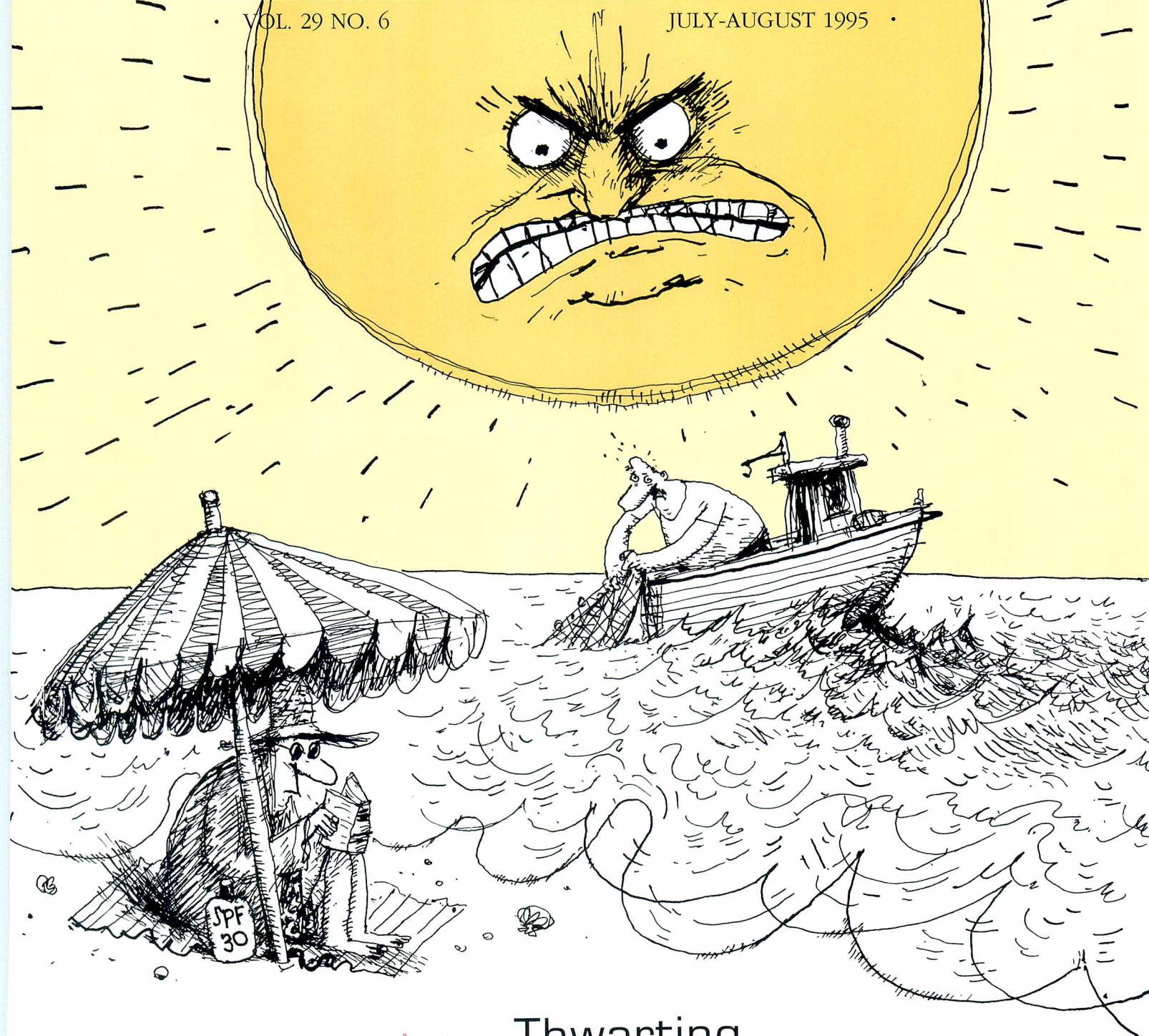


FDA CONSUMER

THE MAGAZINE OF THE U.S. FOOD AND DRUG ADMINISTRATION

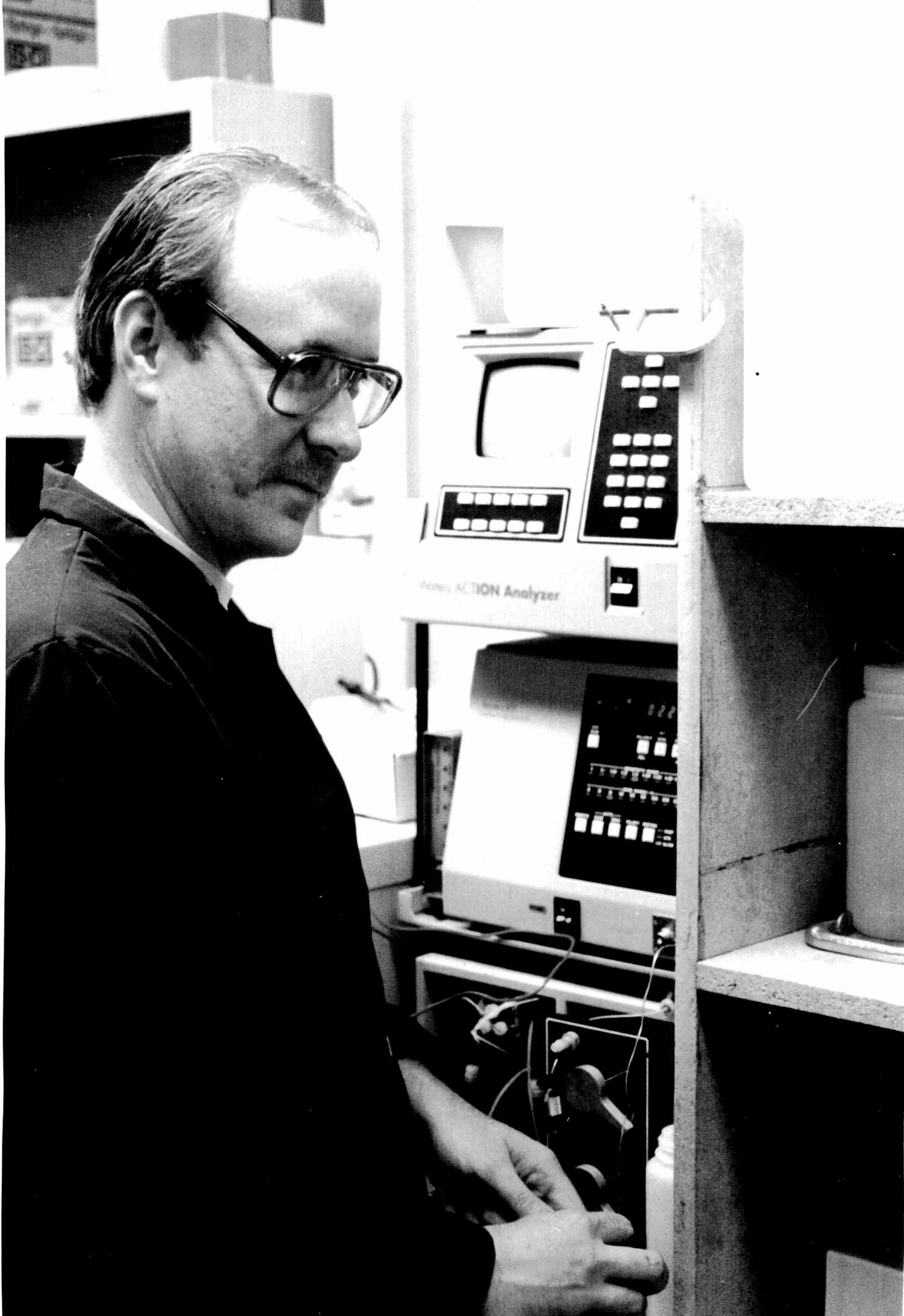
VOL. 29 NO. 6

JULY-AUGUST 1995



26 CH
just enough

Thwarting
SKIN CANCER
With Sun Sense



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FDA's Forensic Center: Speedy, Sophisticated Sleuthing 5
Thirty chemists and three biologists in Cincinnati spearhead FDA's efforts to unravel the scientific mysteries of tamperings and other criminal activities. Their careful observations have high-tech help.

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Skin cancer is now about as common as all other cancers combined. Fortunately, early diagnosis is easy, and most types are highly curable. But prevention is also easy and more desirable.

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Making It Easier to Read Prescriptions 25
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Inside Front Cover Photo: David Jackson, a chemist with FDA's Forensic Chemistry Center, adjusts an ion chromatograph to analyze a sample contaminated with household bleach. For more on the Forensic Center, see page 5.



Think Twice About Eating Raw Oysters

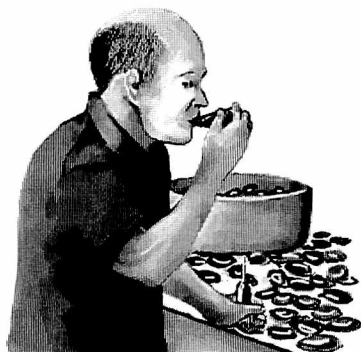
For some people, eating raw oysters can cause serious illness—even death. The reason: *Vibrio vulnificus*, a bacterium that occurs naturally in Gulf of Mexico waters and oysters.

The bacteria are not a result of pollution, so although oysters should always be obtained from reputable sources, such sources, clean waters, and high turnover of oysters in restaurants do not provide protection against the bacteria.

Certain health conditions put people at high risk for infection. These conditions are:

- liver disease
- hemochromatosis, an iron disorder
- diabetes
- stomach problems
- cancer
- immune disorders, including infection with HIV
- long-term steroid use (as for asthma or arthritis).

People who drink moderate to heavy amounts of alcoholic drinks also may be at increased risk. According to the 1993 *Special Report to Congress on Alcohol and Health*, and the National Institute on Alcohol Abuse and Alcoholism, drinking two to three alcoholic beverages each



day can cause liver disease, which often has no signs or symptoms. People with liver disease are almost 200 times more likely to die from *Vibrio vulnificus* infection than those without liver disease.

Check with a doctor if you're unsure of your risk, and, if you're at increased risk, do not eat raw oysters. Fully cooking oysters kills the bacteria.

For more information, call the FDA Seafood Hotline, (1-800) FDA-4010.

Stop to Marketing Quinine For Night Leg Cramps

Less than a year after ordering a halt to the marketing of over-the-counter (OTC) quinine sulfate for night leg cramps based on its serious risks, FDA ordered a stop to the marketing of prescription quinine for this use because even under a doctor's care, its risks outweigh any possible benefits.

In January, FDA sent warning letters to 44 companies stating that it is unlawful to market their quinine sulfate products for night leg cramp relief because FDA has not approved the drug for this use. By the end of March, all major manufacturers and distributors had stopped labeling their products for this use, including Marion Merrell Dow, the manufacturer of the original and best-known quinine drug, Quinamm.

From 1969 through June 1992, FDA received 157 reports of health problems related to quinine use, including 23 that resulted in death. Nonserious problems included temporary sight and hearing disturbances, dizziness, fever, nausea, vomiting, and diarrhea. Serious problems included thrombocytopenia, a destruction of blood platelets that can lead to massive bleeding and sometimes death.

After weighing the benefits and risks

of OTC quinine sulfate for night leg cramps, FDA concluded that quinine is not safe and effective for this use because:

- No studies demonstrate that quinine is effective against night leg cramps.
- Night leg cramps are not a threat to life or health.
- Health risks outweigh any small potential benefits.

Based on this finding, the agency published a rule in the Aug. 22, 1994, *Federal Register* prohibiting OTC marketing of the drug for leg cramps.

FDA also proposed to stop OTC marketing of quinine for another use—to prevent or treat malaria. The public has until July 3 to comment on the proposal, published in the April 19, 1995, *Federal Register*. The agency based the proposal on its conclusion that physician monitoring is essential to the safe and effective treatment of this serious, potentially life-threatening disease. Written comments may be sent to: FDA Dockets Management Branch (HFA-305), Rockville, MD 20857.

7 Companies, FDA Test HACCP

Seven major food companies are working with FDA in a pilot program to test a procedure to enhance food safety.

The pilot will help FDA determine if the approach, called Hazard Analysis Critical Control Point, or HACCP, is practical for wider application in the food industry.

Under the HACCP plan, companies analyze their manufacturing processes to identify where problems are most likely to occur and where preventive measures need to be focused. The idea behind HACCP is to build safety into the manu-

facturing process, rather than rely on inspections and sampling to identify unsafe products after they've been made.

Companies participating in the voluntary pilot program and their products are:

- Alto Dairy, Wapun, Wis.—hard cheese
- Campbell Soup Company, Camden, N.J.—refrigerated salad dressing
- Campbell-Taggart, Inc., St. Louis, Mo.—pan breads
- Con Agra, Omaha, Neb.—flour



- Ocean Spray Cranberries, Lakeville-Middleboro, Mass.—pasteurized juice
- Pillsbury, Minneapolis, Minn.—bakery products
- Hans Kisse Foods, Wilmington, Mass. (in cooperation with the Massachusetts Department of Health)—quiche

FDA Suspends Blood Center License

Serious violations of federal regulations designed to safeguard donors and the blood supply led to the suspension of blood product licenses for a regional blood center in Midland, Texas.

FDA's suspension on April 20 of the establishment and product licenses of

Midland County Hospital District, also known as Permian Basin Regional Blood Center, prevents the center from shipping blood or blood components interstate.

An FDA inspection of the center from March 14 through April 11, 1995, found violations such as improper and unsterile blood collection and processing, inadequate follow-up of donor adverse reactions, inaccurate record-keeping, and inadequate staff training.

The license suspension does not stop the center from procuring U.S.-licensed blood and blood components from another acceptable source, provided that appropriate measures are taken to ensure proper storage and distribution.

If the center develops a plan to correct the violations, FDA will review the plan and decide what further action should be taken.

Report on Rotavirus Vaccine

An investigational vaccine prevented more than 80 percent of the most severe diarrheal illnesses among infants caused by rotaviruses, according to a study reported in the *Journal of the American Medical Association*.

The vaccine was developed and patented by the National Institute of Allergy and Infectious Diseases (NIAID), a part of the National Institutes of Health.

An effective vaccine would annually prevent more than 1 million cases of severe rotaviral diarrhea in U.S. children under 5, including 65,000 hospitalizations. In developing nations each year, moderate to severe rotaviral diarrhea affects 18 million youngsters, killing more than 870,000.

The vaccine, RRV-TV, was developed

in 1986 by Robert Chanock, M.D., Albert Kapikian, M.D., and others at NIAID's Laboratory of Infectious Diseases. Chanock is chief of the laboratory, and Kapikian is assistant chief. NIAID patented the vaccine in 1988.

In the study, reported in the April 19 *Journal of the American Medical Association*, researchers at 23 U.S. medical centers compared a placebo to the RRV-TV vaccine, which uses four important human rotavirus strains, and to another investigational vaccine, the RRV-S1, which uses only one of the strains, serotype 1. Chanock and colleagues developed the RRV-S1 in 1985, and NIAID patented it in 1987.

During the testing, both vaccines protected against serotype 1 disease, but only the RRV-TV protected against disease caused by the other strains during the second year after immunization, according to the report's authors, led by David Bernstein, M.D., of the J.N. Gamble Institute of Medical Research, in Cincinnati.

Specifically, the two vaccines provided the following protection:

- all cases of rotaviral diarrhea—RRV-TV, 57 percent; RRV-S1, 40 percent
- less serious cases—RRV-TV, 49 percent; RRV-S1, 31 percent
- most severe cases—RRV-TV, 82 percent; RRV-S1, 73 percent
- episodes longer than three days—RRV-TV, 92 percent; RRV-S1, 36 percent
- cases requiring medical visits—RRV-TV, 78 percent reduction; RRV-S1, 67 percent reduction.

The researchers enrolled 1,006 healthy infants, ages 4 to 26 weeks, between August 1989 and February 1990. Of those enrolled, 898 received three

oral doses of one of the vaccines or the placebo at least two weeks apart, with the final dose by age 30 weeks. The researchers followed the 898 children for one year and 864 for two years, until June 1991. Neither researchers nor parents knew which product a child received until the study ended.

Through a cooperative research agreement with NIAID, Wyeth-Ayerst Laboratories, of Philadelphia, produced both vaccines for the study. The firm had requested to meet with FDA and, after that meeting, chose not to pursue developing the RRV-S1 vaccine product.

Gallup Survey Says Children Aware of Healthy Lifestyle

American children have beneficial attitudes and behaviors about food, nutrition, and physical activity, according to a nationwide survey of children aged 9 to 15.

The telephone poll, conducted by the Gallup Organization last November and December, queried 410 children about topics such as eating habits, parents' influence on diet, and the school's role in food and fitness.

According to the poll:

- Ninety-seven percent agreed that a balanced diet is "very important" for good health, and 98 percent said the same about physical activity.
- Sixty-six percent said they like eating "many different kinds of foods," while 74 percent agreed that eating "a lot of bread, cereal, and other grains is good for you."
- Sixty-four percent rated their own eating habits "good to excellent," and 76 percent said the same about their parents' eating habits.

- Forty-nine percent said they eat meals with their families every day, while 13 percent said they eat with their families only once a week or less.
- Sixty-four percent agreed that foods good for them "don't taste good," a 14 percent rise from a 1991 survey.
- Eighty percent want to do more physical activity this year.

Children reported getting nutrition information from schools and teachers (90 percent), parents (77 percent), television (64 percent), books (60 percent), and health professionals (59 percent).

Survey results are encouraging, says Doris Derelian, Ph.D., president of the American Dietetic Association, a survey sponsor. "Children understand that they can enjoy a wide variety of foods eaten in moderation," she says.

"Children need encouragement from their family, friends and teachers to ... participate regularly in moderate-to-vigorous physical activity," says Sylvia Rowe, president of the International Food Information Council, another survey sponsor.

The third survey sponsor, the President's Council on Physical Fitness and Sports, will mail a free brochure to

help children plan a healthy lifestyle. For a copy, send a self-addressed, stamped business-sized envelope to: 10 Tips for You
P.O. Box 1144
Rockville, MD 20850

New Publications Available

Five free publications are now available from FDA.

They are two *FDA Consumer* reprints—one on prostate cancer, the other on the new food label; a poster on iron poisoning; a backgrounder on the new food label; and a brochure on mammography published by the Agency for Health Care Policy and Research.

The publications and their FDA publication numbers are:

- Prostate Cancer: New Tests Create Treatment Dilemmas (FDA) 95-1220
- The New Food Label: Better Information for Special Diets (FDA) 95-2291
- Protect Your Child from Iron Poisoning (FDA) 95-1221P
- The New Food Label (BG 95-12)
- A Woman's Guide: Things to Know About Quality Mammograms (FDA) 95-8286

For single copies, write to FDA, HFE-88, Rockville, MD 20857. For two to 100 copies, write to FDA, HFI-40, at the same address, or fax your order to (301) 443-9057. Include the publication number.



FDA Consumer welcomes comments from readers. Send letters to: Editor, *FDA Consumer*, HFI-40, Rockville, MD 20857.

FDA's Forensic Center

Speedy, Sophisticated Sleuthing

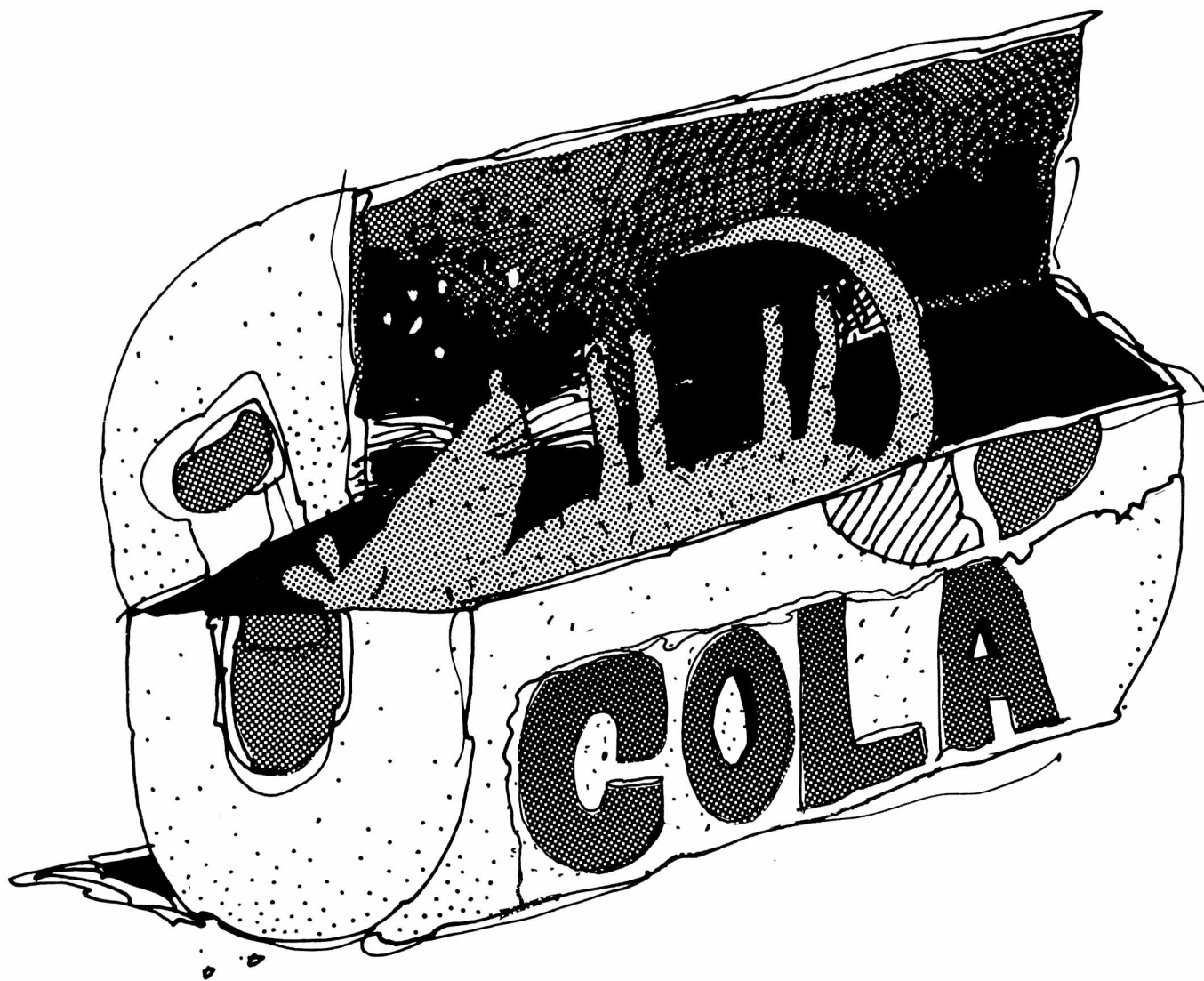
by Isadora B. Stehlin

By the time the mouse and its Pepsi-can coffin reached FDA, Fred L. Fricke and his team of chemists and microbiologists didn't have much to work with.

The mouse, found dead in a can of Diet Pepsi in New York, had already been examined by Pepsi officials. From there it went to a veterinarian on the East Coast. Next stop was a pathologist

in Utah. Finally, the dissected mouse was sent to Fricke at FDA's Forensic Chemistry Center in Cincinnati.

Fortunately, the mouse's teeth were still intact. "We measured the spacing between the teeth and the pattern of bite marks on the can," explains Karen A. Wolnik, director of the center's inorganic chemistry branch. "From those



OTHER ACTIVITIES, SUCH AS ILLEGAL SALE AND USE OF UNAPPROVED DRUGS, COUNTERFEIT DRUGS, AND ECONOMIC FRAUD, REQUIRE THE LAB'S EXPERTISE.

measurements it was determined that his lower teeth had left marks on the inside of the can and his upper teeth had gnawed the outside, right at the pull-tab opening."

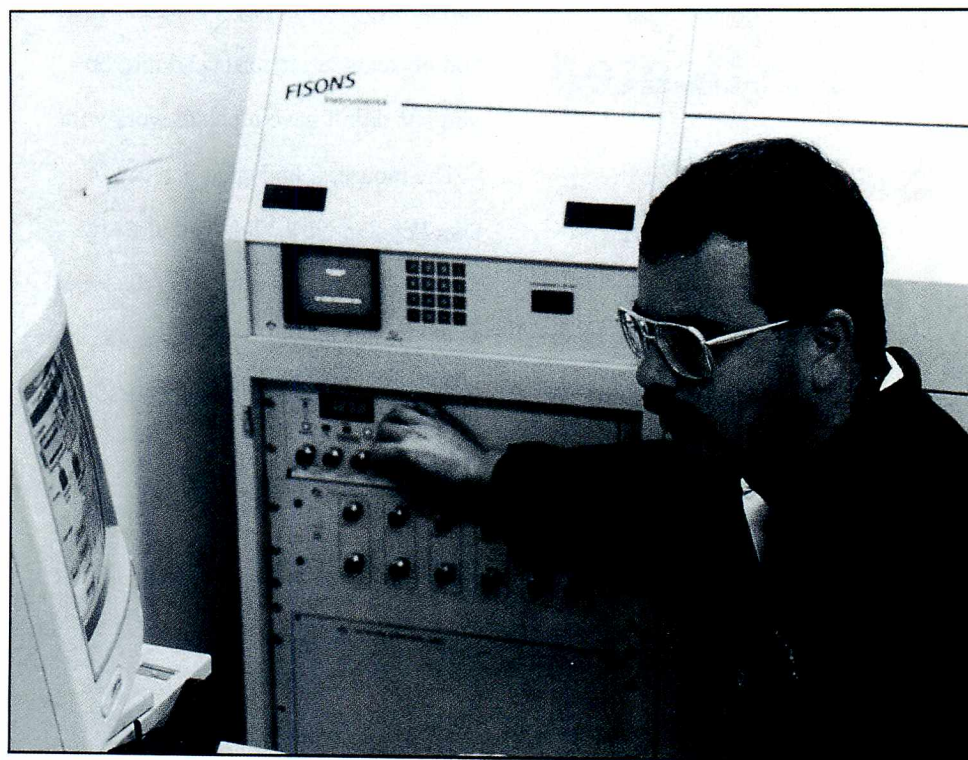
Wolnik says that pattern demonstrated the mouse had been inside the can when it bit the lid. But because the can lid with the pull-tab opening is in one intact piece throughout manufacturing, the mouse couldn't have bitten the lid or gotten into the can until after it was opened. The evidence was used to convict a tamperer who had falsely claimed to have found the mouse inside the can when she opened it. (Under the Federal Anti-Tampering Act, it is a felony to tamper with foods, drugs, devices, cosmetics, and other consumer products.)

"Every week we get something that's suspected tampering," says Fricke, director of the forensic center. "It never slows down."

FDA established the center in 1989 to provide the agency with a team of forensic science experts who can respond immediately to all tampering incidents and provide expert advice and scientific evidence to FDA officials. The 30 chemists and three biologists unravel the scientific mysteries of tamperings and other criminal activities involving FDA-regulated products through careful observation and high-tech instruments.

The center has inorganic chemistry and organic chemistry branches. The organic branch uses organic analytical detection methods—such as infrared spectroscopy, gas and liquid chromatography, and mass spectrometry—to separate and identify the components of mixtures. The inorganic branch uses tools such as digital image analysis and scanning electron microscopy to detect physical evidence of tampering or counterfeiting, and ion chromatography, atomic absorption, and inductively coupled plasma *spectrometry* to measure inorganic components of mixtures. (See accompanying article.)

Most cases require the expertise of both branches. "There's no division [of



Doug Heitkemper, Ph.D., uses inductively coupled plasma/mass spectrometry to identify a trace element "fingerprint" for a counterfeit drug.

responsibilities] that's really sacred," says R. Duane Satzger, director of the organic branch. "When we get a case, both branches sit down and talk about it and decide how to address the situation."

For example, he explains, a syringe might first be examined by the inorganic group. Wolnik's staff would use light microscopy to examine the syringe. If, during this examination, they observed some kind of liquid in the needle of the syringe, Satzger's staff would use chromatographs or mass spectrographs to identify the liquid. Electron microscopy might be used to detect decomposition and other physical changes to the syringe that might have occurred if the syringe had been submerged in soda or come in contact with poison.

Tylenol, Grapes and Cyanide

In 1980, Fricke, Satzger and Wolnik worked at the forensic center's predecessor, FDA's Elemental Analysis Research Center in Cincinnati, where they conducted research and developed procedures for detecting toxic and nutritional trace elements in foods and drugs.

In 1982, when the first Tylenol tampering occurred, FDA chemists developed elemental "fingerprinting" techniques that allowed the authorities to trace the cyanide back to the manufacturer and the distributor. "The identity and relative amounts of various elemental constituents in a suspect sample form a distinct pattern that can be used for comparison with other samples, much like actual fingerprints," explains Wolnik.

"EVERY WEEK WE GET SOMETHING THAT'S SUSPECTED TAMPERING."

—FRED L. FRICKE, DIRECTOR, FORENSIC CHEMISTRY

The next few years saw more cases of cyanide in Tylenol and other pain relievers, as well as other types of tampering. "We applied the "fingerprinting" techniques to various poisons," says Fricke. They also developed "fingerprints" for inorganic substances such as metal and glass.

By the time cyanide was discovered in Chilean grapes in 1989, the center had developed expertise in detecting cyanide and other poisons in drugs and processed foods. But they had very little knowledge about what effect the cyanide would have on the fruit and vice versa. Would the poison become more or less toxic? Would it do something to the fruit that would be obvious to consumers?

"We didn't have a lot of answers at that time about what would happen," says Fricke. To keep FDA from being caught off-guard in the future, the agency redirected the focus of Fricke's lab from elemental to forensic research.

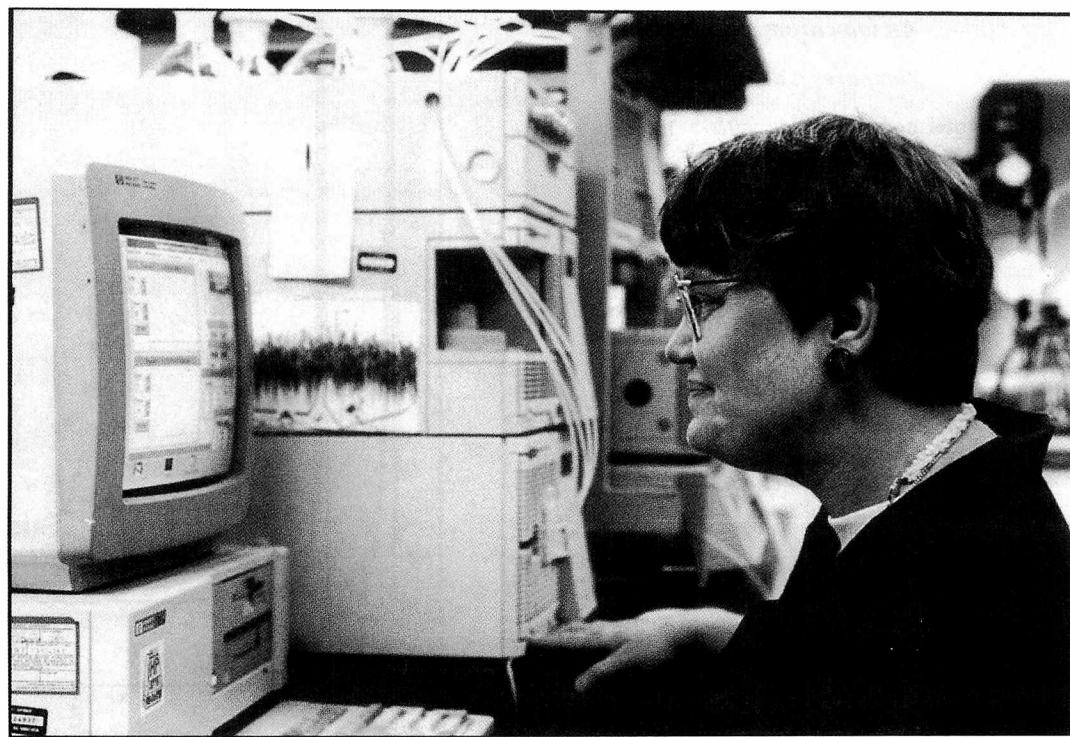
The lab's primary function shifted to research on what happens when poisons are added to foods and drugs. The "fingerprinting" technique used for comparing items of evidence was expanded to include many chemicals. In addition, the lab began developing screening methods for poisons so it could respond rapidly to any suspected tamperings. Since then, the lab has developed techniques to screen for more than 250 of the most toxic poisons commonly available to the public.

The forensic lab is also the only laboratory facility in FDA especially equipped for, and experienced in, ultra-trace elemental analysis. Using a specialized type of mass spectrometry called inductively coupled plasma/mass spectrometry, the lab's chemists can find contaminants in amounts as small as parts per trillion.

Tracking Down the Source

There are three points at which a foreign object or other contaminant can get into a product.

- *During manufacturing.* "There are le-



Lorrie Lin, Ph.D., uses high performance liquid chromatography to examine the results from a screen for poisons.

gitimate things that can go wrong during manufacturing," says Wolnik, "and there are rare occasions of employee sabotage."

- *While the product is in distribution.*

These are cases in which someone tampers with a product and returns it to the store shelf looking as untouched as possible so the purchaser is unlikely to detect the tampering. Frequently the perpetrator has a single victim in mind but tries to make the crime look like random tampering. "It's a crime similar to blowing up an airplane to kill one person," says Wolnik.

- *After purchase.* Those are the false report cases, such as the false claims of Pepsi tamperings during the summer of 1993.

Many clues help the forensic lab's

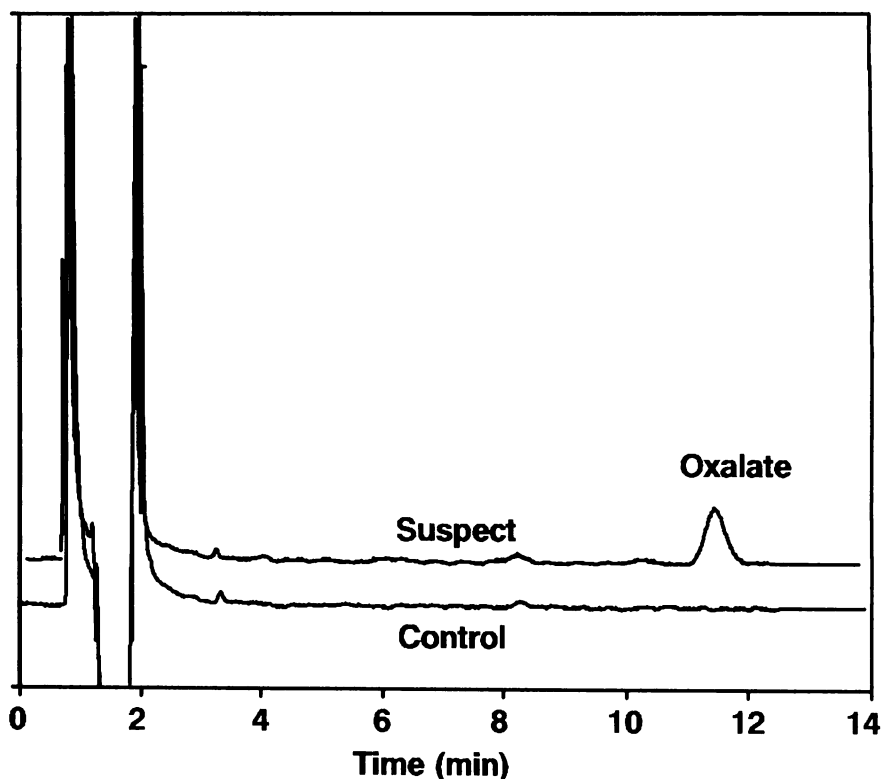
people zero in on the time and place of contamination, including the amount of physical deterioration of foreign objects, the breakdown of poisons into chemical components, and physical measurements of containers. But they won't tell the public what those clues are. "We don't want to hand out a blueprint to would-be tamperers," says Fricke.

The process for identifying poisons and other chemical contaminants is something the scientists will share. Separation of the different chemical components of a mixture is one of the most frequent techniques used and requires some type of chromatography.

Chromatography separates complex mixtures by measuring migration rates of component molecules through columns and through coatings on chroma-

ONE OF THE TOUGHEST OBSTACLES THE FORENSIC LAB FACES IS THE CONDITION OF SAMPLES WHEN THEY REACH THE LAB.

An ion chromatogram compares a drug contaminated with oxalate (a potentially toxic substance) and the non-contaminated (control) drug.



tography plates. “We’ll compare those components with a control and we’ll be looking for differences,” explains Satzger. “We won’t try to identify everything in the sample. So if there are 20 components that we can separate in the suspect sample and only 18 in a control, we’ll zero in on those two extra components.”

Identification usually requires infrared spectroscopy or some form of mass spectrometry. Gas chromatography/mass spectrometry is used for volatile components. Liquid chromatography/mass spectrometry is the usual choice for nonvolatile ones. Ion chromatography and atomic spectrometry are used for inorganic components.

Even after suspect components are identified, the sleuthing may not be over. Sometimes components that show up in lab tests are part of a bigger picture.

“We’ve done studies to show that when you put sodium hypochlorite (bleach) in soft drinks it breaks down into several different components,” says Wolnik. “So we look for elevated break-

down products of the sodium hypochlorite. That’s where the sophistication [of our lab] comes in. Any lab can run a test for bleach in soft drinks. But if they don’t find any bleach it doesn’t necessarily mean bleach wasn’t in there. It just means that [the bleach] may have been changed by the material.”

Even when the final lab results are in, FDA’s work may not be done. “A lot of what we do isn’t the be all and end all,” says Wolnik. “It just really helps focus the investigation. We work closely with [FDA] agents and investigators so we know what kinds of questions they’re interested in answering. As we learn things, we provide information to the investigators which may help direct their investigation.”

Leftovers

One of the toughest obstacles the forensic lab faces is the condition of samples when they reach the lab. Like the mouse in the Pepsi can, samples have frequently been studied by other authorities first, leaving very little for

the forensic lab to work with.

“It’s infrequent that we get the sample first,” says Wolnik. “That alone makes our analysis difficult. We have to spend some time thinking about what analyses we want to do, and what order we want to do them in. We can’t afford to waste what little sample is left.”

Another problem is damage or contamination of the samples. For example, Wolnik says during the 1982 Tylenol tampering incident, the medical examiner unintentionally contaminated the cyanide from some of the poisoned capsules with sodium during his analysis. He then sent the contaminated capsules to FDA.

“In forensics, you want the evidence as close to the condition in which it was originally found as possible, and you want to preserve that,” says Wolnik.

That was not the case on March 19, 1993, when Bobby Joe Johnston of Oklahoma City, suffered burns to his lips and tongue after drinking from a can of Pepsi. The hospital where he was treated took a sample of Pepsi from the

THE LAB HAS DEVELOPED TECHNIQUES TO SCREEN FOR MORE THAN 250 OF THE MOST TOXIC POISONS COMMONLY AVAILABLE TO THE PUBLIC.

High-Tech Tools

FDA's forensic scientists use a number of analytical methods, including:

Chromatography (thin-layer, gas, liquid, and ion)

Separation of complex mixtures based on physical and chemical interaction with a solid adsorbent material (for example, activated carbon, alumina gel, or silica gel) on a plate or in a column.

Mass Spectrometry

Identification of chemical structures and quantitative elemental analysis based on the mass of ionized (charged) molecules, ionized fragments of molecules, and ionized elements.

Infrared Spectroscopy

Measurement and identification of molecules by means of the molecules' interaction with infrared radiation.

Atomic Spectroscopy

Determination of elements based on the emission or absorption of electromagnetic radiation (for example, ultraviolet and visible light) by atoms.

Capillary Electrophoresis

Separation of chemicals by movement through a glass capillary tube in a solution under the influence of an electric field.

Microscopy (light and electron)

Production of magnified images of objects using light or electrons. ■

can and determined it was highly caustic. The hospital called the fire department, which retrieved the can and the rest of the six-pack Johnston had purchased. The fire department treated the cans as hazardous materials instead of forensic evidence, however.

"They put the five unopened cans in a glass container, set the open can on top of the others, and went home for the weekend," says Wolnik. "When they checked it on Monday, the corrosive material had eaten through the open can and dribbled onto and through another can, causing the second one to explode. When we finally got the sample, we had

to reconstruct what came from the contaminated can and what came from the other previously unopened can. It ended up being fairly tricky."

However, the lab was eventually able to confirm that sodium hydroxide (lye) had been added to the can after it was opened and could not have been in any of the unopened cans. "We did studies to see how long it would take [for sodium hydroxide] to eat through a can," says Wolnik. The FDA chemists found that highly caustic solutions such as lye ate through the can in a matter of hours. "That proved that it couldn't have happened during manufacturing." Johnston

was convicted of tampering on June 3, 1993.

Beyond Tampering

While tampering cases are the main focus of the forensic lab, there are other activities—such as illegal sale and use of unapproved drugs, counterfeit drugs, and economic fraud—that require the lab's expertise.

For example, the drug clenbuterol, which isn't approved in the United States for any use in either people or animals, is sometimes used illegally in show animals, including cattle, pigs and sheep to increase muscle. If those animals are subsequently slaughtered, anyone who eats the tainted meat might experience symptoms such as increased heart rate, muscle tremors, dizziness, nausea, fever, and chills. "We developed methods to analyze animal retinas for clenbuterol residues," says Fricke. This is significant, he explains, because while clenbuterol residues may show up in various tissues, almost any use will leave residues in the retina.

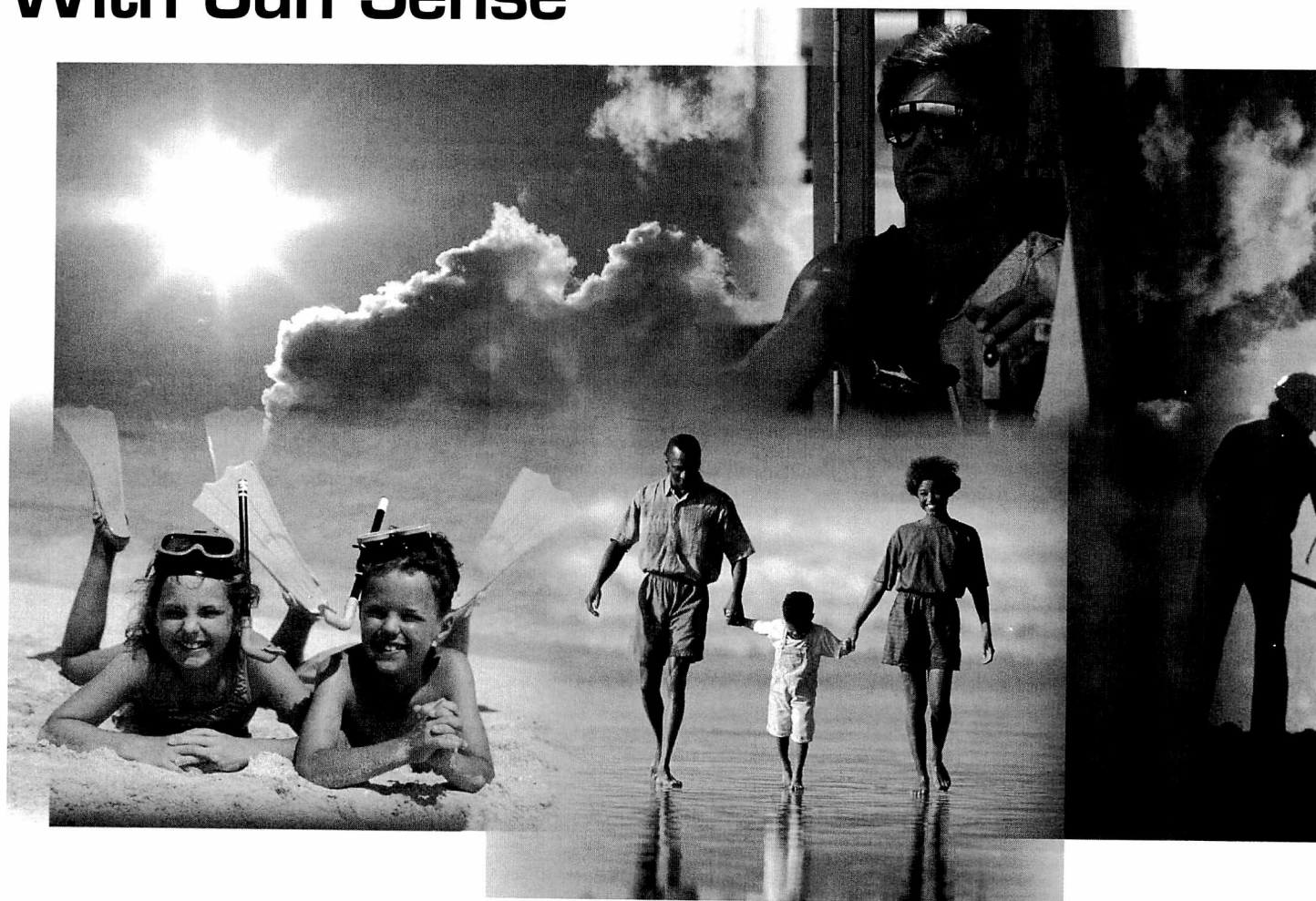
Counterfeit products require a combination of high-tech analysis to compare ingredients with the real product and careful study of the labels and packages.

The lab has uncovered evidence to support charges of economic fraud as well. Two such cases involved standard stainless steel on imported surgical instruments and purported nutritional products that didn't contain any of the listed ingredients.

The procedures and techniques the forensic lab has developed better prepares the agency to meet these types of emergencies. Still, "every sample that comes in is like a separate research project," says Fricke. "We have to decide what procedures and methods to apply, and there still are many cases that require new procedures. And, always, we have to do this as quickly as we can." ■

Isadora B. Stehlin is a staff writer for FDA Consumer.

Thwarting *Skin Cancer* With Sun Sense



by Carolyn J. Strange

Skin cancer is the most prevalent of all cancer, and it's increasingly common.

"This looks like skin cancer," the dermatologist told the woman as he examined the spot on her leg. Later, after removing the tumor and several other precancerous growths from her face and hands, he looked her in the eyes and said, "You've had enough sun."

More and more people are hearing similar messages from their doctors. Viewed as an undeclared epidemic by dermatologists, skin cancer is the most prevalent of all cancers, and it's increasingly common. About a million Americans will develop skin cancer this year.

"Skin cancer is now about as common as all other cancers combined," says

Martin A. Weinstock, M.D., Ph.D., director of Brown University's Dermatoepidemiology Unit and Chief of Dermatology at the Providence (R.I.) Veterans Affairs Medical Center. And there's no evidence that the epidemic has peaked.

But there is a bright side. Skin cancer is quite curable when treated early. More than 90 percent of skin cancers are completely cured. Even better, it's largely preventable, simply by avoiding sun and sunlamp exposure.

As more consumers become sun smart, they're finding new ways to protect themselves. For example, FDA

Not only is there no such thing as a safe tan, "There's no known safe amount of sun," Weinstock says.

Americans are getting the message. Increasingly, we're protecting ourselves from the sun, according to a 1994 survey commissioned by the American Academy of Dermatology. But we're not all sun savvy yet. Only 2 in 5 people consistently use sunscreen whenever they're in the sun. Fewer people say they sunbathe, but about 1 in 5 adults still does. And some people have the mistaken impression that sunlamps or tanning salons are somehow better or safer than natural sunlight. They aren't. No matter what the source, UV exposure increases your risk of skin cancer. (See "Sunlamps—Not a Bright Idea.")

There are three main types of skin cancer. Melanoma is the least common but most serious because this killer is responsible for three-quarters of the nearly 10,000 skin cancer deaths per year. The other two types—basal cell and squamous cell carcinomas—are often referred to together as non-melanoma skin cancer. Basal cell cancer is by far the most common skin cancer, followed by squamous cell carcinoma, which can also become a killer. Between 1980 and 1989, the incidence of non-melanoma skin cancers increased 65 percent, and melanoma 21 percent. And skin cancer is striking at ever younger ages. One-quarter of the more than 30,000 people

expected to develop melanoma this year will be 39 or younger.

A fourth type of growth, actinic or solar keratosis, is also of concern because it can progress into cancer. It's the most common pre-malignant skin condition, occurring in more than 5 million Americans.

UV's Double Whammy

While there's no question that UV damages DNA, scientists had long suspected that it delivers a double whammy. Recent research supports that idea. Developing skin cancer is at least a two-step process, involving initiation and promotion of malignant growth. "UV plays both roles," says Douglas Brash, Ph.D., a biophysicist at Yale University School of Medicine. In studies with mice, Brash and colleagues showed that UV harms a mechanism for repairing cell damage. Once the repair system is impaired, cells become increasingly vulnerable to injury. Subsequent UV exposures just make matters worse, and can initiate malignancy.

After UV exposure, the repair mechanism normally directs damaged cells to commit suicide. That's why skin peels after a sunburn. "It's a mop-up operation," says Brash. But previously damaged cells with a malfunctioning repair system escape this mop up. Genetic damage accumulates as normal cells die and abnormal ones survive.

Brash said the level of UV used in their experiments was about equivalent to exposure from a day at the beach. Skin doesn't have to be badly sunburned, he said, adding that such damage also accumulates with chronic, everyday exposure.

To increase awareness of the damaging potential of UV radiation, the Environmental Protection Agency and the National Weather Service developed the UV Index. Besides skin cancer, UV radiation also increases the risk of cataracts and certain other eye problems, and can suppress the immune system. And although dark-skinned people are generally less likely to get skin cancer than light-skinned people, they are just



Images provided by © 1994 PhotoDisc, Inc.

has cleared for marketing one manufacturer's clothing for sun protection. Eating a healthier diet can't hurt—less fat, more fruits, vegetables and grains—and preliminary studies indicate it may help. And the National Weather Service provides a measure of ultraviolet (UV) exposure with its UV Index, which is part of the daily weather forecast for many cities.

Experts agree that sunlight, particularly the UV wavelengths, damages the skin. UV radiation causes the obvious short-term damage seen in a sunburn or a tan, as well as the long-term damage that accumulates with each exposure.

Weather Service UV Index	
UV Index Number	Exposure Level
0 - 2	minimal
3 - 4	low
5 - 6	moderate
7 - 8	high
9 - 10+	very high

as susceptible to cataracts or immune suppression.

The UV Index number, ranging from 0 to 10+, indicates the amount of UV radiation reaching the Earth's surface during an hour around noon. (See "UV or not UV.") It's forecast daily for 58 cities, based on local predicted conditions. The UV Index is valid only for about a 30-mile radius from the city, and, as with any forecast, local variability in cloud cover and other factors may change actual levels experienced. But it serves as a reminder to take precautions against UV exposure.

For many people, sunscreens are the first line of defense.

"With most sunscreens it's important to apply them before you're in the sun," says FDA microbiologist Jeanne Rippere, who evaluates over-the-counter drugs, including sunscreens. They should be applied liberally, and reapplied at least every two hours (more often if you're sweating) or after swimming or toweling off. Sunscreens are rated by an SPF (sun protective factor) number, which is a multiplier of your skin's exposure time before burning. For example, an SPF of 4 means you can stay in the sun four times longer before burning than if you were wearing no sunscreen. Keep in mind that you can't add SPF numbers. If an SPF 4 product gives you an hour in the sun, reapplying won't give you another hour. Your time's up. If you want longer exposure, next time use a higher SPF before going into the sun.

Something else to remember is that two types of UV radiation reach the Earth, UVA and UVB. Both contribute

to skin damage, including skin cancer. There are no "safe" UV rays. But the SPF numbering system was devised as a guide to protect against sunburn, which is caused mostly by UVB. Because sunscreens allow you to stay out in the sun longer without burning, you may be increasing your exposure to UVA.

FDA has not approved a rating system for UVA protection because experts haven't reached a consensus as to what constitutes a good test. FDA is working to develop one, but until such a test exists, there's no way to compare products or verify claims made for UVA protection. Manufacturers are allowed to claim

TEST YOUR RISK FROM UV RADIATION

Your risk of skin cancer is related to your skin type and the amount of time you spend in the sun. How sensitive are you?

	YES	NO
* I have blond or red hair	<input type="checkbox"/>	<input type="checkbox"/>
* I have light-colored eyes (blue, gray, green)	<input type="checkbox"/>	<input type="checkbox"/>
* I freckle easily	<input type="checkbox"/>	<input type="checkbox"/>
* I have many moles	<input type="checkbox"/>	<input type="checkbox"/>
* I had two or more blistering sunburns as a child	<input type="checkbox"/>	<input type="checkbox"/>
* I spent lots of time in a tropical climate as a child	<input type="checkbox"/>	<input type="checkbox"/>
* There is a family history of skin cancer	<input type="checkbox"/>	<input type="checkbox"/>
* I work outdoors	<input type="checkbox"/>	<input type="checkbox"/>
* I spend a lot of time in outdoor activities	<input type="checkbox"/>	<input type="checkbox"/>
* I like to spend as much time in the sun as I can	<input type="checkbox"/>	<input type="checkbox"/>

▲ Score 10 points for each "YES"

▲ Add another 10 points if you go to tanning parlors or use a sun lamp

(Test courtesy of Dr. Neil Shear, University of Toronto)

SCORE:

80-110: The high-risk zone. Limit your time in the sun, always wear a sunscreen outdoors, and use protective clothing and a hat.

40-70: Increased risk. Use a sunscreen and hat regularly. Avoid exposure at midday when the sun is most intense.

10-30: Still at risk. Use a sunscreen regularly.



PARTNERS FOR SUN PROTECTION AWARENESS

UVA or broad-spectrum protection on a product, as long as it contains an ingredient that absorbs UVA.

The American Academy of Dermatology recommends that everyone use a broad-spectrum sunscreen having an SPF of at least 15, and advises consumers to check for ingredients that screen UVA: benzophenone, oxybenzone, sulisobenzene, titanium dioxide, zinc oxide, and butyl methoxydibenzoylmethane (also called avobenzone and known by the trade name Parsol 1789).

"People should not depend totally on sunscreens," Rippere says.

While sunscreens protect against sunburn, they don't necessarily prevent cancer. If you use sunscreens to spend more time in the sun, your skin could collect about the same total exposure to damaging radiation. So it's still a good idea to stay out of the sun at midday, and to protect yourself with a wide-brim hat and clothing.

Wear Some Shade

Clothing offers the advantages of even, non-sticky protection that you don't have to remember to reapply. But many summer-weight fabrics don't give enough protection. Some are well below the minimum SPF 15 that dermatologists recommend. And fibers like cotton offer even less protection when wet.

"You can't just put on any old shirt and expect it to protect you," says Julian Menter, Ph.D., research professor of medicine at Morehouse School of Medicine in Atlanta, Ga. "Fabrics can differ greatly in their ability to shield you from UV radiation."

The ideal sun protective fabrics are lightweight, comfortable, and protect against exposure even when wet. Clothing that is labeled or promoted as providing protection against the sun or limiting exposure to UV rays is considered a medical device and is regulated by FDA. Sun Precautions, Inc., of Seattle, Wash., has received FDA clearance to market its Solumbra clothing for sun protection and is allowed to claim an SPF of 30 for its products.

Sunlamps—Not a Bright Idea

Tanning salons and sunlamp manufacturers beckon to consumers with the lure of a quick, indoor tan. Some may even imply a "safe" tan. But that's just not possible.

Like the sun, sunlamps give off UV radiation—both UVA and UVB—and can be harmful. Exposure to UV radiation from sunlamps adds to the total amount of UV radiation your skin accumulates during your lifetime, and increases the risk of skin cancer. Other risks include premature skin aging, skin and eye burns, allergic-type reactions, cataracts, reduced immunity, and blood vessel damage.

FDA has a radiation safety performance standard for sunlamp products. Such products must have a warning label, an accurate timer, an emergency stop control, and include an exposure schedule and protective eyewear.

Tanning devices aren't recommended

for anyone, and should **never** be used if:

- You sunburn easily and don't tan. Skin that doesn't tan in the sun probably won't tan with sunlamps either.
- You get frequent cold sores. UV radiation may cause them to appear more frequently.
- You're taking medicines that can make you more sensitive to UV radiation. Check with your doctor or pharmacist.

If you choose to ignore the risks and seek an indoor tan, follow all the safety precautions. Stick to your time limit. Be sure to wear the goggles provided, making sure they fit snugly and aren't cracked.

Remember that there's no safe tan and there's no safe UV radiation. That's why tanning devices are best avoided altogether. ■

—C.J.S.

In an experiment with mice, Menter and colleagues compared a so-called "typical" summer clothing fabric (a tightly woven cotton used in a gardening shirt) with the Solumbra fabric, a proprietary, tightly woven synthetic. With an SPF of 6.5, the cotton fabric protected mice against short-term UV effects, but it didn't protect against long-term skin damage, including skin cancer. In fact, the incidence of tumors in these mice was comparable to that of the mice who received no UV protection. Mice not subjected to any UV radiation and the mice protected by the Solumbra fabric showed no signs of skin damage.

How do fabrics block UV? "It's a combination of factors—fabric thickness, composition of the fiber itself, and

especially tightness of weave," says Deborah F. Lumbardo, an FDA biomedical engineer. Dye can be a factor too, she says.

"But remember that you still need to be using sunscreen on whatever areas are exposed," Lumbardo says.

Inside-Out Protection?

Some studies estimate that diet may be involved in 40 to 60 percent of all cancers. More specifically, a high-fat diet has been implicated in colon and breast cancers. In animal studies, a high fat intake increased the likelihood of skin cancer after exposure to UV radiation, while switching to a low-fat diet after exposure reduced the incidence of skin cancer.

UV or Not UV?

It's a good rule of thumb to guard against overexposure whenever sunlight is strong enough that you can see your shadow. But you can't rely on your perception of brightness and shadows to gauge UV exposure because your eyes can't see UV wavelengths. Up to 80 percent of UV radiation can pass through clouds. The UV Index can help.

While you should always guard against UV exposure, be extra vigilant when the UV Index is 5 or higher. Remember that exposure doesn't come only from above—snow, sand, water, and even concrete reflect UV radiation. Also, UV radiation increases at higher elevations. The UV Index for mountain cities takes this into account, but keep it in mind if you travel.

Protect your eyes and skin from UV radiation with these simple safeguards:

- Wear a wide-brim **hat** to protect your eyes, ears, face, and the back of your neck.
- Wear **sunglasses** that block 99 to 100 percent of UV radiation. Check the label.
- Protect as much of your skin as possible with **clothing**.
- Use **sunscreen** with an SPF of 15 or higher. Reapply every two hours and after swimming.
- **Avoid midday sun**—10 a.m. to 2 p.m.—when UV radiation is strongest. ■

—C.J.S.

Homer S. Black, Ph.D., a researcher at the Veterans Affairs Medical Center in Houston, and his colleagues found a dietary effect in humans as well. In their study, published in the *New England Journal of Medicine*, a low-fat diet decreased the incidence of actinic keratosis in non-melanoma skin cancer patients. "The risk factors for actinic keratosis and non-melanoma skin cancer are basically the same," says Black.

The high-fat group ate their usual diet, consuming 36 to 40 percent of their caloric intake as fat, about average for Americans. In the low-fat group, no more than 20 percent of total caloric intake was fat. Overall, the high-fat group had a nearly five times greater risk of developing one or more actinic keratoses during the two-year study.

"Reduced incidence of this common skin tumor is just another added benefit to a long litany of those that can be attributed to a low-fat diet," Black says.

The National Academy of Sciences recommends a diet in which 30 percent or less of calories come from fat. The National Cancer Institute, the American Cancer Society, the American Heart Association, and other health organizations support this recommendation.

Although many researchers are studying the effects of certain vitamins and various other nutrients on skin cancer, it's too soon to make specific recommendations. But so far, the research trends point toward what we already know to be a healthier diet—less fat, more fruits, vegetables and grains.

Once cancer develops, early detection

and treatment are the best defense. Get familiar with your skin and your own pattern of moles and freckles with monthly skin self-exams. If any growth, mole or discoloration appears suddenly or begins to change, or if a sore appears that doesn't heal, see a dermatologist.

For any type of skin cancer, treatment involves removing the lesion, usually in an outpatient procedure. The treatment goal is to remove or destroy the growth completely with as little damage as possible to healthy tissue. Doctors evaluate numerous factors in planning treatment. Considerations include type of cancer, tumor size and location, extent of disease, whether it's new or recurrent, potential for scarring, and the patient's overall health.

Types of surgery include cryosurgery (destruction by freezing), laser surgery (using a laser beam to cut away or vaporize growths), and curettage and electrodessication (using a spoon-like blade to scoop out the growth, followed by destruction of surrounding tissue with an electric needle). Occasionally, other treatments, such as radiation therapy or chemotherapy, may be used alone or in combination.

Even after successful treatment, people who have had skin cancer remain at increased risk of developing it again. Protecting their skin from UV exposure is critical in helping to prevent a recurrence. It should become a life-long habit. ■

Carolyn J. Strange is a science writer in Saratoga, Calif.

***Skin cancer
is largely
preventable,
simply by
avoiding
sun and
sunlamp
exposure.***

Not A Cure-All

EYE SURGERY HELPS SOME SEE BETTER

by Marian Segal

"Men seldom make passes at girls who wear glasses," Dorothy Parker observed in 1926. True or not, when the writer penned her now famous line, the only alternative to glasses was poor sight. Things are rosier—but not perfect—in 1995.

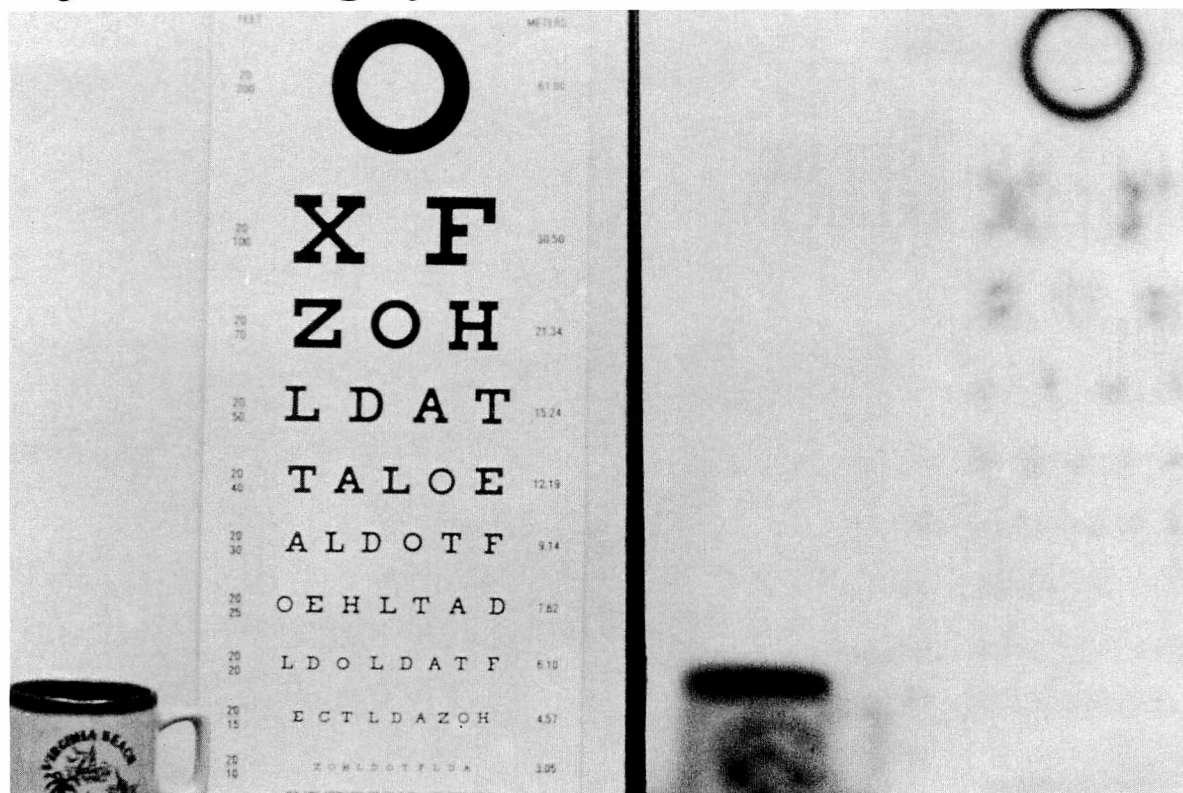
Today, growing numbers of women and men alike are opting for refractive eye surgery to correct their myopia (nearsightedness) in hopes of abandoning their glasses or contact lenses. The most common procedure is called radial keratotomy, or RK, and the National Eye Institute says about 250,000 are done each year in the United States, up from 30,000 just five years ago.

Pursuit of a mate, however, is not cited by either gender as major motivation for surgery. A report by the American Academy of Ophthalmology pub-

Mary Taylor, who teaches horseback riding in Boyds, Md., doesn't worry about losing eyeglasses anymore, since she had refractive eye surgeries in the fall of 1993 and spring of 1994.



Refractive Surgery



The chart at the left shows what a person with “normal,” or 20/20, vision would see at 20 feet. At the same distance, a person with 20/200 would see the chart as shown at right.

(Photo courtesy of American Academy of Ophthalmology)

lished in the July 7, 1993, issue of *Ophthalmology* states: “In two studies, approximately 75 percent of the patients who were interviewed about their reasons for seeking radial keratotomy stated that they wished to see well without physical dependence on ... spectacles or contact lenses. Patients also sought radial keratotomy to improve their performance in profession or sport, to improve cosmetic appearance, for simple convenience, or at times to meet the visual requirements for occupations such as law enforcement and firefighting.”

David Euley, a 52-year-old Darnestown, Md., kitchen designer and home remodeler, began to consider RK when he found himself becoming increasingly frustrated with his glasses, particularly at work.

“It was difficult to go back and forth from blueprints to taking measurements to working on a computer,” he says, adding that he needed a separate prescription for computer work.

Euley talked with several ophthal-

mologists before deciding to have the surgery last December. Interviewed four months later, he was delighted with the results: “This is the first time in 25 years I’ve been able to see the titles on television without glasses. I can read license plates. I can see the deer in my backyard. And my glasses are sitting on a shelf somewhere.”

Six incisions in each cornea (the clear covering over the front of the eye) left Euley with uncorrected vision improved from 20/800 in both eyes to 20/20 in the right and 20/25 in the left. (A person with 20/40 vision, for example, would see an object from 20 feet that another with perfect vision—20/20—could see at 40 feet. Some people see even better than 20/20.)

RK is often done in the doctor’s office. As in Euley’s case, surgeries on each eye are usually scheduled a few weeks apart, as a precaution in case there are complications. The patient is given anesthetic eye drops to numb the eye. Using a high-precision diamond

blade knife, the surgeon makes from four to eight spoke-like incisions in the cornea, while the patient focuses on the light of the operating microscope. The surgery takes about 10 to 15 minutes.

I Can See Clearly Now

Euley can read those license plates without glasses now because the incisions changed the shape of his corneas. Normally, the cornea and lens bend light rays to focus directly on the retina—the tissue at the back of the eye that receives the image. If the cornea or lens is too rounded, or the eyeball is elongated, the light focuses in front of the retina, blurring distant objects. RK reduces or eliminates the myopia by flattening the cornea and redirecting the light to focus on the retina.

The patient may have some pain or discomfort for 24 to 48 hours after surgery, possibly requiring medication. Glare, starbursting, or a halo effect, especially at night, is common for a few months and occasionally persists a year

or more. Vision also commonly fluctuates during the day, with acuity best in the morning and diminishing somewhat at night. This decreases in severity during the first year, but may last for many years.

Notwithstanding some claims to the contrary, RK is not a cure-all. (The Federal Trade Commission is investigating the problem of misleading claims in advertisements.) Reputable ophthalmologists will tell prospective patients the procedure is not completely risk-free, and perfect vision cannot be guaranteed.

Is RK Safe and Effective?

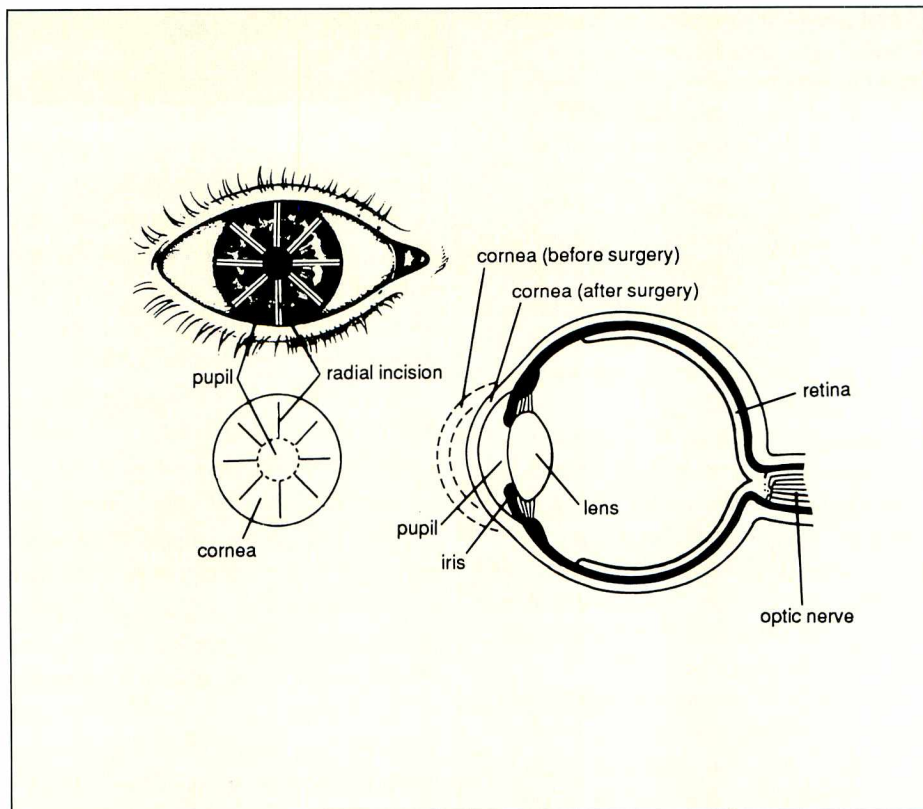
"FDA does not regulate radial keratotomy because it is a medical procedure, not a medical device," says Emma Knight, an ophthalmologist and medical reviewer with FDA's Center for Devices and Radiological Health. "The knife used in RK had been cleared by the agency for general corneal surgery."

The National Eye Institute (NEI), however, concluded from a 10-year study called "Prospective Evaluation of Radial Keratotomy (PERK)" that RK is "reasonably safe and effective ... with serious complications being rare."

All patients in the study had -2 to -8 diopters and could be corrected to 20/20 vision or better with glasses or contact lenses. (A diopter is the unit of measurement of spectacle or contact lens power. A minus value indicates nearsightedness; plus indicates farsightedness, or hyperopia. Euley's correction was -3.25 diopters.)

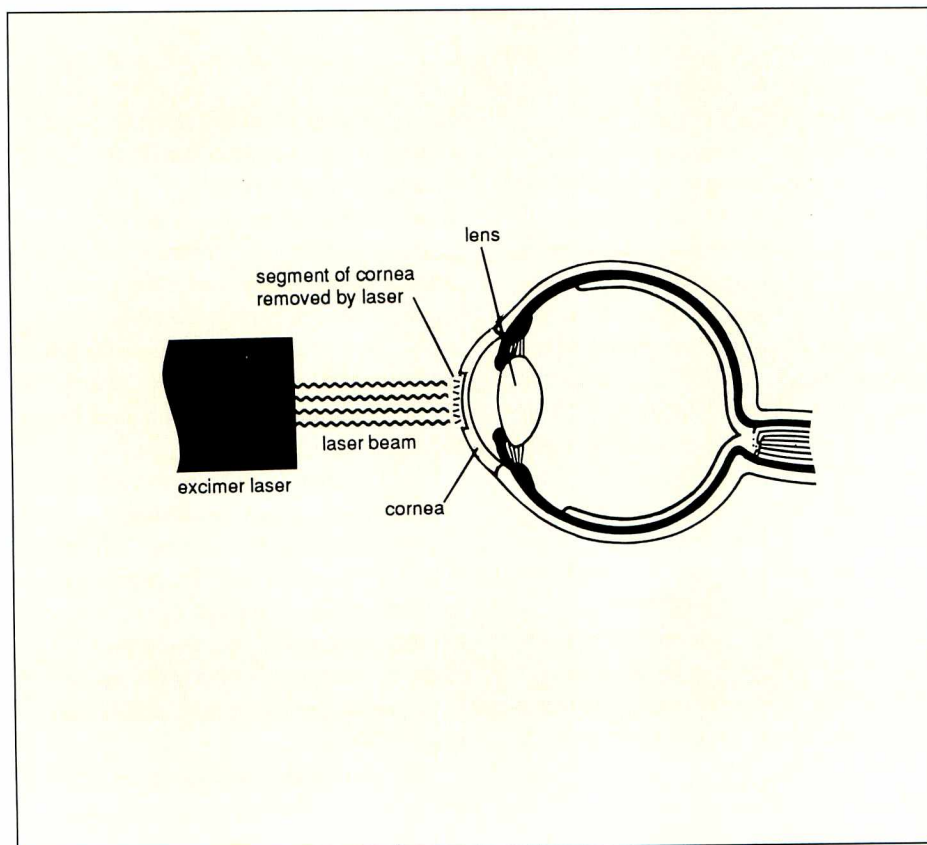
Results of the NEI-sponsored multicenter trial were reported by study investigator George Waring III, M.D., and colleagues in the October 1994 *Archives of Ophthalmology*. Among 374 patients (with 693 operated eyes) who returned for the 10-year follow-up:

- 70 percent said they did not wear glasses or contact lenses for distance vision.
- 53 percent had 20/20 vision without glasses.
- 85 percent had at least 20/40 vision without glasses—the acuity most states require for driving without glasses.
- Of the total 793 eyes operated (including data from the most recent examination of those who didn't return for the 10-year follow-up), 143 lost one line



Top: In radial keratotomy, the ophthalmologist usually makes four to eight incisions in the cornea. **Bottom:** In photorefractive keratectomy, ophthalmologists use a laser beam to remove a thin layer of cornea.

(Illustrations courtesy of the American Academy of Ophthalmology)



of best spectacle-corrected vision on the standard eye chart, 19 lost two lines, and four lost three lines. (Best corrected vision in all but 16 eyes was 20/20—they previously had better than 20/20 corrected vision. Thirteen eyes were corrected to 20/25 and three to 20/30.) This means that, although eyesight *without* glasses was improved from pre-surgery acuity, residual nearsightedness could not be corrected *with* glasses to pre-surgery acuity, probably due to haze or other effect of surgery.

- 38 percent of patients were corrected within one-half diopter of the predicted result; 60 percent were within 1 diopter.
- 43 percent developed “hyperopic shift”—a gradual change toward farsightedness (1 or more diopters between 6 months and 10 years) at a younger age than would be expected.

The cornea is weakened by radial keratotomy, increasing the risk of eye rupture from physical trauma. According to the article by the American Academy of Ophthalmology, however, there have been reports of severe eye trauma without damage to the incision wounds. The report also says that potentially blinding complications, such as corneal infection or perforation are rare.

More recent studies using newer RK techniques have achieved better optical results, says Peter Hersh, M.D., director of keratorefractive surgery at Montefiore Hospital, Bronx, N.Y.

Surgeons have designed improved methods for calculating the number and length of incisions and the diameter of the optical zone (the central clear zone that has no cuts) that will produce the best results in a given patient, he says.

“We’ve had numbers reported as high as 95 percent or so for 20/40 as the procedure has evolved,” Hersh says. “The most important variable is patient age. Younger patients tend to heal their incisions better and more quickly, and therefore get less of an effect. Also, patients with lower degrees of myopia do better than high myopes,” he says. Some other factors that may be considered when determining surgical procedure include corneal curvature, topography and thickness, and ocular pressure.

The Laser Method

An alternative to radial keratotomy

New Progress with an Old Idea

Refractive surgery is not a new idea. Little wonder, since about one-fourth of the world’s population is nearsighted—about 63 million in the United States alone. According to a report in the October 1994 *Archives of Ophthalmology* on the results of a 10-year study on radial keratotomy, the procedure was first described by European ophthalmologists in the late 1800s. It was further developed in Japan in the 1940s and 1950s, evolved into its modern form in Russia in the 1960s and 1970s, and was first done in the United States in 1978.

Despite RK’s long history, refractive surgery is still in its “early toddlerhood,” says Jeffrey Robin, M.D. Head of the department of refractive surgery at the Cleveland Clinic, Robin foresees a broader spectrum of procedures, pending laser approval, that will include RK, PRK, and others now under study.

“There’s a growing menu of approaches that can potentially help people with a variety of refractive errors—low, moderate and high nearsightedness, farsightedness, and even presbyopia [farsightedness associated with aging],” he says, noting that surgeons are also combining the knife and laser techniques to try to achieve better accuracy and effectiveness, especially for very nearsighted people.

For example, in an experimental procedure called laser in situ keratomileusis (LASIK), the surgeon uses a knife to cut a flap of corneal tissue, lases targeted cells beneath it, and then replaces the flap.

“Possible advantages of LASIK are better results with high myopia, less chance of scarring and haze, faster recovery, and less pain than simple PRK,” says FDA’s Emma Knight, M.D., an ophthalmologist with the agency’s Center for Devices and Radiological Health. “From FDA’s standpoint, we want to know not just if LASIK is a good enough procedure, but if it is as good or better than PRK. So we’ve asked people to do randomized studies.” ■

—M.S.

that may soon become available in the United States is photorefractive keratectomy, or PRK.

In this procedure, the surgeon operates an excimer laser programmed to deliver bursts of ultraviolet light that vaporize precisely targeted corneal cells. The effect, as in RK, is to flatten the cornea. Also like RK, PRK takes about 15 minutes and is done under topical anesthesia.

Last October, FDA’s ophthalmic devices advisory panel recommended conditional approval of one firm’s excimer laser for refractive surgery, pending reformatting and reanalysis of some of the data. The panel also asked the manufacturer to submit a training program for surgeons and a patient information booklet.

“This is the first time the agency has critically assessed safety and effectiveness data of any device for refractive

surgery,” says FDA’s Knight, “and the meeting was long and full of debate.”

The primary differences expressed by panel members concerned effectiveness criteria. Some felt the laser was somewhat more precise than RK, and so the criteria should be tighter than what the community had accepted for RK, Knight says. “We may decide there shouldn’t be one single criterion, but that it’s important instead for patients to know their probability of achieving, say, 20/20, 20/25 or 20/40,” she says. For instance, Knight explains, “Someone who can’t see the clock beside the bed might be very happy with 20/40 vision—being able to get around without glasses except maybe to drive, whereas someone with very low myopia probably won’t be happy if they have to wear glasses after surgery. It really depends on patient expectation.”

According to the American Academy

of Ophthalmology, RK results are best in patients with low to moderate nearsightedness and generally is not recommended for people with a correction higher than -5 diopters. Data presented at the meeting indicate that PRK may be effective for people with myopia too severe for RK.

Mary Taylor had her first PRK in November 1993. The highly myopic 42-year-old Winchester, Va., woman had worn glasses since second grade. Her correction was -9.5 diopters in one eye and -10 in the other.

"I tried contacts a few times, but never really got comfortable with them," she says, "and, although I didn't especially mind wearing glasses, I was bothered by how helpless I felt without them. The thought of losing them if something happened while I was driving or swimming—even if I had a spare pair—was always a worry in the back of my mind."

Taylor says she received about 700 laser bursts at periodic intervals during the procedure. Then the doctor put a soft "bandage" contact lens in her eye to be worn the next few days until the surface cells healed. She was given a nonsteroidal anti-inflammatory eyedrop for pain and a prescription for additional pain medicine, if needed.

"That first day I felt a mild discomfort, like a residual scratchiness after removing a piece of sand from the eye. It was gone when I woke up the next morning," Taylor says. Although her vision improved greatly immediately, it took about a month or two, she says, before she was seeing 20/20. Six months after the first operation, she returned for surgery in the second eye.

As of October 1994, according to Taylor's doctor, her vision was 20/25 without glasses and 20/20 with glasses, and her correction was -0.75 diopter. Taylor says she still has some trouble with night glare and needs glasses to drive at night, but she's delighted with the results. "For the first time in my life that I could remember, I could see my feet in the shower," she says.

RK vs. PRK

Jeffrey Robin, M.D., has a unique perspective on RK and PRK. Head of the department of refractive surgery at the Cleveland Clinic, Robin has done both

procedures on patients in clinical trials and has, himself, undergone both procedures.

"I've worn glasses since I was eight, and started wearing contact lenses when I was 17 or 18," Robin says. "I went through many pairs of lenses—tore them, slept in them. I was not a good contact lens patient and I detested wearing my glasses, basically because I didn't perceive I was seeing well with them," he says.

About four years ago, at age 35, Robin had an 8-incisional RK in his right eye. A year later, he had PRK in the left. He felt only minor, temporary discomfort after both surgeries, but says that before anti-inflammatory drops were used with PRK, that procedure often produced intense post-surgery pain.

"With RK, vision is almost instantaneously improved—I went from about 20/800 to better than 20/20 the morning after surgery," Robin says. "After PRK, I had better than 20/20 after about 10 days to two weeks. The big difference with the laser is that the correction is solid—there's no visual fluctuations and really no starbursting like you get with RK. Except for the couple of weeks after my RK when I used night driving glasses, I haven't worn glasses since. I've almost forgotten I ever wore them."

Hersh and Robin agree that PRK may prove more effective than RK for higher myopia and may carry less risk for substantial complications such as infection or cataract. Also, hyperopic shift has not been seen with PRK, nor is the cornea weakened as it is in RK. On the other hand, Robin says, "we have 15 or 16 years of experience with RK as opposed to about four years with PRK. Between 1 million and 2 million Americans have had RK and probably only 4,000 to 5,000 have had PRK, so we kind of know the warts—the good and bad sides—of RK whereas we don't really know all those things with our more limited experience with PRK."

Both refractive surgeries are considered cosmetic procedures and are not covered by insurance. Robin says that RK generally varies from \$600 to \$1,500 per eye and laser surgery costs around \$2,000 per eye.

Prospects for 20/20 in 2020

Visions of a world entirely without glasses in the foreseeable future are probably premature; refractive surgery is not for everyone.

"From a medical standpoint, we are most concerned about people who have wound healing problems," Robin says, "because in all these procedures, the results are ultimately affected by two things—what we do as surgeons, and

People who are not comfortable with the possibility that they may still need glasses or contact lenses at least part-time after refractive surgery are probably not good candidates.

then how the patient's body reacts to the laser or knife wounds."

For this reason, patients with connective tissue diseases such as rheumatoid arthritis or lupus erythematosus probably would not be good candidates, nor would people who are taking oral corticosteroids or immunosuppressive drugs or who are immunosuppressed from illness such as HIV infection. People with severe eye diseases, such as poorly controlled glaucoma, macular disease, retinal problems, extremely dry eyes, and certain corneal problems likely would be ruled out also.

Robin, Hersh and Knight all agree that people who are not comfortable with the possibility that they may still need glasses or contact lenses at least part-time after surgery are probably not good candidates. Prospective patients should carefully weigh their hoped-for benefits against the calculated risks. After all, no surgeon can guarantee 20/20 vision except for hindsightedness. ■

Marian Segal is a member of FDA's public affairs staff

CONDITIONS MEN GET, TOO

by John Henkel

Seymour Kramer noticed a patch of what looked like blood on his pajama top three years ago and thought he had cut himself. But he wasn't scratched. His doctor tested the discharge and told the New Jersey man he had breast cancer.

Dan, 70, a retired Michigan engineer who asked that his last name not be used, was pulling weeds three years ago. For no apparent reason, he fractured two vertebrae. Doctors told him his bones were wasting away. He has osteoporosis.

As a teenager, Gary Grahl was obsessed with having a trim, "athletic" body. The Wisconsin resident shunned food and exercised excessively. Sometimes he'd do situps and pushups for three hours before school. He ate little and shrank from 160 to an unhealthy 104 pounds. Over a six-year period, he was hospitalized four times. Now 26, Grahl says he is "completely recovered" from his eating disorder.

What do these men have in common? They all suffer from illnesses typically thought of as "women's diseases." Breast cancer, osteoporosis, and eating disorders all occur in men, too, though their prevalence is much greater in the female population. As a result, many men, unaware that the diseases affect both sexes, may fail to recognize symptoms. Likewise, doctors and families often don't suspect these illnesses. This can delay therapy and make disorders difficult to treat.

Medical experts say men may shy away from seeking medical treatment



Following his breast cancer

treatment three years ago,

Seymour Kramer mounted what

he calls "a crusade" to inform

men that breast cancer is not

just a woman's disease.

Many men, unaware these diseases affect both sexes, may fail to recognize symptoms.

for disorders they feel are unmasculine. In support groups, men use terms like “very scared” and “ashamed” to describe initial feelings about their illnesses. Others express frustration at the difficulty in finding information and therapy.

Osteoporosis

High on the list of such conditions is osteoporosis. Though women are four times more likely to acquire it, about 5 million men in this country have osteoporosis, according to the National Osteoporosis Foundation. A disorder in which bones become weakened, osteoporosis is sometimes called the “silent disease” because it has no symptoms. It often manifests itself in fractures of the hip, wrist, spine, and other bones. Among both sexes, it is responsible for 1.5 million fractures a year.

Scientists are still piecing together just how osteoporosis develops, but it is well known that a key factor is deficiency of the mineral calcium. Leo Lutwak, M.D., Ph.D., a medical officer in FDA’s Center for Drug Evaluation and Research, emphasizes that calcium intake over a person’s lifetime is crucial to preventing bone loss. Ideally, he says, a diet adequate in calcium starting in childhood “can maximize peak bone mass,” helping to ensure strong bones and make osteoporosis less likely. The revised food label that went into effect in 1994 can help consumers pinpoint calcium-rich foods (see the May 1993 issue of *FDA Consumer*).

About 99 percent of the body’s calcium is stored in bones and teeth. Bone is continually being broken down and rebuilt. If the amount of calcium absorbed equals the amount lost, a state of balance occurs. When calcium absorption is greater than losses, the body accrues a “positive balance” that it can use for bone growth and repair. But when dietary intake of calcium can’t meet the body’s needs, the body draws the mineral from bones to allow a constant

bloodstream supply. Ultimately, the breakdown process can exceed deposits, causing a possible reduction in bone mass and density.

Osteoporosis is seen less often in men than in women for several reasons. Men generally have greater bone mass than women, and in males, bone loss begins later and advances more slowly. But men do have a hormonal drop-off in testosterone similar to women’s reduction of estrogen after menopause. Testosterone may diminish as a result of hypogonadism, a condition marked by decreased function of the testicles. Testosterone levels may naturally become lower as a man ages.

“Loss of sex hormone results in accelerated bone loss in whomever it occurs, whenever it occurs, for whatever reason,” says Michael Kleerekoper, M.D., deputy associate chairman of internal medicine at Wayne State University. “Whether that translates to osteoporosis depends on how much

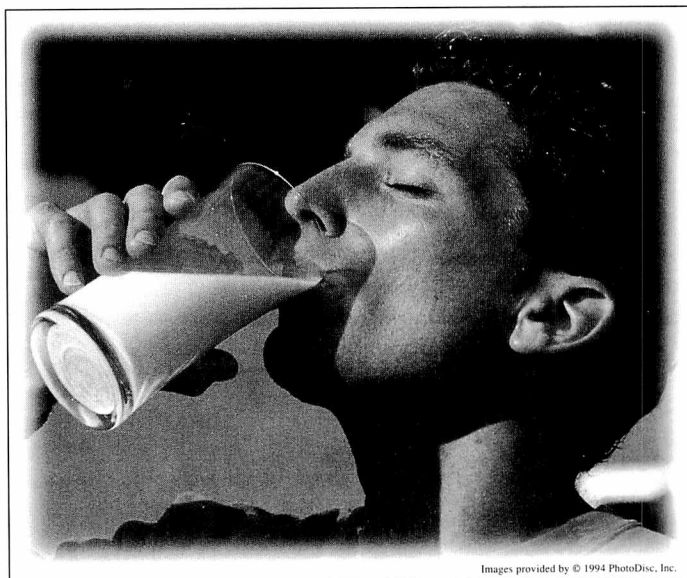
bone you have when the loss begins and how quickly you lose it.” Women find relief from osteoporosis with estrogen therapy, and some men respond to testosterone injections. But successes with hormone therapy come most often from “seeing young men in the early stages” of the condition, Kleerekoper says.

Another therapy shown to slow bone breakdown and reduce pain associated

with fractures attributed to osteoporosis is the drug calcitonin, marketed as Miacalcin or Calcimar. FDA has not approved these drugs specifically for men, though some doctors prescribe them to males if they feel the patient will benefit. Currently under study for osteoporosis treatment are sodium fluoride, which some researchers think may help increase bone mass; vitamin D, which helps the body absorb calcium; and a nasal spray version of calcitonin.

Dan, the Michigan osteoporosis patient, receives biweekly testosterone injections and takes daily supplements of 1,500 milligrams of calcium with vitamin D. He also exercises in a swimming pool, where water provides a beneficial resistance to movement. He says his two fractured vertebrae three years ago made him realize that osteoporosis gives no warnings.

Factors that raise the risk of osteoporosis include cigarette smoking, alcohol consumption in excess of two



Experts say a diet adequate in calcium starting in childhood is one of the best ways to help prevent osteoporosis. An excellent source of calcium is milk, preferably low-fat or skim.

**“Men need to get the word that, yes, this is a woman’s disease.
But you’re not immune. It can happen to you.”
—Seymour Kramer, breast cancer patient**



*Dried beans, broccoli, spinach,
sardines, and skim or low-fat dairy
products are all good dietary sources
of calcium.*

drinks a day, advanced age, and an inactive lifestyle.

Eric, 45, says years of inactivity helped bring on his osteoporosis. In his early 20s, the New York resident (who asked that his last name not be used) had several sports accidents that seriously impaired his mobility. An eating disorder in college also encouraged development of the condition, he suspects. Now, his bone loss is so severe that “anytime I have an x-ray, the doctors go into shock,” he says. He risks injury by simply taking a walk and cannot stand barefoot on a hard floor without excruciating pain. He is taking calcitonin, which he hopes will stabilize his bone loss and allow him to do more walking.

Though osteoporosis cannot be cured, it can be slowed down and steps can be taken to prevent it. The National Osteoporosis Foundation suggests these preventive measures:

- Eat a balanced diet rich in calcium.
- Exercise regularly, especially in weight-bearing activities.
- Don’t smoke.
- If you drink alcohol, do so in moderation.

Breast Cancer

Primarily associated with women, breast cancer also occurs in men, although rarely. According to the American Cancer Society (ACS), men will make up 1,400 of the 183,400 new cases of breast cancer expected in 1995.

Men typically do not perform breast self-examinations to detect tumors, and doctors do not ordinarily examine men for breast cancer during physicals. Unlike women, men do not get routine mammograms. Consequently, a tumor may be present and go undiscovered.

As with breast cancer in women, symptoms include the presence of a breast lump that is usually firm and painless. The nipple can have an abnormality such as retraction, crusting, or a discharge. Patients frequently are over 60.

Men with eating disorders often are medically obese at some point in the illness and feel pressure to be thin.

Seymour Kramer was 70 when a gooey, bloodlike discharge from his nipple prompted him to seek medical attention. After analyzing the secretion, doctors told him he had breast cancer and recommended a lumpectomy, in which the nipple and a small amount of breast tissue are taken out. He also had several lymph nodes removed, and he underwent five weeks of radiation therapy to help ensure that residual cancer cells were killed. Though his prognosis appears very good, Kramer won't say he's been cured. But he expresses optimism: "Just because I had cancer doesn't mean my life is over."

The ACS says risk factors for male breast cancer include:

- hyperestrogenism, or abnormal secretion of the hormone estrogen
- Klinefelter's syndrome, a male disorder characterized by reduced or absent sperm production, small testicles, and enlarged breasts
- gynecomastia, or enlargement of the male breast. Though medical professionals typically don't recommend detection exams for the general male population, doctors may advise men with gynecomastia to perform periodic breast self-examinations.

Because in men the disease is often detected at an advanced stage when the tumor has spread, radical mastectomy—removal of breast tissue and pectoral muscle—is often the initial treatment. But if the cancer is found before it spreads to surrounding tissue or to the lymph nodes, a lumpectomy can be performed. Radiation sometimes is used without surgery, but the verdict is still out on its effectiveness. As in Kramer's

case, radiation also can be employed after surgery to reduce the chance of local recurrence and to relieve symptoms in advanced cases. If cancer has spread into the lymph nodes, some physicians use chemotherapy. A therapeutic "tumor vaccine" for men and women to treat breast cancer that has already spread is in clinical trials now.

Possible complications after surgery or radiation include decreased shoulder function, fluid retention in the arm, and pain or stiffness in the operated or radiated area. The ACS emphasizes that besides tending to the physical conse-

quences of breast cancer therapy, "attention should be paid to the psychological aftereffects."

Patients also need follow-up monitoring—including regular exams, blood chemistry, imaging (such as magnetic resonance imaging), and bone scans—to discover any recurring tumors quickly.

Kramer says his experience of being blindsided by the disease put him on "a crusade" to inform men and medical professionals about breast cancer in males. "During a routine physical exam, I think doctors should run their hands across a man's breast to see if there's anything irregular," he says. "I'm not saying men have to go out and get wholesale mammograms. But [as a rule] doctors don't do this [touch test] and men don't inspect themselves. Those men who are not aware need to be shocked into the fact that, 'Hey, guys, this could happen to you.'"

Eating Disorders

Though many people associate eating disorders with women, these illnesses also occur in males. In one disorder, anorexia nervosa, the person limits food intake to the point of starvation. In another, bulimia nervosa, sufferers alter-

nate between eating large amounts of food and ridding the body of it through vomiting or laxative use. About half of those with anorexia also have bulimia symptoms.

According to the National Association of Anorexia Nervosa and Associated Disorders (ANAD), men make up about 1 million of the 8 million Americans with eating disorders.

"It's a myth that these are illnesses of



In a procedure called a lumpectomy to treat breast cancer, Seymour Kramer's left nipple and surrounding tissue were removed. Several lymph nodes under the arm also were taken out.

Men will make up 1,400 of the 183,400 new cases of breast cancer expected in 1995.

rich, white, perfectionist women,” says Chris Athas, ANAD vice president. “Just as a man or woman may become an alcoholic, either may fall victim to an eating disorder.”

Medical professionals say the disorders most often surface during the teen years, but in rare cases, men as old as 60 and boys as young as 8 can be afflicted. In both sexes, the illnesses can lead to lifelong medical and psychological complications. An estimated 6 percent of cases result in death. Most people find it difficult to halt the behavior without professional assistance. Though some men ultimately seek help, many continue untreated with the disorders, often for years, and sometimes for a decade or more.

Diagnosis is complicated by a reluctance some men have to seek medical help for disorders that are “still primarily women’s,” Athas says. “We live in a ‘macho’ society. Many men simply are ashamed to have an illness of this type.” Thus, they suffer in silence.

Another problem, says ANAD, is that a great number of doctors and health-care professionals are not trained to identify or treat male eating disorders, especially anorexia. Families, too, often fail to see the diseases’ symptoms. The illnesses then can progress to a more advanced stage where they are harder to treat.

During recovery, men sometimes are unwilling to participate in support-group sessions because the groups are mostly female. “Men as a whole are not comfortable in eating disorder support groups,” says Athas. “But we encourage them to go anyway.”

Unlike many women, who acquire eating disorders because they “feel” fat, men often are medically obese at some point in the illness and feel pressure to be thin. Sometimes athletic activities induce this struggle to be lean, prompting not only the eating disorder but also compulsive exercising. Men also may adopt disease behaviors when teased or

For More Information

Sources of information and support for the disorders described in this article include:

- National Association of Anorexia Nervosa and Associated Disorders, Box 7, Highland Park, IL 60035—Offers free programs to help victims and families, including counseling, support groups, health-care referrals, and a newsletter; telephone (708) 831-3438.
- National Osteoporosis Foundation, 1150 17th St., N.W., Suite 500, Washington, DC 20036—Will send information packet and can refer patients to support groups; telephone (1-800) 223-9994.
- The Cancer Information Service, 550 N. Broadway, Suite 300, Baltimore, MD 21205-2004—Will provide information on male breast cancer and can refer callers to cancer centers and support groups; telephone (1-800) 4-CANCER. ■

criticized about being fat at critical development stages, such as puberty.

Treatment can be very effective, according to Arnold Andersen, M.D., an expert on eating disorders in men who has written a book on the subject. He describes a regimen of inpatient or outpatient hospital treatment, depending on the illness severity. Conditions such as anemia or depression are treated, and patients gradually relearn proper eating habits. Treatment also usually includes psychotherapy, which helps patients understand why they have the illness.

One antidepressant drug, Prozac (fluoxetine hydrochloride), is under review by FDA as a treatment for bulimia. Other antidepressants also are being studied. One, Wellbutrin (bupropion), was shown to induce seizures in both anorexia and bulimia patients. Doctors sometimes prescribe tricyclic drugs—a class that includes Elavil (amitriptyline), Tofranil (imipramine), and Norpramin (desipramine). FDA has approved tricyclics for other uses but not specifically for eating disorders. However, doctors may prescribe approved drugs for

“off-label” uses if, in their judgment, the patient will benefit.

Patients also undergo what Andersen calls “nutritional rehabilitation,” which allows them to regain a desirable body weight. Treatment is followed by weeks, months, even years of follow-up to ensure complete recovery.

Men in support groups for eating disorders, as well as those for breast cancer and osteoporosis, say the public gradually is becoming more aware that these disorders can occur in men. They also say there’s a long way to go. Some think doctors need to be enlightened. Others bemoan the lack of research. But most seem to agree that men should be educated about the disorders and how to detect them.

As breast cancer patient Seymour Kramer says: “Men need to get the word that, yes, this is a woman’s disease. But you’re not immune. It can happen to you.” ■

John Henkel is a staff writer for FDA Consumer.

Making It Easier To Read Prescriptions

by Dixie Farley

Sig: $\dot{\tau}$ tab po qid pc & hs

Unless you have a medical background, that bunch of letters probably looks like gobbledygook. In fact, it's several abbreviations for Latin terms used on prescriptions (see chart), in this case telling the pharmacist, "Label the container for this patient's medication with the following instructions: Take one tablet 4 times a day, after meals and at bedtime."

But if some health professionals get their way, prescriptions may soon be easier to read—and therefore safer, since improved readability helps prevent medication mix-ups.

In separate efforts, the Food and Drug Administration and the American Medical Association recently urged medication prescribers to take new precautions with prescriptions.

Patients should take precautions, too, says Thomas McGinnis, R.Ph., associate director for pharmacy affairs at FDA. "If the directions written on a prescription seem confusing, ask your doctor or pharmacist to explain, until you fully understand how to take the medication."

The Rx

The Drug Enforcement Administration requires that prescriptions for controlled substances (drugs regulated by the Federal Controlled Substances Act) state the patient's name and address, date, name of the prescribed drug, dosage strength and form (such as 10-milligram tablets), amount to be dispensed, directions for use, number of allowed refills, and the prescriber's name, address, DEA registration number, and signature.

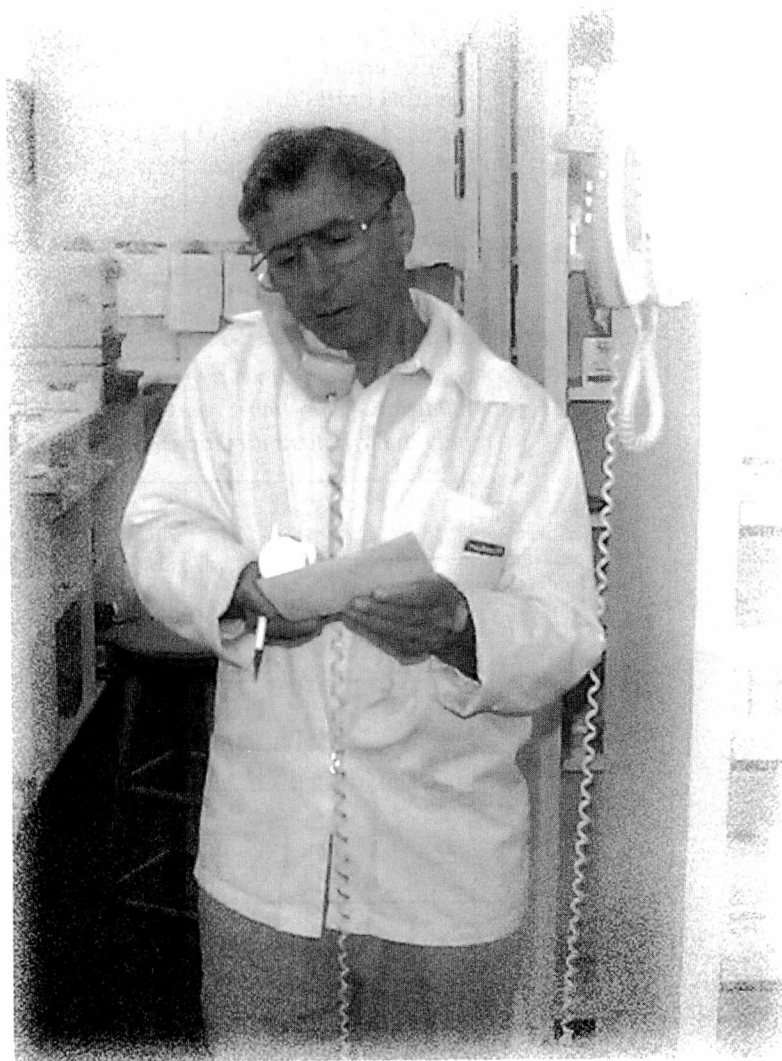
States may make additional require-

ments. And they regulate the information on other prescriptions.

Since September 1993, for instance, all Texas prescriptions have had to include the intended use of the drug, unless the prescriber decides this inclusion is not in the patient's best interest.

"At the same time, we strengthened the confidentiality portion of our statute," says Steve Morse, R.Ph., assistant director of compliance with the Texas State Board of Pharmacy, in Austin.

About 2 in 100 prescriptions are unclear, warranting a call to the doctor, says registered pharmacist Sol Chalom at the Rockville, Md., pharmacy where he practices.



"The law makes it very clear that pharmacists may not share usage information except as the patient directs, or with other health-care professionals when the pharmacist determines that passing this information on would be in the best interest of the patient, or with certain regulators, such as DEA, as required by law."

The Institute for Safe Medication Practices, in Warminster, Pa., also advocates putting the intended use on prescriptions, says pharmacist Michael Cohen, president of the institute. Many prescribers agree with this practice, Cohen says, while others argue against it. A number of states already require the use to be on drug orders for patients in long-term care facilities, he says.

"There's no question in my mind," Cohen says, "that if the doctor generally included the drug's use on the prescription, most drug name mix-ups that occur would never happen."

Look-Alike Names

Mix-ups of drugs whose names look alike in handwriting or sound alike have also been a concern to FDA, which has received numerous reports. Jerry Phillips and other colleagues on FDA's Medication Error Subcommittee began tracking this type of medication error in June of 1992.

"We review each report," Phillips says, "and, if warranted, we may call for the manufacturer to change a product's labeling and packaging, or even its name."

Examples of look-alike names and the

approximate number of reports are:

- Norvasc (amlodipine besylate) for high blood pressure, and Navane (thiothixene) for psychosis, 35 reports
- Levoxine (levothyroxine) for low thyroid, and Lanoxin (digoxin) for heart failure, 25 reports
- Prilosec (omeprazole) for duodenal ulcer, and Prozac (fluoxetine) for depression, 12 reports.

In the February 1995 *FDA Medical Bulletin*, the agency advised printing or typing prescriptions for drugs with look-alike names. "It's the handwritten or verbal orders that have been misinterpreted," Phillips says. Including the diagnosis on these prescriptions also could help prevent mix-ups, he says.

At FDA's request, Levoxine's manufacturer changed the name to Levoxyl. Also at FDA's request, Prilosec's name was changed in 1990 from Losec, which was being confused with the diuretic Lasix (furosemide).

In addition, some doctors today may be able to send prescriptions directly to pharmacies by computer, bypassing handwritten prescribing.

More Clarifying

The American Medical Association, at its annual meeting in 1994, recommended ways to make prescription writing clearer.

AMA's recommendations include:

- If handwriting is illegible, use a com-

Anatomy of a Prescription

States may vary in what they require on a prescription. This example was made up to show most types of possible information. Latin terms appear only in the patient directions, and ambiguous terms are discouraged.

Prescriber's Printed Name and Address	HELEN R. WALSH, M.D. 620 BEACHWOOD DRIVE, SUITE 30 ALEXANDRIA, VA. 22307		DEA Number (required for controlled substances)
	(703) 329-4567	DEA# AH1234567	
Patient Identification	NAME <u>John Smith</u>	AGE <u>10</u>	
	ADDRESS <u>18 Wye Ct Reston VA 22090</u>	DATE <u>6-21-95</u>	Date
Inscription (drug name and strength)	R <u>Tylenol #3</u> <u>#15 (fifteen) tablets</u>		
Signa (patient directions)	<u>Sig: 1 tab po q6h c food</u> <u>prn pain</u>		
	<input type="checkbox"/> Dispense As Written <input type="checkbox"/> Voluntary Formulary Permitted	Refill <u>0</u> Times <input type="checkbox"/> Label	Refills Authorized Signature of Authorized Prescriber
	<u>Helen R Walsh MD.</u> Signature of prescriber		
If neither box is marked, a Voluntary Formulary product must be dispensed. (Source: Institute for Safe Medication Practices, Warminster, Pa.)			

Prescription Symbols

Latin served a good purpose on prescriptions when they were first written in the 1400s. Spread widely by Roman soldiers and traders, Latin was the main language of western Europe for hundreds of years. It was unlikely to change, because it was a “dead” language, and it was unlikely to be misinterpreted, because it was exact in its meaning. Of course, the patients who didn’t know Latin probably didn’t have the vaguest idea what they were taking.

The only part of a prescription where Latin appears today, however, is in the directions for taking the drug. This use has become a kind of medical shorthand. (See chart.) Some of these abbrevi-

ated terms have the potential to cause medication errors because they look so similar in handwriting, so their use is on the decline.

Where does the “Rx” for “prescription” come from? Its origins are given variously as an abbreviation of the Latin word “recipe,” meaning “take,” or as a representation of the astrological sign of Jupiter, ♃. This sign was placed on ancient prescriptions to invoke that deity’s blessing on the medicine to help the person get well. More recently, the cross at the end of the “R” has been explained as a substitute period. ■

—D.F.

puterized medication order system, if available. Otherwise, print or type prescriptions.

- Write out instructions rather than use ambiguous abbreviations. (For example, write “daily” rather than “qd,” an abbreviated Latin term for “every day,” which could be misinterpreted as “qid,” meaning “4 times a day,” or “od,” meaning “right eye.”)
- Avoid vague instructions, such as “take as directed.”
- Use the USAN-approved generic drug name, official name, or trademarked name if a specific product is required, rather than a locally coined name or unestablished abbreviated drug name. (For example, use “didanosine,” the generic name of an AIDS drug, or its trade name, “Videx,” instead of the abbreviation “DDI.” USAN stands for United States Adopted Names, a nonproprietary designation for any compound used as a drug, established by negotiation between the manufacturer and the USAN Council.)
- Avoid apothecary or chemical symbols, such as “K,” the chemical symbol for potassium.
- Use a leading “0” in decimals expressing less than one, as in “0.5 mL” (milliliter), but never an ending “0,” as in “5.0 mL.”
- Avoid decimals when possible. (For example, prescribe “500 mg” [milligrams], rather than “0.5 g” [grams].)
- Spell out the word “units” rather than write “u.”
- Use the metric system.

When verbal orders are necessary, AMA recommends that they be fully, clearly and articulately dictated, and then read back by the person receiving the order. (For example, say “three times daily,” rather than the Latin abbreviation “tid.”)

While Latin terms such as “Sig,” for *signa* (“write”) or *signetur* (“let it be labeled”), are still commonly seen on prescriptions, prescribers who follow the new recommendations may soon retire some of these terms and otherwise clarify their drug orders. “Let it be labeled correctly” is the expected result. ■

Dixie Farley is a staff writer for FDA Consumer.

Common Latin Rx Terms

Latin	Abbreviation	Meaning
ante cibum	ac	before meals
bis in die	bid	twice a day
gutta	gt	drop
hora somni	hs	at bedtime
oculus dexter	od	right eye
oculus sinister	os	left eye
per os	po	by mouth
post cibum	pc	after meals
pro re nata	prn	as needed
quaque 3 hora	q 3 h	every 3 hours
quaque die	qd	every day
quater in die	qid	4 times a day
ter in die	tid	3 times a day
ṭ, ṭṭ, or ṭṭṭ		1, 2, or 3 (of the dosage form, such as tablets)



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

■ **Food label placement** will be permitted greater flexibility on packaged foods, according to an FDA final rule effective last May 5. The rule allows the label to be placed on any panel that can be readily seen by the consumer in situations where the principal display and information panels cannot accommodate all required labeling information, and the package has a total surface area of more than 40 square inches. (FR April 5)

■ **Names of patients and those reporting** to FDA adverse events associated with regulated products will not be disclosed by the agency, according to a final rule effective July 3, 1995. The rule helps maintain FDA's ability to collect information about safety risks of human drugs, biologicals, and medical devices. The rule also preempts state or local laws requiring disclosure of an individual's name. (FR April 3)

■ **Jaguar brand bicycle helmets**, model 3060, are being recalled by Protective Technologies International, Inc. (PTI), because the helmet liners failed head impact tests and may not prevent injuries. In cooperation with the Consumer Product Safety Commission, PTI, the manufacturer, is recalling 25,000 helmets sold nationwide at Toys 'R' Us and Target stores from September 1994 to January 1995. Consumers should call PTI at (1-800) 515-0074 to receive a

United Parcel Service tag to return the helmet. PTI will send consumers a new helmet that meets safety standards.

■ **A cumulative orphan products list** is available from FDA. The list, updated monthly, identifies the drugs and biologics granted orphan status under the Food, Drug, and Cosmetic Act. Free copies are available from FDA, Office of Orphan Products (HF-35), Rockville, MD 20857; telephone (301) 443-4718. (FR April 19)

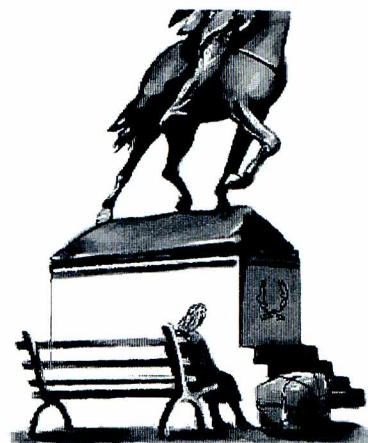
■ **Manufacturers of licensed biological products** can find out about reporting changes in a *Federal Register* document, "Changes to be Reported for Product and Establishment License Applications; Guidance." The document provides manufacturers of licensed biological products guidance on manufacturing changes that don't need prior approval by FDA's Center for Biologics Evaluation and Research director and on changes that do need approval. (FR April 6)

■ **Over-the-counter products** to treat pancreatic enzyme deficiency are not generally recognized as safe and are misbranded, according to an FDA final rule that takes effect Oct. 24, 1995. After that date, no such OTC products may be initially introduced or delivered for introduction into interstate commerce unless they have been approved by FDA. (FR April 24)

■ **Testicular prostheses** can no longer be distributed unless the manufacturer or importer has filed with FDA a premarket approval application or a notice of completion of a product development protocol, according to an agency final

rule effective last April 5. The prostheses are generic, surgically implanted medical devices intended to simulate the presence of a testicle within the male scrotum. (FR April 5)

■ **Homelessness and migrancy** have been added to the list of predisposing risk conditions to qualify a person for the Special Supplemental Nutrition Program for Women, Infants and Children, according to a final rule from the U.S. Department of Agriculture's Food and Consumer Service. The rule was effective last April 19. (FR April 19)



■ **The Social Security Administration** became an independent agency in the U.S. government's executive branch, according to a final rule effective last April 14. Social Security, formerly a part of the Department of Health and Human Services, continues to be responsible for administering the old-age, survivors, and disability insurance and the Supplemental Security Income programs. (FR April 14)



Device Maker Receives Five-Year Sentence in Fraud Case

by John Henkel

A scheme to market ineffective medical diagnostic kits has landed a Pleasant Hill, Calif., man in prison for five years. Following a two-week jury trial, he was convicted on 21 felony counts of fraudulently marketing medical devices, wire fraud, mail fraud, falsifying clinical test data, and violating probation.

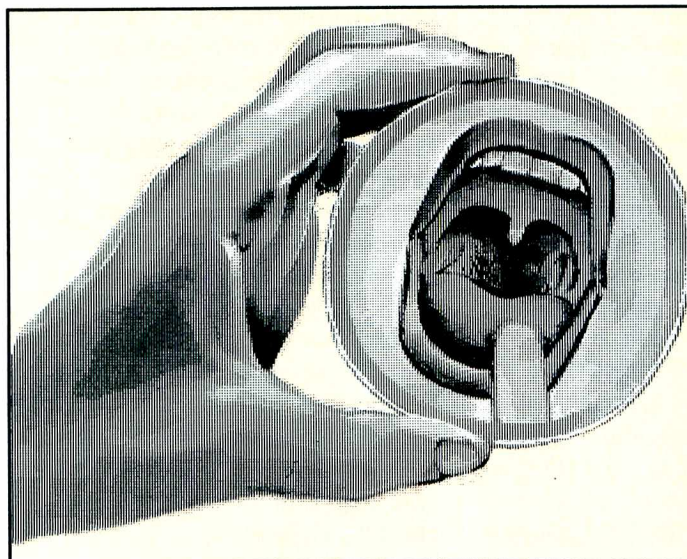
Robert F. Hird, 50, formerly president of Diversified Diagnostics Inc. (DDI), also was ordered to pay \$386,878.25 in restitution to three medical device firms he had defrauded. He began his prison term last March.

Seven years earlier, Hird had pleaded guilty to medical device-related misdemeanor charges and was on probation when charged with the felony offenses in 1993.

The previous conviction resulted from an FDA investigation in the mid-1980s of Biospec, a firm Hird then owned. The investigation showed that culture media manufactured by Biospec for laboratory identification of bacteria was adulterated and ineffective.

FDA secured an injunction ordering the firm to stop selling the adulterated devices and later, through the Justice Department, filed a criminal action charging Hird with 16 misdemeanor counts. These included filing false documents and distributing adulterated devices.

In September 1987, Hird pleaded guilty to the charges and received five years' probation, which included a stipulation barring him from participating in the manufacture of medical devices.



By the time of the probation, however, Hird had already formed DDI and was seeking partners to produce and distribute various medical devices.

The preceding April, before pleading guilty to the misdemeanor charges, Hird received FDA approval to market a kit called the Chromagen culture test. The device checks for strep throat by growing bacteria from a patient's throat swab on a culture plate and testing typical bacteria colonies with chemical reagents to confirm the presence of *Streptococcus*.

In May 1988, FDA rejected Hird's application for approval of a similar device called the Chromagen direct test, designed to detect *Streptococcus* bacteria by applying chemical reagents di-

rectly to the throat swab. FDA told Hird that sale of the Chromagen direct test would be illegal.

Despite this, Hird entered into an agreement in February 1988 with California Integrated Diagnostics (CID) for that company to assemble Chromagen direct test kits using chemical reagents made by DDI. During negotiations with CID, Hird falsely claimed that FDA had approved the Chromagen direct test. Unaware the kits were illegal, CID began assembling and delivering them to Hird.

At the same time, Hird similarly misled officials from Port Washington, N.Y.-based Henry Schein Inc. (HSI) into believing FDA had approved Chromagen direct tests for marketing. As a result, HSI began test-marketing

the devices and, in August 1988, signed an agreement with Hird's company giving exclusive license to make and sell products using DDI-developed technology, including the Chromagen direct test.

DDI shipped the unapproved devices to HSI and collected approximately \$600,000 for the kits, research and development, and loans. HSI distributed the test kits for about a year, unaware that they were not approved devices.

By early 1989, FDA had received complaints claiming the Chromagen devices didn't work. The agency traced the devices to Hird's company and conducted an inspection of the facility between April and May 1989.

The inspection revealed that the Chromagen device being sold was not cleared by FDA and that Hird had violated the terms of his earlier probation. FDA confronted Hird, who called HSI and told officials there about FDA's findings. HSI quickly cut off all business with Hird, stopped selling the test kits, and, in August 1989, sued Hird for civil damages. (The suit went to trial in January 1993, and in June of that year the court awarded HSI \$300,000 in damages.)

Hird then petitioned FDA to reconsider clearing the Chromagen direct test. In November 1989, the agency rejected the petition and, around the same time, referred Hird's case to the U.S. Probation Office in San Francisco. After a hearing, the case was referred to the U.S. Attorney's Office, which directed FDA to investigate the case further to determine the full extent of

Hird's criminal activities.

Between March and October 1991, Hird negotiated with Troy Biologicals, of Troy, Mich., to market the Chromagen direct test kit under the Troy label. Again, Hird falsely claimed that FDA had approved the test. Troy agreed to market the kits and bought 300 of them.

That November, an HSI employee saw the Troy version of the Chromagen direct test, marketed as the Micro-Swab Strep Kit, and recognized it as Hird's uncleared, ineffective device. The employee notified FDA, which went to Troy and asked for documentation showing FDA had cleared the device. Troy contacted Hird, who faxed a fraudulent certification. FDA then prepared to seize devices on Troy's premises, but later found the inventory had been moved to a firm in Massachusetts that had invested in Hird's operations. In February 1992, U.S. marshals seized the kits from the Massachusetts company.

Earlier, Hird had signed a marketing agreement with Bioclinical Systems Inc., of Annapolis Junction, Md., to sell a device that tests for *Chlamydia*, a sexually transmitted bacterium. Between March 1989 and October 1990, DDI conducted studies needed to clear the device. Hird altered the study data to show the *Chlamydia* test to be more effective than actual test results demonstrated. Based on a review of documents submitted with the falsified data, FDA cleared the device in April 1991. Because the data were submitted by Bioclinical Systems and Hird's name

was nowhere on the application, FDA officials were not suspicious.

A month later, Bioclinical Systems began to suspect there was "something fishy about the data," says Alex McCormick, compliance officer in FDA's San Francisco district. Bioclinical ran its own tests and found the *Chlamydia* kit didn't work. In May 1991, after running further tests, the company notified FDA, which investigated the clinics Hird used for the trials. Comparing data sheets for patients on file at the clinics with Hird's submitted data, FDA officials determined that Hird had skewed the data. Hird had claimed a 94 percent effectiveness rate for the test, but FDA found it to be 66 percent—"not much better than flipping a coin," says McCormick.

In September 1992, the U.S. Attorney's Office filed a probation revocation with the U.S. District Court for the Northern District of California. By that December, FDA and the U.S. Attorney's Office were examining further charges and negotiating with Hird for a possible plea bargain. Hird rejected a plea and was indicted in September 1993. In September 1994, a jury found him guilty on 21 felony counts, and he was sentenced the following December.

Because the companies Hird worked with were unaware of the fraudulent aspects of the agreements, none was considered liable.

John Henkel is a staff writer for FDA Consumer.

Canadian Firm Gets Fined For Selling Mail-Order Drugs

A Toronto-based mail-order firm has received a \$500,000 fine—the maximum amount allowed—in federal court for one count of shipping and selling an unapproved generic drug.

Medicine Club International Inc. also was ordered by the U.S. District Court for the District of Maryland last Jan. 5 to pay nearly \$340,000 for investigative costs incurred by the U.S. government. The firm must maintain a \$1 million letter of credit that will be forfeited to the U.S. Treasury if the company manufac-

tures, advertises or distributes adulterated or misbranded drugs during a five-year probation.

The company, which also operated under the name Interpharm Inc., was affiliated with the major Canadian generic drug manufacturer, Apotex Inc.

Medicine Club International practiced

what is commonly called "off-shore pharmacy." From at least January 1991 to August 1993, the company routinely promoted and shipped more than 75 unapproved new drugs into the United States from Canada. Among the drugs were generic versions of Prozac (fluoxetine), used to treat depression; Retrovir (zidovudine), used to treat AIDS; and Tagamet (cimetidine), used to treat ulcers.

The company took consumer orders over an 800 telephone number that it publicized through ads in U.S. newspapers, magazines, and direct mailings. The ads targeted the general public, as well as specific groups such as the male homosexual community, senior citizens, and veterans. Between January 1991 and January 1992, ads ran in 24 different gay publications. Drugs were sold at greatly reduced prices and did not require a prescription. Quantities sold generally were limited to a three-month supply.

By law, companies intending to market generic drugs in the United States must file an abbreviated new drug application (ANDA) with FDA and must be authorized to distribute or sell those products. Otherwise, FDA cannot ensure that such products have been properly manufactured and are effective. Medicine Club International had no ANDA on file and did not obtain authorization to sell the drugs. In addition, the drugs the firm sold require a prescription, but Medicine Club customers were not asked for one.

FDA first became aware of the illegal activities in January 1991, when agency officials saw a magazine ad promoting the mail-order products. The company's ads implied that FDA permits such purchases under its "personal use" policy, which allows individuals to import some unapproved drugs for personal use under certain conditions.

FDA traced the 800 numbers to Toronto and Montreal. From interviews with newspapers and magazines in

which the ads appeared, investigators determined that Medicine Club International (then called Interpharm) was placing the ads and shipping products. An investigator from FDA's Buffalo district office bought drugs undercover from the 800 number. Over the next year, officials from nine other FDA field offices around the country bought drugs.

Based on evidence collected, FDA sent Interpharm warning letters in early 1992 telling the company to stop distributing the drugs. FDA also sent the company written notice that the mail-order products did not fall within the agency's "personal use" policy, which pertains only to products not available in the United States.

But the drug sales continued. To elude FDA, the company changed its name and 800 number. "They didn't heed our warning letters, and they dodged surveillance," says David Kiessling, investigator in FDA's Buffalo district office.

In January 1993, the Federal Bureau of Investigation joined the investigation, and the next month, an FBI agent bought 100 fluoxetine tablets from Medicine Club International. That pur-



chase formed the single count of shipping unapproved drugs under which the U.S. government secured a guilty plea in January 1995 from the firm.

—John Henkel

Shrimp Processor Goes to Jail

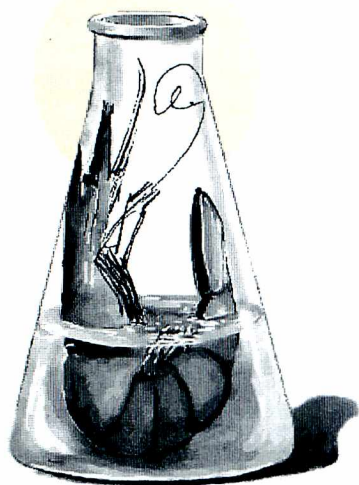
A Massachusetts businessman was sentenced to three years in prison followed by two years' supervised release for selling shrimp that had been illegally treated with chemicals.

The sentencing last March 28 in U.S. District Court for the District of Massachusetts followed an October 1994 conviction of Robert Randazzo, 49, and his firm, New England Shrimp Company, Ayer, Mass., on 101 counts. The charges included conspiracy, making false claims to the U.S. Department of Defense (DoD), distributing shrimp containing sodium hydroxide and sodium tripolyphosphate (STP), distributing Chinese shrimp fraudulently labeled as U.S. shrimp, and filing false tax returns.

Something had "smelled fishy" to federal agents at the firm's processing plant for some time. But it wasn't until suspicious competitors as well as a former employee—fired because he refused to go along with New England Shrimp's illegal activities—complained to federal authorities in February 1992 that FDA and other government agencies got the break they needed.

Acting on the complaints, the Massachusetts U.S. Attorney's Office, DoD, and FDA assembled evidence needed to request a warrant to search the plant. In the early morning of June 30, investigators from FDA, DoD, U.S. Customs, National Marine Fisheries Service, and local law enforcement agencies headed to New England Shrimp to execute the search.

"We had all met the day before to go over the details of the operation," says FDA Boston district investigator John Ridings. "The place was so large that



everyone had to be assigned a specific area to search; the logistics were crazy.”

The search began shortly after 7 a.m., and investigators collected evidence for more than 14 hours. By the end of the search, 136 boxes had been filled with evidence, including production records, financial data, shipping records, memos, and correspondence. They were trucked away to safe storage areas at federal facilities. Also, more than 1.3 million pounds of shrimp, valued at \$2.75 million, was seized.

Investigation of the company’s records and supporting testimony from former employees revealed how New England Shrimp, Randazzo, and former plant manager Daniel Canavan had conspired to violate federal laws.

FDA’s Boston district worked with the U.S. Attorney, DoD, Customs, and the Internal Revenue Service to consolidate the case against New England Shrimp. In early 1994, the government handed down a 101-count indictment.

New England Shrimp had sold more than \$3 million worth of STP-contaminated shrimp to DoD, despite contractual agreements with that agency prohibiting use of the chemical in the shrimp it buys. STP makes the shrimp

retain water, increasing its weight and therefore its price, because shrimp is a weight-based commodity. Also, because STP was used in levels exceeding the limits allowed under good manufacturing practices, the product was regarded as unsafe for human consumption. There were no reports of illness from the shrimp, however.

In April 1994, Canavan pleaded guilty to conspiracy to make false claims against the government in selling the shrimp to DoD, and conspiracy to sell adulterated and misbranded shrimp. He was sentenced to five months imprisonment followed by five months home detention. Randazzo, however, maintained he was innocent and went to trial in October 1994.

During the trial, FDA seafood expert John Noonan demonstrated to the judge and jury how New England Shrimp changed grayish and black-striped shrimp harvested in China to look like pink shrimp from the Gulf of Mexico.

Noonan soaked the Asian-harvested shrimp in containers of sodium hydroxide, chemically burning them to the pinkish-orange color more appealing to American consumers. New England Shrimp labeled and advertised the shrimp as Gulf shrimp.

New England Shrimp Company is no longer in business.

—*Joseph Raulinaitis is a public affairs specialist with FDA’s Boston district office.*

N.Y. Cattle Dealer Caught Selling Adulterated Beef

Cattle dealer George Zabadal, of Binghamton, N.Y., was taking a new tack rounding up cattle for slaughter. If a farmer wasn’t around to sign a certificate declaring an animal free of illegal levels of drug residues, Zabadal just signed the farmer’s name. His last such

signing, for an animal that in fact had illegal residue levels, led him to promise to change his ways.

Caught red-handed, Zabadal agreed to terms of a consent decree of permanent injunction for selling adulterated beef. U.S. District Judge Thomas McAvoy, Northern District of New York, signed the decree last Dec. 23. Zabadal agreed to set up and use a written records system—to be approved by FDA—designed to prevent the illegal marketing. In another decree, the farmer also agreed to improve his drug residue control procedures.

Illegal antibiotic residues in meat can cause life-threatening allergic reactions in people sensitive to those drugs. In addition, they contribute to development of antibiotic-resistant strains of bacteria in people who eat or handle the meat.

“This was a small case, but an important one,” says John Thompson, a compliance officer with FDA’s Buffalo district office. “It’s the first animal tissue residue enforcement action we’ve taken against an animal dealer in New York. Maybe it will send a message to some others who aren’t doing their best that FDA takes this problem seriously.”

On Feb. 26, 1993, William Chilton, an animal tissue monitor in FDA’s Syracuse resident post, inspected Zabadal to investigate a report from the U.S. Department of Agriculture that one of the dealer’s animals had illegal residue levels of penicillin and streptomycin. FDA permits no more than 0.05 parts per million (ppm) of penicillin, but this sample showed 0.13 ppm. FDA allows 2.0 ppm of streptomycin, but the sample showed 21.17 ppm.

USDA inspectors at each slaughtering site obtain tissue samples from the slaughtered animals for analysis at a USDA laboratory. The results are then transmitted to FDA by computer through USDA’s Residue Violation

Information System.

During Chilton's inspection, he learned that for more than 40 years, Zabadal had been buying about 800 cattle a year from local farmers in New York and then delivering them for re-sale, usually to slaughter houses in Pennsylvania. "Zabadal admitted he deals mostly in 'down cows,'" Chilton says. "These were usually sick, lame or injured dairy cows, more likely than others to have been medicated. He had already received several warning letters from FDA and USDA for additional drug residue reports in the 1980s."

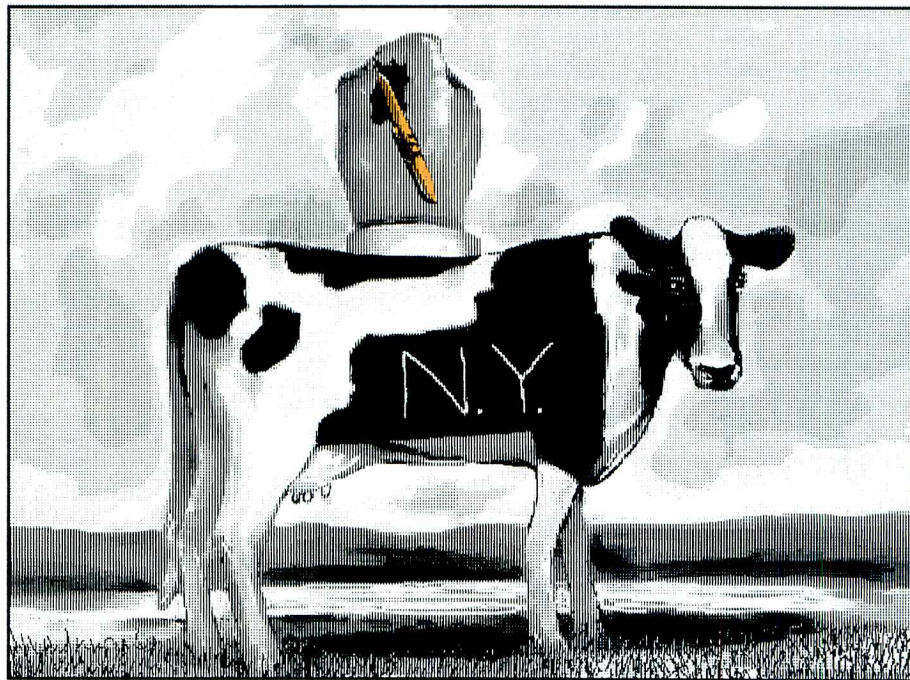
Zabadal had certificates printed, Chilton says, stating that the animal hadn't been medicated or that proper withdrawal time had been observed before a medicated animal was offered for slaughter. "He had his farmers sign this before he'd buy their animals."

Confronted with the new USDA report that found excessive residue levels in one of his cows, Zabadal showed Chilton a certificate signed by the source farmer, Paul Stephen Smith, of Smith Family Farms. Chilton made a copy of the certificate.

In March 1993, Chilton inspected Smith. "I showed him the certificate," Chilton says, "and asked, 'Is that your signature?'" Smith answered, "No. I never signed that." Chilton learned that Zabadal had in fact not even been at the Smith farm that day and that the cow wasn't even there, but at another farm about 70 miles away.

Chilton confronted Zabadal with what Smith had said. Zabadal admitted he signed Smith's name, Chilton says, and that he did this often with his regular sources if a farmer wasn't available or didn't know about the animal's medication status.

Chilton told Zabadal it was his responsibility to ask questions so that he would be certain of every animal's



medication status and to always wait the appropriate drug withdrawal time.

Then, in November 1993, FDA got a notice from USDA that a slaughtered Zabadal cow had an illegal penicillin residue level of 5.08 ppm. Chilton inspected Zabadal again, in January 1994.

"Turns out," Chilton says, "Zabadal had gone to a cattle auction in Sennett, N.Y. When he would buy cows at these sale barns, he'd make no attempt to learn who the owner was to ask about the animal's medication status. But guess who had sold this cow—Paul Stephen Smith."

Chilton again told Zabadal he needed to inquire further about these animals, to be certain he wasn't offering cows with illegal drug residues.

In April 1994, Chilton reinspected Smith and found that his controls to prevent illegal residues were inadequate.

On June 24, Smith signed a consent decree agreeing to develop a records

system for administering drugs, a drug inventory and accountability system, and a system for giving drug records to the cattle buyers, who must certify receiving them. The decree was filed June 27 in the U.S. District Court, Western District of New York.

In July, at FDA's request, a complaint for injunction was filed against Zabadal. The consent decree he signed in December requires a records system that tracks each animal's ear tag number; the date the animal is bought and the seller's name; the date any drug is given and its name, dose, and route of administration; each drug's pre-slaughter withdrawal time; and the date a medicated animal is sold and the buyer's name. Zabadal must obtain from the seller of a medicated animal a signed certificate indicating the animal is drug-free.

FDA is monitoring both the dealer and the farmer.

—Dixie Farley

SUMMARIES OF COURT ACTIONS



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

Summaries of Court Actions are prepared by Food and Drug Division, Office of the General Counsel HHS.

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

SEIZURE ACTIONS

Food/Contamination, Spoilage, Insanitary Handling

PRODUCT: Canned tomatoes, canned peach slices, and canned grapefruit, two seizure actions, at Brooklyn, N.Y. (E.D.N.Y.); Civil No. CV-93-4917.

CHARGED 10-29-93: All of the articles were exported from Canada as part of a salvage lot from a bankruptcy sale and were held at Federation Warehouse in New York, N.Y. The canned tomatoes were adulterated in that they were contained in dented, rusted, swollen, and leaking cans—402(a)(3); the canned peach slices contained *Geotrichum* mold and they were misbranded in that the labels expressed the net quantity of contents in terms of fluid measure rather than in terms of weight measure—402(a)(3) and 403(f). The canned grapefruit contained developed seeds, and the peaches contained pit fragments in excess amount of the applicable standard—403(h)(1). **DISPOSITION:** Default—articles destroyed. (F.D.C. 66764 and 66712; S. Nos. 92-508-941 and 92-508-948; S.J. No. 1)

PRODUCT: Crab meat, frozen, at Philadelphia, Pa. (E.D.Pa.); Civil No. 87-6155.

CHARGED 9-30-87: While held at Blue Grass Distribution Center in Philadelphia, Pa., the article was adulterated after interstate shipment in that the food contained *Listeria monocytogenes*—402(a)(1); the article was prepared, packed and held under insanitary conditions where the food was contaminated with *Escherichia coli*—402(a)(4); the article was misbranded in that the labeling of many of the cartons incor-

rectly identified the product as frozen shrimp instead of crab meat—403(b); and the label failed to state the place of business of the manufacturer, packer or distributor—403(e).

DISPOSITION: Default—article destroyed. (F.D.C. 65261; S. No. 87-441-827; S.J. No. 2)

PRODUCT: Lobster meat, frozen, at Chicago, Ill. (N.D.Ill.); Civil No. 91C703.

CHARGED 7-26-91: While at Americold Corporation in Chicago, Ill., the article was adulterated in that it consisted in part of a decomposed substance—402(a)(3).

DISPOSITION: Default—article destroyed. (F.D.C. 66218; S. No. 91-575-999; S.J. No. 3)

PRODUCT: Sturgeon in tomato sauce, perch-pike, stuffed eggplant in tomato sauce, and stellated sturgeon low-acid canned foods, at Brooklyn, N.Y. (E.D.N.Y.); Civil No. CV-92 4967.

CHARGED 10-20-92: While held for sale at M & A International, Inc., in Brooklyn, N.Y., the articles were adulterated in that they were prepared and packed under conditions which might have rendered them injurious to health due to inadequate processing—402(a)(4); the perch-pike, eggplant in tomato sauce, and stellated sturgeon were misbranded before and after interstate shipment in that they were in package form and failed to bear labels containing the name and place of business of the manufacturer, packer or distributor—403(e)(1); the label of the eggplant in tomato sauce did not appear in English, and the labels of the stuffed eggplant and eggplant in tomato sauce were not expressed in terms of weight—403(f); the label for the perch-pike failed to identify the food by its common or usual name—403(i)(1); and all of the articles were made from two or more ingredients that were not listed on the labels by their common or usual names—403(i)(2).

DISPOSITION: Decree—articles destroyed. (F.D.C. 66462; S. No. 92-638-500; S.J. No. 4)

PRODUCT: White fragrant rice, at Los Angeles, Calif. (C.D.Calif.); Civil No. 89 7136.

CHARGED 12-11-89: While held for sale at PFC Foods, Inc., in Los Angeles, Calif., the article was adulterated in that it had been held under insanitary conditions where it might have become contaminated with filth—402(a)(4); and the article contained insects, insect pupae, insect larvae, and insect skins—402(a)(3).

DISPOSITION: A consent decree of condemnation released the article to the claimant, who voluntarily destroyed and re-

conditioned parts of the article. (F.D.C. 65787; S. No. 90-556-488; S.J. No. 5)

Drugs/Human Use

PRODUCT: Amaphen with codeine No. 3 capsules, at Pittsburgh, Pa. (W.D.Pa.); Civil No. 86-1364.

CHARGED 6-26-86: While held after interstate shipment at Trimen Laboratories, Inc., in Pittsburgh, Pa., the articles were new drugs without an approved new drug application—505(a) and (b).

DISPOSITION: A summary judgment ordered the articles destroyed. (F.D.C. 64732; S. No. 85-419-342; S.J. No. 6)

PRODUCT: Colon Cleanser, Liv-Flush, Kidney Flush, Arthritis Nutrient Formula, Prostate Plus, Cata-Rx, and Aloe/Cranberry Flush, at Long Island City, N.Y. (E.D.N.Y.); Civil No. CV-91-4802.

CHARGED 12-4-91: While held after interstate shipment at L&H Vitamins, Inc., in Long Island City, N.Y., the articles were new drugs without an approved new drug application—505(a) and (b).

DISPOSITION: A decree of forfeiture ordered the articles destroyed. (F.D.C. 65955; S. No. 90-626-621; S.J. No. 7)

PRODUCT: Hauck G-2 and G-3 capsules, at Alpharetta, Ga. (N.D.Ga.); Civil No. 86-1305A.

CHARGED 6-10-86: While held after interstate shipment at W.E. Hauck, Inc., in Alpharetta, Ga., the articles were new drugs without an approved new drug application—505(a) and (b); and the articles were misbranded in that their labeling failed to give adequate directions for use—502(f)(1).

DISPOSITION: A summary judgment ordered the articles forfeited and condemned. The articles were destroyed. (F.D.C. 64698; S. No. 82-482-515/516; S.J. No. 8)

PRODUCT: Liv-Flush, PressuRest, ProZaine, Kidney Flush, Heart-Ex, ChromMate, Blood Cleanser, Whole Dried Cranberry Fruit, Ester C., Bee Pollen, Kyolic, and PROZ Personal Oxygen System, at Brooklyn, N.Y. (E.D.N.Y.); Civil No. CV-91-4802.

CHARGED 12-4-91: While held after interstate shipment at L&H Vitamins, Inc., in Long Island City, N.Y., the articles were new drugs without an approved new drug application—505(a) and (b); the articles were misbranded while held for sale after shipment in that their labeling was false and misleading since they represented and suggested that the articles were safe and effective for their intended use—502(a); and the articles' labeling failed to bear adequate directions for use—

502(f)(1). The Personal Oxygen System was misbranded while held for sale after shipment of one or more of its components—503(b)(4).

DISPOSITION: A portion of the articles was seized on 12-23-91. A consent decree ordered the seized drugs condemned, forfeited and destroyed. As to the drugs that were not seized, the claimant affirmed they did not fill any orders after 12-23-91, they returned any monies received for such orders, and they returned to the vendors the articles in stock or which it might have subsequently received. Furthermore, the claimant informed the vendors that the government considered the articles unlawful. The claimant destroyed any remaining articles. (F.D.C. 66060; S. No. 90-600-481; S.J. No. 9)

PRODUCT: Margensic No. 3 tablets, at Lafayette, La. (W.D.La.); Civil No. 86-1353.

CHARGED 5-29-87: While held after interstate shipment at Marnel Pharmaceuticals, Inc., in Lafayette, La., the articles were new drugs without an approved new drug application—505(a) and (b).

DISPOSITION: A summary judgment ordered the articles destroyed. (F.D.C. 64695; S. No. 85-314-085; S.J. No. 10)

Drugs/Veterinary

PRODUCT: Prozyme enzymatic protein supplement, at Kansas City, Mo. (N.D.Mo.); Civil No. 91-0595-CV-W-8.

CHARGED on or about 7-2-91: While held for sale after interstate shipment at Veterinary Companies of America, Inc., in Kansas City, Mo., the article was adulterated in that it was an unsafe, new animal drug without an approved new drug application—501(a)(5); and the article was misbranded in that its labels failed to bear adequate directions for use—502(f)(1).

DISPOSITION: Default—article destroyed. (F.D.C. 66159; S. No. 90-596-962; S.J. No. 11)

Medical Devices

PRODUCT: Lithotriptor Spark Plugs, at Frederick, Md. (D.Md.); Civil No. B-92-1849.

CHARGED 7-1-92: While held at Frederick Self Storage, in Frederick, Md., the articles were adulterated in that they were class III devices that did not have an application for premarket approval—501(f)(1)(B); and the articles were misbranded in that the labeling failed to bear adequate directions for use, and they were not manufactured in a registered establishment—502(f)(1) and 502(o).

DISPOSITION: A default decree of forfeiture condemned the articles, forfeited the rights and interests of the manufacturer,

and ordered the articles destroyed. (F.D.C. 66430; S. No. 92-516-233; S.J. No. 12)

CRIMINAL ACTIONS

DEFENDANTS: Par Pharmaceuticals, Inc., at Baltimore, Md. (D.Md.); Criminal No. HAR-91-0433.

CHARGED 12-6-91 by grand jury: *Count 1*: The defendant adulterated the drug Cloridine HCl in that it manufactured and processed the drug using methods and controls that did not conform to good manufacturing practices—301(a) and 303(a)(2); *Count 2*: The defendant shipped in interstate commerce the generic drug megestrol acetate, which was adulterated in that the employees prepared and maintained false product batch records and manufactured the drug by adding an ingredient that was not included in the approved formula—301(a) and 303(a)(2).

Counts 3-8: The defendant made false statements to FDA by (a) failing to accurately state the manner, order and instructions by which the drug thioridazine was milled and mixed, (b) failing to correctly show where the drug haloperidol was produced, (c) misrepresenting the batch size of the drug leucovorin calcium, (d) misrepresenting the batch and proportion size of lactose anhydrous NF, Starch 1500, povidone USP, Aerosil 200, stearic acid NF, zinc stearate, Green Caffeine Granulation with Starch, and Orphengesic Forte, (e) falsely creating batch records of the drug methyldopa that did not reflect the unapproved addition of magnesium stearate, and f) recreating batch records, falsifying accelerated stability data, and laboratory reports of the generic drug triameterene/hydrochlorothiazide—18 U.S.C. 1001.

Count 9: The defendant influenced, obstructed and impeded an inspection of its drug manufacturing facility in that its agents and employees falsely represented a batch of tablets to an FDA investigator in order to conceal the fact that the batch did not contain sodium bicarbonate and the fact that the product had not been submitted for bioequivalency testing—18 U.S.C. 1505.

Count 10: The defendant adulterated the drug Tolazamide in that it failed to comply with good manufacturing practices, by preparing and maintaining false batch records—301(k) and 303(a)(2).

DISPOSITION: Guilty plea; a \$2,500.00 cumulative fine and a special assessment of \$200 for each of the 10 counts. (F.D.C. 65712; S.J. No. 13)

DEFENDANT: Padam Bansal, director of research and development, Baltimore, Md. (D.Md.); Criminal No. HAR-92-066.

CHARGED 3-19-93 by grand jury: In connection with Par

Pharmaceuticals, Inc., defendant was charged with obstructing an FDA investigation by giving false and misleading testimony to the grand jury regarding the batch record for the drug triameterene/hydrochlorothiazide—18 U.S.C. 1503.

DISPOSITION: Guilty plea; two years' probation, sentenced to six months home confinement, and ordered to pay a \$50 special assessment. (F.D.C. 66533; S.J. No. 14)

DEFENDANTS: Edward Boden Sr., Edward Boden Jr., and Roger Walsh Jr., Chicago, Ill. (N.D.Ill.); Civil Nos. 89 CR 645-1; 89 CR 645-2, and 89 CR 645-3.

CHARGED 2-23-90 and 3-2-90 by a grand jury: Conspiracy by the three defendants to increase the sales and profits of Bodine's Inc., and their salaries by falsely representing that low-cost adulterated and misbranded products manufactured and sold by Bodine's Inc. were 100% pure orange juice products—301(a) and (k), and 303(b). Foods labeled as orange juice, orange juice from concentrate, and frozen concentrated orange juice were adulterated in that orange juice and orange juice concentrate were omitted from the product and replaced by inferior and cheaper ingredients—402(b)(1) and 402(b)(2).

DISPOSITION: Guilty pleas; Edward Boden Sr. was sentenced to two years in prison, a \$250,000 fine, 1,000 hours of community service, five years' probation, and a special assessment of \$150. Edward Boden Jr. was sentenced to two years' probation, a \$200,000 fine, 200 hours of community service, and a special assessment of \$125. Roger Walsh Jr. was sentenced to two years' probation and 200 hours of community service. (F.D.C. 64573, S. No. 85-499-315; S.J. No. 15)

DEFENDANT: John Sadlon, vice president of operations, Baltimore, Md. (D.Md.); Criminal No. HAR-92-0336.

CHARGED 6-21-95 by grand jury: In connection with Par Pharmaceuticals, Inc., defendant was charged with aiding and abetting in the interstate shipment and adulteration of the drug methyldopa in that it did not conform to good manufacturing practices—301(k) and 303(h).

DISPOSITION: Guilty plea; ordered to pay a \$3,000 fine and a \$50 special assessment; two years' probation and 500 hours of community service. (F.D.C. 66560; S.J. No. 16)

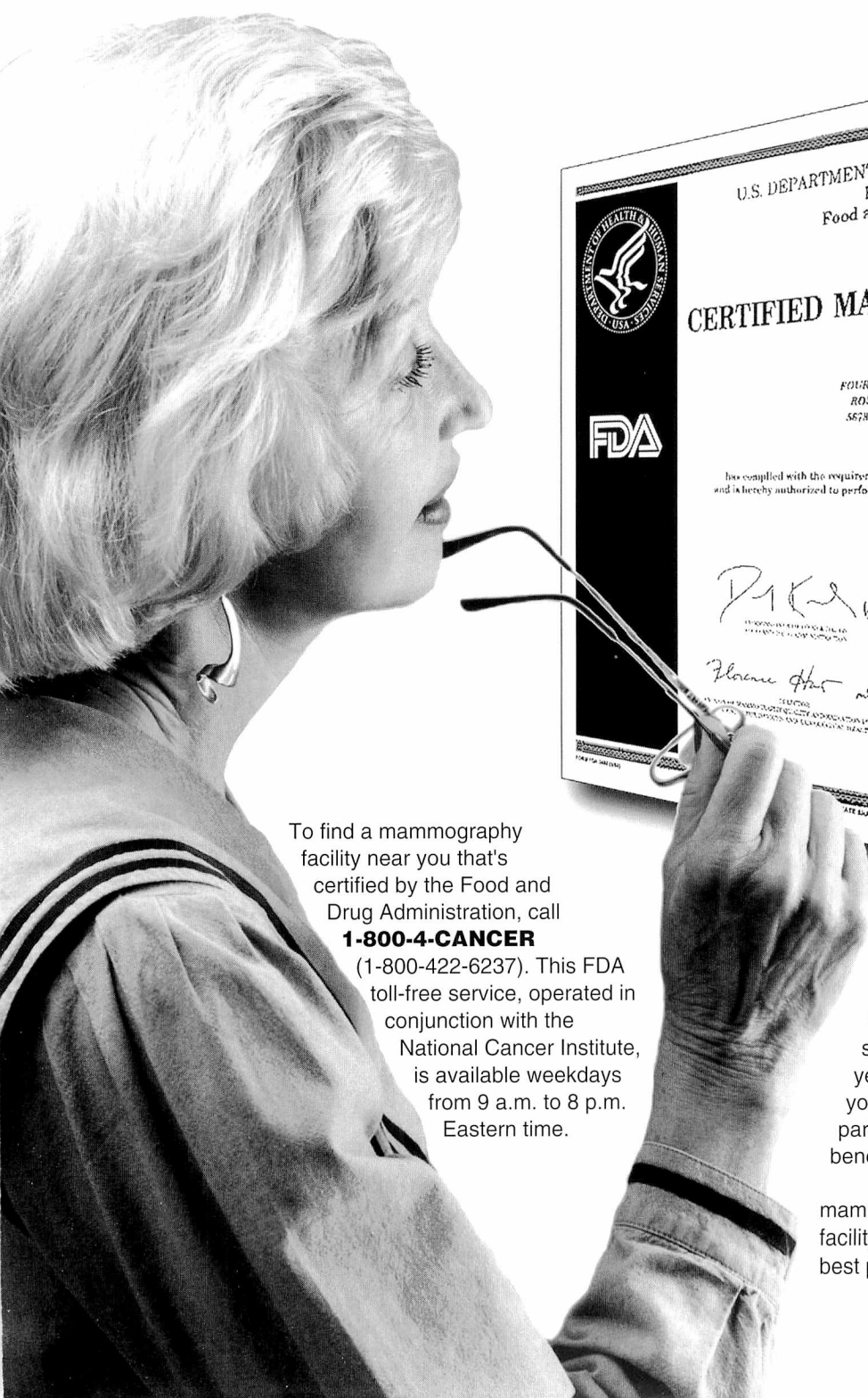
DEFENDANT: Atul Shah, director of analytical research and developmental laboratory, Baltimore, Md. (D.Md.); Criminal No. HAR-92-0337.

CHARGED 3-5-93 by grand jury: In connection with Par Pharmaceuticals, Inc., defendant was charged with making false statements to the grand jury regarding the pilot batch of the drug triameterene/hydrochlorothiazide.

DISPOSITION: Guilty plea; two years' probation and ordered to pay a \$50 special assessment. (F.D.C. 66561; S.J. No. 17)

M Help In Getting A Quality MAMMOGRAM

1 - 8 0 0 - 4 - C A N C E R



U.S. DEPARTMENT OF HEALTH & HUMAN SERVICES
Public Health Service
Food and Drug Administration

CERTIFIED MAMMOGRAPHY FACILITY

This certifies that

FOUR CORNERS RADIOLOGY CLINIC
ROSEWOOD MEDICAL BUILDING
5878 TELEGRAPH LANE, SUITE 410
WASHINGTON, D.C. 20065

has complied with the requirements of the Mammography Quality Standards Act of 1992
and is hereby authorized to perform mammography examinations, pursuant to 42 U.S.C. 283h.

[Signature]
DIRECTOR, CENTER FOR DEVICE EVALUATION
U.S. FOOD & DRUG ADMINISTRATION

[Signature]
FACILITY REPRESENTATIVE

The Center has been accredited by

Facility ID Number:

Expiration Date: November 16,

Patients may report comments/complaints to:

DATE SHALL BE PROMINENTLY DISPLAYED IN THE MAMMOGRAPHY FACILITY

To find a mammography facility near you that's certified by the Food and Drug Administration, call **1-800-4-CANCER** (1-800-422-6237). This FDA toll-free service, operated in conjunction with the National Cancer Institute, is available weekdays from 9 a.m. to 8 p.m. Eastern time.

A mammogram is the best way to find breast cancer early, when it can be treated most successfully. Mammography screening is recommended every one to two years for women over 50, and for some younger women as well. And Medicare covers part of the cost of mammograms for its beneficiaries.

Look for the FDA certificate at the mammography facility you use. It shows that the facility meets federal standards to assure you the best possible mammogram.