

FDA CONSUMER

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

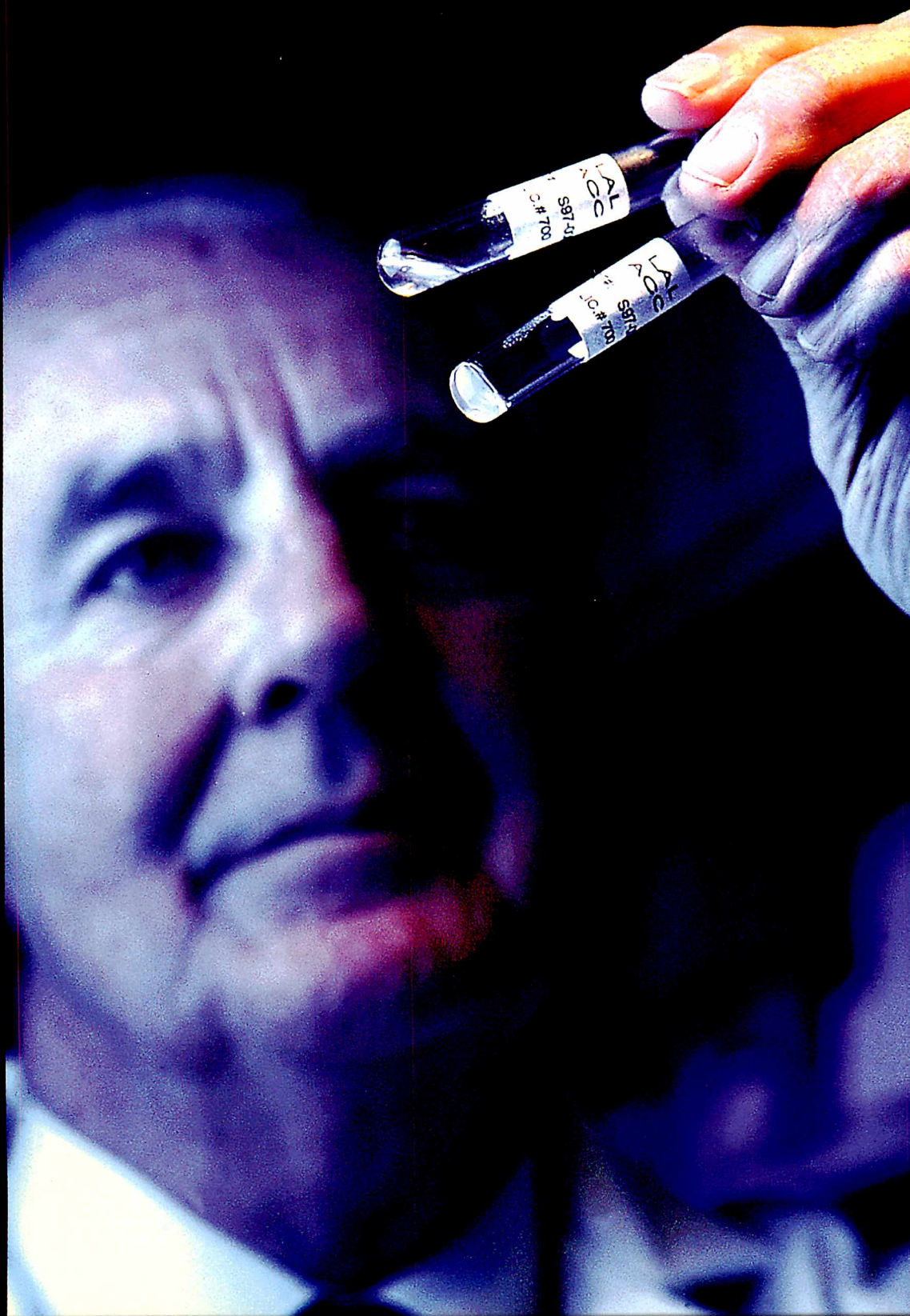
• VOL. 32 NO. 1

January-February 1998 •



Skimming the **MILK LABEL**

Fat-Reduced Milk Products Join the
Food Labeling Fold



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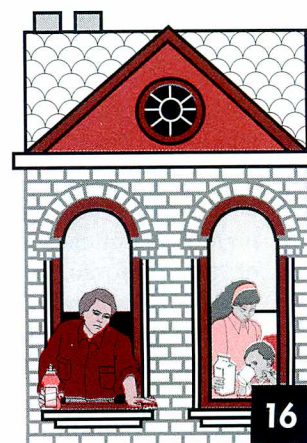
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Which test tube in Don Hochstein's hand holds deadly toxins? The test that tells him it's the lower of the two is one of many medical treasures from the sea. See page 30.



Herbal Fen-Phen Warning

Because so-called "herbal fen-phen" products have not been shown to be safe or effective and may contain ingredients associated with injuries, FDA is taking action to remove these products from the market.

The agency considers the products to be drugs because their names reflect that they are intended for the same use as the anti-obesity drugs fenfluramine and phentermine, which in combination are commonly referred to as "fen-phen."

FDA warned consumers last November about "herbal fen-phen." The agency believed that an increase in use of these alternative products might follow from the September withdrawal based on safety concerns about fenfluramine (Pondimin) and another prescription anti-obesity drug, dexfenfluramine (Redux). In addition, promotion of these products over the Internet and through weight-loss clinics, print ads, and retail outlets is on the rise.

The main ingredient in most herbal fen-phen products is ephedra, also called Ma Huang. Ephedra is an amphetamine-like compound with potentially powerful stimulant effects on the nervous system and heart. Since 1994, FDA has received more than 800 reports of adverse events associated with ephedrine alkaloid-containing products, ranging from high blood pressure and headaches to heart attacks and death.

Many ephedra-containing herbal fen-phen products also contain *Hypericum perforatum*, often called St. John's Wort or "herbal Prozac," which has not been studied under carefully controlled trials.

Other herbal fen-phen products contain 5-hydroxy-tryptophan. This compound is closely related to L-tryptophan, which was pulled from the market after being linked to 1,500 cases, including about 38 deaths, of a rare blood disorder.

New FDA Labeling Rules For Dietary Supplements

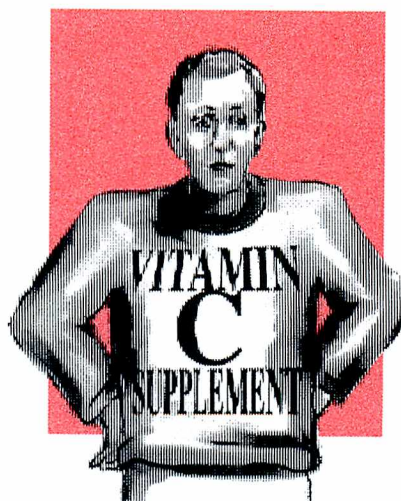
A Supplement Facts panel, modeled after food labeling's Nutrition Facts panel, is among new FDA labeling requirements for vitamins, minerals, herbs, amino acids, and other dietary supplements.

Labels also must identify these products as dietary supplements (for example, "Vitamin C Supplement") and when products have botanical ingredients, the part of the plant used must be identified, according to final FDA rules in the Sept. 23, 1997, *Federal Register*.

The rules, which take effect March 23, 1999, will implement several key provisions of the Dietary Supplement Health and Education Act of 1994.

The Supplement Facts panel must provide information about:

- the appropriate serving
- 14 nutrients, such as vitamins A and C, calcium, iron, and sodium, when present in more than insignificant amounts
- other vitamins and minerals, if they are added or referred to in a label claim
- other dietary ingredients for which there are no FDA-established Reference Daily Intakes.



Also, products must meet certain criteria to be labeled with the terms "high potency" and "antioxidant."

"High potency" will be allowed to describe both individual vitamins and minerals or multinutrient products. When describing an individual vitamin or mineral, it will mean that 100 percent or more of the Daily Value for the nutrient is present in each serving. For multinutrient products, it will mean that one serving provides more than 100 percent of the Daily Value for two-thirds of the vitamins and minerals present.

"Antioxidant" may be used with the already defined claims "good source of" and "high" to describe a nutrient for which a Reference Daily Intake value has been established (for example, vitamin C) and the nutrient is shown by scientific evidence to inactivate free radicals or to prevent free-radical-initiated chemical reactions in the body after a sufficient quantity of the nutrient has been absorbed.

Warnings Added To Seldane Labels

People taking a new hypertension drug or several other drugs should not take the antihistamine Seldane or the antihistamine/decongestant Seldane-D, according to new warnings on Seldane's labeling.

The hypertension drug, Posicor (mibefradil dihydrochloride), joins antibiotics such as erythromycin and antifungals such as ketoconazole, which have long been associated with severe risks when taken with Seldane, Seldane-D, or generic versions containing the antihistamine terfenadine.

The new labeling also warns against taking the antihistamine at the same time as these drugs:

- HIV protease inhibitors such as Crixivan (indinavir), Norvir (ritonavir), Invirase (saquinavir), and Viracept (nelfinavir)
- serotonin re-uptake inhibitors such as Luvox (fluvoxamine), Zoloft (sertaline), and Serzone (nefazodone)
- Zyflo (zileuton)
- Propulsid (cisapride)
- Zagam (sparfloxacin).

In addition, no one should take Seldane, Seldane-D, or the generics with grapefruit juice, and patients with kidney difficulties should not take more than one tablet daily.

FDA is in the process of removing all terfenadine products from the market because of the approval of a safer alternative, Allegra (fexofenadine hydrochloride). (See "Antihistamine Poses Possible Safety Risk" in the Updates section of the April 1997 *FDA Consumer*.) Both Allegra and Seldane are manufactured by Hoechst Marion Roussel Inc.

FDA urges health-care providers to report any terfenadine-related adverse events to the manufacturer by calling 1-800-633-1610 or to FDA's MedWatch program by calling 1-800-FDA-1088.

Final Rules Will Improve Mammography Quality

Final FDA rules on mammography facilities will lead to further improvements in the quality of mammography in the United States.

Under the Mammography Quality Standards Act of 1992, FDA has strengthened the interim rules by which it has certified and inspected almost all 10,000 U.S. mammography facilities. According to the final rules:

- Medical records and reports of mam-

for contents and wording. Facilities must provide the reports to patients, including patients who have not designated a health-care provider. Facilities must make reasonable attempts to notify both patients and health-care providers as soon as possible of reports when results are "suspicious" or "highly suggestive of malignancy."

- Doctors who interpret mammograms must have 60 hours of training in mammography.

- Technologists must average 200 mammograms every two years to keep their skills current.

- Medical physicists who survey the equipment and facilities must meet initial and ongoing training requirements.

- Better defined equipment requirements include specifications for motion of the tube-image receptor assembly, magnification, compression, automatic exposure control, and x-ray film.

- Mobile mammography units must follow quality controls that are more stringent than before.

- At the patient's request, original mammograms must be made available to other medical facilities, allowing comparison with new mammograms.

- Facilities must provide for consumer complaints, so that patients or their representatives (such as family members or referring doctors) have an opportunity to be heard, and serious complaints investigated and resolved.

FDA published its final rules in the Oct. 28, 1997, *Federal Register*.

To obtain names and locations of FDA-certified facilities, call the Cancer Information Service at 1-800-4-CANCER or visit <http://www.fda.gov/cdrh/dmgrp.html> on FDA's Website.

Liver Injuries Prompt Warning for Diabetes Drug

Following reports of liver injury associated with a new diabetes drug, the manufacturer changed the prescribing information and added a warning to the labeling.

Rezulin (troglitazone), approved by FDA in January 1997, is used in combination with insulin or sulfonylurea in patients with adult-onset diabetes mellitus whose blood glucose levels are not adequately controlled by these other therapies alone. (See "Diabetes Demands a Triad of Treatments" in the May-June 1997 *FDA Consumer*.)

The 35 reports of liver injury, as of Oct. 21, 1997, ranged from mildly elevated blood levels of the liver transaminase enzymes to liver failure leading to one liver transplant and one death. It is not yet known if the drug alone caused the liver injury or if other medical factors contributed.

FDA and the drug's manufacturer, Parke-Davis, recommend checking patients' serum transaminase levels routinely for the first one to two months of Rezulin treatment, every three months for the rest of the first year, and periodically after that. Liver function tests should be done if a patient develops symptoms of liver dysfunction, such as nausea, vomiting, abdominal pain, fatigue, loss of appetite, or dark urine.

Patients should stop taking Rezulin if they develop jaundice or their laboratory tests indicate liver injury.

About 2 percent of patients are expected to have to stop taking Rezulin because of elevated liver enzymes. If the drug is stopped, few, if any, of these patients will develop permanent liver damage.

Health-care providers should report

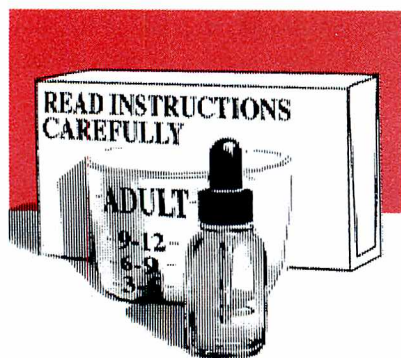
any Rezulin-related adverse events, especially those that suggest liver injury, to Parke-Davis by calling 1-800-223-0432, or to FDA's MedWatch program by calling 1-800-FDA-1088.

New Labels for Children's Tylenol, Motrin Stress Safety

The manufacturer of Children's Tylenol (acetaminophen) and Children's Motrin (ibuprofen) is modifying the labeling of these over-the-counter analgesics to ensure their safe and effective use. Overdoses of Tylenol have been associated with liver damage and deaths in children.

McNeil Consumer Products Co., of Fort Washington, Pa., announced recently it would:

- Add the warning "Read the instructions carefully" to the front panel of all Children's Tylenol dosage forms.
- Change the language to emphasize the importance of using the specific dosing device—for example, dropper or cup—that comes with the product.
- Add the statement "Taking more than the recommended dose (overdose) will not provide more pain or fever relief and could cause serious health risks" to ensure that parents and other caregivers understand that there is no advantage to exceeding recommended doses.
- Change the front panel of Infants'



Tylenol drops to read "Concentrated Drops" instead of "Suspension Drops."

(For more information on children and drug dosing, see "How to Give Medicine to Children" in the January-February 1996 *FDA Consumer*.)

Don't Buy Unapproved Home Test Kits, FDA Warns

Two home-use kits distributed by Lei-Home Access Care of Sunnyvale, Calif.—one intended to test for the AIDS virus and the other for the hepatitis A virus—are unapproved, unreliable, and should not be used, FDA warns.

The agency asked pharmacies last September to remove these two kits from their shelves: the "Lei-Home Access HIV Test," advertised on the Internet as the "Personal HIV Test Kit," and the "In-home Hepatitis A Test Kit."

The only HIV home test approved by FDA is the Home Access HIV-1 Test System, made by Home Access Health Corp., Hoffman Estates, Ill. Users send a blood sample obtained from a finger prick to a laboratory for testing. Confidential results are given over the phone, with a trained counselor available.

FDA has not approved a hepatitis A test kit for use in the home. Hepatitis A, usually transmitted by food, causes a mild, rarely serious, liver disease.

Consumers who used either of the unapproved kits should consult their doctors for retesting.

First Combination Drug Approved for AIDS and HIV

Approval by FDA of the first combination drug for treating AIDS and HIV infection would decrease the number of pills patients need to take each day.

The new drug, Combivir, combines AZT (zidovudine) and 3TC (lamivudine), two drugs commonly pre-

scribed with one another in "drug cocktails" as treatment.

Patients take one pill twice a day. Patients may need to take up to eight pills a day when taken separately.

AZT and 3TC are members of the nucleoside analog class of drug compounds, and both interfere with the replication of HIV, the virus that causes AIDS. Side effects of these drugs include: nausea, diarrhea, anemia, low white blood cells, pancreatitis, and neuropathy. Combivir was approved on Sept. 26, 1997, and is manufactured and marketed by Glaxo Wellcome of Research Triangle Park, N.C.

Final Rule Adds Warning On Devices Containing Latex

Surgical gloves, adhesive bandages, intravenous catheters, and other medical devices containing latex will have to start carrying a warning for people allergic to the rubber substance, according to an FDA final rule.

Beginning Sept. 30, 1998, labels of latex-containing medical devices will have to state, "Caution: This Product Contains Natural Rubber Latex Which May Cause Allergic Reactions." Similar labeling will be required on medical devices containing dry natural rubber and medical device packaging that contains latex.

Also, the rule will prohibit use of the claim "hypoallergenic" on labels of latex-containing medical devices. As now used on devices with reduced latex levels, the claim implies that such products are safe for latex-sensitive people. But even reduced amounts of latex can cause allergic reactions in susceptible people.

During the past decade, FDA received more than 1,700 reports of severe allergic reactions, including 16 deaths in children with spina bifida, related to



medical devices containing latex. Health-care workers and children with spina bifida and other conditions requiring multiple surgeries are at greatest risk of allergic reaction because of their constant exposure to latex-containing devices. For the general public, the risk of allergic reaction is less than 1 percent.

FDA published the rule in the Sept. 30, 1997, *Federal Register*.

Devices Have Record Year

Increased approvals, quicker reviews, and no backlogs made 1997 a record year for medical devices at FDA.

The agency's Center for Devices and Radiological Health approved 48 premarket approval applications in fiscal year 1997, five more than in 1996 and 18 more than in 1995. Key approvals included the first implant to restore partial hand movement in quadriplegics, a deep brain stimulator to help control tremors from Parkinson's disease, a nerve stimulator to reduce severe epileptic seizures, a temporary skin substitute for severe burns, and two fetal bladder stents to treat urinary tract obstruction in unborn babies. The center also cleared the first laser system for treating tooth decay.

Average review time for premarket approval applications was 16.6 months, down from 25.9 months in 1996, with 17 applications approved within 180 days

or less. Average review time to clear 510(k) devices—those similar to existing products—was 97 days, down from 110 days in 1996, with 98 percent having an initial review decision within 90 days or less during the first three quarters of the fiscal year.

The center eliminated its approval application backlogs and continued, for the second year, a “zero” backlog of 510(k) clearances. Approval time for 70 percent of investigational device exemptions was 30 days or less, the quickest ever.

Unapproved Lasers Seized

To ensure that only approved excimer lasers are used to treat nearsightedness and other eye conditions, FDA initiated the seizure of unapproved lasers worth millions of dollars.

Consumers should make sure any laser surgery they undergo is done only with approved lasers or in an FDA-monitored clinical study. Unapproved lasers pose a risk of serious eye injury.

FDA has approved only two lasers as safe and effective for eye surgery. One is manufactured by Summit Technology Inc., of Waltham, Mass., the other by VISX Inc., of Santa Clara, Calif. Several others are in FDA-sanctioned clinical trials.

The lasers treat nearsightedness with photorefractive keratectomy (PRK), a procedure in which the surgeon reshapes the cornea with ultraviolet light bursts from the laser.

At press time, U.S. marshals, on behalf of FDA, had seized unapproved lasers from these sites:

- Photon Data Inc., Winter Park, Fla.—nine lasers and components valued at more than \$3 million seized June 9
- Woodhams Eye Clinic, Atlanta, office of J. Trevor Woodhams, M.D.—one laser seized July 1

- Neumann Eye Institute, Deland, Fla., office of Albert C. Neumann, M.D.—one laser seized Aug. 28

- Pro Cargo, Miami, a private freight firm—one additional Photon Data laser seized Aug. 28

- St. George Corrective Vision Center, Chicago, office of Nicholas Caro, M.D.—one laser seized Sept. 2.

FDA continues to investigate unapproved lasers.

Proposal: Don't Exclude Women from Drug Studies

A rule proposed by FDA aims to ensure that women of reproductive age are not automatically excluded from studies of drugs and biologics for treating life-threatening diseases such as AIDS.

If made final, the rule would permit FDA to stop a company from conducting or continuing a study if women or men were being inappropriately excluded based only on the risk of damage to their reproductive organs or to the health of potential offspring. It would not apply to certain studies, such as those designed to look only at healthy volunteers or to test drugs for use exclusively by one gender, such as prostate cancer drugs.

FDA wants to expand access to new treatments for life-threatening diseases, believing that patients and their doctors can themselves weigh the risks and benefits of such treatments when given complete information during the informed consent process.

The agency hopes that diversity in drug studies will provide better information about how the drug will affect the people who will use it.

The proposed rule, published in the Sept. 24, 1997, *Federal Register*, provided a public comment period that ended Dec. 23.

Free Report on Women's Health

FDA Consumer subscribers may order one free copy of the *FDA Consumer Special Report: Your Guide to Women's Health*, Third Edition. Write to FDA, HFI-40, Rockville, MD 20857, or fax your order to 301-443-9057. Include the publication number, (FDA) 97-1181.



Incontinence Implant Approved

Adults who suffer a serious type of urinary incontinence have a new treatment option: an implantable nerve stimulator.

FDA approved the Sacral Nerve Stimulation System last Sept. 29 to treat urge incontinence. This sudden, uncontrollable loss of urine is due to involuntary bladder wall contractions, which may result from such nerve conditions as spinal cord injury, stroke, and multiple sclerosis, or from other bladder problems. The device requires major surgery and is for use only when less invasive treatments, such as drugs and diet changes, fail. Of the 5 million adults, mainly women, who experience urge incontinence, 20 percent may benefit from the new treatment.

The battery-operated device consists of a pacemaker-size generator for implanting in the abdominal wall and a

wire lead for attaching to the nerves near the sacrum, the large bone at the bottom of the spine. The generator sends electric impulses along the lead to the sacral nerves to help control bladder contractions.

After six months into clinical studies of 86 implanted patients, 47 percent of patients were dry, and an additional 28 percent had 50 percent fewer leakage episodes. Results were similar after 12 months and 18 months. In safety studies of 157 implanted patients, about a third had problems requiring at least a second surgery. Doctors could usually resolve the most common problem, pain, by repositioning the device.

The manufacturer, Medtronic Inc., of Spring Lake Park, Minn., must do a five-year study of the device to determine long-term effects.

FOI Reading Room Added To Remodeled www.fda.gov

A new electronic Freedom of Information Act "reading room" is part of FDA's expanded and redesigned Website at www.fda.gov.

Internet users can now directly access such documents as warning letters, inspection operation manuals, monthly import detention lists, medical device reports, and other often-requested materials without having to go through the time and paperwork of filing a traditional FOI request. Users can reach the Electronic Freedom of Information Reading Room directly from the FDA homepage.

FDA has also revised its homepage to include a greatly expanded index and special menus for such groups as consumers, health professionals, and industry. (For a quick peek at FDA's new homepage, see inside back cover.)

Drug Approval Process, Food Label Win Accolades

Quicker and more new drug approvals and the design of food labeling's Nutrition Facts panel garnered two recent awards for FDA.

The Innovations in American Government Awards Program, sponsored by the Ford Foundation and Harvard University's John F. Kennedy School of Government, recognized the agency for its efforts to speed the review of, and access to, new medicines. In addition to cutting approval times nearly in half, the agency has doubled the number of new drugs approved in a year.

The Nutrition Facts panel, now found on virtually all food labels, was tapped for the Presidential Design Achievement Award because of its useful, consumer-friendly design. The award recognizes exemplary achievements in federal design in such areas as architecture, interior design, urban planning, and graphic design.

Correction

The article "Bone Builders," in the September-October 1997 *FDA Consumer*, included an incorrect TDD number for the Osteoporosis and Related Bone Diseases National Resources Center. The correct TDD number is 202-466-4315.

FDA Consumer welcomes comments from readers. Send letters to: Editor, *FDA Consumer*, HFI-40, 5600 Fishers Lane, Rockville, MD 20857.

Direct To You

TV Drug Ads That Make Sense

by Tamar Nordenberg

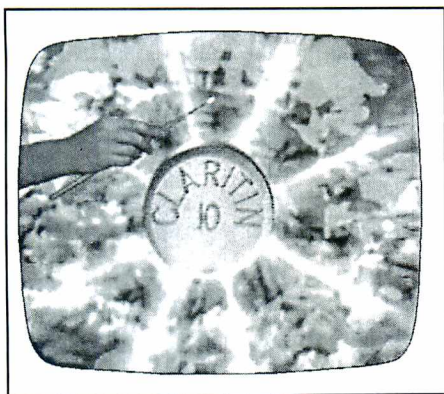
The secret's out. The prescription drug Claritin is an antihistamine for seasonal allergies, new TV commercials reveal. Before August 1997, the Claritin television ads said little beyond, "At last, a clear day is here" and "It's time to see your doctor."

Not much to go on in those earlier ads, and the commercials for Claritin's main competitor, Allegra, were equally unrevealing. Why the secrecy? Because, by stating the drug's name but not what it was used for, the ads were exempt

Giaquinto, senior vice president for worldwide regulatory affairs for Schering-Plough Corp., the drug's manufacturer. "You'd be surprised. We got calls from gynecologists saying patients were asking if they were candidates for Claritin."

In part because of the consumer confusion and concerns that some TV and radio advertisements might be misleading, FDA reviewed its policies on broadcast ads and, in August 1997, issued a draft guidance for public comment. The

A consumer-directed ad may be considered misleading unless it explains the drug's benefits and risks in words that people who aren't medical professionals can understand.



Before August 1997, many TV commercials for prescription drugs stated little more than the product's brand name and "ask your doctor" (left). Now, drug companies are airing TV commercials that tell viewers not just the name of the drug, but also the medical condition it is used to treat (right). (Source: Schering Corp.)



from a Food and Drug Administration regulation that generally requires prescription drug advertisements to disclose the risks of the medication as well as its benefits. From the drug companies' perspective, it was impractical to include detailed risk information in a 30- or 60-second TV spot.

But the so-called "reminder ads" for Claritin and other drugs left consumers puzzled. "We used to get a tremendous amount of phone calls saying, 'What is Claritin? What is it for?'" says Alex

new guidance describes how prescription drug companies can advertise a product directly to consumers on TV or radio, including the product's use, without scrolling the type of detailed risk information that accompanies magazine and other print advertisements.

The makers of Claritin and Allegra soon began airing revised ads. "Only one tablet means 24-hour, nondrowsy seasonal allergy relief," announced the new Schering-Plough commercial.

Not everyone agrees that these "direct-to-consumer" ads are beneficial. At a 1995 public hearing on consumer-directed advertising, FDA heard from scientists, drug companies, patient advocates, and medical professionals. Some objected to direct-to-consumer ads, saying that they mislead consumers because they don't provide a complete picture of the drug. Others favored the ads, telling the agency that a consumer-directed ad can be an important educational tool in an era when patients want to be more in-

volved in their own health care.

But, says Nancy Ostrove, a public health analyst in FDA's division of drug marketing, advertising, and communications, "Direct-to-consumer advertising is not inherently bad or good. It can be useful or harmful, depending on how it's done."

Truth in Advertising

FDA has regulated the advertising of prescription drug products since 1962, under the Federal Food, Drug, and Cosmetic Act and related regulations. Most other advertising, including the advertising of over-the-counter drugs, is regulated by the Federal Trade Commission, under a different set of rules.

FDA generally interprets the term "advertisement" to cover information other than labeling that promotes a product. The term includes promotions broadcast on television or radio, conducted by telephone, or printed in magazines or newspapers. (Also see "Drug Promotion in Cyberspace.")

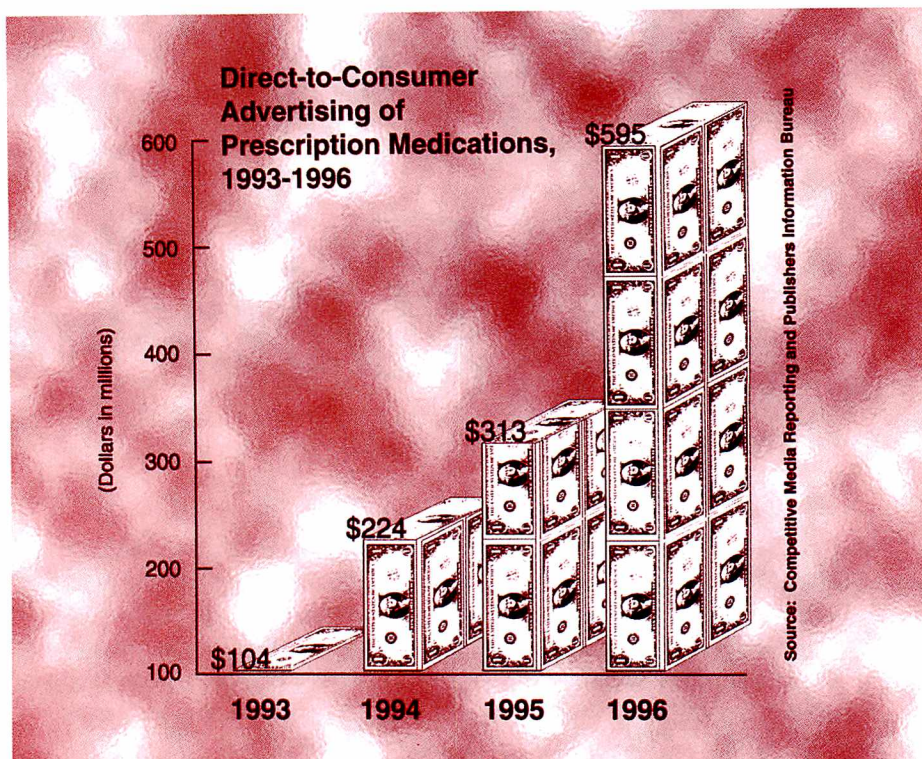
For many years, prescription drug makers promoted their products exclusively to health-care professionals. But about 15 years ago, some manufacturers began to produce ads targeted to consumers.

Since then, direct-to-consumer advertising has become a popular promotional tool. In 1996 alone, prescription drug manufacturers spent almost \$600 million on this type of advertising, according to Competitive Media Reporting, which projects 1997 spending to be at least twice that.

And consumer-directed ads seem to be capturing consumers' attention. In a 1996 study by drug industry consultant Scott-Levin, three-quarters of the doctors surveyed said their patients have talked about drug ads they heard or saw.

FDA regulates consumer-directed ads under the same regulations as professional-directed ones. Like promotions directed to health-care providers, consumer ads may only make claims that are supported by scientific evidence and that are not inconsistent with the FDA-approved product labeling. And, like professional-directed advertisements, they may not be false or misleading.

FDA oversight helps ensure that consumers understand both the benefits and



In Trouble with FDA

Generally, FDA does not require pre-clearance of promotional materials. But the agency often reviews drug companies' draft promotional materials at their request.

If FDA finds that an advertisement a company is using is false or misleading, the agency may take enforcement action against the company. The agency regulates all of a drug company's prescription drug promotions, including the promotional tactics of its salespeople.

For the least serious violations of advertising regulations, FDA will send the drug company an "untitled letter" outlining FDA's findings.

For more serious violations, FDA may issue a "warning letter" requesting that the company immediately stop the violative advertising and, in many cases, take other corrective steps.

For example, the company may be asked to send a "Dear Doctor" letter to alert those who prescribe the medication to FDA's finding. The company may also be asked to run corrective advertisements setting forth FDA's concerns and bringing the ad's language into compliance. Finally, a warning letter may request that a company send its future promotional materials to FDA for clearance before they are used.

Beyond sending untitled letters and warning letters, FDA may stop violative promotions by seizing affected products or enjoining the use of promotions that make the same or similar claims. These actions and the most serious remedy, criminal prosecution of the company or the individuals involved, are used rarely—generally when intentional and serious misstatements are involved.

The threat of agency action isn't the only thing that keeps companies honest, says John Kamp of the American Association of Advertising Agencies. "A drug company won't play fast and loose with the rules because its most important asset is its reputation with the American people." ■

—T.N.

limitations of an advertised drug. (See "In Trouble with FDA.") The agency monitors ads to make sure they are tailored for the target audience. For example, a consumer-directed ad may be considered misleading unless it explains the drug's benefits and risks in words that people who aren't medical professionals can understand.

FDA regulations call for "fair balance" in every ad. FDA reviewers look at the entire advertisement to see if it is balanced. The risks as well as the benefits must be clearly identified, with the risks presented prominently and readably so that the benefits are not unfairly emphasized.

Under the Federal Food, Drug, and Cosmetic Act, most ads must include a "brief summary" describing the effectiveness of the drug and its risks. In print ads, drug companies usually meet the requirement by including entire risk-related sections of the approved labeling. Many people have expressed concern to FDA that, because drug labeling is primarily written for doctors, much of it cannot be understood by consumers.

"The brief summary might be fine for someone who went through medical school," says Linda Golodner, president of the National Consumers League. Even then, she says, "you have to get out a magnifying glass to try and sort out the information."

FDA is considering what steps can be taken toward a more consumer-friendly format. In the meantime, says Ostrove, "We encourage manufacturers to write the brief summary information to be more understandable to consumers."

Help-seeking ads like this one let people know treatments exist for a medical condition, but don't name a specific drug.

(Source: Roche Products Inc.)

TV Reality

In a short television or radio ad, manufacturers have found it difficult to meet the brief summary requirement. "Scrolling a long, detailed brief summary on a television screen is not practical on commercial television," writes drug law expert Wayne Pines in the Thompson Publishing Group's *Advertising and Promotion Manual*.

So, for television commercials and sometimes print ads, companies have historically opted for two types of ads—"reminder" ads and "help-seeking" ads—that are exempt from the brief summary requirement.

Reminder ads, like the original version of the Claritin commercial, call attention to a drug's name, but don't state the condition it is used to treat.

Help-seeking ads tell consumers only that there are treatments available for a particular condition and encourage them

to talk to a health-care professional. To be considered a help-seeking advertisement, an ad may not state or imply the name of a particular product, although it can mention the manufacturer's name. One such magazine ad said simply, "Life without ulcers. It is now possible. See your doctor."

The reminder and help-seeking ad "each has only part of the information a consumer wants, which can create a lot of confusion," Ostrove says.

Completing the Puzzle

FDA regulations have always permitted sponsors of television and radio ads to present a brief summary. Or, instead, they could make "adequate provision" for interested people to get the approved labeling.

Before August 1997, FDA had not described "adequate provision" for consumer-directed ads, so drug companies

were not taking advantage of the option because they were uncertain about whether their ads would meet FDA's standards.

The draft guidance doesn't change the regulation, but rather describes one way to meet the requirement. Under the approach described in the guidance, "adequate provision" is accomplished if the ad contains the following:

- a toll-free telephone number so consumers can request the approved package labeling by mail, fax, or prerecorded telephone message
- a reference to print ads about the product in consumer magazines so consumers can read more detailed drug information, or to brochures containing the package labeling that a consumer can find conveniently in public places such as libraries, pharmacies, doctors' offices, and grocery stores
- a statement that additional product information is available from a doctor or pharmacist
- an Internet address where package labeling can be found.

Whether the brief summary or "adequate provision" is used, however, the most important risk information must always be included in the ad itself. This information is often referred to as the "major statement."

Joint Responsibility

Some consumer-directed ads can raise awareness that drugs are available to treat certain conditions, including diseases such as seasonal allergies that might not require a doctor's care, and undertreated conditions such as depression and impotence. "We have a huge patient population for which there are drugs available to help them live longer and better lives," says John Kamp of the American Association of Advertising Agencies. He adds that government agencies and medical professionals "can use their tools until they're blue in the face and not reach the people who will be reached through television."

While a doctor's prescription is necessary to get these medications, some at the 1995 public hearing expressed a concern that this alternative source of drug information would interfere with the doctor-patient relationship. The National Consumers League's Golodner and

others, however, feel that consumers will communicate with their physicians more, not less, if they are aware that a drug exists for their condition.

"In health care," Golodner says, "there is a general trend toward having consumers more responsible for their own health. Now, consumers can go to their physicians with a little more information."

A related issue raised at the 1995 public hearing is whether such ads would lead to patients pressuring doctors to prescribe unneeded medications. Many speakers emphasized the doctors' duty to advise their patients responsibly. Mary Jane Sheffet, from Michigan State University's marketing department, told FDA, "The doctor needs to be there as a gatekeeper."

With the health concerns of both supporters and opponents in mind, the agency continues to review its policies on direct-to-consumer promotion. FDA will finalize the draft guidance on con-

Drug Promotion in Cyberspace

Like many other companies, prescription drug marketers are beginning to take advantage of the extensive reach of the Internet to promote their products. FDA monitors the Internet to check the quality of the information provided, and encourages consumers to remain vigilant to separate the good information from the bad. (See "Health Information On-Line" in the June 1996 *FDA Consumer*.)

"Generally, FDA is treating Internet promotion like it does other forms of promotion," says Melissa Moncavage, a public health advisor with FDA's division of drug marketing, advertising, and communications. "Although the Internet is brand new, the promotion content issues are largely the same as print, broadcast, and other traditional media."

To address those issues that are unique to the Internet, FDA held a public meeting in October 1996 to hear from consumers, patient groups, health professionals, manufacturers of FDA-regulated products, and others.

The questions discussed at the meeting included:

- Where should promotional product information be located on a company's Website?
- How can promotional information on the Internet be clearly distinguished from other information?
- How can Internet users be ensured access to a balanced presentation of risks and benefits?
- Should Websites distinguish between Internet promotions directed to health professionals and consumers? How?
- How should the promotional materials of multinational companies be addressed to ensure compliance with U.S. drug laws and regulations?

Also, in a Sept. 16, 1996, *Federal Register* notice, FDA requested written comments on some of these same Internet-related drug promotion issues. The agency is considering the written comments, suggestions of meeting participants, and information received since the meeting, and plans to publish a draft guidance to clarify its policies. ■

—T.N.

sumer-directed broadcast advertising, the first step of the review, after considering all comments received during the 60-day comment period, which ended last Oct. 14.

As more ads have been reviewed by FDA, Ostrove says, the agency "has become more and more confident that the appropriate information, including risk information, can reach consumers and be helpful to them."

But the foremost goal of advertisers will always remain the same: to get people to use their products. So Ostrove urges consumers to regard prescription drug ads with thoughtfulness.

"These are prescription drugs with real potential downsides," she says. "We don't want people going to their doctor and saying, 'I want this drug.' The message should be, 'I saw this ad. Is it right for me?'" ■

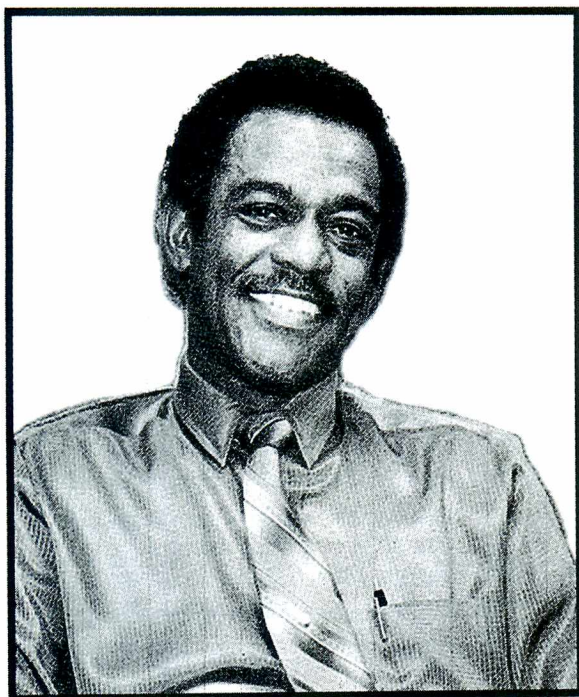
Tamar Nordenberg is a staff writer for *FDA Consumer*.

Living Day-to-Day With

Kidney Dialysis

Quality Improvements Continue for Devices and Clinics

by Rebecca D. Williams



Tony Robinson

As he has for the last seven years, Tony Robinson, 47, heads straight from work on Monday, Wednesday and Friday afternoons to a nearby hemodialysis center in Orlando, Fla.

A nurse gives him a checkup, then Robinson settles into one of the recliners circling the room. Propping his left arm up, he allows a technician to slip two needles into blood vessels near his wrist. The needles—one to capture the blood and the other to return it—are attached to plastic tubes leading to a dialysis machine beside the chair.

For the next three hours, this device, which looks like a tall, narrow, automated teller machine, removes wastes and extra fluid from Robinson's blood. He passes the hours by reading, watching the evening news, and sometimes dozing.

Robinson was born with only one kidney. It failed when he was in his 30s, as did a kidney transplant. For now, dialysis keeps him alive.

Except for the initial needle stick, the procedure doesn't hurt. "You never get used to the needles, you just learn to handle them," he says with a laugh. "Sometimes I feel sick on my stomach if my blood pressure drops, but other

than that, it's not bad."

Robinson is one of approximately 217,000 Americans who receive ongoing dialysis, at an annual cost of \$11.1 billion nationwide. Since the late 1960s, the procedure has been used in place of kidneys lost to disease, birth defects, or injury. It can be used temporarily until the kidneys resume function or the patient receives a transplant, or for years if those options are not available.

With dialysis, Robinson and many others like him can live full and active lives. In fact, Robinson works full-time as an investigator with the Food and Drug Administration's Orlando office. His job requires him to walk distances through production plants, climb ladders, and lift boxes to inspect products. He travels to cities all over Florida to conduct inspections. The overnight trips are not a problem as long as he schedules dialysis ahead of time in the cities he visits.

"If a dialysis patient is otherwise healthy, they should be afforded the opportunity to work," says Robinson. "No one should say you're disabled or restricted to certain areas. I travel, go to training, do inspections—and I have since 1990. I've gotten adjusted to arranging things around the treatments."

Dialysis Under Scrutiny

Since the 1960s, surveillance studies have consistently shown that American dialysis patients do not live as long as those in other countries—the U.S. mortality rate for dialysis patients is about

23 percent, twice the rate of patients in Western Europe or Japan.

A number of factors seem to be the cause. As a whole, American clinics perform hemodialysis treatments for a shorter length of time than in other countries, both because reimbursement doesn't increase for lengthier treatments and patients don't want to sit for five or six hours, according to Dr. Garabed Eknayan, president of the National Kidney Foundation and professor of medicine at Baylor College of Medicine in Houston, Texas. "If you talk to any of the patients, you'll find it's hard to con-

vince them to stay five hours. They come in late and want to leave early."

In addition, says Barbara McCool, a nurse and senior scientist in FDA's Office of Device Evaluation, we dialyze older and sicker patients than do other countries, including AIDS patients, who do not withstand the rigors of dialysis very well. And because of the need to cut costs, American dialysis clinics reuse much of the dialysis equipment and employ staff who have minimal technical training. Many experts say this may be a risk to patient care.

The quality between clinics within the

United States varies as well. Most clinics operate for profit; others don't. Some are located in teaching hospitals, while some are in more remote rural areas. Some have doctors on site every day, while others only have them on call. These factors result in a wide range of quality of care. "We may all read the same books and have the same science, but we're using it differently," says Eknayan.

In response to these concerns, many scientific and medical groups, including the National Kidney Foundation and FDA, are working to improve the quality of dialysis care nationwide.

FDA has increased its involvement in regulating the reuse of dialysis equipment. The agency does not inspect dialysis clinics—that is the responsibility of each state health department. FDA approves the equipment used in dialysis, and the agency has begun requiring that hemodialyzer filters and tubes be tested and approved in realistic clinical situations. For example, in about 80 percent of hemodialysis treatments, the equipment is reused to cut costs, although it was originally tested, labeled and approved for one-time use only. FDA is now requiring manufacturers to prove that filters and tubes are safe and effective when reused. FDA is also taking a closer look at water purifying equipment used in dialysis. Pure water is crucial to hemodialysis, since impurities can kill a patient. FDA has recently begun enforcing regulations that require the manufacturers of water purifiers to prove their devices are safe and effective.

FDA has produced numerous training videos and documents to inform dialysis clinicians about the importance of making sure their equipment is used properly and meets FDA requirements. In addition, the agency has met with many manufacturers of dialysis equipment to help them meet requirements for marketing their devices in the United States. FDA also maintains MedWatch, an adverse events reporting hot line that helps the agency track medical device problems.

"We're hoping to enhance communications with dialysis providers and consumers," says Marie Reid, a nephrology nurse in FDA's Office of Surveillance and Biometrics. "Whenever there's an



Publishers Depot © Bob Daemrich

Pulitzer prize-winning author James Michener, above, began dialysis when his kidneys failed in 1993. He died in October 1997 after discontinuing the life-sustaining treatments.

Take Care of Your Kidneys

Healthy kidneys are the body's cleaning crew. Located under the rib cage in the lower back, these twin bean-shaped organs, each the size of a fist, filter out extra water, minerals, and toxins dumped into the blood by the body's other organs.

Kidneys process 18 gallons of blood each hour with a sophisticated method of excretion, absorption and re-absorption. By the end of each day, they can produce as much as 7 gallons of urine.

The kidneys are reddish-brown, their concave sides facing each other. They are cushioned in fat, with only the tops of them protected by the rib cage. Perched on top of each kidney is an adrenal gland, which produces many hormones vital to life. The right kidney is a little lower than the left because it must squeeze under the liver, a large organ that occupies a large section of the upper right abdominal cavity.

In the concave section of the kidney is a depression containing blood vessels, nerves and the ureter, a small tube that

carries urine away from the organ and down to the bladder. The blood-filtering units of the kidney are microscopic tubes called nephrons.

The leading causes of end-stage renal (kidney) disease are diabetes and high blood pressure. These two conditions take a toll on blood vessels, and the kidneys are rich with blood vessels. Managing these diseases can go a long way toward preventing kidney failure and the need for dialysis. (See "Diabetes Demands a Triad of Treatments" in the May-June 1997 *FDA Consumer*.)

If your kidneys are normal, they don't need special care. A healthy, balanced diet and enough water to quench thirst are adequate to keep kidneys working fine. Fad diets, such as those very high in protein, however, can hurt your kidneys. Drinking very little water, or an overabundance of water (more than 8 quarts a day), may also damage these organs.

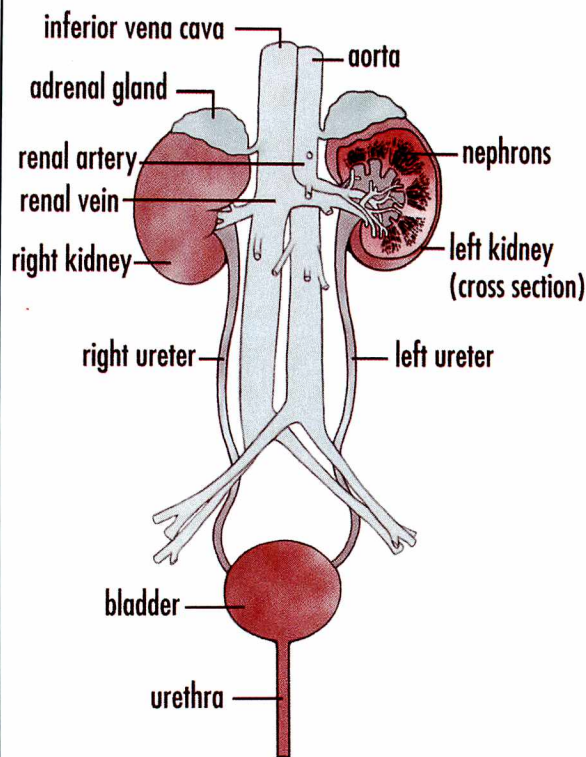
Other than illnesses, the real kidney killers are drugs—they must pass through the kidney to be filtered out of the bloodstream. Some antibiotics, anesthesia medications, and antipsychotic drugs may damage kidneys. Even over-the-counter painkillers, if taken in large doses, may lead to kidney failure.

Common household chemicals can

also hurt your kidneys. Chemical solvents, wood alcohol, toluene, carbon tetrachloride (a cleaning fluid), and ethylene glycol (antifreeze) can damage kidneys if ingested or inhaled. Be very careful handling any chemical and use it according to directions. ■

—R.D.W.

Urinary System



Approximately 217,000 Americans receive on-going dialysis, at an annual cost of \$11.1 billion.

adverse event, we look at it to identify the problem and learn how we can help prevent it from happening again."

The National Kidney Foundation, as well as others in the renal (kidney) care community, has been trying to improve quality in dialysis clinics nationwide. The foundation led an extensive project for the last two years to develop quality guidelines for dialysis treatment nationwide. If dialysis providers adopt the voluntary guidelines, experts say patients will benefit because the latest information on quality treatment will be avail-

able in even the smallest dialysis clinics.

How Dialysis Works

Dialysis acts as an artificial kidney. There are two types of treatment: hemodialysis and peritoneal dialysis. About 90 percent of dialysis patients receive hemodialysis, in which the blood is circulated outside the body and cleaned inside a machine before returning to the patient.

Before hemodialysis can be done, a doctor must make an entrance, called an access, into the patient's blood vessels.

This is done by minor surgery in the leg, arm or sometimes neck. The best access for most patients is called a fistula. Minor surgery is performed to join an artery to a vein under the skin to make a larger vessel.

If no vessels are suitable for a fistula, the doctor might use a soft plastic tube called a vascular graft to join an artery and vein under the skin. For temporary dialysis in the hospital, a patient might need a catheter implanted into a large vein in the neck. Once the access is made and healed, two needles are in-



serted in the fistula or graft, one on the artery side and one on the vein side.

Blood drains into the dialysis machine to be cleaned. The machine has two parts, one side for blood and one for a fluid called dialysate. A thin, semipermeable membrane separates the two parts. As dialysate passes on one side of the membrane, and blood on the other, particles of waste from the blood pass through microscopic holes in the membrane and are washed away in the dialysate. Blood cells are too large to go through the membrane and are returned to the body.

The benefits of hemodialysis are that the patient requires no special training, and he or she is monitored regularly by someone trained in providing dialysis.

The other type of treatment, peritoneal dialysis, uses the patient's own peritoneal membrane as a filter. The peritoneal membrane is a sac around the abdominal organs. This membrane (like the dialysis machine membrane) is semipermeable. Waste particles can get through it, but larger blood cells cannot.

The patient has a plastic tube called a peritoneal catheter surgically implanted into the belly. He or she slowly empties about two quarts of dialysate fluid through the catheter into the abdomen. As the patient's blood gets exposed to the dialysate through the peritoneal membrane, impurities in the blood are drawn through the membrane walls and into the dialysate. The patient drains out the dialysate after three or four hours

Kris Robinson shares more than genes and family memories with her dad, James. He gave her one of his kidneys when the one kidney she was born with began to fail.

and pours in fresh fluid. The draining takes about half an hour and must be repeated about five times a day. This is called Continuous Ambulatory Peritoneal Dialysis (CAPD).

The main benefit of CAPD is freedom—the patient doesn't have to stay at a dialysis clinic several hours a day, three times a week. The dialysate can be exchanged in any well-lit, clean place, and the process is not painful. The drawback to this treatment is that some people get an infection of their peritoneal lining, and the process may not work well enough on very large people.

Children often do a similar type of dialysis called Continuous Cycling Peritoneal Dialysis (CCPD). Their treatments can be done at night while they sleep. A machine warms and meters dialysate in and out of their abdomens for 10 hours continuously. Then they are free from treatments during the day.

As a college student in the spring of 1985, Kris Robinson chose CAPD when her kidney (she was born with only one) began to fail.

Doctors quickly determined Robinson would need dialysis until a kidney transplant could be done. Robinson's father was willing and able to give her one of his kidneys, and for several months before the operation was arranged, she drained dialysate in and out of her abdomen five times a day. She became adept at draining it out in the shower, putting fresh fluid in during breakfast, and so on throughout the day.

"I'm extremely independent," Robinson says. "This let me be in charge of my own dialysis. I knew I could do it, and I wanted to be responsible for my own care. I didn't like to have to sit for four hours, three times a week, and I didn't like the idea of dealing with my own blood in such an open way as in hemodialysis."

The transplant from her father was successful and today Robinson, now 32, still has her kidney transplant and is the executive director of the American Association of Kidney Patients in Tampa, Fla., a nonprofit organization dedicated to patient education about dialysis and kidney disease.

One thing all dialysis patients must know a great deal about is diet. They need a good amount of protein and

lower amounts of potassium and phosphate, which tend to accumulate in the blood and cannot be removed very well with treatment. French fries, for example, are off-limits, and ice cream and cheese must be eaten with caution. Dialysis patients also must limit fluids because the treatment removes only a certain amount of water. Excess fluids make body tissues swell.

Dialysis in the Future

The first successful artificial kidney was developed in the 1940s by a Dutch physician, Willem J. Kolff. Because of World War II and the Nazi occupation of his country, he improvised many materials. For example, he used sausage-link casing for the semipermeable membrane. Since then, the process of dialysis has been fine-tuned over the years, and semipermeable membranes and dialysate have improved.

Still, dialysis is not a cure. If a

pressure. Some patients receive transplants only to have them rejected by their immune system later. Some patients refuse transplants. For them, says Robinson, dialysis may be something of a social gathering and a way to be monitored and cared for by a group of health-care providers that become like friends.

Dialysis survival in the United States after one year is 77 percent, according to the National Center for Health Statistics. After five years it is 28 percent, and after 10 years it is about 10 percent. Transplant survival rates are higher: 77 percent of patients survive 10 years after a living-relative donor. Many experts point out there is room for improvement in the survival rate and quality of life for American dialysis patients.

"I think everything will be different in the future," predicts Eknayan of the National Kidney Foundation. "People

To report a problem with dialysis equipment, call MedWatch at 1-800-FDA-1088.

person's kidneys are temporarily damaged, dialysis can give them a rest and a chance to recover. But for chronic, end-stage renal disease, a kidney transplant is the only long-term solution that frees a patient from dialysis.

Living relatives can donate a kidney if their remaining organ is healthy. Even with a kidney from a close relative, however, a transplant recipient must take drugs to suppress the immune system from rejecting the organ. There are about three times as many people waiting for transplants as there are kidneys available.

Some dialysis patients are not well enough for the rigors of a transplant operation and the drugs that follow, according to Robinson of the American Association of Kidney Patients. In fact, 20 percent of dialysis patients are over 65. More than half suffer from other illnesses, such as diabetes and high blood

pressure. Some patients receive transplants only to have them rejected by their immune system later. Some patients refuse transplants. For them, says Robinson, dialysis may be something of a social gathering and a way to be monitored and cared for by a group of health-care providers that become like friends.

Perhaps kidney transplants, always in shortage, will become easier to get if animals such as pigs are used as donors, Eknayan adds. But the best treatment, of course, is to protect healthy kidneys in the first place. Diabetes and high blood pressure account for more than half of all cases of end-stage renal disease. Both of these conditions usually can be managed with proper medical care (see accompanying article, "Take Care of Your Kidneys").

Says Eknayan, "Prevention is going to be a big part of the answer." ■

Rebecca D. Williams is a writer in Oak Ridge, Tenn.

Dangers Of Lead Still Linger

by Dixie Farley

The hazardous substance lead was banned from house paint in 1978. U.S. food canners quit using lead solder in 1991. And a 25-year phaseout of lead in gasoline reached its goal in 1995.

As a result of such efforts, the number of young children with potentially harmful blood lead levels has dropped 85 percent in the last 20 years, as shown in National Health and Nutrition Examination Surveys conducted by the National Center for Health Statistics. Interested in measuring the impact of lead solder's removal from food cans, the Food and Drug Administration funded collection of the data during the 1976–1980 period and has continued to support the survey efforts.

Similarly, FDA's 1994–1996 Total Diet Studies showed that, since 1982–1984, daily intakes of lead from food dropped 96 percent in 2- to 5-year-olds (from 30 micrograms a day to 1.3) and nearly 93 percent in adults (from 38 micrograms a day to 2.5).

Yet in 1997, FDA approved a new, portable blood lead screening test kit for health professionals to use. In the face of so much success, why is another screening tool even necessary?

The answer: Lead is still around.

Lead paint abounds in older housing. The deteriorating paint exposes youngsters indoors to lead-laden dust and paint chips and outdoors to exterior paint lead residues in nearby soil—residues that remain unless removed. Lead par-

ticles emitted by the past use of leaded gasoline are also in the soil, especially near major highways. Lead persists at some work sites and, occasionally, in drinking water, ceramicware, and a number of other products.

"The risk of lead exposure remains disproportionately high for some groups,

including children who are poor, non-Hispanic black, Mexican American, living in large metropolitan areas, or living in older housing," the national Centers for Disease Control and Prevention noted in its Feb. 21, 1997, *Morbidity and Mortality Weekly Report*. Indeed, CDC reports that nearly a million children under 6 still have blood lead levels high enough to damage their health. While CDC considers the blood lead level of concern in adults to be 25 micrograms per deciliter (mcg/dL) of blood, this level in young children is only 10 mcg/dL.

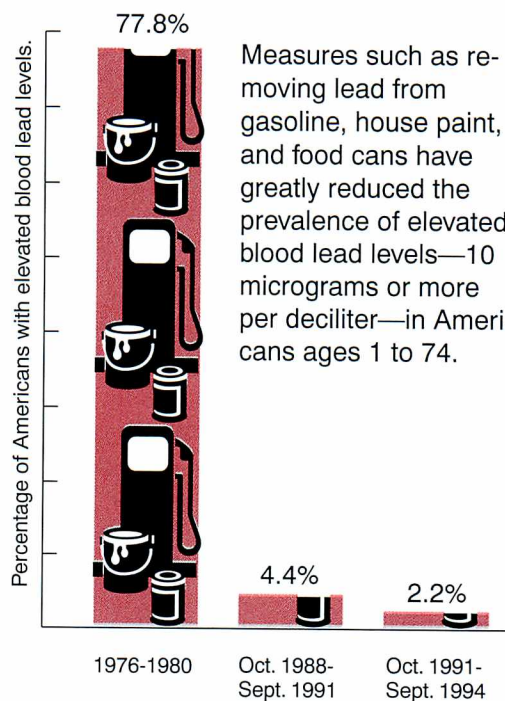
Based on CDC's levels, FDA's "tolerable" daily diet lead intakes are 6 mcg for children under age 6, 25 mcg for pregnant women, and 75 mcg for other adults. However, some risk exists with *any* level of lead exposure, says toxicologist Michael Bolger, Ph.D., chief of FDA's contaminants branch in the Office of Plant and Dairy Foods and Beverages.

And harmful levels need never occur, according to Sheryl Rosenthal, M.S.P.H., R.D., a lead educator at FDA's Center for Food Safety and Applied Nutrition. "Lead poisoning is preventable and just should not happen today," she says.

Lead Absorption

While adults absorb about 11 percent of lead reaching the digestive tract, children may absorb 30 to 75 percent. When lead is in-

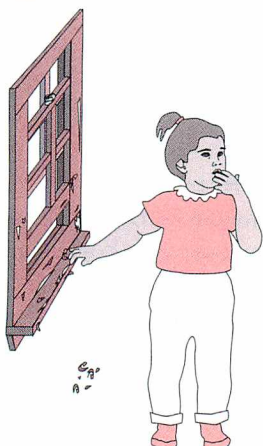
Getting The Lead Out



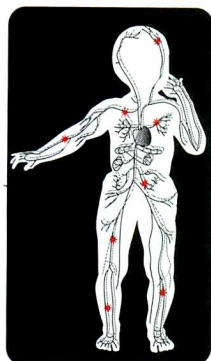
(Source: National Health and Nutrition Examination Surveys, National Center for Health Statistics)

Lead In The Body

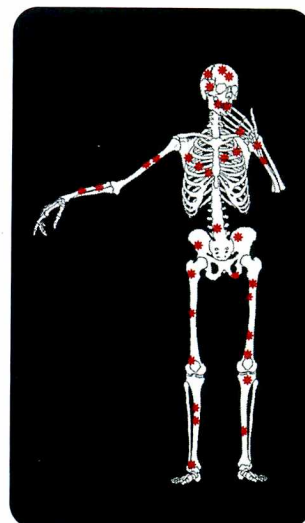
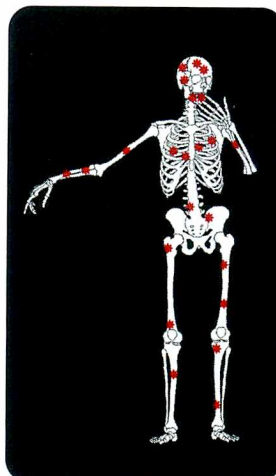
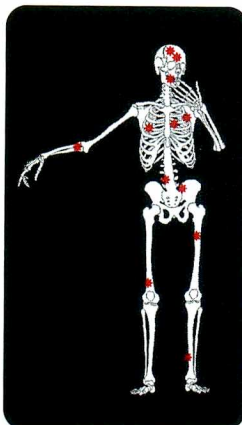
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3



(1) Lead is ingested or inhaled.

(2) The bloodstream carries it throughout the body.

(3) After a few weeks, lead not excreted is absorbed mainly into bone, a little into the brain, teeth and kidneys. Lead may accumulate in bone for decades.

haled, up to 50 percent is absorbed, but less than 1 percent of lead is absorbed when it comes in contact with the skin. The body stores lead mainly in bone, where it can accumulate for decades. (See illustration, "Lead in the Body.")

"Anyone in poor nutritional status absorbs lead more easily," adds Cecilia Davoli, M.D., a pediatrician with Kennedy Krieger Institute's Lead Poisoning Prevention Program, in Baltimore. Calcium deficiency especially increases lead absorption, as does iron deficiency, which can also increase lead damage to blood cells. A high-fat diet increases lead absorption, and so does an empty stomach.

The Risks of Lead

Lead disrupts the functioning of almost every brain neurotransmitter, says David Bellinger, Ph.D., a psychologist and epidemiologist at Children's Hospital in Boston. Neurotransmitters are chemical messengers between the body's nerve cells. The messenger calcium, for example, is essential to nerve impulse transmission, heart activity, and blood clotting, but if it doesn't work right, affected systems may also be askew.

"Lead fits into binding sites that calcium should," Bellinger says, "so it can

Screening and Treatment

Decisions about who needs lead screening should be made by individual doctors as well as state health departments, who can examine local lead hazards and conditions to determine which children are at risk of lead exposure, according to 1997 guidance issued by the national Centers for Disease Control and Prevention.

A new screening test is especially suited for use in isolated U.S. rural areas and in developing countries. In September 1997, FDA approved the LEADCARE In Office Test System, a portable blood lead screening kit for health professionals' use in areas lacking refrigeration and other complex equipment needed with previously approved tests. Manufacturers developed the quick, easy and reliable kit in conjunction with CDC.

FDA has approved three drugs that bind to, or chelate, lead molecules so the body can remove them in urine and stool. Calcium Disodium Versenate (edetate calcium disodium) requires injections or intravenous infusion in the hospital. Along with this drug, BAL (dimercaprol), also injected, may be used. The pediatric oral drug Chemet (succimer) may be taken at home, but it's important to eliminate the lead sources. Like other chelator drugs, Chemet should not substitute for effective environmental assessment and removal of the source of lead exposure.

These drugs may have side effects, however, so doctors closely monitor their patients during treatment. ■

—D.F.

By the time symptoms appear, damage from lead is often already irreversible.

disturb cellular processes that depend on calcium. But there's no unifying theory that explains in detail what lead does to the central nervous system, which is where lead typically affects children."

Bellinger estimates that each 10 mcg/dL increase in blood lead lowers a child's IQ about 1 to 3 points.

"Evidence is less clear," he says, "on whether mild blood lead elevations in pregnancy cause permanent effects on the fetus. Studies have tended not to find that early developmental delays related to minor fetal exposure carry through to school age, when IQ is measured." Studying middle- and upper-middle-class children exposed before birth to mild lead levels, Bellinger and colleagues found delays in early sensory-motor development, such as grasping objects, but did not find such effects by school age.

However, he adds, "When lead exposure in the uterus is quite high, the impact can be devastating on the fetus, causing serious neurological problems."

High lead exposures can cause a baby to have low birth weight or be born prematurely, or can result in miscarriage or stillbirth.

"Symptoms of lead poisoning can be highly variable depending, in part, on the age of the child, the amount of lead to which the child is exposed, and how long the exposure goes on," says pediatrician Randolph Wykoff, M.D., FDA associate commissioner for operations. Children exposed to lead may have no symptoms, he says, or may report sometimes vague symptoms, including headache, irritability or abdominal pain.

While a child's chronic exposure to relatively low lead levels may result in learning or behavioral problems, Wykoff says that "higher levels of exposure can be associated with anemia and changes in kidney function, as well as significant changes in the nervous system that may, at extreme exposures, include seizures, coma and death."

In adults, lead poisoning can contribute to high blood pressure and damage to the reproductive organs. Severe lead

poisoning can cause subtle loss of recently acquired skills, listlessness, bizarre behavior, incoordination, vomiting, altered consciousness, and—as with children—seizures, coma and death. Poisoning without severe brain effects can cause lethargy, appetite loss, sporadic vomiting, abdominal pain, and constipation.

By the time symptoms appear, damage is often already irreversible.

"The most important thing for families to do," says Baltimore's Davoli, "is to learn what steps they can take to prevent lead poisoning. We don't want to get to treatment. And they should take their children to the doctor regularly for checkups and, if the children are at risk, get blood lead tests done."

Critical to prevention is focusing on the important lead sources. FDA's Rosenthal says, "Dealing with sources of lead means recognizing them in your family's environment, knowing which ones contribute significant exposures, and eliminating or avoiding those exposures."

Top Contaminator: Lead Paint

America's No. 1 source of lead exposure in children is deteriorating lead paint in older housing. Because young children frequently put their thumbs and fingers and objects they handle in their mouths, they are easily poisoned from chronic ingestion of lead paint chips and house dust or soil that may have lead particles in it.

The Consumer Product Safety Commission (CPSC) banned house paint having more than 0.06 percent lead in 1978. But housing built before then, particularly before 1950, may contain lead paint. The Environmental Protection Agency and Department of Housing and Urban Development require owners of pre-1978 housing to give prospective buyers or renters federally approved information on the risk. Buyers must have 10 days to inspect for lead-based paint before being obligated by a contract.

Improper housing renovation increases exposure. The riskiest practices

are sanding, scraping or removing lead paint with a heat gun, which taint the air with lead paint dust. CPSC warns: *There is no completely safe method for do-it-yourself removal of lead paint.* Only experts should remove lead paint. (See illustration, "Protect Your Family from Lead Poisoning.")

Occupational Hazards

Clark Carrington, Ph.D., of FDA's dairy foods and beverages contaminants branch, names workplace exposure as the next major potential source of lead. Besides their own exposures, workers may bring lead dust home on clothes, hands or hair, exposing children in the household.

Occupations that may expose workers to lead include painting, smelters, firearms instruction, automotive repair, brass or copper foundries, and bridge, tunnel and elevated highway construction.

To help protect workers from such exposure, the Occupational Safety and Health Administration calls for removal of workers from the workplace if their blood lead levels reach 50 mcg/dL. EPA limits lead emissions from certain industries.

Keeping Drinking Water Safe

Certain drinking water systems can also pose a lead risk.

Under EPA rules, if lead exceeds 15 parts per billion (ppb) in more than 10 percent of public water taps sampled, the system must undergo a series of corrosion control treatments. The main culprits are corroded lead plumbing, lead solder on copper plumbing, and brass faucets. Lead is highest in water left in pipes for a long time—for example, when the faucet isn't used overnight.

FDA's quality standard for bottled water requires that lead not be present at 5 ppb, the lowest concentration that generally available methods for water analysis can reliably measure. If bottled water contains lead above this level, it is subject to regulatory action, including removal from the marketplace.

Lead in Ceramicware

Some ceramicware has lead in the glaze and may introduce small amounts of lead in the diet, which the body can tolerate, says Carrington. "The major problem with ceramicware is the rare

poorly made piece with very high levels of leaching lead."

Bolger adds that even with these pieces, risk varies. "A plate coming in brief contact with food is not an issue," he says, "but storage of food in such a bowl or pitcher is a risk." It's especially wise to avoid storing acidic foods like juice and vinegar in ceramicware, as acids promote lead leaching.

FDA has established maximum levels for leachable lead in ceramicware, and pieces that exceed these levels are subject to recall or other agency enforcement action. The levels are based on how frequently a piece of ceramicware is used, the type and temperature of the food it holds, and how long the food stays in contact with the piece. For example, cups, mugs and pitchers have the most stringent action level, 0.5 parts per million, because they can be expected to hold food longer, allowing more time for lead to leach. Also, a pitcher may be used to hold fruit juice. And a coffee mug is generally used every day to hold a hot acidic beverage, often several times a day.

Michael Kashtock, Ph.D., chief of FDA's Office of Plant and Dairy Foods and Beverages enforcement branch, says, "FDA allows use of lead glazes because they're the most durable. But we regulate them tightly to ensure their safety. Commercial manufacturers ... employ extremely strict and effective manufacturing controls that keep the lead from leaching during use." Small potters often can't control the firing of lead glazes as well, he warns, so their ceramics are more likely to leach illegal lead levels, although many do use lead-free glazes. "The best advice is to stick to commercially made products. If you are going to buy something hand-made or hand-painted, get assurance that lead-free glazes were used," he says.

Antique ceramicware may leach high levels of lead. Consumers can use a lead test kit from a hardware store on such pieces and on other hand-painted ceramicware they may already own. Avoid using such items—particularly cups, mugs or pitchers—if the glaze develops a chalky gray residue after washing.

"And you want to make sure," says Rosenthal, "that you know whether an item is for food use, or if it's for decora-

tive use only." FDA requires high-lead-leaching decorative ceramicware to be permanently labeled that it's not for food use and may poison food. Such items bought outside the United States may not be so labeled, potentially posing serious risk if used for food.

Other Lead Sources

- ***Tin-coated lead foil capsules on wine bottles***

FDA banned these capsules in 1996 after a study by the Bureau of Alcohol, Tobacco and Firearms found that 3 to 4 percent of wines examined could become contaminated during pouring from lead residues deposited on the mouth of the bottle by the foil capsule.

U.S. winemakers stopped using lead foils before the ban, but older bottles with the foils may still be around. "Remove the entire foil before using such wines," says attorney Martin Stutsman, a consumer safety officer in FDA's dairy foods and beverages enforcement branch. "Then before uncorking the bottle, wipe its neck and rim and the top of the cork with a clean wet cloth."

- ***Lead-soldered food cans***

Despite U.S. food canners' voluntary elimination of lead solder and a 1995 FDA ban on lead-soldered cans, requiring their removal from shelves by June 1996, this source of lead in the diet hasn't been fully eliminated. Some countries still use lead-soldered cans for food, and these food items may still occasionally be imported, albeit illegally, into the United States. Also, some small vendors may still stock old inventories of food in lead-soldered cans. In fact, a 1997 FDA investigation found more than 100 such cans in ethnic grocery stores in California alone.

- ***Glassware***

Lead crystal glassware may leach lead. "The crystalware industry has established voluntary lead-leaching limits for crystalware," says Kashtock, "that most foreign and domestic manufacturers follow." As a precaution, children and pregnant women should avoid frequent use of crystal glassware. Lead crystal baby bottles should never be used.

Also, FDA intends to issue industry guidance in 1998 to prohibit use of lead-based (and cadmium-based) pigments

Want More Information?

Centers for Disease Control and Prevention

1-888-232-6789

<http://www.cdc.gov/nceh/programs/lead/lead.htm>

Consumer Product Safety Commission

1-800-638-CPSC

TDD: 1-800-638-8270

<http://www.cpsc.gov/>

Environmental Protection Agency's Safe Drinking Water Hotline

1-800-426-4791

<http://www.epa.gov/opptintr/lead/index.html>

National Lead Information Center

1-800-LEAD-FYI

clearinghouse: 1-800-424-LEAD

TDD: 1-800-526-5456

<http://www.nsc.org/ehc/lead.htm>

for decorating the lip rim area of glassware, says Kashtock. "Use of the pigments may pose only a negligible risk, but it is avoidable."

- ***Calcium products***

Some people have expressed concern about lead in calcium supplements. Lead is a common contaminant in calcium from such natural sources as dolomitic limestone and oyster shells, but levels vary considerably from trace amounts to higher levels. However, FDA's Carrington says, "Since calcium intakes decrease lead absorption, supplements that correct low calcium intakes may reduce lead absorption, even though they contain small amounts of lead."

Lead is also found in other calcium sources. For example, lead in milk is usually too low to measure, but FDA's yearly Total Diet Study of foods in grocery stores sometimes detects lead in milk, says Carrington.

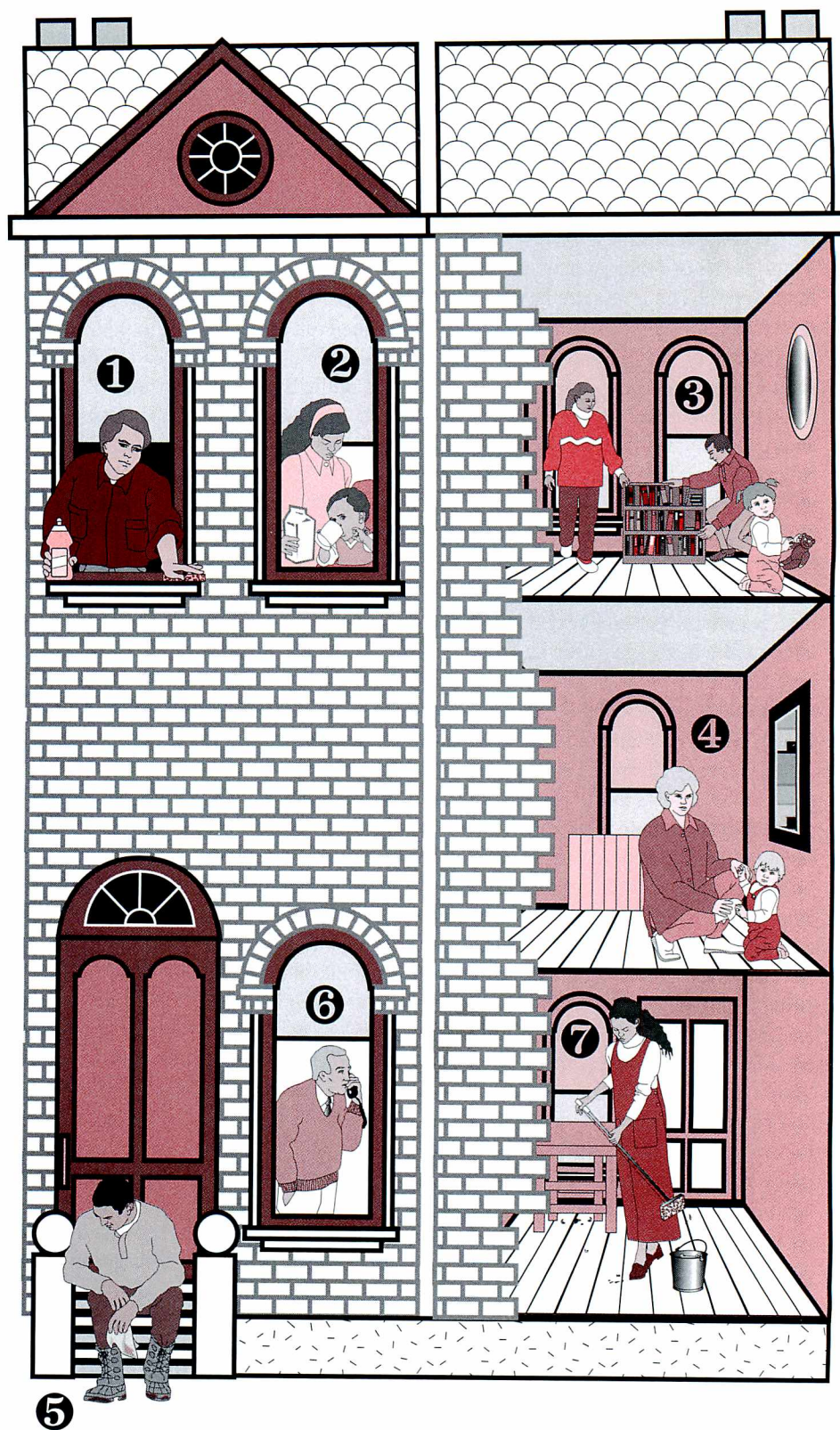
FDA has been petitioned to establish
(Continued on page 21)

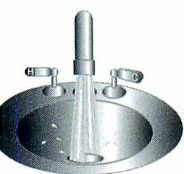
Protect Your Family from Lead Poisoning

The greatest source of lead poisoning in young children is deteriorating lead paint in older housing. *But lead poisoning is preventable.* If your house was built before 1978, follow this advice from the National Lead Information Center.

1. Wash floors, windowsills, and other surfaces weekly with warm water and detergent.
2. Feed children healthy, timely meals low in fat and high in iron and calcium.
3. Keep children from chewing painted surfaces.
4. Wash children's hands, bottles, pacifiers, and toys **often**.
5. Wipe soil off shoes before entering the house. Cover soil with grass, mulch or other barrier.
6. Ask your doctor or health department whether your children should be tested for lead, even if they seem healthy.
7. Immediately clean up paint chips.

Call 1-800-LEAD-FYI for a list of experts certified by the Environmental Protection Agency to inspect the house and soil for lead and remove lead paint. Move out of the house until the renovation and clean-up is completed. *Never remove lead paint yourself.*



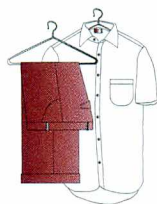


If you suspect your **water pipes** are leaching lead, use cold water for drinking and cooking, running it 30 seconds before use. Ask your state health agency about testing your drinking water for lead.

Remove **lead foil capsules from wine bottles** before pouring. Before removing the cork, wipe the bottle neck and rim and the cork top with a clean wet cloth.



Never use **ceramicware** that gets chalky after washing. Avoid storing acidic foods like juice and vinegar in ceramic holloware. If pregnant, avoid daily use of ceramic mugs for hot beverages like coffee and tea. Stick to commercially made items. If you buy a craft piece, ask if it's lead-free. If you're unsure whether a food serving item is made from lead-based materials, you can check with the manufacturer. Test antiques with a kit from a hardware store. And never use items marked "decorative" for food.



If your **occupation** exposes you to airborne lead, change clothes and wash before coming home.



In homes with young children, make sure cartons of **imported vinyl mini-blinds** have terms like "non-lead formula" or "no lead added." Discard blinds you're unsure of. Blinds with lead may form lead dust as they deteriorate.



Children and pregnant women should avoid frequent use of **crystal glassware**.

Never feed babies from **crystal baby bottles**.

Keep all **hair dyes**, especially those with lead acetate, away from children.



Never expose children to the **Middle East eye cosmetic dyes** kajal, kohl or surma or to the **foreign remedies** Alarcon, Azarcon, Coral, Greta, Liga, Maria Luisa, or Rueda.



(Continued from page 19)

a tolerance level for lead in calcium sources used in dietary supplements. According to Robert Moore, Ph.D., of the agency's Office of Special Nutritionals regulatory branch, two petitions propose different tolerance levels—one similar to current industry standards and one considerably lower. FDA is reviewing the issues raised in the two documents.

- **Progressive hair dyes**

Applied over time to gradually color the hair, these dyes contain lead acetate. After studying information on their safety, FDA found that lead exposure from these dyes was insignificant and that the dyes could be used safely, says John Bailey, Ph.D., director of FDA's Office of Cosmetics and Colors. "But we restricted how much could be in the product, and we required specific labeling instructions, including a warning to keep it out of the reach of children."

- **Kajal and surma, or kohl**

These unapproved dyes in certain eye cosmetics from the Middle East contain potentially harmful amounts of lead. A 7-month-old in 1992 had a 39 mcg/dL blood lead level due to surma applied to the lower inner eyelid. Bailey says, "They are sold in stores specializing in Middle East products or brought into the country in personal luggage." He stresses that people using these cosmetics "need to understand the potentially serious health risk."

- **Foreign digestive remedies**

Certain unapproved foreign digestive remedies containing lead include Alarcon, Azarcon, Coral, Greta, Liga, Maria Luisa, or Rueda. Greta, for example, is 99 percent lead oxide.

FDA orders the detention at U.S. borders of items known to possibly contain potential harmful levels of lead, including the Middle East eye cosmetics, the foreign digestive remedies, lead crystal baby bottles, and many other prohibited items. Lead sources outside FDA's purview include lead-based artists' paints, lead solder used in electronics work and stained glass, fishing weights, lead toy soldiers, and old painted toys and furniture.

Reflecting that these many lead sources are not all in every family's environment, new CDC screening guidance calls for state lead-poisoning prevention programs to identify communities at risk of high exposure and recommend appropriate screening. (See the accompanying article, "Screening and Treatment.") To this end, CDC funded 30 state and 10 local programs in 1996.

When announcing the new guidance, Health and Human Services Secretary Donna E. Shalala said, "Lower lead levels for America's children constitute a public health achievement of the first importance. But a significant number of children are still at risk for high lead exposure, and we have to finish the job on their behalf." ■

Dixie Farley is a staff writer for FDA Consumer.

Skimming

THE MILK LABEL

Fat-Reduced Milk Products Join The Food Labeling Fold

by Paula Kurtzweil

The goal of the labeling changes is to help consumers select milk products that can help them lower their fat and saturated fat intakes to recommended levels.

Milk, that all-American food, is taking on some all-American names—like “fat free,” “reduced fat” and “light.”

Starting Jan. 1, 1998, the labeling of fat-reduced milk products will have to follow the same requirements the Food and Drug Administration established almost five years ago for the labeling of just about every other food reduced in fat. From now on:

- 2 percent milk will become known, for example, as “reduced fat” or “less fat” instead of “low fat”
- 1 percent milk will remain “low fat” or become, for example, “little fat”
- skim will retain its name or be called, for example, fat-free, zero-fat, or no-fat milk.

Also, the regulations that implement the labeling changes give dairy processors more leeway to devise new formulations. As a result, consumers may see a broader range of milk and other dairy products, including “light” milk with at least 50 percent less fat than whole, or full-fat, milk and other reformulated milks with reduced fat contents but greater consumer appeal.

“I expect that there are going to be many more milk products for consumers to choose from” says Michelle Smith, a food technologist in FDA’s Office of Food Labeling. “This is positive for milk consumption in general, and it’s likely that consumers will be able to find a lower fat milk product that they like.” (See accompanying article.)

FDA issued a final rule in November

1996 that revoked the standards of identity—the prescribed recipes that manufacturers of a particular food must follow—for many fat-reduced milk and other dairy products. This allowed the agency to bring milk labeling in line with existing labeling requirements for nutrient content claims, such as “fat free,” “low fat,” “high protein,” and others.

Lower fat milk products will still need to be nutritionally equivalent to full-fat milk and provide at least the same amounts of the fat-soluble vitamins A and D as full-fat milk. Vitamins A and D are lost when milk fat is reduced or removed.

“[Milk] is just as nutritional as before,” says LeGrande “Shot” Hudson, dairy plant manager for the Landover, Md.-based Giant Food Inc. “[The milk industry] just changed the name[s] a little.”

Joint Effort

FDA’s final rule was prompted in part by a petition filed jointly by the Milk Industry Foundation and the Center for Science in the Public Interest (CSPI), a consumer advocacy group, and a separate petition filed by the American Dairy Products Institute. The petitions asked FDA to lift the labeling exemption provided for in the Nutrition Labeling and Education Act of 1990 for lower fat dairy products.

FDA agreed to revoke the standards of identity for low-fat milk and 11 other

“It takes only five seconds at the dairy case to move your hand to the fat-free (skim) or low-fat (formerly 1 percent) milk.”

—Margo Wootan, senior scientist for the Center for Science in the Public Interest

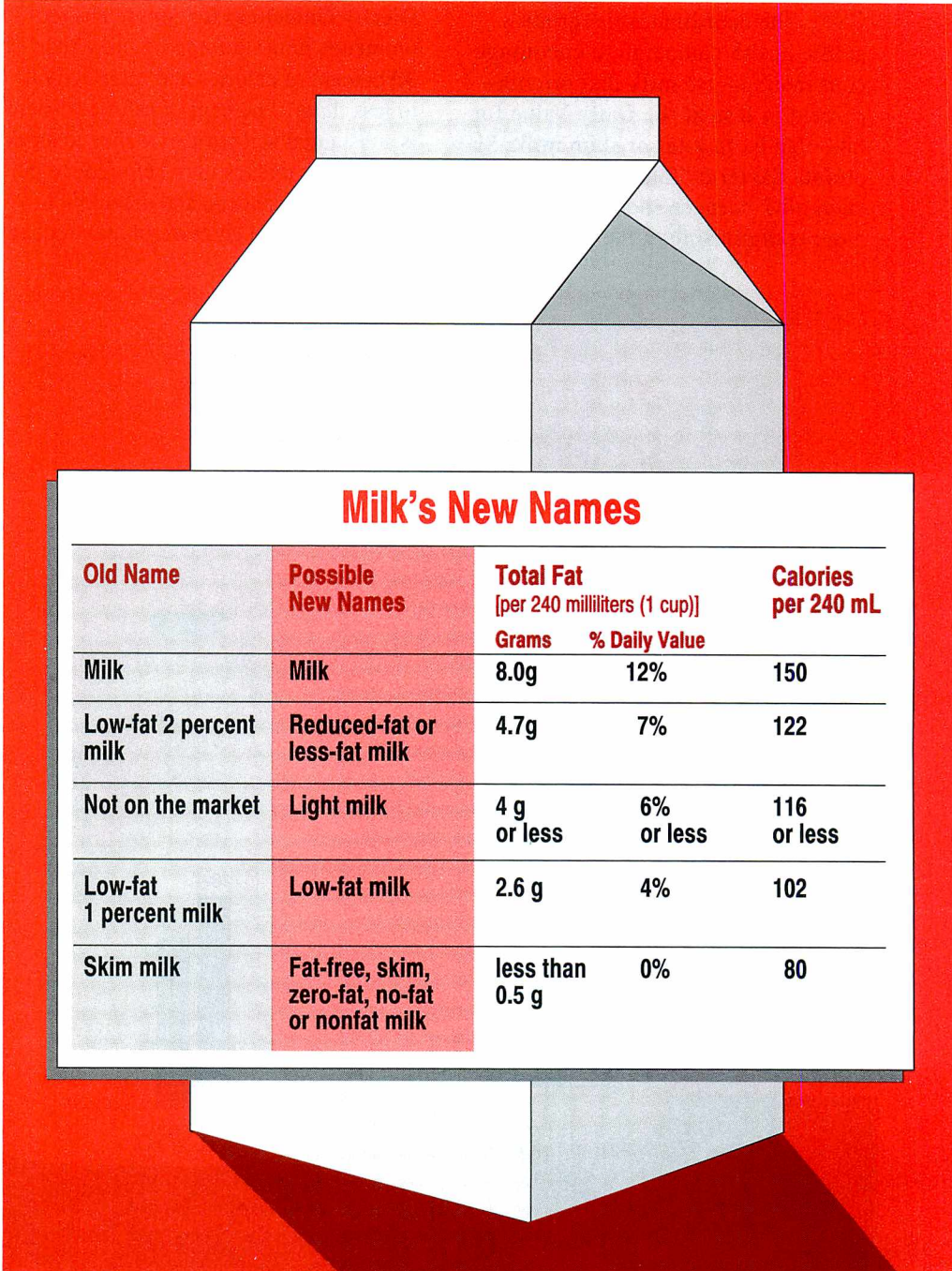
lower fat dairy products, including low-fat cottage cheese, sweetened condensed skimmed milk, sour half-and-half, evaporated skimmed milk, and low-fat dry milk. These products are now bound by the “general standard” for nutritionally modified standardized foods. This means the nutrients that lower fat milk products provide, other than fat, must be at least equal to full-fat milk before vitamins A and D are added.

FDA also agreed to allow manufacturers to use “skim” as a synonym for “fat free” in the labeling of dairy products because, the agency concluded, most consumers realize that skim milk means no fat.

The changes do not affect lower fat yogurt products. FDA decided to keep the standards of identity for the time being to further consider manufacturers’ concerns about fortifying yogurt with vitamin A, a nutrient found in full-fat yogurt.

FDA, along with the milk industry and nutrition educators, believes the label changes will give consumers more accurate, useful information about milk. Because claims on milk labels will be consistent with claims on other foods, consumers will know, for example, that “low-fat” milk (formerly known as 1 percent milk) will be similar in fat content to “low-fat” cookies. (Both can provide no more than 3 grams of fat per serving. The serving size for each is listed on their label’s Nutrition Facts panel.)

The improved accuracy of milk labeling is particularly important for skim milk, experts say, because “skim” carries a negative connotation for many



| Milk's New Names | | | | |
|-------------------------------|--|--|-----------------------|--------------------------------|
| Old Name | Possible New Names | Total Fat [per 240 milliliters (1 cup)] | | Calories per 240 mL |
| | | Grams | % Daily Value | |
| Milk | Milk | 8.0g | 12% | 150 |
| Low-fat 2 percent milk | Reduced-fat or less-fat milk | 4.7g | 7% | 122 |
| Not on the market | Light milk | 4 g or less | 6% or less | 116 or less |
| Low-fat 1 percent milk | Low-fat milk | 2.6 g | 4% | 102 |
| Skim milk | Fat-free, skim, zero-fat, no-fat or nonfat milk | less than 0.5 g | 0% | 80 |

Lower fat milk products will still need to be nutritionally equivalent to full-fat milk and provide at least the same amounts of the fat-soluble vitamins A and D.

consumers. "They think it is skimmed of all its good nutrients," says Brad Legreid, executive director of the Wisconsin Dairy Products Association. "That it's flat and tasteless. But that's not it at all."

Or, they view it in the same negative light as dry powdered milk, says Margo Wootan, a senior scientist with CSPI. She coordinates the group's public health campaign to encourage consumers to use milk that provides 4 percent or less of the Daily Value for fat—that is, low-fat or skim milk. She prefers the term "fat-free" to describe skim milk because she says: "It is more recognizable to the public. And

"fat-free" better describes the benefits of skim milk."

Dietary Significance

The goal of the labeling changes, as many nutrition experts see it, is to help consumers select milk products that can help them lower their fat and saturated fat intakes to recommended levels. The Dietary Guidelines for Americans recommends limiting fat to no more than 30 percent of calories and saturated fat to less than 10 percent of calories. There is substantial scientific evidence to show that low fat intakes may help reduce the risk of some cancers, and diets low in saturated fat and cholesterol may reduce

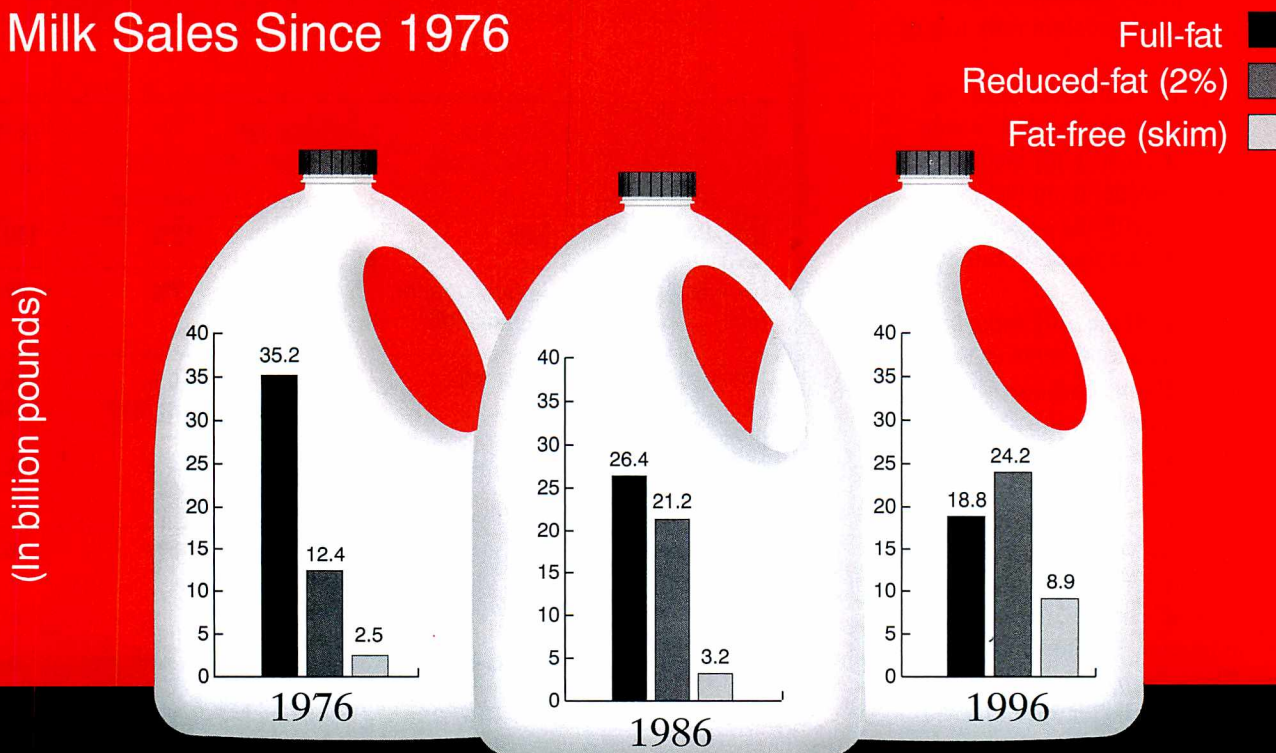
the risk of heart disease.

Switching from higher fat to lower fat milk products can have a particularly significant impact on lowering fat and saturated fat intakes because milk plays such an important role in the American diet, CSPI's Wootan says. She says that milk is a major contributor of saturated fat to the American adult's diet. Only cheese and beef contribute more.

Considering that 240 milliliters (one cup) of full-fat milk provides 26 percent of the Daily Value for saturated fat, while fat-free milk provides none, switching from full-fat to fat-free milk can drop saturated fat intake considerably, she says.

Make Mine Less-Fat Milk

Milk Sales Since 1976



Source: U.S. Department of Agriculture Economic Research Service

Raising Milk Consumption

While the new labels may promote greater consumption of the lower fat milk products, some nutrition experts—and industry members in particular—hope the changes will increase milk consumption overall.

LeGrande “Shot” Hudson, dairy plant manager for Giant Food Inc., in Landover, Md., notes that the industry already has taken steps to entice consumers, especially teens and young adults, to drink more milk. It’s undertaken major advertising campaigns and, in an effort to make milk more palatable to people who dislike the taste of plain milk, has begun marketing novel flavored products, such as banana, blueberry, raspberry, strawberry, and mocha milk products.

“We don’t all wear the moustache,” he says, alluding to the industry’s current milk advertisements in which celebrities tout their preference for plain milk.

Michelle Smith, a food technologist in FDA’s Office of Food Labeling, believes that milk processors will have even more flexibility to develop products with greater consumer appeal, now that the standards of identity for lower fat milks have been revoked. For example, processors will be able to add fat substitutes, stabilizers or thickeners to give lower fat milks a creamier texture and better sensation in the mouth or coloring to make the products whiter. When added, these ingredients must be listed on the label.

“There are many ways to modify a food,” she says. “So, if you come across a reduced-fat product, and you want to know how they did it, look at the ingredient list.”

With greater product development comes greater product choices for consumers, she says, and that will allow consumers to make better, lower fat choices that they can enjoy. ■

—P.K.

“It’s an easy way to lower fat intake,” she says. “It doesn’t take a lot of time. No preparation skills are needed. It takes only five seconds at the dairy case to move your hand to the fat-free [skim] or low-fat [formerly 1 percent] milk. It’s a good first step towards healthy eating.”

Wootan believes that the revised milk labeling will make especially clear to consumers the difference between reduced-fat (formerly 2 percent low-fat milk) and low-fat (1 percent low-fat milk). “A lot of people use 2 percent milk thinking it is the same as 1 percent,” she says, because the previous labels referred to both as “low fat.” However, reduced-fat milk provides almost twice the amount of fat and saturated fat as low-fat milk.

The new labels will “show a difference,” she says, “and, [I think,] more people will go to drinking 1 percent or skim milk.”

New Names in the Dairy Case

But first, they’ll need to get used to milk’s new names. Joan Taylor, consumer affairs manager for Schnuck Markets Inc., of St. Louis, recalls the confusion that arose when manufacturers began relabeling ice milk as “low-fat” ice cream in 1994, under another FDA rule. The company received a number of calls from shoppers wanting to know why they had stopped selling ice milk, she says. “We hadn’t,” she says. “We only changed the name.”

Some groceries and milk processors plan to educate consumers about the label changes. Schnuck Markets, for example, was planning at press time to post signs at their stores’ dairy cases explaining what the new names mean. And its dairy plant planned to label, at least at first, lower fat milk with both the new name, followed by its former name or the milk’s fat content. An example might be “reduced-fat milk, contains 2 percent milk fat.”

Efforts such as these should help consumers catch on quickly to the new names, but nutrition and industry experts hope the new labels’ potential benefits will be longer lasting.

“This is not just a cosmetic change,” CSPI’s Wootan says. “This is an important strategy to healthier eating.” ■

Paula Kurtzweil is a member of FDA’s public affairs staff.

Dunagin’s People



“Is this the milk formerly known as low fat?”

Reprinted with permission.

Air aid

Medical Kits Reach New Heights

by Tamar Nordenberg



Heart-related problems rank among the most common types of in-flight emergencies.

"Is there a doctor on board?" Not one, but two doctors responded to the plea when, on April 23, 1995, Benjamin Talit suffered sudden cardiac arrest in flight. Despite the medical expertise of a heart-lung surgeon and the other doctor who came forward, the 43-year-old Talit died en route to Los Angeles aboard Northwest Airlines flight 339.

Ben—"a thoughtful, loving husband of 20 years, exemplary father, valued professional, and truly good citizen"—died needlessly before reaching medical help on the ground, his wife Lynn told Congress at a May 1997 hearing about

airplane medical kits, because the plane did not carry a device called a defibrillator to restart his heart. It is a "bitter irony," she said, that Ben, himself a volunteer firefighter and emergency medical technician, died "for the lack of exactly the preparedness he supported and practiced every day of his life."

Based on Federal Aviation Administration surveys, an average of 15 medical emergencies may occur daily on U.S. airlines. Medical emergencies have more than doubled in the last decade, according to FAA, which says the increase may be due at least in part to improved airline accommodations for medically-at-risk disabled and elderly passengers.

"The number of emergencies is small in the statistical sense," says Jerry Hordinsky, M.D., head of FAA's aeromedical research division. "But when an event does occur, with a person potentially dying in flight because of a lack of medical equipment, it is very dramatic and attracts a great deal of public attention."

Lynn Talit disagrees. Because airlines are not required to report medical emergencies, people underestimate their scope, she told Congress, pointing out that the number of people who die in flight each year "far exceeds" airline crash deaths.

Cardiac Care Aloft

Along with neurological problems such as strokes and seizures, heart-related problems rank among the most common types of emergencies. In sudden cardiac arrest, the heart stops pumping blood, often without warning in

people like Ben Talit with no known heart problems.

According to the American Heart Association, more than 250,000 Americans die each year from sudden cardiac arrest. "And not all of them happen to suffer their cardiac emergency in a hospital waiting room," Lynn Talit says.

Fewer than 7 percent of those suffering cardiac arrest outside a hospital survive, a statistic which the association attributes to the unavailability of a defibrillator, a device that restarts the heart by delivering an electric shock.

As David McKenas, M.D., American Airlines corporate medical director testified before Congress, a person's chance of survival drops 7 to 10 percent with each passing minute. Even if someone's heart stopped right after the plane left its gate, McKenas said, it would be too late to save the person by the time the plane returned to the gate. An on-board defibrillator would offer the best chance of survival.

In September 1996, the Food and Drug Administration cleared an "automatic external defibrillator" (commonly called "AED") for in-flight use and has since cleared another. While defibrillators have been used in ambulances and other nonhospital settings since the 1960s, the unique environment of a plane in flight prompted FDA to require additional testing.

According to Carole Carey, a scientific reviewer in FDA's division of cardiovascular and respiratory devices, the maker of a defibrillator for airplane use must show FDA that:

- the defibrillator can physically withstand in-flight environmental demands, such as vibration and variations in temperature and altitude
- the device will not electronically interfere with the airplane's instruments
- the airplane's instruments will not electronically interfere with the functioning of the device.

Based on this evidence, a defibril-

The goal during serious in-flight medical emergencies is to stabilize the patient while further emergency care is sought.

lator's labeling was permitted to state that the device was environmentally tested for use in planes. Only after FAA added its approval could the device actually be used in flight.

In July 1997, American Airlines became the first U.S. airline to carry automatic external defibrillators and the third internationally, after Britain's Virgin At-

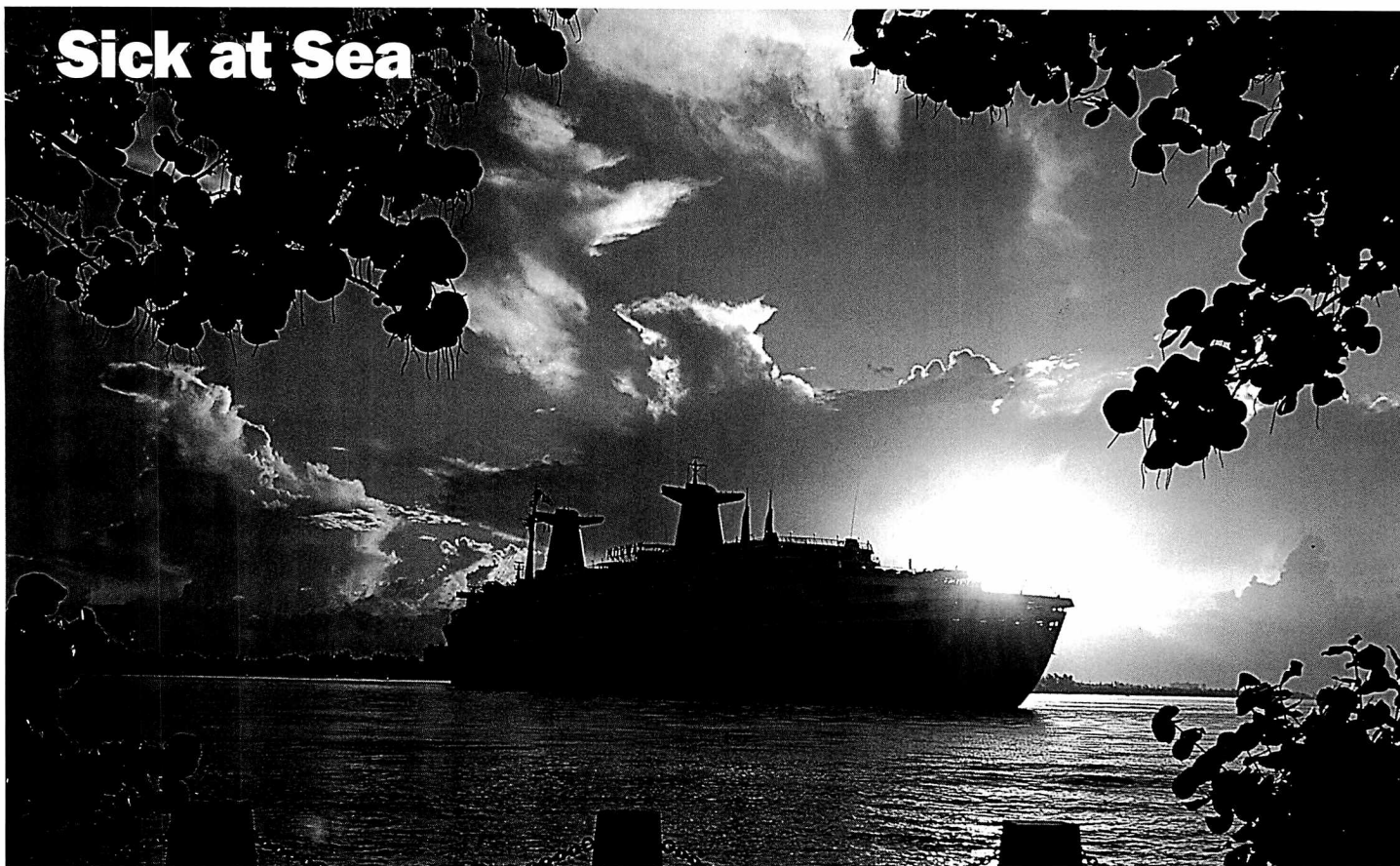
(Continued on page 29)



With an onboard defibrillator like the small, easy-to-use ForeRunner (demonstrated on the model above), people who suffer sudden cardiac arrest on an airplane have a better chance of surviving until they reach medical help on the ground.

(Courtesy: Heartstream Inc.)

Sick at Sea



Publishers Depot©Alon Reininger

More than 4 million passengers took a cruise in 1996, according to the Cruise Line Industry Association. The organization estimates that by the year 2000, cruises will attract as many as 7 million passengers each year.

Based on the sheer volume of travelers, some are bound to get sick. "In addition to seasickness and sunburn, which are the big leaders, we see all the things you would normally see in an emergency department on land," says Theodore Harrison, M.D., who heads the cruise ship and maritime medicine section of the American College of Emergency Physicians.

While Coast Guard regulations cover the safe navigation and design of a cruise ship, the government does not regulate the quality of on-board medical treatment. In 1996, the American College of Emergency Physicians and a major industry group, the International Council of Cruise Lines, developed the first meaningful standards for cruise ship medical facilities.

Under the ICCL guidelines, a ship should have:

- licensed medical staff qualified to administer cardiac care and life support, who are fluent in the language spoken by most of the passengers and crew
- adequate infirmary space based on the ship's size
- wheelchairs, stretchers, cardiac monitor, portable defibrillator, and other important equipment and emergency medications.

Harrison says that most cruise ships already meet the voluntary guidelines, and he expects that virtually all the ships will meet them in time. "Before the guidelines, everybody was pretty much on their own in determining what medical capabilities were needed. The guidelines leveled the playing field for everybody."

The guidelines may help cruise medical staff address the day-to-day medical needs of passengers, but for complicated cases, many cruise lines are associated with a hospital that can provide emergency consultation 24 hours a day. "We help the ship's medical staff make a decision when they call us about an unusual condition," says Abdul Memon, M.D., the associate director of the emergency department of Florida's

Jackson Memorial Hospital, which provides medical emergency advice to Royal Caribbean Cruise Lines.

"The medical care will be pretty good on most cruise ships, under the circumstances," Harrison says. But he cautions travelers to not expect the level of medical care they could get in a New York City hospital. "A cruise ship is just a one or two thousand person little town out there. And people should expect the same medical care as they would expect in a little town in the middle of nowhere."

To help ensure a safe cruise, passengers may want to take some precautions. If you have medical concerns and are considering going on a cruise, Memon recommends:

- discussing your travel plans with a doctor
- carrying adequate supplies of medications you may need
- calling the cruise line's medical department to make sure the ship can accommodate your special medical needs. ■

—T.N.

The in-flight defibrillator comes with simple pictures and a digital voice to guide a rescuer through the steps.

(Continued from page 27)

lantic and Australia's Qantas airlines. American put defibrillators on its planes that fly over-water routes to Europe, Japan, the Caribbean, Central and South America, and some domestic destinations.

Manufactured by Seattle-based Heartstream Inc. and sold under the brand name ForeRunner, the new model purchased by American weighs about 4 pounds, half the weight of most defibrillators. And the ForeRunner has a longer-lasting battery and requires much less maintenance than older models, according to Carey.

It's also easier to use, she says, making it possible for trained flight attendants to deal with some cardiac emergencies. "Flight attendants obviously aren't physicians, nurses or paramedics. But to use this prescription device, they must receive training in emergency care and use of the defibrillator."

Flight attendants can use the ForeRunner with minimal training because, unlike most defibrillators, it comes with simple pictures and a digital voice to guide a rescuer through the steps. The rescuer simply puts two pads on the victim's chest and rib area. The device measures the heart's rhythm to check for ventricular fibrillation, which requires a shock to the heart, then directs the user to push a button if a shock is needed.

American has trained 2,300 lead flight attendants in use of the defibrillator and plans to train its other flight attendants, according to Nestor Kowalsky, M.D., American Airlines' Chicago area medical director. At least one trained person will be on each flight that carries the device, he says.

American has not decided whether to add the device to the medical kit on all its domestic aircraft. "Right now, the airline is following this first phase of the program to see how successful it is," Kowalsky says. "Then a decision will be made about expanding it to other airplanes."

Several other U.S. airlines have said that they are considering carrying defibrillators on their aircraft.

Medical Minimum

Most U.S. airlines carry little more than the medical equipment currently required by FAA: one to four first-aid kits, depending on the number of passengers, and one medical kit per aircraft.

Each first-aid kit must be accessible to the flight attendants and include:

- bandages
- compresses for applying pressure, moisture, heat, or cold
- antiseptic swabs
- arm and leg splints
- tape
- scissors.

An airplane's medical kit must be accessible to the flight crew, but is for use only by medical professionals. It must include:

- blood pressure cuff
- stethoscope
- plastic airways to deliver oxygen to help with breathing
- nitroglycerin tablets for chest pain
- dextrose solution for hypoglycemia
- epinephrine for asthma or allergic reactions
- injectable diphenhydramine HCl for serious allergic reactions
- hypodermic needles
- protective latex gloves.

The goal during serious in-flight medical emergencies is to stabilize the patient while further emergency care is sought. The pilot may decide to make an emergency landing, called "diverting" the plane, depending on factors such as the passenger's apparent medical condition, weather conditions, turbulence, air traffic, and the distance from adequate ground medical facilities.

To help with medical decisions, most airlines have 24-hour access to a physician on the ground. In the future, airlines may decide to use a computerized system developed by a Michigan surgeon

for air-to-ground transmission of passengers' vital signs.

But "there is nothing the people on the ground could tell the doctor on board if the right equipment doesn't exist," says Talit, who wants Congress to require enhanced medical kits that would include defibrillators.

One airline voluntarily carrying defibrillators on its overseas flights is not enough, according to Talit. The automated defibrillator, she says, "should be as commonplace as fire extinguishers, and as accessible in case of emergency. Not every public building catches fire—few do—but do we not have a fire extinguisher in these public places?"

Joan Sullivan Garrett, who is president of MedAire Inc., a firm that provides emergency medical guidance to commercial airlines, is also in favor of updating the federal regulations. "Emergency physicians and flight crews," she told Congress, "are using first-aid kits circa 1924 to deal with 1997 realities."

In addition to the automated defibrillator, her recommendations include an automated blood pressure cuff and stethoscope so laypersons can check a person's pulse and an albuterol metered-dose inhaler in case someone suffers an asthmatic attack.

At press time, Congress was still exploring whether to require additional on-board medical equipment, including defibrillators. FAA is working with the airline industry to evaluate the costs and health benefits of additional medical tools on board. But, Hordinsky says, until FAA gets more information, the agency cannot impose additional rules.

So, for now, it is up to the airlines if they want to upgrade their medical kits beyond legal requirements. Regardless of what medical equipment is on board, people with medical conditions that put them at risk should consult their doctors before flying. They should also bring their own medications on board. Even the best-equipped airlines have limited medical capabilities. As MedAire's Garrett testified at the congressional hearing, "It's important to remember that an aircraft cannot be a flying hospital." ■

Tamar Nordenberg is a staff writer for FDA Consumer.

DRUGS

Of The Deep

Don Hochstein raises a thin glass tube up to his eye level and flicks it with a fingernail. Inside the pencil-width vessel, a substance with the texture of gelatin shimmies and wobbles but doesn't move from the tube's bottom.

"There's endotoxin in there, you can bet on it," he says, slipping the tube back into a rack.

Hochstein, former deputy director of product quality control (he retired last Sept. 3) in the Food and Drug Administration's Center for Biologics Evaluation and Research, is demonstrating a simple analytical test. It's one that medical professionals, drug companies, pharmacies, and others use worldwide to detect the presence of endotoxins—dangerous toxic byproducts of "gram-negative" bacteria such as *Salmonella* and *E. coli*.

The test is the limulus amebocyte lysate assay and is, Hochstein says, "remarkable" for its origin: the horseshoe crab. The limulus test, along with an osteoporosis treatment derived from salmon and a bone filler made from coral, are approved medical products that come from the sea.

Until recently, virtually all medical products had terrestrial sources. For example, organisms found in soil have yielded products such as penicillin, amoxicillin, and other antibiotic compounds responsible for saving millions of Americans from suffering and death.

Sea-based products are rare, but some experts say the world's oceans and waterways may harbor the next generation of drugs, biologics, and even a few medical devices. Dozens of promising products, including a cancer therapy made from algae and a painkiller taken from snails, are in development at research laboratories right now. Other products, such as an anti-inflammatory drug extracted from an organism called the Caribbean sea whip, are under FDA

Treasures of the Sea Yield Some Medical Answers and Hint at Others

by John Henkel

review. Three approved products already have brought the healing power of the sea successfully into the world of public health.

A Lucky Horseshoe

Along the Eastern Seaboard of the United States, it's not unusual when strolling on the shore to find horseshoe crabs that have "beached" or shed their shells. These crabs, the *limulus* species, are important players in the ecology and marine life of shore areas from Maine to Florida. Their importance increased when, more than two decades ago, researchers discovered that, due to some unique properties, the crabs' blood could be used to detect dangerous endotoxins in drugs, medical devices, and even water.

Endotoxins are produced when *E. coli* and other gram-negative bacteria break down. The effect on humans exposed to the toxins ranges from fever to hemorrhagic stroke. "This underscores the importance of the test in finding these toxins before they can do any damage," says Hochstein.

Before the limulus amebocyte lysate (LAL) test was marketed, medical professionals gauged endotoxin presence by injecting the substance being analyzed into a rabbit's ear. If the animal developed a fever, endotoxins were present. Rabbit tests still are done but are "falling out of favor," says Hochstein, because "they are just too

complicated." The tests take four to five hours, and labs must keep caged rabbits on hand.

By contrast, the LAL test uses a glass tube and takes only one hour. Drawing blood from horseshoe crabs causes the animals no harm, and they can be returned to their habitat within 48 hours.

By many accounts, the discovery of the LAL test was serendipitous. In 1971, National Institutes of Health researcher Jack Levin was studying various marine animals when he discovered that blood in horseshoe crabs exposed to *E. coli* bacteria had clotted. He then drew fresh blood from some horseshoe crabs and exposed it to *E. coli* in the laboratory. The blood clotted to a gel-like consistency. Further experiments in the NIH Bureau of Biologics, which later became part of FDA, confirmed that if any endotoxins are present, the blood will clot.

Hochstein was a major participant in those early tests, and he recalls setting up shop at a NASA facility on the Eastern Shore of Virginia to catch and draw blood from 1,000 horseshoe crabs at a time. He and his colleagues also kept as many as 200 crabs in tanks filled with ocean water in labs outside Washington, D.C., to ensure an available blood supply.

The team ultimately developed a method for separating amebocytes, which are similar to human white blood cells, from the rest of the crab's blood. These cells then were spun in a centri-



This “blood donation center” (really an FDA laboratory) collects blue-green blood from horseshoe crabs to make a test that detects dangerous toxins. These blood donations don’t harm the crabs, and the lab quickly returns them to their habitats.

A Coral Performance

Scuba divers and snorkelers have long marveled at the intricate patterns of coral reefs in the Pacific, Caribbean, and other exotic locations. These patterns are now a marvel for people with certain kinds of bone injuries. A product made from the rigid exoskeletons of marine coral can fill voids caused by fractures or other trauma in the upper, flared-out portions of long bones.

Called hydroxyapatite (HA), the material is similar in structure to human bone. FDA approved the HA product Pro Osteon Implant 500, made by Interpore International, in 1992. When HA is implanted into a bone void, its web-like structure allows surrounding bone and fibrous tissue to infiltrate the implant and make it biologically part of the body.

The implants, which are either blocks in pre-cut sizes or granules used to fill in the spaces not covered by the blocks, must be used with reinforcement devices such as steel rods to ensure that the fracture remains stable until it heals. “Otherwise,” says Nadine Sloan, biomedical engineer in FDA’s restorative devices branch, “the implant may crack when you walk or put any weight on it. It wouldn’t have sufficient strength to support the weight until bone grows into it or the fracture heals.”

Although it is possible for patients to donate bone from other sites on their body to repair a fracture, this causes extra trauma, says Sloan. “One of the real advantages of using [coral-based] implants is that they avoid a second surgery that would be necessary if a donor site is used.”

FDA also has approved coral-derived implants for applications such as bone loss around the root of a tooth and in certain areas of the skull.

fuge to intentionally rupture them and create a “lysate,” the essence of the LAL test, which is freeze-dried and looks like grains of salt.

In 1973, FDA published regulatory guidelines for producing the LAL test, and in 1977, the agency licensed the first LAL product to Massachusetts-based Associates of Cape Cod. Five other companies have developed their own LAL products since then. Hochstein says FDA’s LAL work is an excellent example of transferring technology from the public to the private sectors.

The test has a large market in drug companies that use LAL to detect endotoxin contamination in injectable products, says Melissa Juntunen, marketing coordinator for Associates of Cape Cod. “Probably every major pharmaceutical company uses it,” she says. Medical device firms also use the test to ensure that catheters, pacemakers, and other invasive devices are endotoxin-free.

From Fish to Pharmacies

Osteoporosis, a crippling disease marked by a wasting away of bone mass, affects as many as 25 million Americans, 90 percent of them women, at an expense of \$10 billion a year, according to the National Osteoporosis Foundation. The disease may be responsible for 1.5 million fractures of the hip, wrist and spine in people over 50, the foundation says, and may cause 50,000

deaths. Given the pervasiveness of osteoporosis and its cost to society, experts say it is crucial to have therapy alternatives if, for example, a patient can’t tolerate estrogen, the first-line treatment.

Enter the salmon, which, like humans, produces a hormone called calcitonin that helps regulate calcium and decreases bone loss. For osteoporosis patients, taking salmon calcitonin, which is 30 times more potent than that secreted by the human thyroid gland, inhibits the activity of specialized bone cells called osteoclasts that absorb bone tissue. This enables bone to retain more bone mass.

Though the calcitonin in drugs is based chemically on salmon calcitonin, it is now made synthetically in the lab in a form that copies the molecular structure of the fish gland extract. Synthetic calcitonin offers a simpler, more economical way to create large quantities of the product.

FDA approved the first drug based on salmon calcitonin, Calcimar, an injectable form marketed by Rhône-Poulenc Rorer, in 1975. Since then, two drugs made by Novartis and marketed under the trade name Miacalcin—one injectable form and one administered through a nasal spray—were approved. An oral version of salmon calcitonin is in clinical trials now. Salmon calcitonin is approved only for postmenopausal women who cannot tolerate estrogen, or for whom estrogen is not an option.

On the Horizon

Research into new products from the sea, including medical products, is in "high gear" in labs across the United States, says Linda Kupfer, program officer for the National Sea Grant College Program. A unit of the Commerce Department's National Oceanic and Atmospheric Administration, Sea Grant is a network of 29 university-based programs in coastal and Great Lakes areas that involves more than 300 institutions. Though research into medical products is only part of the program's focus, some "very promising work" with medical potential is under way in Sea Grant-supported labs, Kupfer says.

For example, researchers at the University of Hawaii have created what may be a novel cancer treatment from blue-green algae. Using compounds

Dozens of promising **sea-derived products** are in development now, including a cancer therapy and a painkiller.

called cryptophycins extracted from the algae, researchers have treated mice implanted with cells that cause prostate and breast cancer. The compounds appear to affect the cancer cells' internal structure, possibly keeping the disease from spreading. Much work remains before a drug treatment could be created, but at least one major pharmaceutical company has shown interest in developing the compounds as an anti-cancer therapy.

At the University of Rhode Island, professor Yuzuru Shimizu is developing a culturing system that will ensure an adequate supply of sea-based organisms that

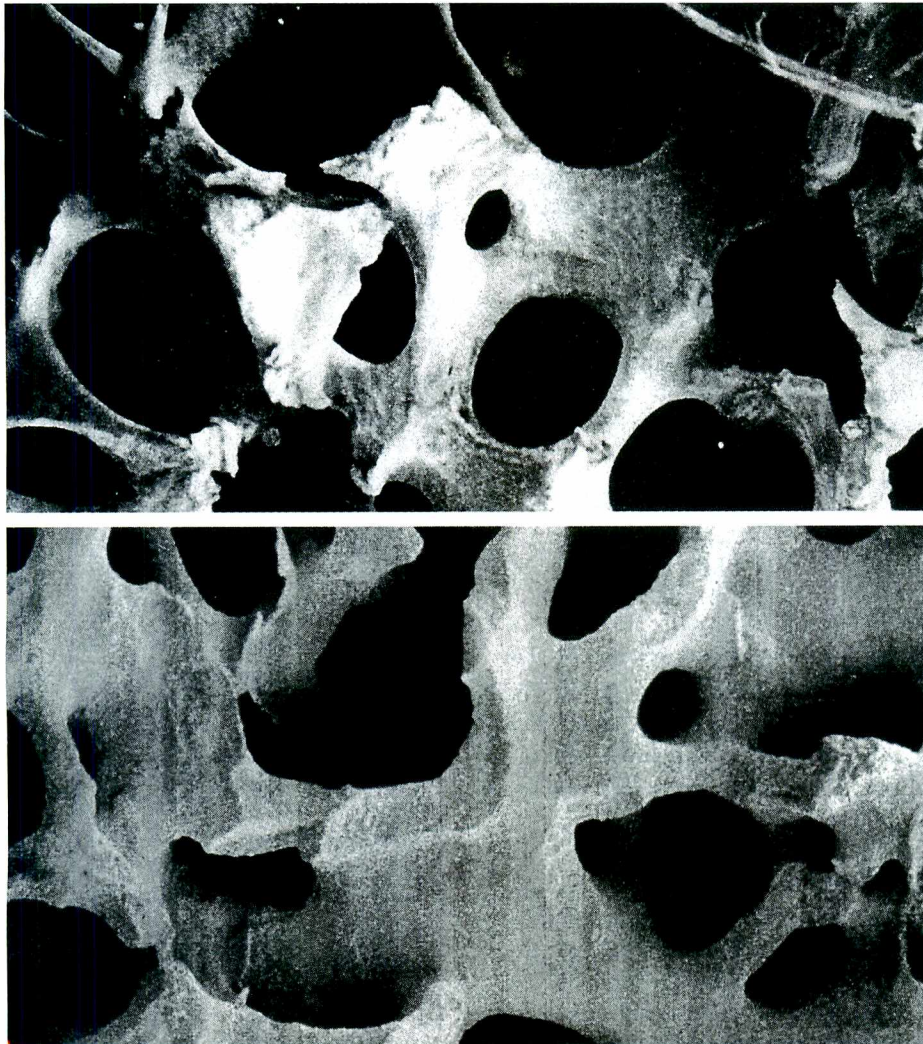
show anti-tumor properties. Shimizu is examining metabolites of single-celled plankton called dinoflagellates, which National Cancer Institute tests have shown to have cancer-fighting potential.

Scientists at the University of California's Santa Barbara and San Diego campuses are researching compounds called pseudopterosins. Extracted from the Caribbean sea whip, a type of coral that resembles shrubbery on the sea floor, the compounds are being investigated for use in skin-care products. They also appear to have anti-inflammatory properties and could see use someday as treatment for skin irritations resulting from injury or infection. One pseudopterosin-based product, licensed from the university, is in clinical trials now. The researchers hope to take their work even further: "Our next attempt will be to develop drugs for inflammatory diseases such as arthritis and asthma, among others," says William Fenical, an organic chemist at UC San Diego.

Other important sea-based medical product work is in progress outside the Sea Grant program. For instance, the National Cancer Institute is sponsoring clinical trials of five substances derived from marine invertebrates such as sea hares and bryozoans that may have use in the future as cancer treatments. Elsewhere, one drug company is testing a neurotoxin obtained from a seagoing snail common in the Pacific as a potent painkiller. Early clinical trials have shown that the substance relieves some of the worst kind of chronic pain and could someday be an alternative to morphine.

For the time being, the sea's potential as a medicine cabinet remains largely in the realm of experimentation. But science is moving quickly, and many experts say the world's waterways may soon yield some effective medical treatments, if not some miracle cures. ■

John Henkel is a staff writer for FDA Consumer.



These highly magnified samples show the similarity between human bone (top) and coral (bottom). The weblike structure of coral makes it ideal as a bone implant because it becomes biologically integrated into the human body.

(Photos courtesy of Interpore International)



■ A new test that can detect the potentially deadly ***E. coli* O157:H7 bacterium** in less than an hour is in development by FDA scientists. The Anti-body direct epifluorescent filter test improves on many current methods such as culturing, which can take four to five days for results.

■ Americans of all ages may be at risk for **pneumococcal diseases**, the leading cause of 40,000 vaccine-preventable deaths that occur each year. These diseases include pneumonia, bacteremia (blood infection), and meningitis (infection of the brain lining). The national Centers for Disease Control and Prevention urges vaccination for everyone over 65. Others should ask their doctors if they need the vaccine.

■ **Home-monitored blood pressure readings** tend to be more accurate than those taken in a doctor's office, report researchers at the Katholieke Universiteit Leuven in Belgium. Many patients experience a rise in blood pressure caused by office visit stress. The falsely elevated readings can lead to unnecessary treatment for high blood pressure. (*Journal of the American Medical Association*, Sept. 30)

■ Twenty percent of Americans over age 12 carry the **genital herpes virus**, report researchers at the national Centers for Disease Control and Prevention. The alarming occurrence of the virus—a 30 percent increase over a 1970s' study—is partly the result of young people not practicing safe sex, the report states. Herpes can be transmitted through sexual activity

and also by touching and kissing. The disease cannot be cured. (*New England Journal of Medicine*, Oct. 16)

■ A **reduced-fat mozzarella cheese** that retains "meltability" and "springiness" is now being used on pizzas and other foods for school lunch programs nationwide. Developed by the U.S. Depart-



ment of Agriculture, the new cheese contains less than half the fat found in whole-fat mozzarella.

■ A series of **drug education materials** for students in grades five through nine is available free from the National Institute on Drug Abuse. NIDA's "Mind Over Matter" campaign offers six glossy magazines that unfold into posters and explore the effects of drugs on the brain. The campaign aims to encourage interest in the neuroscience profession and includes a teacher's guide. For copies, call NIDA at 1-800-729-6686.

■ **Tuberculosis** can be transmitted by contaminated bronchoscopes, which are devices used to examine the lungs, according to a study by the national Centers for Disease Control and Prevention. CDC says medical facilities can reduce or eliminate this threat by adhering to

sterilization standards established by the Association for Practitioners in Infection Control. (*Journal of the American Medical Association*, Sept. 30)

■ Unattended **bathtub seats** caused 29 infant drownings between 1983 and 1995, according to the Consumer Product Safety Commission. More than a million of the seats are sold yearly. CPSC warns consumers to never leave a child alone in the tub. (*Pediatrics*, October 1997; the article is available in the October issue on the Pediatrics Electronic Pages at www.pediatrics.org/content/vol100/issue4/)

■ **Senior citizens** may keep their weight in check by eating more frequent, but smaller, meals. A study sponsored by the U.S. Department of Agriculture found that both women in their 20s and women in their 60s and 70s burned about the same amount of fat after eating 250- and 500-calorie meals. But the older group burned about 30 percent less fat after a 1,000-calorie meal. (*American Journal of Clinical Nutrition*, October 1997)

■ The antidepressant drug Zyban (bupropion), which FDA approved last May, may double smokers' chances of **quitting smoking**, according to a study at the Mayo Clinic and elsewhere. In the study, 615 volunteers who were not depressed but wanted to give up smoking took either Zyban or a placebo for six weeks. After a year, 23 percent of the Zyban group had not smoked, but only 12 percent of the placebo group had not smoked again. (*New England Journal of Medicine*, Oct. 23)



Manufacturer Sentenced for Selling Unsterilized Surgical Instruments

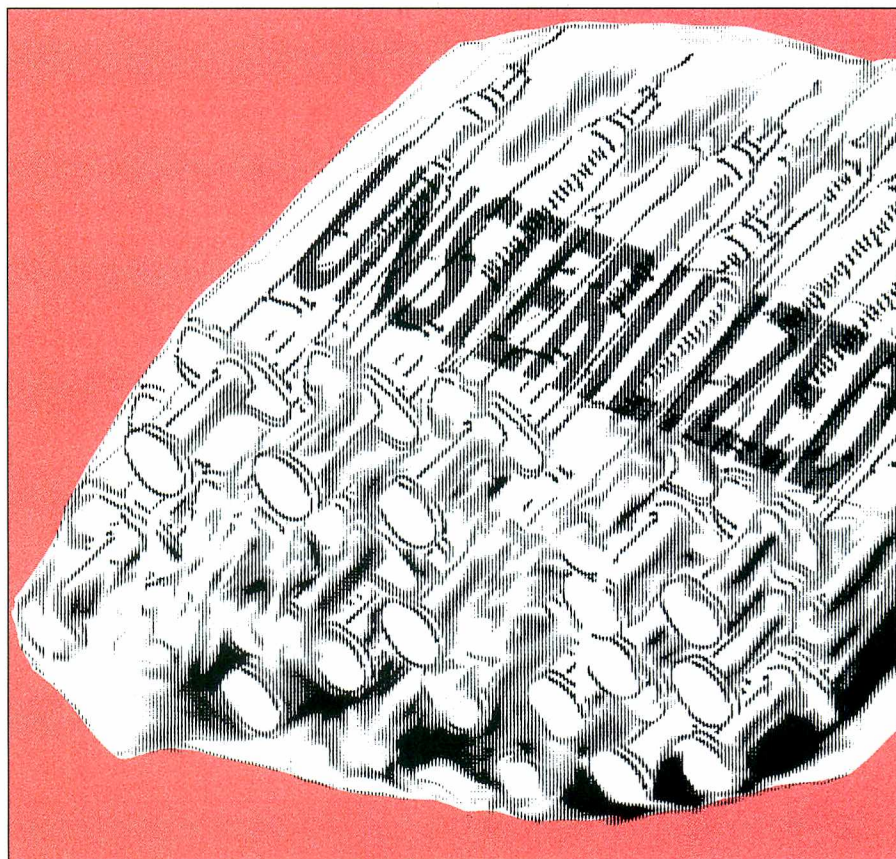
by Dixie Farley

A manufacturer of gynecological surgical devices was sentenced to a 15-month prison term after pleading guilty to intentionally selling unsterilized instruments labeled as "sterile" and providing FDA false information.

The manufacturer and the company also were ordered to pay \$37,004 each to the hospitals and clinics that had returned the instruments. All the unsafe devices were recalled, seized and destroyed under FDA supervision.

After hearing testimony at the Sept. 17, 1997, presentencing hearing, Judge Frederick Scullin, of the U.S. District Court for the Northern District of New York, also placed International Medical Technologies Group Inc. (IMTG) on five years' organizational probation and ordered its president, John Sturgeon, to withdraw his device marketing clearances and avoid involvement in the manufacture of drugs and devices for one year after serving his sentence.

IMTG sold syringes, aspiration catheters, surgical tubing, cervical dilators, curettes for sampling tissue, and tissue collection sets for use in surgical gynecological procedures such as abortion, treatment of abnormal uterine bleeding, and uterine sampling for diagnosing cancer. These are considered sterile surgical procedures, and doctors have traditionally demanded sterile instruments for performing them. The risk of infection is one of the major hazards of these procedures because infection may lead



to blood poisoning, infertility and death.

At the hearing, Eugene Williams, M.D., an obstetrician-gynecologist now retired from FDA's Center for Devices and Radiological Health, testified that the unsterilized devices created a serious risk of harm from infection and that data gathered by the agency's Buffalo, N.Y., district office indicated that a fourfold increase in infections at one clinic was

likely due to the use of unsterilized IMTG devices the clinic had received.

The company's poor practices came to FDA's attention in January 1993, when three former IMTG employees complained to the agency's Albany, N.Y., resident post that the company was shipping unsterilized products labeled as "sterile."

Early in 1993, Nancy Saxenian and

Michael Sinkevich, investigators with FDA's Buffalo district office, inspected IMTG.

Initially, Sturgeon gave the investigators company records showing that surgical devices labeled as sterile and distributed to hospitals and clinics had been sterilized by Medical Device Sterilization Inc., of Saratoga, N.Y. But when Saxenian and Sinkevich tried to locate the company, they could find no evidence of its existence. Confronted with this finding, Sturgeon admitted that he'd fabricated the records, intentionally giving false information and knowingly labeling the unsterilized devices as sterile. FDA's approvals of the devices called for them to be sterilized with ethylene oxide, but Sturgeon said sterilization was too costly.

The investigators examined Sturgeon's records, noting that one load of curettes had been sent to a Northborough, Mass., company for sterilization. But the records also showed that, of a batch of 1,825 curettes, only 1,500 had been sterilized. When FDA asked Sturgeon to identify which instruments had been sterilized and which were in commercial distribution, Sturgeon was unable to do so. As a result,

FDA urged Sturgeon to recall from the market all curettes made by the company.

As the inspection progressed, the investigators found other problems, including:

- no records of production, quality control, packaging, and labeling specifications
- inadequate records of product specification testing and dates and number of products made
- no written procedures for inspecting finished devices
- failure to receive FDA marketing clearance for tissue collection and uterine injector sets.

Sinkevich recalls that Sturgeon appeared "vague, evasive, inconsistent and uncertain" in answering questions and providing records. Eventually, Sturgeon admitted that the company had distributed other unsterilized products labeled as sterile. At FDA's urging, he recalled from the market all remaining products made by the company.

At the end of the inspection, the investigators reported their findings to Sturgeon, who gave them copies of written manufacturing procedures he said he intended to put in place to meet FDA requirements.

However, FDA found the procedures to be inadequate and decided to take further action.

"In light of the extensive manufacturing problems and Sturgeon's history of falsifying records and shipping potentially hazardous unsterilized devices as sterile, particularly when faced with economic incentives, we decided to go for seizure," says James Kewley, a compliance officer with FDA's Buffalo district office.

Accompanied by Saxenian and Sinkevich, a U.S. deputy marshal seized the devices in August 1993. Saxenian witnessed destruction of the devices, valued at \$100,000, in February 1994.

FDA continued to investigate Sturgeon and IMTG through a federal grand jury in New York. "We interviewed many current and former employees," says John Thompson, a team leader in FDA's Buffalo district. "From the interviews, we learned that Sturgeon had engaged in a coverup involving not only false sterilization records but also false manuals on standard operating procedures."

Sturgeon and IMTG were indicted in August 1996. They pleaded guilty four months later.

Dixie Farley is a staff writer for FDA Consumer.

Probe Proves Effective Against Antibiotic Smuggling Scheme

A scheme to make money by smuggling counterfeit antibiotics into the United States from China backfired on a New Jersey-based company and four of its principals and key employees when they were fined sums totaling more than \$1 million. They also were

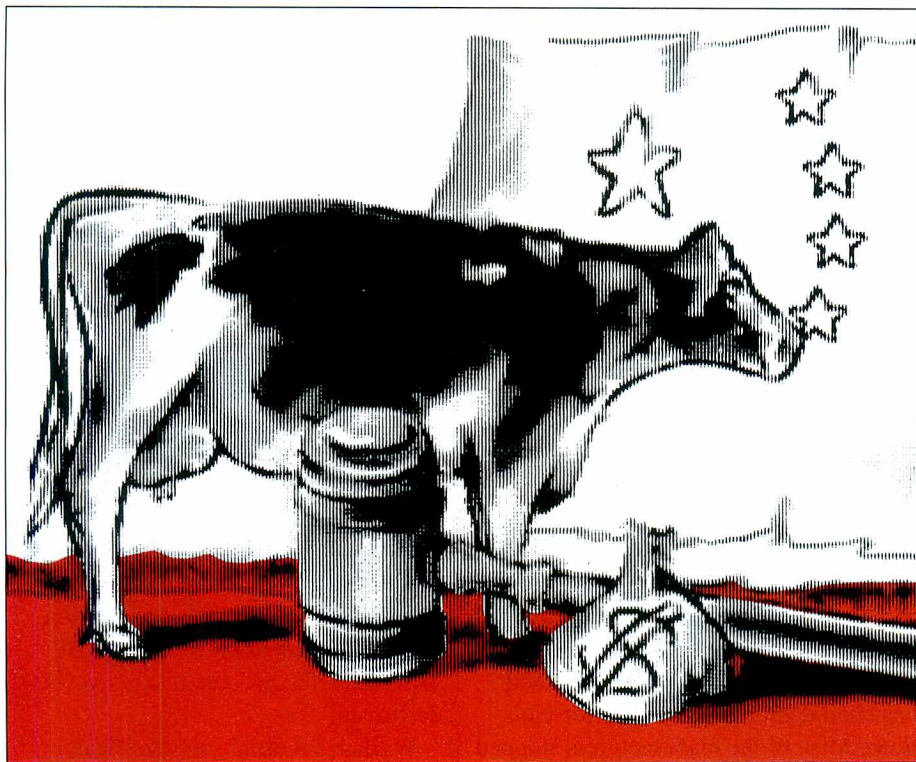
given prison sentences or probation.

An FDA investigation begun in 1990 revealed that the company's illegal activities cost end-user companies more than \$1.7 million in product losses.

Judge Joseph E. Stevens Jr., of the U.S. District Court for the Western District of Missouri, imposed the most recent fines last April. He ordered the company, Flavine International Inc.,

Closter, N.J., to pay \$925,000; its owner, Gerd Weithase, \$75,000; and vice president, Wolf Vogel, \$10,000. He also sentenced Weithase to two years in prison and Vogel to home detention for six months and gave both probations of as much as three years.

The men were part of a scheme in which Flavine bought bulk amounts of a veterinary antibiotic ingredient, oxytet-



racycline (OTC) base, and the human antibiotic gentamicin sulfate from unapproved sources in China for substantially less than the price of legitimate products. The company then resold them to U.S. drug companies at inflated rates.

Besides constituting economic fraud, the scheme posed a risk to food animals and humans because these counterfeit drugs are of unknown quality and potency.

The case began in May 1990, when an industry source contacted FDA's Omaha, Neb., resident post with information linking Flavine to the counterfeit OTC base. The source stated that Flavine had imported about 310 metric tons of OTC base from China in 1989. But the company's legitimate Chinese manufacturer, Long March Pharmaceutical Plant, which is approved by FDA, had made only 100 metric tons of the chemical that year. Thus, officials say, at least part

of the shipments likely came from unknown, unapproved sources.

In June 1991, FDA investigator Michael Spangenberg visited the Long March plant in China and took pictures of legitimate bulk OTC containers. After he returned to the United States, he inspected SmithKline Beecham Animal Health, in Omaha and determined that the bulk materials there were counterfeit because the containers were different from those in China.

Over the next three years, FDA and U.S. Customs officials seized suspected counterfeit materials from five end users and warehouses. The material came from Flavine and other possible suppliers. Among the seizure sites were the Port of Baltimore; Fermenta Animal Health, Elwood, Kan.; and Sanofi Animal Health, Le Sueu, Minn. Much of the material was later destroyed after being proven counterfeit.

In May 1993, after establishing probable criminal activity, special agents from FDA's Office of Criminal Investigations (OCI) and the U.S. Customs Service executed a search warrant at Flavine's New Jersey headquarters. At the same time, agents executed searches at the company's Kansas City, Mo., offices and at the residence of company vice president Ira "Rip" Siegel in Parkville, Mo.

In reviewing records seized during the search, OCI and Customs agents learned that Flavine was using a North Carolina company to repackage some of the 20-kilogram drums of counterfeit OTC base into 25-kg drums. The agents concluded that the company used this maneuver to hide its sale of counterfeit products by repackaging materials to look like they were from Long March, the legitimate Chinese manufacturer, which packs its OTC materials only in 25-kg drums.

Between December 1993 and February 1994, OCI also analyzed import information, determining that out of all the company's OTC base shipments, almost half—277,325 kg—of the shipments came from Chinese sources other than the legitimate supplier and were likely counterfeit.

These suspicions were backed up in May 1994, during an OCI and Customs interview with Long March official Dejun Meng. He confirmed that numerous shipments of OTC base, sold by Flavine under the Long March name, were not made by Long March. He outlined for agents several ways they could distinguish Long March materials from counterfeit by examining the products' certificates of analysis.

In December 1994, OCI, Customs, and the Justice Department's Office of Consumer Litigation interviewed former Flavine employee W. Mark Paradise. He verified that numerous shipments of

OTC base had not been produced by Long March but were sold in the United States as such.

Agents also reviewed Flavine's shipment record of other bulk drugs it bought from overseas. They found that Flavine had counterfeited several other drugs, including gentamicin sulfate, an antibiotic used to treat bacterial infections, such as those caused by *Streptococcus pneumoniae*, in humans and animals. Long March also makes gentamicin sulfate, and, again, Meng verified for agents that some of the bulk gentamicin sulfate sold by Flavine under the Long March name was not made by his company.

On Jan. 24, 1995, a federal grand jury returned an 11-count indictment charging Flavine International, Weithase, and several of his associates with conspiracy, smuggling, misbranding, and other federal drug violations.

In September 1995, French police arrested Weithase in Paris, where he had fled after escaping to Germany to avoid prosecution. Accompanied by U.S. marshals, Weithase returned to the United States in January 1996 after being turned over to U.S. authorities by the Justice Ministry of France.

Initially, Weithase pleaded not guilty to the charges. But on March 20, 1996, he, along with his company and associates Vogel and John Milhard, Flavine's traffic manager, admitted guilt to charges of conspiracy, money laundering, and counterfeiting. They were sentenced last April 9. Milhard was placed on probation for one year and fined \$5,000. Two days earlier, Flavine employee W. Mark Paradise was sentenced for his part in the counterfeiting scheme to six months' home detention, a \$25,000 fine, and five years' supervised probation.

Flavine International Inc. is still in business and now deals in legitimate products, FDA officials say.

—John Henkel

FDA Takes Dim View Of Glow-in-the-Dark Makeup

If the scary monsters that came trick-or-treating last Halloween glowed in the dark, they may have unknowingly painted their faces with an illegally marketed makeup.

The Face Colours Glow-in-the-Dark Cream Makeup, manufactured by Zauder Brothers Inc. of Freeport, N.Y., contained an unapproved color additive, zinc sulfide, added to the makeup to achieve a glowing appearance.

While FDA has not received any reports of injuries from the makeup, the agency considers zinc sulfide unsafe until it concludes that studies have been submitted to prove its safety.

Zauder Brothers recently sought approval of zinc sulfide by submitting a color additive petition, as stated in an Oct. 6, 1997, *Federal Register* notice.

FDA has been aware of these glow-in-the-dark makeups since the 1970s and has cited eight manufacturers for violations. Most of the manufacturers stopped making the products after FDA contacted them.

FDA first inspected the Zauder Brothers' facility in October 1993, after an informant complained to the agency about the sale of the illegal makeup. Investiga-

tors with FDA's New York district office collected product samples, and FDA lab tests confirmed that the product contained zinc sulfide.

In a March 4, 1994, warning letter, FDA cautioned Zauder Brothers that the agency might take further action if the company continued to manufacture and sell the illegal product.

But the company didn't stop making and selling it, as evidenced by continuing tips from informants and an FDA reinspection of the Zauder facility in October 1996.

In April 1997, FDA filed a complaint against the glow makeup in the U.S. District Court for the Eastern District of New York, and U.S. marshals, accompanied by FDA investigators, seized 185 cartons of the makeup, valued at \$3,800.

In September 1997, Zauder Brothers entered into a consent decree under which the U.S. Marshals Service will destroy the seized glow makeup. At press time, the makeup had not yet been destroyed.

William Friedrich, an investigator with FDA's New York district office, anticipates that his office will inspect the company's facility again as the next Halloween season approaches.

—Tamar Nordenberg



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: Honey, at New Munster, Wis. (E.D. Wis.); Civil Action No. 97-C-0536.

CHARGED 5-5-97: While held for sale after shipment in interstate commerce at Best Bargains, Inc., in New Munster, Wis., the article was adulterated in that another substance, cane or corn sugar syrup, had been substituted in whole or in part for honey—402(b)(2). The article was misbranded in that the name on its labeling, honey, was false and misleading as applied to an article of food which was not pure honey and which consisted largely of another substance—403(a)(1).

DISPOSITION: The article was destroyed. (F.D.C. No. 67186; S. No. 97-562-238; S.J. No. 1)

PRODUCT: Infant Formula, at Wampum, Pa. (W.D. Pa.); Civil Action No. 95 1814 and 95 1991.

CHARGED 12-8-95: While held for sale after shipment in interstate commerce at Gateway Commerce Center, in Wampum, Pa., the articles were misbranded in that their labeling was false and misleading—403(a)(1).

DISPOSITION: The articles were either destroyed or reconditioned. (F.D.C. No. 67110; S. No. 96-787-061; S.J. No. 2)

PRODUCT: Peppers, at Brooklyn, New York (E.D. N.Y.); Civil Action No. CV-96-1230.

CHARGED 3-18-96: While held for sale after shipment in in-

terstate commerce at Adamba Imports International, in Brooklyn, N.Y., the articles were adulterated in that they had been shipped and held under insanitary conditions whereby they might have been rendered injurious to health—402(a)(4).

DISPOSITION: The articles were destroyed. (F.D.C. No. 67124; S. No. 95-752-931; S.J. No. 3)

PRODUCT: Sodium Citrate, at Springfield, Mo. (W.D. Mo.); Civil Action No. 94-3152-CV-S-4.

CHARGED 4-12-94: While held for sale after shipment in interstate commerce at G.S. Robins and Company, in Springfield, Mo., the article was adulterated in that it was unfit for food because of the presence of foreign material, including plant matter and a rubber-like material visible to the naked eye—402(a)(3).

DISPOSITION: The article was reconditioned for nonfood use. (F.D.C. No. 66954; S. No. 94-688-047; S.J. No. 4)

Drugs/Human Use

PRODUCT: An article of drug, at Eau Claire, Wis. (W.D. Wis.); Civil Action No. 96 C 1016 S.

CHARGED 12-17-96: While held for sale after shipment of one or more of their components in interstate commerce at Radix Laboratories, Inc., in Eau Claire, Wis., the article was adulterated in that it was a new animal drug within the meaning of 201(v)(1) and was unsafe within the meaning of 512(a)(1)(A) because no approval of an application filed pursuant to 512(b) was in effect with respect to its intended use.

DISPOSITION: The article was destroyed. (F.D.C. No. 67158; S. No. 96-718-764; S.J. No. 5)

Medical Devices

PRODUCT: Test Kits, at Irvine, Calif. (C.D. Calif.); Civil Action No. CV 97-0524-ABC (VAP).

CHARGED 1-27-97: While held for sale after shipment in interstate commerce at IBEX Medical Group, in Irvine, Calif., the articles were adulterated in that they were a class III device without an application for premarket approval—501(f)(1)(B). The articles were misbranded in that the label failed to contain the name and place of business of the manufacturer, packer or distributor—502(b)(1), and failed to bear the established name of the device—502(e)(2). Also, notice or other information respecting the device was not provided to the Food and Drug Administration at least 90 days prior to its introduction into interstate commerce—502(o).

DISPOSITION: The articles were destroyed. (F.D.C. No. 67161; S. No. 97-683-594; S.J. No. 6)

PRODUCT: Test Kits, at Beverly Hills, Calif. (C.D. Calif.); Civil Action No. CV 97-1751-GHK (RCx).

CHARGED 3-18-97: While held for sale after shipment in interstate commerce at the residence of David Rudich, in Beverly Hills, Calif., the articles were adulterated in that they were a class III device without an application for premarket approval—501(f)(1)(B). The articles were misbranded in that the label failed to contain the name and place of business of the manufacturer, packer or distributor—502(b)(1), and the label failed to bear the established name of the device—502(e)(2). Also, notice or other information respecting the device was not provided to the Food and Drug Administration at least 90 days prior to its introduction into interstate commerce—502(o).

DISPOSITION: The articles were destroyed. (F.D.C. No. 67173; S. No. 97-789-608; S.J. No. 7)

INJUNCTION ACTIONS

DEFENDANT: Central Grocers Cooperative, Inc., Robert J. Wagner, Joseph Caccamo, and individuals, at Franklin Park, Ill. (N.D. Ill.); Civil No. 97-C-2052.

CHARGED 3-25-97: While held for sale after shipment in interstate commerce at Central Grocers Cooperative, Inc., in Franklin Park, Ill., the articles were adulterated in that they had been shipped and held under insanitary conditions whereby they might have been contaminated with filth—402(a)(4).

DISPOSITION: A consent decree of permanent injunction was granted. Central Grocers Cooperative, Inc., was ordered to pay all civil penalties in this action. (Inj. No. 1411; S. No. 97-759-321; S.J. No. 8)

DEFENDANTS: MinXray, Inc., and Keith R. Kretchmer, at Northbrook, Ill., (N.D. Ill.); Civil Action No. 96 C 1062.

CHARGED 2-23-96: While held for sale after shipment in interstate commerce at MinXray, Inc., in Northbrook, Ill., the defendants manufactured and distributed x-ray units that did not comply with the applicable performance standards—538oo(a)(1); they also issued certificates that were false and misleading—538oo(a)(5)(B); and they failed to notify the purchasers that the units did not comply with applicable performance standards, failed to bring the units into compliance without charge, and failed to replace them or to refund the cost of the units—538oo(a)(2).

DISPOSITION: A consent order and judgment of permanent injunction was granted. And MinXray, Inc., was ordered to pay civil penalties in this action. (Inj. No. 1384; S. No. 95-741-232; S.J. No. 9)

Statement of Ownership, Management, and Circulation

(Required by 39 U.S.C. 3685)

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