diaphragms were found in boxes labeled as containing size 70 devices. Dia-

phragms are prescription contraceptive devices, generally used with a spermicidal cream or jelly. Using the wrong size diaphragm could result in an unwanted—and possibly hazardous—pregnancy. The firm agreed to recall the kits after the investigator found that all size 65 diaphragms in lot 18-8—which also included four other sizes of the device—may have been incorrectly boxed. The firm has sent recall letters nationwide to family planning clinics, pharmacists, and doctors advising them to return the kits, which consist of diaphragms and a lubricant, for proper packaging. Consumers can identify the mislabeled product by the lot number (18-8), which appears on the rim of the device.

### REGION III

*Delaware, District of Columbia, Maryland, Pennsylvania, Virginia, West Virginia*

The blizzard of 1979 dropped 1 and 2 feet of snow on the east coast, and, on the day of that big snow, firemen in Harrington, Delaware, fought a fire at Burris Warehouse Co., a refrigerated food warehouse. Heavy soot from smoldering urethane settled over the food after the fire burned into the building's insulation. Water from the firemen's hoses, combined with heat from the flames, started a premature thawing process. The Delaware Health Department, handicapped by the snow, requested assistance from FDA's **Philadelphia District** and the U.S. Department of Agriculture in evaluating the damage caused by the fire. Investigators from both agencies inspected the warehouse and recommended a mass seizure since all the products were badly damaged by fire and water. Approximately \$4 million worth of food was eventually seized.

A U.S. marshal seized 190 cases of misbranded and adulterated canned pears, valued at \$1,000, at Draper Foods, Inc., a warehouse in Milford, Delaware. The Philadelphia District filed for seizure after a routine in-



spection revealed that the cans were leaking, swollen, and improperly labeled.

## REGION IV

*Alabama, Florida, Georgia, Kentucky, Mississippi, North Carolina, South Carolina, Tennessee*

Sale of contaminated soybeans was averted through cooperative efforts by FDA's **Atlanta District** and the U.S. Department of Agriculture (USDA). USDA inspectors discovered the problem while inspecting over 600,000 pounds of soybeans intended for export by Lapeyrouse Grain Corp., Loxley, Alabama. The inspectors noticed that some of the beans, intended for consumption by humans or animals or both, were dyed pink. Seed grains treated with fungicides are required under FDA regulations to be dyed pink, or some other identifying color, to indicate their toxicity and to prevent marketing as a food. USDA halted the planned exportation and then requested assistance from FDA to help prevent domestic distribution. Analysis by the Atlanta District revealed that some of the beans had been treated with captan, a poisonous fungicide used to inhibit molding or rotting of seed grain. The District initiated seizure of the beans, valued at \$75,000.

## REGION V

*Illinois, Indiana, Michigan, Minnesota, Ohio, Wisconsin*

Following up a trade complaint, FDA's **Cincinnati District** checked out a diagnostic x-ray system in a Cincinnati doctor's office. The investigation confirmed that the system, manufactured by the General Electric Co., was in violation of the Radiation Control for Health and Safety Act. The violations included failure of the firm to file a list of the certified components and the required assembly report with FDA. At the District's request, General Electric corrected the violations and reviewed all assembly reports for the previous

6 months to make sure no other violative systems had been distributed.

## REGION VI

*Arkansas, Louisiana, New Mexico, Oklahoma, Texas*

FDA's **New Orleans District** inspected Bill's Institutional Commissary after a consumer complained that there were rats in the warehouse. When inspection of the New Orleans firm confirmed widespread rodent infestation, the District asked the Louisiana Department of Health and Human Resources to embargo all products in the firm's dry storage warehouse and cooler. The products, valued at over \$200,000, included cracker meal, flour, and dry cereal. Under State supervision, the firm then separated contaminated foods from undamaged products. Most of the foods were salvaged, and the small portion that was too badly contaminated to be reconditioned was buried in a local sanitary landfill.

## REGION VII

*Iowa, Kansas, Missouri, Nebraska*

"The evidence of conspiracy was overwhelming," the U.S. District Court in Missouri ruled. James C. Jamieson, Sr., and James C. Jamieson, Jr., officers of four pharmaceutical companies in St. Louis, were found guilty of manufacturing and selling counterfeit drugs and drugs that were adulterated, misbranded, and dangerous to health.

FDA's **Kansas City District** requested criminal prosecution of the Jamiesons and the four companies after a series of inspections during investigation of a trade complaint revealed a large number of serious violations. Investigators found that the defendants were selling a drug labeled as "Motrin"—the Upjohn Company's brand name for ibuprofen—that, in fact, contained magnesium salicylate instead of ibuprofen. The defendants had substituted penicillin for ampicillin, and tetracycline for clindamycin; had used brand names for generic drugs without

being authorized to do so; and had changed the expiration dates on antibiotics from 1975 to 1977. In addition, few—if any—manufacturing and control records were maintained as required by FDA regulations.

Judge John G. Nangle deliberated nearly 11 months before announcing his decision, but his ruling was clear. "The individual defendants engaged in a vast plan to substitute less expensive drugs for more expensive ones," he stated in his opinion. "Contrary to defendants' assertions, these actions were not taken in a sincere desire to save money for patients, but instead were the result of defendants' desire to reap profits. There can be no claim that defendants had a patient's interests in mind when said defendants sold drugs past their expiration date or substituted one drug for another."

The Jamiesons were each sentenced to 8 years in prison and fined \$50,000 apiece; and a \$22,000 penalty was levied against each company (Jamieson-McKames Pharmaceutical, Inc.; Pharmacare, Inc.; Payless Pharmacy, Inc.; and Pharmacare Generic Drugs, Inc.). The total fine assessed by the court (\$188,000) represents one of the highest penalties ever ordered by a U.S. District Court for violations of the FDC Act. The defendants are appealing the decision.

## REGION VIII

*Colorado, Montana, North Dakota, South Dakota, Utah, Wyoming*

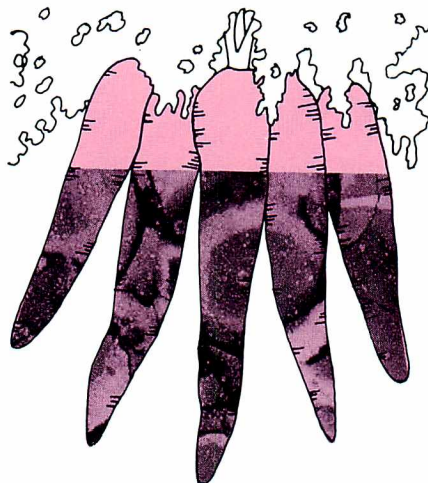
A U.S. marshal seized all food and food packaging materials stored at Weaver Potato Chip Co., Longmont, Colorado, a food storage warehouse and processor of snack foods including popcorn, roasted nuts, corn puffs, and cheese puffs. FDA's **Denver District** filed for seizure after a routine inspection revealed widespread rodent infestation, structural defects in the building that permitted rodents to enter easily, and crowded storage conditions that encouraged rodent nesting. More than \$100,000 worth of goods were seized.



## REGION IX

*Arizona, California, Guam, Hawaii, Nevada*

After analysis by FDA's **Los Angeles District** detected residues of an illegal pesticide on samples of imported carrots, 180 cartons of the vegetable, valued at \$8,000, were returned to the Mexican shipper, *Asociación Agrícola Y Gandra Del Valle*, San Luis, Mexicali, Baja, California. District inspectors collected the samples at Calexico, California, on the Mexican border, and sent them to the Los Angeles District laboratory, which found traces of pentachloronitrobenzene (PCNB), a pesticide not registered with the Environmental Protection Agency for use on carrots. When the District advised the shipper of the problem, the firm requested the return of the carrots and added that it would stop



shipping carrots to the United States.

## REGION X

*Alaska, Idaho, Oregon, Washington*  
A complaint that a jar of "hot

peppers" had erupted upon opening culminated in the seizure of 170 1 gallon jars of the product at a restaurant in Bellingham, Washington. Pete's Sandwich Shop reported to the Whatcom-Bellingham Health District that lids on the jars containing vinegar-packed peppers were bulging and one jar had actually erupted when it was opened. The Health District notified FDA's **Seattle District** of the problem, and an investigator went out to the restaurant to collect samples. Subsequent analysis revealed that the jar contents were under high pressure and contained a large quantity of carbon dioxide and an unidentified white precipitate. The District filed for seizure on a charge that the product was unfit for food because of the swollen containers, and \$862 worth of the peppers, distributed by A. Russo, Reading, Pennsylvania, was eventually seized.

# State Actions

*State Actions reports on important regulatory and administrative actions conducted by State and local government agencies to provide health and economic protection to consumers of foods, drugs, cosmetics, and medical devices.*

## Food Poisoning Investigated

When 47 people developed symptoms of food poisoning after attending a wedding reception in Naranjito, Puerto Rico, Puerto Rican health officials and a Naranjito physician set to work to determine the cause.

The reception had featured a variety of home-cooked foods—including marinated green bananas, rice and green pigeon peas, and ham with pineapple—any of which could have been the source of the problem.

About 3 hours after the reception men, women, and children appeared in large numbers at local health clinics, complaining of weakness, stomach aches, diarrhea, and vomiting—all signs of food poisoning. The phy-

sician at the Naranjito Health Center, an epidemiologist, notified the Puerto Rico Health Department, which began testing for bacterial contamination. The problem was finally traced to *staphylococcus* in the ham. Since several people who had eaten the ham before the reception had not become sick, authorities concluded that the meat must have become contaminated during the reception.

## Aftermath of a Tornado

Shortly after 6 p.m. on Tuesday, April 10, the city of Wichita Falls, Texas, was hit by a tornado that killed 49 people, injured hundreds more, and left an estimated 5,000 homeless. Property damage exceeding \$100 million was sustained by hundreds of businesses, including 20 retail grocery stores, 25 restaurants, 5 retail pharmacies, and 1 medical clinic.

Accounts of the tornado and its fury received national media play. These overshadowed the follow-up

work of State and Federal officials who, in the aftermath of the storm, had to deal with massive amounts of damaged goods. In the week following the tornado, 10 investigators from FDA's Dallas District and 12 officials from the Texas Health Department and the Wichita Falls City Health Department combined to inspect the damaged foods and drugs.

The damage was as varied as it was extensive. Many foods contained tiny shards of glass or were contaminated by polluted water; frozen foods thawed and refrigerated products spoiled when the storm knocked out electrical power; vacuum-packed canned goods were ruined when the pressure of the tornado broke their seals; and bottled soft drinks were found that inexplicably had tiny particles of dirt, glass, and debris inside although the lids were intact.

When the inspections were over the participants estimated that almost \$1 million worth of food and \$100,000 worth of drugs were irreparably damaged.

# 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 of a complaint 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 30 actions to remove from the consumer market products charged to be violative was reported in May. These actions included 16 of foods; all 16 involved charges concerning contamination. Others included 13 of drugs, and 1 of prophylactics.

PRODUCT, DISTRICT & DATE FILED	FIRM & PLACE OF BUSINESS	CHARGES
<b>FOOD/Contamination, Spoilage, Insanitary Handling</b>		
Beans, black, and red beans/U.S. District Court for the Southern District of New York 3/9/79	Summit Import Corp./New York, N.Y.	Held under insanitary conditions; rodent and/or insect contaminated.
Beans, pink/U.S. District Court for the District of Puerto Rico 3/21/79	Goya de Puerto Rico/Bayamon, P.R.	Held under insanitary conditions; rodent contaminated.
Cheese, and white kidney beans/U.S. District Court for the District of Massachusetts 3/14/79	Musolino LoConte Co./Cambridge, Mass.	Held under insanitary conditions; cheese is rodent contaminated.
Flour/U.S. District Court for the Southern District of Florida 3/5/79	Star Bakery, Inc./Miami, Fla.	Held under insanitary conditions; rodent contaminated.
Flour, and texturized vegetable protein/U.S. District Court of Puerto Rico 4/3/79	Productos Cuquis/Rio Piedras, P.R.	"
Garlic, and salt/U.S. District Court for the District of Puerto Rico 3/21/79	Empresas Coqui, Inc./Toa Baja, P.R.	Held under insanitary conditions; garlic contains insects and is decomposed.
Hot peppers/U.S. District Court for the Western District of Washington 3/29/79	Shipped from Reading, Pa.	Contained in swollen containers.
Popcorn kernels, yellow/U.S. District Court for the Eastern District of Virginia 2/12/79	Richter Distributing Co./Norfolk, Va.	Held under insanitary conditions; rodent contaminated.
Rice/U.S. District Court for the Eastern District of New York 3/1/79	Daiei Trading Co., Inc./Woodside, N.Y.	Held under insanitary conditions; contains the nonconforming food additive Dursban.
Rice/U.S. District Court for the Western District of Oklahoma 4/6/79	Tommies Cello-Pak, Inc./Oklahoma City, Okla.	Held under insanitary conditions; rodent contaminated.
Rice/U.S. District Court for the District of Maryland 4/2/79	East West Food Products, Inc./Columbia, Md.	Held under insanitary conditions; rodent and insect contaminated.
Rolls, and other breads/U.S. District Court for the District of South Carolina 3/23/79	Bean Distributing Co./Hanahan, S.C.	Held under insanitary conditions; rodent contaminated.
Soup mix, vegetable, dehydrated/U.S. District Court for the Northern District of California 3/9/79	Dah Chong Hong Trading/New York, N.Y.	Contains insects.
Soup stock, protein base, gin, petroleum jelly, and other food, drug & device, and cosmetic stocks/U.S. District Court for the Eastern District of Virginia 4/11/79	Barge load from Baltimore, Md., cap-sized into harbor water/Norfolk, Va.	Held under insanitary conditions. For some foods labeling lacked name and place of business of manufacturer, packer, or distributor, lacked accurate quantity of contents statement, and lacked common or usual name of food.



PRODUCT, DISTRICT, & DATE FILED	FIRM & PLACE OF BUSINESS	CHARGES
Sugar, potato slices, rice, and other food-stocks/U.S. District Court for the Southern District of Indiana 4/5/79	Rolling Mills, Inc./Indianapolis, Ind.	Held under insanitary conditions; rodent contaminated.
Wheat, bulk/U.S. District Court for the District of Minnesota 4/5/79	Shipped from Jamestown, N. Dak.	Insect contaminated.
<b>DRUGS/Human Use</b>		
Bee pollen/U.S. District Court for the Central District of California 3/28/79	A-1 Honey Co./Honolulu, Hawaii	Labeling contains false and misleading claims of therapeutic usefulness, and fails to bear adequate directions for use. New drug without an effective approved New Drug Application. Article processed in unregistered establishment.
Diethylpropion HCl T.D. tablets/U.S. District Court for the Northern District of California 3/8/79	Pharmadyne Laboratories, Inc./Hackensack, N.J.	New drug without an effective approved New Drug Application.
Diethylpropion HCl T.D. tablets; furosemide tablets; and chlorothiazide with reserpine tablets/U.S. District Court for the District of Massachusetts 3/20/79	"	New drugs without effective approved New Drug Applications.
Diuretic pills, laxatives, analgesics, other drugs, and drug components/U.S. District Court for the Western District of New York 3/23/79	Brown Manufacturing Co., Inc./LeRoy, N.Y.	Circumstances of the drugs' manufacture not in conformity with current good manufacturing practice.
Furosemide tablets/U.S. District Court for the Northern District of California 3/29/79	Pharmadyne Laboratories, Inc./Hackensack, N.J.	New drug without an effective approved New Drug Application.
Furosemide tablets, and diethylpropion HCl tablets/U.S. District Court for the Southern District of Florida 3/27/79	"	New drugs without effective approved New Drug Applications.
Hair Medicine Grow Aid products, and ingredients/U.S. District Court for the Eastern District of Pennsylvania 1/24/79	Alfonso's Products, Inc./Philadelphia, Pa.	Circumstances of manufacture, processing, packing, and holding not in conformity with current good manufacturing practice.
Lyophrin epinephrine bitartrate for ophthalmic solution/U.S. District Court for the Northern District of Texas 3/1/79	Alcon Laboratories/Fort Worth, Tex.	Circumstances of drug's manufacture not in conformity with current good manufacturing practice; subpotent.
Perphenazine & amitriptyline HCl combination tablets in various strengths/U.S. District Court for the Southern District of Florida 3/5/79	MD Pharmaceutical, Inc./Santa Ana, Calif.	New drug without effective approved New Drug Application.
Perphenazine & amitriptyline HCl combination tablets/U.S. District Court for the District of Connecticut 3/21/79	"	"
Perphenazine & amitriptyline HCl combination tablets/U.S. District Court for the Northern District of Georgia 3/28/79	"	"
Perphenazine & amitriptyline HCl combination tablets of various strengths/U.S. District Court for the Northern District of California 3/29/79	"	New drugs without effective approved New Drug Applications; labeling fails to bear adequate directions for use and articles not exempt due to their new drug status.
Providone-Iodine Surgical Scrub/U.S. District Court for the Eastern District of Michigan 4/4/79	North American Pharmacal/Dearborn, Mich.	Circumstances of production not in conformity with current good manufacturing practice, and false and misleading expiration date, since the date is not based on appropriate stability testing.
<b>Prophylactics</b>		
Prophylactics, rubber, Trojan-Enz/U.S. District Court for the District of Colorado 3/12/79	Youngs Rubber Corp./Trenton, N.J.	Quality falls below article's purported quality; and false and misleading claims for preventing pregnancy and venereal disease, since article contains holes.

# Don't drink to the health of your baby

Drinking alcoholic beverages while pregnant can be harmful to the baby. Why take chances? For information or for help, write: National Clearinghouse for Alcohol Information, Rockville, Md. 20857





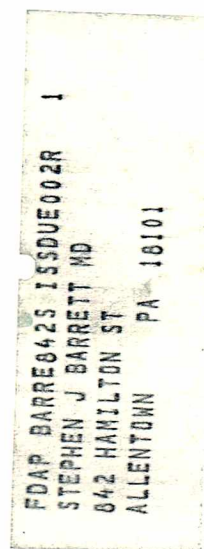
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