

FDA CONSUMER

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

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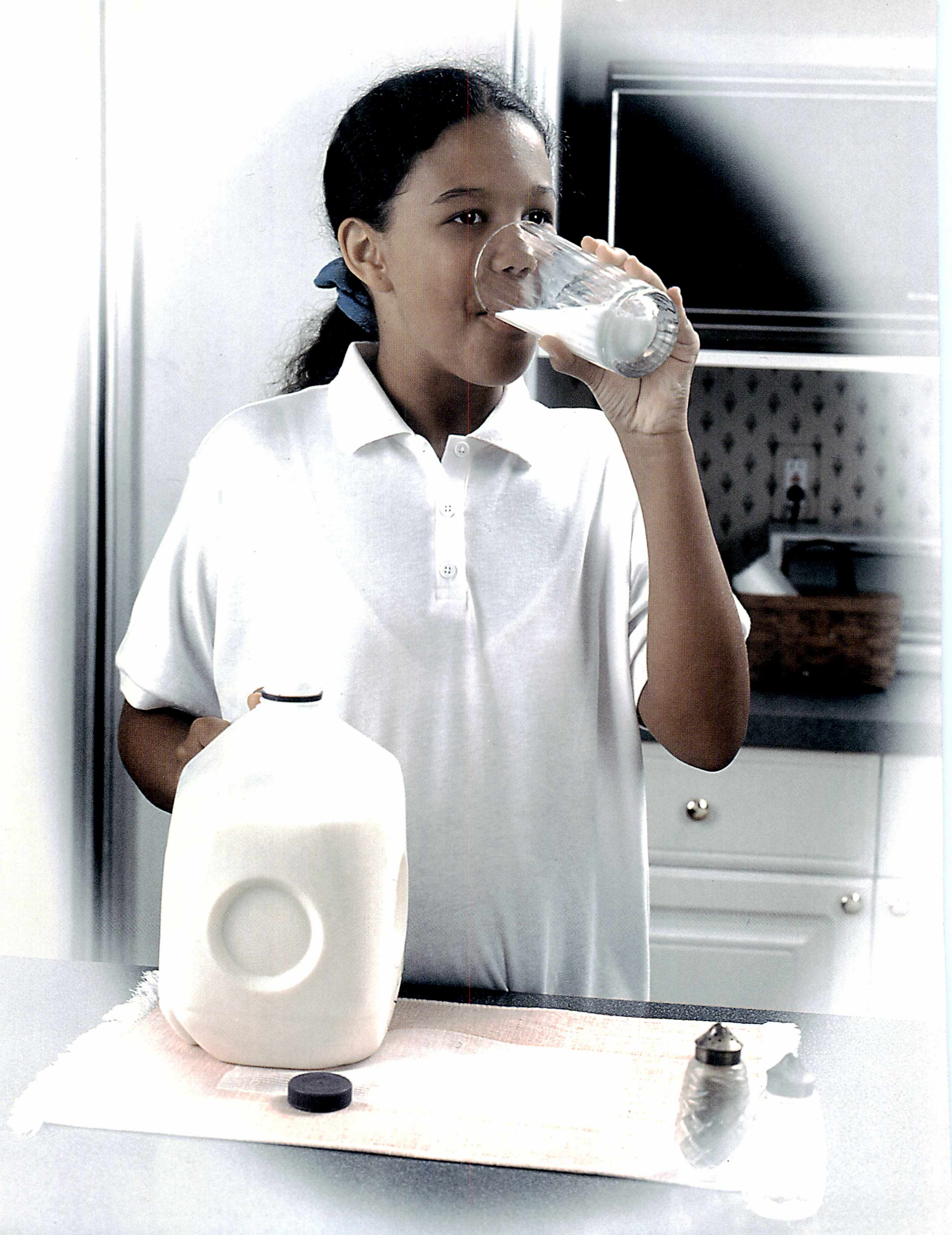
SEPTEMBER-OCTOBER 1997 •

WHY SHOULD FDA

REGULATE

DRUGS?

An Interview
with Janet
Woodcock,
M.D.



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

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SEPTEMBER–OCTOBER 1997

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From farmers to families, everyone needs to be vigilant in the battle to make and keep food safe.

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That's a question many people raise as FDA strives to maintain a delicate balance between too much regulation and not enough. The answer is explained in an interview with the director of FDA's drug center.

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To make and keep your bones strong, nothing beats a tall, icy glass of milk. But other foods and exercise are important, too. See page 27.



New Safety Standard For Device Electric Wires

Under a new FDA safety standard, manufacturers must protect the electric wires connecting patients to their medical devices so the wires cannot be mistakenly plugged into a live electric outlet.

The wires, called electrode lead wires and patient cables, have an electrode at one end attached to the patient, with the other end attached to the device. Without protection, this other end could be mistakenly plugged into an electrical outlet while the electrode is attached to the patient, possibly burning or even electrocuting the person.

Although many manufacturers voluntarily protect the wires and cables, accidents have occurred in both hospitals and homes. Between 1985 and 1994, 24 infants and children received severe electric shocks from unprotected wires, and five died.

Most of the cables and wires must meet the standard within three years. However, protection must be in place within one year for the 10 highest-risk

devices: breathing frequency monitors, apnea monitors, electrocardiographs, physiological signal radio transmitters and receivers, heart monitors, electrocardiograph electrodes, transducer and electrode cables, medical magnetic tape recorders, arrhythmia detectors and alarms, and electrocardiograph telephone transmitters and receivers.

FDA published the mandatory standard in the May 9, 1997, *Federal Register*.

Prison, Fines for Perpetrators Of Food and Drug Fraud

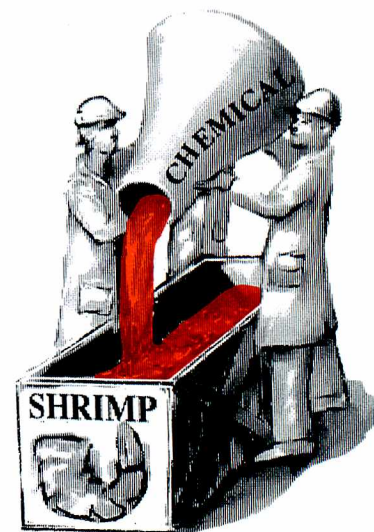
Three men face up to three years in prison for selling rotten shrimp and an unapproved drug touted as a cure-all for serious diseases. Those who sold the rotten shrimp were fined, and the company was ordered to pay \$1 million.

Charles R. Pixley, a New York book publicist found guilty of selling the unapproved drug 714X, lost his appeal and will serve one year and one day in federal prison, as ordered in 1996.

The U.S. Court of Appeals for the 2nd Circuit, based in New York, affirmed Pixley's conviction May 7, stating that because 714X was promoted as a treatment for cancer, AIDS and other diseases, it is subject to FDA's new drug approval requirements. FDA's case against Pixley was reported in the Investigators' Reports section of the November 1996 *FDA Consumer*.

In another case, reported in the April 1997 *FDA Consumer*, a company and three employees were sentenced for selling rotten imported Chinese shrimp that had been chemically treated and passed off to consumers as "fresh frozen."

Sigma Corp. Inc. of St. Petersburg, Fla., and Sigma managers William A. Walton and Charles Sternisha were sentenced May 9 in the U.S. District Court



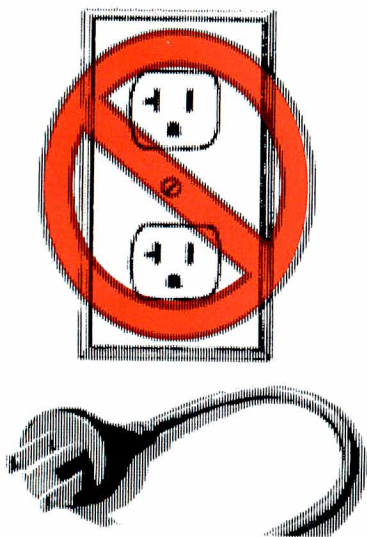
for the Middle District of Florida. Robert Fields, a salesman, had been sentenced March 24.

The corporation was fined \$1 million, placed on five years' probation, and ordered to pay \$160,916 in prosecution fees, special assessments, and restitution. Walton was sentenced to three years, five months in prison and two years' probation and fined \$10,600. Sternisha was sentenced to two years, three months in prison and two years' probation and fined \$6,250. Both men remain free without bond, pending their appeals. Fields was sentenced to two years' probation and fined \$2,500.

Urgent Factor VIII Recall

Possible contamination with penicillium mold recently prompted the Hyland Division of Baxter Healthcare to recall three lots of Recombinate (recombinant human Factor VIII). Recombinate is injected intravenously to treat the blood disorder hemophilia A.

The possible contamination, announced by FDA last July, may cause infection and, in patients allergic to penicillin, allergic reaction. Both could be



Report Problems to MedWatch: To report serious health problems associated with products in the following updates, health professionals should call FDA at (1-800) FDA-1088, or report by fax at (1-800) FDA-0178.

Mixing Diet Drugs Calls for Caution

Reports of heart valve disease in women taking the obesity drugs fenfluramine and phentermine together have prompted FDA to advise doctors to closely monitor patients on this therapy.

In a letter to doctors, FDA noted that as of July 8 it had received reports of 33 cases of unusual abnormalities in heart valves in women ages 30 to 72 taking both drugs together for 1 to 28 months. The course of the disease when the drugs are stopped is unknown.

There is no conclusive evidence of a cause-effect relationship between use of the drugs and development of this disease. However, because of the seriousness of the heart problems and their rarity in otherwise healthy obese women, FDA believes patients and health professionals need this information. The agency will continue monitoring adverse events reports.

FDA approved each drug for use alone and short term, not in combination or for long term. In accordance with approved labeling, only obese patients should take these drugs, and they should also follow a weight-loss regimen that includes a reduced-calorie diet and an exercise program. (See "Losing Weight Safely" in the January-February 1996 *FDA Consumer*; "New Weight-Loss Drug" in the Updates section of the July-August 1996 issue, and "Redux Relabeling Notes Higher Risk" in the Updates of the November 1996 issue.)

Health professionals should give patients on this therapy thorough heart evaluations and, if heart disease develops, pursue further such evaluation. They also should report any heart valve disease or other serious problems associated with the use of phentermine, fenfluramine, and also dexfenfluramine to FDA's MedWatch program.

Editor's Note: Herbal "fen-phen" is

not similar to the prescription drug combination of fenfluramine and phentermine. Herbal fen-phen is marketed as a combination of herbals and, like all products sold as dietary supplements, can be marketed without FDA review of safety or effectiveness, in accordance with the Dietary Supplement Health and Education Act of 1994. For further information on a specific dietary supplement product, contact the manufacturer. Check with your health-care professional about use of the product.

Health Advisory On Newest AIDS Drugs

Drugs called protease inhibitors may contribute to increases in blood sugar and diabetes in HIV-infected patients, and doctors should closely monitor patient glucose levels, FDA has advised doctors.

The agency informed doctors in June that it received reports of 83 cases of new or exacerbated diabetes mellitus and hyperglycemia in HIV patients taking the drugs. While many patients who discontinued protease inhibitor therapy saw a reduction in their symptoms, a clear causal relationship between the drugs and onset of the conditions has not been established. Many patients had confounding medical conditions, some of which required therapy with agents that have been associated with the development of diabetes mellitus or hyperglycemia.

Of the 83 patients, 27 were reported to require hospitalization, including six life-threatening cases. Five cases resulted in ketoacidosis, a serious diabetes-related condition. Protease inhibitors will carry revised labeling that delineates this potential side effect.

HIV patients on protease inhibitor therapy should be aware of the warning signs of hyperglycemia and diabetes: increased thirst and hunger, unexplained weight loss, increased urination, fatigue,

and dry, itchy skin. These symptoms occurred in the reported cases, on average, in approximately 76 days from starting protease inhibitor therapy, but FDA is aware of cases where symptoms appeared as early as four days after starting this therapy. FDA will continue to monitor for additional events. Health-care professionals should report any cases of diabetes, hyperglycemia, or any other serious toxicity associated with the use of protease inhibitors to FDA's MedWatch program.

(See also "New Ways to Prevent and Treat AIDS" in the January-February 1997 *FDA Consumer*.)

Don't Buy Abortion Kits Over the Net, FDA Warns

Consumers should not purchase home abortion kits or female self-sterilization kits sold over the Internet, FDA warns. These unapproved products pose significant, possibly life-threatening health risks.

The abortion kit is inaccurately advertised as a "complete kit for early pregnancy termination without surgery ... scientifically proved safe and unrisky." The kit provides drugs not approved by FDA to terminate pregnancy.

The agency assessed the product and concluded that using the kit without a physician's supervision could cause heavy vaginal bleeding and even death. Birth defects also can result if a pregnancy is carried to term after using these drugs.

The self-sterilization kit claims to use a method similar to inserting an intrauterine device and to have a lower risk than surgical sterilization. The kit uses an unapproved drug, quinacrine hydrochloride, which can cause ectopic pregnancy, abnormal pregnancies, and permanent damage to reproductive organs.

FDA is continuing to investigate and monitor both products.

severe and even life-threatening.

The recalled lots are:

- Lot 2938M228AA, 976 International Units (IU) per vial
- Lot 2938M229AA, 291 IU per vial
- Lot 2938M230AA, 1,130 IU per vial.

Anyone who has these lots should return them to the place where they obtained them. Patients and customers with questions may call the company at (1-800) 423-2090.

Catfish Cleared of Dioxin; Eggs Still Being Sampled

Catfish that had consumed feed inadvertently contaminated with the toxic chemical dioxin are now cleared by FDA for processing and shipping. FDA had originally halted sale of these fish, but new data show that dioxin levels are below the level of concern. At press time, the agency still had not cleared for sale eggs from poultry that ate the contaminated feed.

The detected dioxin levels pose no immediate health hazard, and consumers should not hesitate to consume catfish or eggs bought on the retail market.

After finding elevated levels of dioxin in two of 80 poultry samples, FDA on July 7 told makers of the tainted animal feed to stop further distribution and use of the feed. The agency told catfish and egg producers not to ship their products if the fish or chickens had eaten the feed. The agency said the companies could resume shipping only if they showed through testing that the human food contained less dioxin than 1 part per trillion.

Investigation by FDA and other federal and state agencies showed that the dioxin source was "ball clay," a common anti-caking agent added to soybean meal. The ball clay was traced to a Mississippi clay mine, which stopped shipping the clay for feed use.

"Dioxin" refers to a class of chemical pollutants created as byproducts of

chemical manufacturing, incineration, chlorine bleaching of paper pulp, and other industrial processes. Dioxins exist in the environment at low levels and are known to accumulate in the food chain. Continued high exposure to dioxins can increase the risk of cancer and other health problems.

States Join FDA In Enforcing Tobacco Rule

Florida and Washington are FDA's first state partners for enforcing the agency's 1996 rule to protect children from tobacco.

The rule prohibits the sale of cigarettes and smokeless tobacco to children under 18 and requires retailers to check photo ID's of anyone under age 27. (See "Saving Our Children from Tobacco" in the October 1996 *FDA Consumer*.)

Under contracts with FDA, announced in June, each state will conduct about 300 unannounced retail checks monthly for eight months. Children ages 15 and 16, accompanied by an adult, will try to purchase cigarettes or smokeless tobacco in retail stores throughout the respective state.

FDA will issue a warning the first time a retailer is found selling to children and will plan repeat inspections. The agency will seek a \$250 fine for the second violation and greater fines after that.

Unapproved Lasers Seized From Florida Manufacturer

As part of a crackdown on the sale and use of lasers not approved for eye surgery, U.S. marshals, on behalf of FDA, seized nine excimer lasers and components valued at more than \$3 million from Photon Data Inc., of Winter Park, Fla.

The lasers, which FDA had not reviewed for safety and effectiveness, were being sold to reshape the cornea to

treat nearsightedness and other eye conditions. They were seized June 9.

FDA is concerned about the potential for serious eye injury from unapproved excimer lasers because manufacturers have not submitted success rates, number of adverse events, critical safety engineering data, and other information FDA requires to show the devices are safe and effective. Physicians using unapproved excimer lasers might not have enough information to counsel patients adequately on the benefits and risks of the treatment.

FDA's concern about unapproved excimer lasers has been heightened by recent reports of serious eye injuries from the devices such as permanently damaged eyesight or temporary blindness requiring a corneal transplant. The agency asks patients who have been injured, or doctors aware of such injuries, to inform FDA's MedWatch service by phone, (1-800) FDA-1088; by fax, (1-800) FDA-0178; or by modem (1-800) FDA-7737.

Currently, FDA has approved only two lasers for photorefractive keratectomy (PRK), a surgical procedure that treats nearsightedness. The laser manufacturers, Summit Technology Inc., of Waltham, Mass., and Visx Inc., of Santa Clara, Calif., conducted clinical studies to show that their lasers were safe and effective. (See "Laser Procedure for Nearsightedness" in the Updates section of the January-February 1996 *FDA Consumer*.) FDA also has approved a Visx laser to treat astigmatism.

Several other lasers for eye surgery are currently in FDA-sanctioned clinical trials.

Patients considering laser surgery for nearsightedness or astigmatism should ask their doctors if the laser is an approved Summit or Visx product. If not, they should make sure the laser is part of an FDA-sanctioned clinical study.

At press time, only the Photon Data

devices had been seized, but FDA plans to take enforcement action against other unapproved excimer lasers on the market.

Risk of Tick-Borne Illness Prompts Blood Recall

The possibility of transmitting tick-borne disease through blood transfusions recently prompted a voluntary recall of blood products from six states.

United Blood Services, also known as Blood Systems Inc., collected the potentially infected blood at Fort Chafee, Ark., during May and June. The states that may have received the recalled red blood cells, platelets, and recovered plasma are Alabama, Arizona, Louisiana, Mississippi, Oklahoma, and Texas.

In addition, other blood and plasma collections sites may have received potentially infected blood from individuals in training at Fort Chafee from April through June. FDA and the national Centers for Disease Control and Preven-

tion advised that individuals who donated blood within four weeks of leaving the fort should immediately notify the center where they donated. If notified, a center should take immediate steps to retrieve the potentially affected blood and blood components intended for transfusion.

Patients who received these blood products should have been notified by their physicians in July and told to report any illness. All tick-borne infections can cause fever, as well as headache, muscle pain, and sometimes a rash. While the majority of infections are mild, often without symptoms, a small number can be serious and even fatal.

People with questions about the source of blood products they received should contact their doctors. Health professionals should report any adverse events associated with these products to FDA's MedWatch program.

Supplements with Plantain May Pose Danger, FDA Warns

Consumers should stop buying and using certain dietary supplements labeled as containing plantain because they may contain Digitalis, a plant that contains powerful heart stimulants.

FDA issued this warning after finding Digitalis in samples of raw material labeled as plantain and used by various manufacturers in herbal laxatives, poultices and tea. Some of the suspect plantain also was distributed to retailers who sell it in bulk for making tea. The labels of suspect products may list plantain as an ingredient.

Consumers who have herbal laxatives or tea labeled as containing plantain should contact the store where the products were bought to learn whether or not the product is from one of the manufacturers or distributors believed to

have received the mislabeled raw material. Consumers also can get an updated list of manufacturers and distributors of suspect products from FDA's Consumer Hotline, (1-800) FDA-4010, or on FDA's World Wide Web site at <http://www.fda.gov/bbs/topics/NEWS/NEW00570.html>.

Consumers who experience adverse reactions associated with the consumption of plantain-labeled products should see a doctor. Consumers and health professionals can report adverse reactions associated with these products to FDA's MedWatch adverse event reporting line at (1-800) FDA-1088.

FDA investigated the plantain-labeled products after receiving a report of an abnormal heart rate with heart block—a life-threatening condition—in a young woman who ate a dietary supplement labeled as containing plantain. FDA analysis indicated the presence of lanatosides, constituents of the herb *Digitalis lanata*, in raw material.

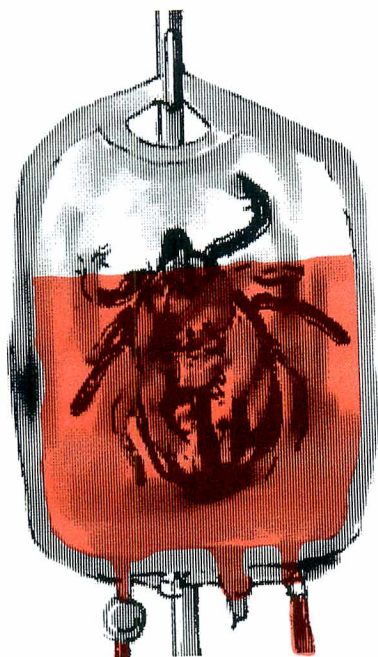
Digitalis is an active ingredient of some prescription heart medicines. It can cause nausea, vomiting, dizziness, headache, confusion, low blood pressure, vision problems, and abnormal heart rate and rhythm, including cardiac arrest.

Plantain is a perennial weed of the genus *Plantago*, which includes more than 200 widely distributed species. It is not the same as the tropical banana plant of the same name whose fruit is cooked and eaten as a vegetable.

Less Foreign Inspection Likely

Recent agreements may reduce dramatically the need for FDA inspection of regulated firms in European Union countries.

The United States and countries in the European Union have agreed that FDA and its EU counterparts may exchange



inspection reports on pharmaceutical and medical device firms. In addition, the agencies may exchange medical device evaluation reports prepared by third parties, based on the existing FDA external review pilot program for selected devices. Appropriate confidentiality will be maintained, as well as public access to certain information.

Currently, FDA and the EU regulatory agencies conduct hundreds of such overseas inspections annually, at considerable expense to their taxpayers. Under the agreements when fully implemented, the agencies would each inspect the appropriate domestic firms and ensure compliance with the regulations of the country to which the firms export.

FDA's readiness to participate in such agreements is based on demonstrated equivalence of EU inspection procedures and good manufacturing practice standards. Equivalence would be assessed during a three-year transition period.

At all times, each agency retains full responsibility for products marketed in its own country and can take action necessary to protect the public health.

1997 Food Code Available

The latest science-based food safety information is available in FDA's 1997 Food Code, a publication that gives food safety guidelines for restaurants, grocery stores, nursing homes, and other institutional and retail food operations.

The Food Code is used by the more than 3,000 state and local regulatory agencies that establish and enforce food safety rules. (See "New Food Code: A Menu of Modern Safety Standards" in the April 1994 *FDA Consumer*.)

The 1997 edition features for the first time separate guidelines on serving safe food to susceptible populations, such as

young children in day care and older adults in long-term health-care facilities. It also gives appropriate wording for consumer advisories on consumption of raw and undercooked foods of animal origin and includes language on in-shell egg pasteurization, a new technology in which eggs are heated long enough to destroy a specific bacterium without actually cooking the eggs.

As in previous editions, the 1997 Food Code guidelines are based on the Hazard Analysis Critical Control Point food safety system, which involves identifying and monitoring the points in food preparation where the risk of food-borne hazards is greatest.

The Food Code is available on FDA's World Wide Web site at <http://vm.cfsan.fda.gov/~dms/foodcode.html> and is provided in several different formats. Spiral-bound copies (order number PB97133656) and a WordPerfect 6.1 version on diskette (order number PB97501274) are available for \$35 each from the National Technical Information Service, Springfield, VA 22161; (703) 487-4650. The e-mail address is orders@ntis.fedworld.gov. To place an order by facsimile, dial (703) 321-8547. For rush orders, call (1-800) 553-NTIS.

Final Feed Rule Reduces Risk of BSE

To protect ruminant animals such as cattle, sheep and goats from transmissible neurological diseases, including bovine spongiform encephalopathy (BSE), and to keep potential human risk very low, an FDA final rule prohibits most mammalian protein from feeds for these animals.

The rule, which also requires controls to ensure that feeds are free of prohibited protein, took effect Aug. 4.

BSE, a transmissible degenerative dis-

ease of the nervous system, has never been documented in cattle in the United States. If it were found here, the rule would prevent its spread through feeds.

The rule excludes animal products that pose minimal risk of transmitting BSE, including blood, blood products, gelatin, milk, and milk products. It excludes inspected meat products originally produced for human consumption, such as plate waste from restaurants and institutions that is then further heat processed before being made into animal feed. Also excluded are pure pork and pure equine protein. Because pigs and horses are not known to have transmissible spongiform encephalopathies, their protein is excluded when it is from facilities that handle only these species.

FDA published the rule in the June 5, 1997, *Federal Register*, and also put it on its web site at <http://www.cvm.fda.gov/fda/infores/updates/bse/6597bse.html>.

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Consumer-Friendly Birth Control Information

This new, easy-to-understand table from FDA compares the effectiveness of birth control methods. FDA is working with manufacturers to include the table in the patient information for all contraceptive products. (See also "Protecting Against Unintended Pregnancy: A Guide to Contraceptive Choices" in the April 1997 *FDA Consumer*.)

Pregnancy Rates for Birth Control Methods

(For One Year of Use)

The following table provides estimates of the percent of women likely to become pregnant while using a particular contraceptive method for one year. These estimates are based on a variety of studies.

"**Typical Use**" rates mean that the method either was *not always used correctly* or was *not used with every act of sexual intercourse* (e.g., sometimes forgot to take a birth control pill as directed and became pregnant), or was *used correctly but failed anyway*.

"**Lowest Expected**" rates mean that the method was *always used correctly with every act of sexual intercourse* but *failed anyway* (e.g., always took a birth control pill as directed but still became pregnant).

Method	Typical Use Rate of Pregnancy	Lowest Expected Rate of Pregnancy
Sterilization:		
Male Sterilization	0.15%	0.1%
Female Sterilization	0.5%	0.5%
Hormonal Methods:		
Implant (<i>Norplant</i>)	0.09%	0.09%
Hormone Shot (<i>Depo-Provera</i>)	0.3%	0.3%
Combined Pill (<i>Estrogen/Progestin</i>)	5%	0.1%
Minipill (<i>Progestin only</i>)	5%	0.5%
Intrauterine Devices (IUDs):		
Copper T	0.8%	0.6%
Progesterone T	2%	1.5%
Barrier Methods:		
Male Latex Condom ¹	14%	3%
Diaphragm ²	20%	6%
Vaginal Sponge (<i>no previous births</i>) ³	20%	9%
Vaginal Sponge (<i>previous births</i>) ³	40%	20%
Cervical Cap (<i>no previous births</i>) ²	20%	9%
Cervical Cap (<i>previous births</i>) ²	40%	26%
Female Condom	21%	5%
Spermicide: (<i>gel, foam, suppository, film</i>)	26%	6%
Natural Methods:		
Withdrawal	19%	4%
Natural Family Planning (<i>calendar, temperature, cervical mucus</i>)	25%	1-9%
No Method:	85%	85%

1 Used Without Spermicide

2 Used With Spermicide

3 Contains Spermicide

Data adapted from: R.A. Hatcher, J. Trussell, F. Stewart, et al., *Contraceptive Technology*, 17th Revised edition, New York, NY: Irvington Publishers Inc. (in press).

Table prepared by FDA: 5/13/97

Focus On

Food SAFETY

Initiative Calls on Government, Industry, Consumers to Stop Food-Related Illness

by Audrey Hingley

Most people don't give much thought to food safety until a food-related illness prompts concern. But the threats are real, numerous and varied, as headlines in recent years have documented: *E. coli* O157:H7 in meat and apple juice, *Salmonella* in eggs and on vegetables, *Cyclospora* on fruit, *Cryptosporidium* in drinking water, and, most recently, Hepatitis A virus in frozen strawberries.

The U.S. food supply is among the world's safest. But as many as 9,000 Americans—mostly the very young and elderly—die each year, and millions more are sickened, as the result of a food-related illness, according to government estimates.

The Clinton administration has proposed an ambitious, \$43-million Food Safety Initiative that, if fully funded by Congress, is designed to reduce the incidence of food-borne illness by strengthening and improving food safety practices and policies. The initiative includes expanded education efforts aimed at consumers, food service workers, and various other segments of the food community; enhanced food safety inspection and monitoring efforts; an increase in research to develop new and more rapid methods to detect food-borne pathogens and to develop preventive techniques; and improved intergovernmental communications and coordination of response to food-borne outbreaks, as well as expansion of the nationwide FoodNet system, which gathers data on the occurrence of food-borne illnesses.

The \$43-million Food Safety Initiative is designed to reduce the incidence of food-borne illness by strengthening and improving food safety practices and policies.



"The Food Safety Initiative is extremely important in reducing food-borne illness in the United States," says Janice Oliver, deputy director of the Food and Drug Administration's Center for Food Safety and Applied Nutrition (CFSAN). "The illnesses and deaths that are occurring [now] are just not acceptable." Joe Madden, Ph.D., CFSAN's strategic manager for microbiology, adds, "We have limited resources but through the Food Safety Initiative, we can identify those foods that cause the most problems. We can direct our resources to focus on those foods from production to processing."

In January 1997, President Clinton announced he would request \$43.2 million for the 1998 budget to fund a nationwide plan aimed at improving the safety of the nation's food supply. A 50-page report, "Food Safety From Farm To Table," was prepared at the president's request by the Department of Health and Human Services, the U.S. Department of Agriculture, and the Environmental Protection Agency; released in May, the report outlines recommendations

on improving U.S. food safety.

The centerpiece of the inspections segment of the initiative revolves around the HACCP (Hazard Analysis Critical Control Point) concept, a science-based preventive approach to safe food production. Industry identifies possible points in food production, manufacturing and transportation where contamination could occur, called "critical control points," and then puts control measures in place. FDA's seafood HACCP regulations go into effect in December 1997, and USDA is in the process of implementing HACCP regulations for meat and poultry. FDA will also propose preventive measures, including HACCP, for the manufacture of fruit and vegetable juices, while USDA and FDA jointly will propose HACCP for eggs and egg products.

"HACCP itself varies from plant to plant and product to product," says Karen Carson, food science policy coordinator on CFSAN's executive operations staff. "HACCP causes a company to go in and analyze the system they're using internally. It's preventive in na-

ture. Rather than depending on end-product testing, HACCP controls can help ensure that the end product is safe."

"Food sampling is not the way to make sure food is safe," explains Madden, "because, if a pathogen is statistically present in low numbers, it will be difficult to locate. For example, if you

For More Information

FDA Food Information Line
(1-800) FDA-4010

USDA's Meat and Poultry Hotline
(1-800) 535-4555

National Food Safety Initiative Website
<http://vm.cfsan.fda.gov/~dms/fs-toc.html>

FDA's Home Page
<http://www.fda.gov/>

have something present in a 0.1 percent level and you look at 60 samples of a given lot, there's a 94 percent chance of not finding it. Pathogens are not homogeneous throughout a food. They form pockets and are found sporadically."

LeeAnne Jackson, Ph.D., science policy analyst with CFSAN, notes that HACCP puts the responsibility for food safety on the food industry. Although the Food Safety Initiative will add 80 new investigators, fewer than 700 investigators and lab personnel now oversee 53,000 U.S. plants and imported foods.

"Current statistics show that FDA-regulated plants are inspected only once every 10 years, on average, because of the sheer enormity of the job," she explains.



HACCP is a more efficient use of FDA inspection resources, says Carson, "because we can focus on the records the company is keeping on these critical control points."

New Problems Emerge

The impact of food-borne infections

can be substantial. Some pathogens give rise to diseases far more serious than the uncomfortable vomiting or diarrhea that accompanies what most people call "food poisoning." Food-borne infections can cause spontaneous abortion, reactive arthritis, Guillain-Barré syndrome (the most common cause of acute paralysis in both children and adults), and HUS (hemolytic uremic syndrome), which can lead to kidney

failure and death.

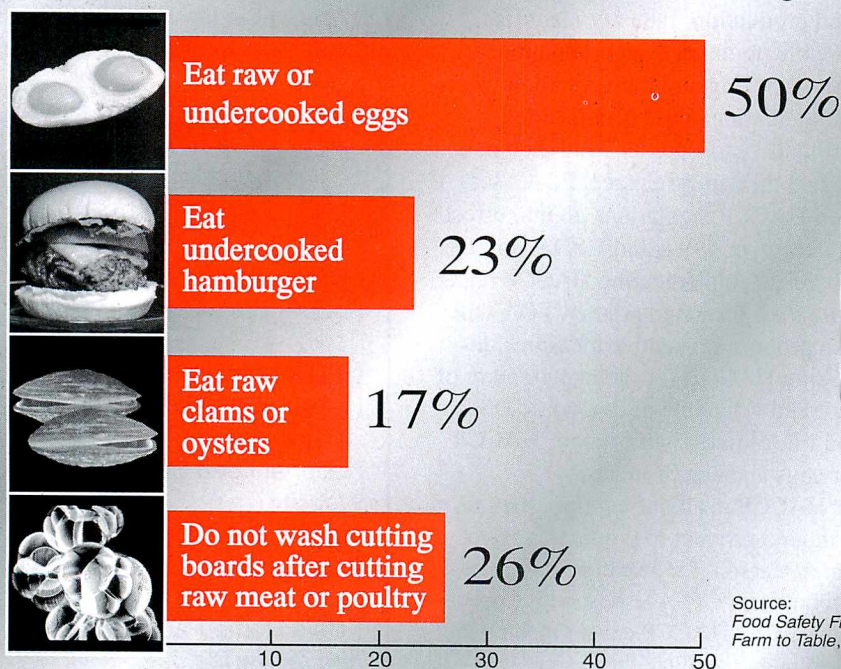
Why has food-borne illness become a significant problem? Reasons identified in the "Food Safety From Farm To Table" report include the emergence of new food-borne pathogens; existing organisms expressing increasing virulence or new ways to evade immune defenses; and the susceptibility of certain people

to food-borne infections (such as pregnant women, children, the elderly, people taking antibiotics or antacids, and people with lowered immunity due to HIV/AIDS, medications for cancer treatment, or organ transplants). Solutions include education for consumers and food service/industry workers; enhanced government coordination when food-related illnesses occur; and more research related to pathogens and organisms that threaten food safety.

Currently FDA, the Centers for Disease Control and Prevention, and USDA's Food Safety and Inspection Service support seven FoodNet (Foodborne Disease Activity Surveillance Network) early-warning sites at state health departments to

Bad Habits

Percent of Consumers Who Practice Unsafe Food Handling



Source:
Food Safety From
Farm to Table, May 1997

track cases of food-borne infections and determine their sources. The Food Safety Initiative calls for new FoodNet sites, creating a powerful network for detection, response and prevention of food-borne illness. Funding in the new initiative will also allow sites to update technology and build a national "fingerprinting" database of bacterial DNA.

"When you find bacteria such as *E. coli* O157:H7 in a product linked to a food-borne illness outbreak," explains Oliver, "you will find that each strain has a specific [DNA] 'fingerprint.' So when microorganisms isolated from individuals [associated with an outbreak] who actually became ill are fingerprinted, researchers can match the fingerprint to the source."

For example, such technology would permit rapid recognition that a bacterium cultured from a patient in Washington is indistinguishable from one isolated from another patient in California, suggesting to public health investigators that a product distributed in both states was contaminated with the same organism.

Because some food-borne pathogens are acquiring resistance to antimicrobial agents, making infections hard to treat, the plan calls for increased surveillance and epidemiologic studies to monitor and reduce the incidence of diseases associated with emerging drug-resistant pathogens.

Education for All

Prevention of pathogens in food requires an understanding of how foods become contaminated during production, processing and distribution. Studies show that over half of all consumers eat raw or undercooked eggs, 23 percent eat undercooked hamburger, 17 percent consume raw clams and oysters, and 26 per-



cent do not wash cutting boards after using them for raw meat or poultry. And often, food preparers and handlers at each stage of the "food chain" lack knowledge about risks and safe food-handling practices.

In May, a "memorandum of understanding" was signed forming the public/private Partnership for Food Safety Education. The partnership members include FDA, CDC, USDA, industry, consumer groups, and the U.S. Department of Education. During September, which is National Food Safety Education Month, the partnership will launch a nationwide food safety education campaign for the general public. Future activities include development of multilingual programs that promote safe food handling and preparation in the food service industry and address the impact of high turnover of employees. The target audiences for these programs will include teen workers, small businesses, and entrepreneurs.

"In both consumer education and the retail/industry level, we'll need to address a variety of literacy levels and multilingual issues: retail food jobs are often the first jobs filled by new immigrants," says Carole Schiffman, director of CFSAN's consumer education staff. "And retail workers are also consumers. So teaching one group will impact the other in positive ways. To reach all the

various groups, we hope to use more of the available new technology, such as the Internet, and e-mail in the future. These can link us easily with food safety educators in all arenas—consumers, health professionals, and retailers."

Future activities may also include research to develop a visual communication tool conveying food safety principles akin to what the dietary guidelines and Food Guide pyra-

mid do to illustrate nutrition principals.

"Consumers have a lot of control to protect themselves from food-borne illnesses," Schiffman explains. "Make some simple practices habits: Wash your hands before handling food, after using the restroom, or after changing baby diapers. Don't let raw foods such as uncooked meat, poultry, and seafood touch ready-to-eat foods, since bacteria from the uncooked food can be spread."

"Keep hot foods hot and cold foods cold," Oliver adds. "Don't use a cutting board for [raw] chicken and then use the same board for [chopping] salad."

Madden is even more succinct when advising consumers: "Treat all foods as if they are potentially contaminated. Keep them refrigerated, watch for any cross-contamination between raw and cooked products, and cook food thoroughly."

Personal responsibility coupled with common sense and education may go a long way in reducing food-borne illness. The Food Safety Initiative promises concrete action designed to reduce the incidence of food-borne illness in this country. It's an important recognition that people have to eat—but they don't have to get sick or die while doing it. ■

Audrey Hingley is a writer in Mechanicsville, Va.

GIVING Thalidomide

A Second Chance

by Herbert Burkholz

In the early 1960s the very mention of the word “thalidomide” was enough to conjure up the vision of a parent’s worst nightmare: the birth of a deformed child. During that period, approximately 8,000 babies were born in Europe with severe defects after their mothers had taken thalidomide. The drug, a sedative, had been virtually untested for its effects on pregnancy. In its reaction to the tragedy, Congress enacted legislation in 1962 that put into place the rigorous testing now required before a pharmaceutical product can be approved in this country.

Today, almost 40 years later, manufacturers are conducting clinical trials to see if thalidomide can treat inflammation common to a host of diseases, and combat weight loss and aphthous ulcers in AIDS patients. Other trials are studying thalidomide’s effect on the eye disease macular degeneration; on breast, prostate and brain cancer; and on Kaposi’s sarcoma (a form of cancer common in AIDS patients). If thalidomide is found to be safe and effective for even one such use, it would represent a remarkable comeback for a drug that once was universally condemned.

The thalidomide story began when a marked increase in the number of infants born with a severe deformity of the limbs called phocomelia was noted in a number of European countries. The deformities eventually were linked to the



**That thalidomide
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FDA’s Frances Kelsey.**

use of thalidomide during pregnancy. Mothers who took the drug during the first trimester, when the limb buds of the fetus are formed, produced children with a wide but distinctive range of deformities. Some had no arms, just flippers extending from the shoulders; others had limbless trunks with toes extending from their hips; others were born with just a head and a torso; and still others had various malformations.

Thalidomide was manufactured by Chemie Grunenthal of Germany, and was sold over the counter and by prescription by many firms in many countries under license from the parent company. In the end, children in 46 countries were affected. The American company that applied to the Food and Drug Administration to market the drug under the brand name Kevadon was Richardson-Merrell.

Thalidomide was not a lifesaving drug, but only one of many tranquilizers that had come onto the market in the decade after World War II. It was promoted by its maker as being nontoxic, with no side effects, and completely safe for pregnant women. Not one of those statements was true. In addition to the effect on the fetus, in adults it caused peripheral neuritis, a painful numbing of the hands and feet that is often irreversible, as a side effect.

There were scientific tests that, had

There were many scientific tests that, had they been conducted, would have shown **thalidomide** to be unsafe.

they been conducted, might have shown thalidomide to be unsafe. The drug companies involved, however, did not perform those tests.

That thalidomide was never marketed in the United States was largely due to the stubborn skepticism of FDA's Frances Kelsey, M.D., Ph.D., whose doubts about the drug kept it out of American pharmacies. Assigned to review the thalidomide application, she fought a dogged defensive battle, blocking and parrying every attempt by Richardson-Merrell to gain approval until the news from the European countries made approval unthinkable.

Kelsey was particularly interested in fetal safety because during the 1940s she had worked on the antimalarial drug quinine and had noted that embryos lacked the ability to metabolize quinine. But she had other concerns. She wanted to know how the drug behaved in the human body. She wanted to know about its stability, about its effect on human metabolism, about its basic chemistry and pharmacology. How the drug worked in laboratory animals was not enough; she wanted to know how it worked in humans. Years later, she recalled that, "... at this time there was growing concern regarding the exposure of the fetus to drugs and other substances to which the mother was exposed during pregnancy. ... Furthermore, the harmful effects of German measles during pregnancy had been recognized The recognition of peripheral neuritis developing particularly after long-term use of thalidomide raised in our mind the question as to what effect the drug might have on the fetus who might be exposed to it for up to nine months."

Kelsey wanted to know the answers to questions that often were not asked in those days. Neither Chemie Grunenthal nor Richardson-Merrell, the American licensee, could or would answer her questions, and so the drug went unapproved in the United States.

Long honored for her role in blocking the approval of the drug, Kelsey, who

still works for FDA as deputy for medical and scientific affairs in the agency's Center for Drug Evaluation and Research, points out that thalidomide was the first drug application to which she was assigned after joining the agency in 1960. "They gave it to me because they thought it would be an easy one to start on," she now recalls. "As it turned out, it wasn't all that easy."

Although thalidomide was unapproved in the United States, it was never ignored by researchers. According to Debbie Birnkrant, M.D., of the agency's division of special pathogens and immunological drug products, "Research on the drug slowed somewhat after the tragedies of the late 1950s and 1960s, but it never really stopped."

One of the reasons for the continued interest centers on the compound Tumor Necrosis Factor (TNF) Alpha, a chemical mediator in the body. Serious infections such as tuberculosis, sepsis and cancer cause the level of TNF Alpha to rise. This elevated level may contribute to the detriment of a patient's condition. In cancer patients it may enhance the wasting process, while leprosy patients may deteriorate because of high levels of TNF Alpha. Thalidomide may have the ability to lower TNF Alpha levels. Results of some test tube and animal trials bear this out.

Another reason is the apparent ability of thalidomide to inhibit the growth of new blood vessels. This could prove useful in cases of macular degeneration, which results from an overgrowth of new blood vessels in the central portion of the retina where focus is controlled.

In the AIDS arena, thalidomide may

have the ability to combat aphthous lesions in the mouth and esophagus. In AIDS patients, these ulcerous sores are large, deep and painful. They are also debilitating, and may lead to malnutrition because the patient cannot eat.

With so many diverse applications being tested, FDA originated a Thalidomide Working Group in 1994 to provide consistency among the agency's various review divisions with a particular emphasis on safety monitoring.

Thalidomide is not approved for use in the United States; however, in appropriate circumstances FDA allows restricted investigational use of the drug to



FDA's Frances Kelsey, M.D., Ph.D., received the President's Award for Distinguished Federal Civilian Service from President John F. Kennedy on Aug. 7, 1962, for her work in helping to keep thalidomide off the market in the United States.

**People participating in the investigational programs
are given strong and unambiguous warnings.**

treat the diseases now under clinical trials. Over the years, thalidomide has been given to hundreds of patients under FDA's program for single-patient investigational new drug applications (INDs). However, as Birnkrant points out, "We're now moving from a state of issuing compassionate INDs for thalidomide to a state where there are actual clinical trials going on."

Given the known serious toxicities of the drug, those people participating in the investigational programs are given strong and unambiguous warnings. Female patients are advised that taking even one thalidomide pill can cause birth defects. They are further warned:

- You must not take thalidomide if you cannot avoid pregnancy.
- Before taking any thalidomide you must have a blood or urine test done by your doctor that shows you are not pregnant.
- You must abstain from sexual intercourse or use two highly effective birth control methods at the same time for at least one month prior to receiving thalidomide, and continuing regularly thereafter, until one month after the last dose of thalidomide.

Female patients are also reminded that no method of birth control is completely reliable except for abstinence, and that if the patient does not practice abstinence or has not had a hysterectomy, she must use birth control even if she believes that she cannot become pregnant. She must also refrain from any other activity, such as fertilization methods, that could result in pregnancy. She is also warned not to take the drug if she is nursing a baby.

A female patient must immediately stop taking thalidomide under the following circumstances:

- If she has a late or an irregular menstrual period.
- If she stops practicing abstinence.
- If she stops using birth control.

- If she thinks that she is pregnant.
- If she does become pregnant.

A female patient is also required to have a blood or urine test for pregnancy on a monthly basis or more frequently if she has irregular menstrual periods. Pregnancy testing will also be done if the patient experiences vaginal bleeding, or if she misses a menstrual period.

Male patients must be willing to abstain from sexual intercourse or use a condom during intercourse while they are taking thalidomide and for at least one month after the last dose, because it is not known if the drug is present in semen.

In general, all patients are reminded that thalidomide has been prescribed for the individual only, and must not be shared with, or given to, others. In addition:

- Thalidomide often causes drowsiness. The patient should avoid drinking alcohol or taking other medications that might induce sleepiness. Also, the ability to operate machinery or participate in activities requiring alertness and clear judgment may be impaired while taking thalidomide.
- Thalidomide causes nerve damage in some patients. In some cases, the nerve damage has proved irreversible even after treatment with the drug is discontinued. Symptoms of nerve damage include numbness or tingling in the arms, hands, legs, and feet.

Any such side effects should be reported by the patient to his or her doctor, as well as additional side effects such as:

mood changes, dry mouth, headache, nausea, constipation, increased appetite, puffiness of the face and limbs, dry skin, itching, low white blood cell count, thyroid problems, blood sugar that is too high or too low, and slow heartbeat.

Although there are risks involved in an investigational program with a teratogenic drug like thalidomide, Birnkrant points out that it is important to explain to the public and to the patients just how the drug should be used. "The goal is to minimize the risk, recognizing that it may never be zero." ■

Herbert Burkholz is a member of FDA's public affairs staff.



Medications And Older Adults

by Rebecca D. Williams

Mary Parker of Oak Ridge, Tenn., is quick to joke about her health problems. Her vibrant smile and upbeat attitude belie her 78 years. But last year she had a health problem she didn't find amusing. The medication she took for her swollen sinuses left her so weak and dizzy she couldn't get out of bed.

"I felt like I wanted to die," she remembers. "It was awful."

She learned an important lesson from the episode. She thinks twice before taking any medication, questions her doctors and pharmacists, and reviews all her medications regularly with her primary physician.



Mary Parker

Adults over age 65 buy 30 percent of all prescription drugs and 40 percent of all over-the-counter drugs.

Parker's attitude is a good one for older adults to have, experts say. As people age, they often develop a number of problems taking medications. Being aware that problems may occur is the first way to minimize them.

"You are a partner in your health care," urges Madeline Feinberg, Pharm.D., a pharmacist and director of the Elder Health program of the University of Maryland School of Pharmacy. "This is a partnership between you, your doctor, and your pharmacist. You need to be assertive and knowledgeable about the medications you take."

The Food and Drug Administration is also working to make drugs safer for older adults, who consume a large share of the nation's medications. Adults over age 65 buy 30 percent of all prescription drugs and 40 percent of all over-the-counter drugs.

"Almost every drug that comes through FDA [for approval] has been examined for effects in the elderly," says Robert Temple, M.D., associate director for medical policy in FDA's Office of Drug Evaluation and Research. "If the manufacturer hasn't done a study in the elderly, we ask for it."

More than 15 years ago, the agency established guidelines for drug manufacturers to include more elderly patients in their studies of new drugs. Upper age limits for drugs were eliminated, and even patients who had other health problems were given the green light to participate if they were able. Also, drugs known to pass primarily through the liver and kidneys must be studied in patients with malfunctions of those organs. This has a direct benefit for older adults, who are more likely to have these conditions.

In several surveys, FDA discovered that drug manufacturers had been using older adults in their drug studies; however, they weren't examining that age

group for different reactions to the drugs. Now, they do. Today, every new prescription drug has a section in the labeling about its use in the elderly.

Says Temple, "The FDA has done quite a bit and worked fully with academia and industry to change drug testing so that it does analyze the data from elderly patients. We're quite serious about wanting these analyses."

When More Isn't Necessarily Better

Of all the problems older adults face in taking medication, drug interactions are probably the most dangerous. When two or more drugs are mixed in the body, they may interact with each other and produce uncomfortable or even dangerous side effects. This is especially a problem for older adults because they are much more likely to take more than one drug. Two-thirds of adults over age 65 use one or more drugs each day, and a quarter of them take three drugs each day.

Not all drug combinations are bad. High blood pressure is often treated with several different drugs in low doses. Unless supervised by a doctor, however, taking a mixture of drugs can be dangerous.

For example, a person who takes a blood-thinning medication for high blood pressure should not combine that with aspirin, which will thin the blood even more. And antacids can interfere with certain drugs for Parkinson's disease, high blood pressure, and heart disease. Before prescribing any new drug to an older patient, a doctor should be aware of all the other drugs the patient may be taking.

"Too often, older people get more drugs without a reassessment of their previous medications," says Feinberg. "That can be disastrous."

There is also evidence that older adults tend to be more sensitive to drugs

What to Ask the Doctor

Before you leave your doctor's office with a new prescription, make sure you fully understand how to take the drug correctly. Your pharmacist can also provide valuable information about how to take your medicines and how to cope with side effects. Ask the following questions:

- What is the name of this drug, and what is it designed to do? Is this a generic or a name brand product?
- What is the dosing schedule and how do I take it?
- What should I do if I forget a dose?
- What side effects should I expect?
- How long will I be on this drug?
- How should I store this drug?
- Should I take this on an empty stomach or with food? Is it safe to drink alcohol with this drug? ■

—R.D.W.

than younger adults are, due to their generally slower metabolisms and organ functions. As people age, they lose muscle tissue and gain fat tissue, and their digestive systems, liver, and kidney functions slow down. All this affects how a drug will be absorbed into the bloodstream, react in the organs, and how quickly it will be eliminated. The old adage "Start low and go slow" applies especially to the elderly.

Older adults who experience dizziness, constipation, upset stomach, sleep changes, diarrhea, incontinence, blurred vision, mood changes, or a rash after taking a drug should call their doctors. The following suggestions may also help:

- Don't take a drug unless absolutely necessary. Try a change in diet or exercise instead. Ask your doctor if there's anything else you can do besides drug therapy for the condition.
- Tell your doctor about all the drugs you take. If you have several doctors, make sure they all know what the others are prescribing, and ask one doctor (such as an internist or general practitioner) to coordinate your drugs.
- Ask for drugs that treat more than one condition. Blood pressure medicine might also be good for heart disease, for example.
- Keep track of side effects. New symptoms may not be from old age but from the drug you're taking. Try another medication if possible until you find one that works for you.
- Learn about your drugs. Find out as much as you can by asking questions and reading the package inserts. Both your doctor and pharmacist should alert you to possible interactions between drugs, how to take any drug properly, and whether there's a less expensive generic drug available.
- Have your doctor review your drugs. If you take a number of drugs, take them all with you on a doctor's visit.
- Ask the doctor, "When can I stop taking this drug?" and, "How do we know this drug is still working?"
- Watch your diet. Some drugs are better absorbed with certain foods, and some drugs shouldn't be taken with certain foods. Ask a pharmacist what foods to take with each drug.
- Follow directions. Read the label

About a quarter of all nursing home admissions are due at least in part to the inability to take medication correctly.

Cutting Costs

The cost of medications is a serious concern for older adults, most of whom must pay for drugs out of pocket. Even those who have insurance to supplement Medicare must often pay a percentage of the cost of their medicines.

For a new prescription, don't buy a whole bottle but ask for just a few pills. You may have side effects to the medication and have to switch. If you buy just a few, you won't be stuck with a costly bottle of medicine you can't take.

For ongoing conditions, medications are often less expensive in quantities of 100. Only buy large quantities of drugs if you know your body tolerates them well. But be sure you can use all of the medication before it passes its expiration date.

Call around for the lowest price. Pharmacy prices can vary greatly. If you find a drug cheaper elsewhere, ask your regular pharmacist if he or she can match the price.

Other ways to make your prescription dollars go further include:

- Ask for a senior citizens discount.
- Ask for a generic equivalent.
- Get drug samples free. Pharmaceutical companies often give samples of drugs to physicians. Tell your doctor you'd be happy to have them. This is especially convenient for trying out a new prescription.
- Buy store-brand or discount brand over-the-counter products. Ask the pharmacist for recommendations.
- Call your local chapter of the American Association for Retired Persons (AARP) and your local disease-related organizations (for diabetes, arthritis, etc.) They may have drugs available at discount prices.
- Try mail order. Mail-order pharmacies can provide bulk medications at discount prices. Use this service only for long-term drug therapy because it takes a few weeks to be delivered. Compare prices before ordering anything. ■

—R.D.W.



Mary Sloane depends on more than her memory to help keep track of her daily medications. She turns the container upside down after taking each pill (left). And when she goes to the doctor, she takes all her medicines with her (above).

every time you take the medication to prevent mistakes, and be sure you understand the timing and dosage prescribed.

- Don't forget. Use a memory aid to help you—a calendar, pill box, or your own system. Whatever works for you is best.

Medicine and Special Needs

Arthritis, poor eyesight, and memory lapses can make it difficult for some older adults to take their medications correctly. Studies have shown that between 40 and 75 percent of older adults don't take their medications at the right time or in the right amount. About a quarter of all nursing home admissions are due at least in part to the inability to take medication correctly.

A number of strategies can make taking medication easier. Patients with arthritis can ask the pharmacist for an oversized, easy-to-open bottle. For easier reading, ask for large-type labels. If those are not available, use a magnifying glass and read the label under bright light.

Invent a system to remember medication. Even younger adults have trouble remembering several medications two

or three times a day, with and without food. Devise a plan that fits your daily schedule. Some people use meals or bedtime as cues for remembering drugs. Others use charts, calendars, and special weekly pill boxes.

Mary Sloane, 78, keeps track of five medications a day by sorting her pills each evening into separate dishes. One is for morning pills, the other for the next evening. Then she turns each medicine bottle upside down after taking the pill so she can tell at a glance if she has taken it that day.

"You have to have a system," Sloane says. "Because just as soon as I get started taking my pills, the phone rings, and when I come back to it, I think, 'Now have I taken that?'"

Drug-taking routines should take into account whether the pill works best on an empty or full stomach and whether the doses are spaced properly. To simplify drug-taking, always ask for the easiest dosing schedule possible—just once or twice a day, for example.

Serious memory impairments require assistance from family members or professionals. Adult day-care, supervised

living facilities, and home health nurses can provide assistance with drugs.

Active Lives

Not all older adults are in danger of drug interactions and adverse effects. In fact, as more and more people live active lives well into their 80s or beyond, many take few medications at all. Among healthy older adults, medications may have the same physical effects as they do in younger adults. It is primarily when disease interferes that the problems begin.

To guard against potential problems with drugs, however, older adults must be knowledgeable about what they take and how it makes them feel. And they should not hesitate to talk to their doctors or pharmacists about questions and problems they have with a medication.

Says the University of Maryland's Feinberg: "We need to have educated patients to tell us how the drugs are working." ■

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

Why Should FDA Regulate Drugs?



An Interview with Janet Woodcock, M.D. Director of FDA's Center for Drug Evaluation and Research

by Tamar Nordenberg

"If you look at speed of introducing new medicines, we're the fastest agency among all the countries in the world with a formal regulatory system."

Is the Food and Drug Administration in need of reform? Some critics of the agency, in Congress and outside, argue that the agency should be overhauled to make it work more efficiently. FDA supporters disagree, pointing to record-setting drug approvals and other agency accomplishments in recent years.

FDA's Center for Drug Evaluation and Research (CDER) is the part of the agency that regulates all drugs marketed in the United States: brand-name and generic, prescription and over-the-counter.

Since June 1994, the center has been directed by Janet Woodcock, M.D., a rheumatologist who worked in FDA's

“CDER’s mission involves not only assuring that safe and effective drugs are available to the public, but that unsafe or ineffective drugs are kept off the market.”

Center for Biologics Evaluation and Research for eight years before becoming CDER’s director.

Despite her center’s record 131 drug approvals in 1996, including new treatments for AIDS, Alzheimer’s disease, and diabetes, and despite a much-reduced median review time of about 15 months in that year, some continue to question the agency’s role in the drug review and approval process. And you, as a consumer, may wonder, “Why should a government agency even be involved in *my* decisions about the drugs *I* want to take?”

In the following interview, Woodcock gives her views on these issues.

Q. Why not trust consumers to decide for themselves which medicines work for them?

A. I don’t think it’s in the government’s best interest to stand between people, especially those who are desperately ill, and their desire to take medicine. But that libertarian issue shouldn’t be confused with the scientific issue of whether patients can tell what medicines work, because with almost any drug treatment we use today, they can’t tell.

Doctors thought for years they could tell what worked. In the 1960s, for example, doctors were convinced that diethylstilbestrol, or DES, was terrific for preventing early miscarriages, and they gave it to thousands of women in pregnancy. “The women had miscarriages before, and I put them on this DES, and some of them didn’t have miscarriages. So obviously, it’s very effective,” doctors thought.

In fact, when DES was actually subjected to scientific testing, it had no effect on miscarriage whatsoever. Not only was it absolutely ineffective, but unfortunately it had delayed negative health effects on the fetus.



We had a more recent experience like this with a heart rhythm drug. After people have heart attacks, they can have extra beats. And it’s known that a percentage of people with those extra beats will have sudden death. Well, drugs were discovered that made the sudden beats go away, and people thought, “Wonderful! Make the beats go away, and sudden death will go away.” The medicine became the standard of practice throughout the United States; everybody was using the drug.

There were some skeptics at the National Institutes of Health and FDA that said the drug ought to be tested. NIH set up a trial, and what they discovered shocked everyone: Yeah, the drugs make the beats go away, but the people who were put on the drugs had sudden death at a substantially higher rate than the people who were just left having the beats. The drugs actually made the problem worse, and maybe more probable.

Even the people who did the trial were later haunted by the fact that they had given some people that drug. They were

people the researchers knew, and some of them died.

So the answer is, many, many very smart people have thought they knew what drugs would help them and what drugs would hurt them, and clinical tests again and again have proven them wrong. They didn’t know.

Q. What is there to lose by giving people with life-threatening diseases like AIDS and terminal cancer access to whatever drugs they want?

A. If we didn’t test drugs—if people could take whatever they wanted without any testing—there would be no way to tell whether any of the thousands, millions, of candidate drugs out there worked. So no one would ultimately benefit.

For people with life-threatening illnesses, even the patient groups don’t agree on where the right balance is between identifying treatments that will really improve patients’ health and allowing people to have immediate access to experiment with drugs that might work for them.

I think AIDS is a good example. We had a lot of discussions with the AIDS activists early on about access to treatments. And FDA put together many programs to allow people early access to those drugs even before they were approved.

But at the same time, companies did pursue testing to see if these agents worked. Ultimately, some drugs were dropped, because they didn’t work or because they were so toxic that the risks outweighed the benefits. And good drugs were found and then approved by FDA.

Now we’re decreasing mortality with HIV. So every person with HIV has a path they know they can take of drugs that will work to improve their health, and have been proven to do so. If we’d

"I don't think it's in the government's best interest to stand between people, especially those who are desperately ill, and their desire to take medicine."

gone down the other path, and everyone had been able to try anything they wanted with no testing, then we'd still be at the same point so much later into the epidemic: Everyone would have total availability to all drugs, but we wouldn't know what worked.

Now some of the AIDS activists are actually telling us they want more rigorous testing because, as they study their disease and the treatments, they realize they need information to make choices about which drugs they should take, even among the approved drugs. They want FDA to mandate more big trials that would include combination therapy. "What if I start this combination early, versus if I take this single drug first? Which would help me to be in better health 10 years from now?" Those are the kinds of questions they want answered, and you can't answer those questions unless you do scientific testing.

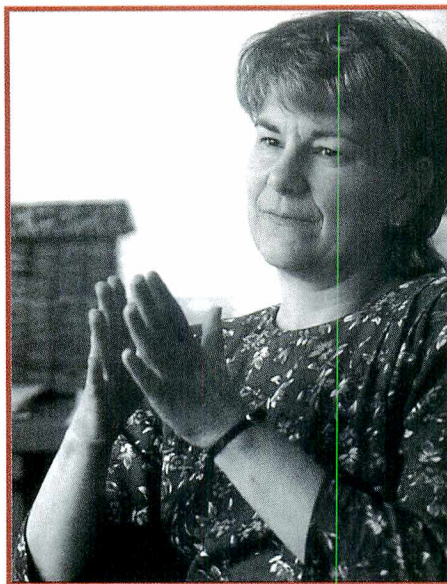
Q. Isn't FDA infringing on drug marketers' freedom of speech when the agency restricts what is said in drug labeling and advertising?

A. There is a category of speech called commercial speech when you're making a sales pitch. So, while some other kinds of speech are less restricted, things that are promotional in nature may have certain constraints legitimately put on them by FDA.

For example, drug labeling and advertising must be balanced and not misleading. In my opinion, consumers want truthful information; they want a lot of information, not hype.

Because people would like to receive all the latest information on a drug from the manufacturer, there has been a lot of debate about uses that are considered "off-label"—not approved by FDA.

Obviously, medical science doesn't happen in spurts, but continuously. Af-



ter a drug is out on the market, health professionals continuously experiment with new uses. FDA thinks that's appropriate and doesn't want to restrict that kind of use of drugs. But we don't currently permit manufacturers to promote these new uses until it's proven that they work and are safe.

To help the situation, we've put out a draft guidance on how much information a manufacturer needs to get a new use put on the label. We think that will help to some extent.

Last year, the center approved 118 new uses for drugs that were already approved, way up from a few years ago. We think that manufacturers are motivated to send in applications for new uses because they know that the agency has been approving them promptly if they work.

Q. Could reforming FDA make it more efficient and save American tax dollars?

A. I think the center's efficiency has come far, but we still have improvements to make. When we talk about legislation

to reform the agency, the first thing that must be done is to identify what problem exists. What problem are you trying to fix?

There has been a lot of rhetoric about FDA reform that hasn't been related to identified problems. Some people are saying the problem is that we're too slow. That clearly isn't the problem. During my three years as director of the center, some important changes have been made to make the center's work proceed faster and more effectively.

We are making as many processes as possible computer-based. But one of the biggest changes is the ever-improving review times for new drugs under the user fee program.

The idea behind user fees is that the industry is getting a service from the government in having their applications for marketing reviewed. And they should contribute directly to that. So five years ago, Congress, the industry, and FDA negotiated this user fee program. Industry would pay fees to add to FDA's resources for reviewing new drug applications. In exchange, FDA made a commitment to meet certain goals for review times.

CDER has been meeting all those goals. In fact, we've exceeded almost all the goals, and we expect to continue to exceed them. Basically, we've doubled the number of new drugs we're approving, and we've halved the review times.

One of the unique things about the user fee program, though, is that Congress only authorized it for five years, which expires at the end of September. So all the stakeholders—Congress, industry, the public—have to decide whether or not they're satisfied enough with the results to continue the program. Most of the interested parties I have talked to support the continuation of the user fee program. [At press time, Congress had not yet reauthorized user fees.]

“If people could take whatever they wanted without any testing, there would be no way to tell whether any of the thousands, millions, of candidate drugs out there worked.”

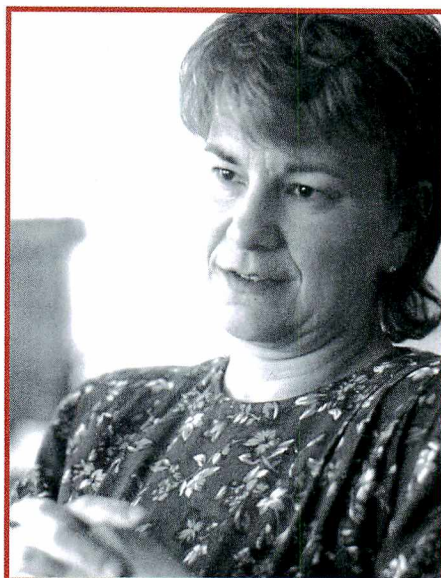
In generic drugs, the workload has also gone up in the last couple of years. We're maintaining our review times—we've had difficulty shortening them on the generic drug side—but the generics staff has started some streamlining strategies over the last year to try to deal with the increased workload. They're working more closely with manufacturers—by faxing them information, communicating more by telephone, and meeting with them if necessary—to try to minimize the back-and-forth when an application has shortcomings.

So we still have work to do, but if you look at speed of introducing new medicines, we're the fastest agency among all the countries in the world with a formal regulatory system.

It takes a long time to change perceptions, though. For years, we were behind other countries in approvals, and there was what is called a “drug lag.” In many cases, it took us years longer to review drugs than certain other countries. And that remains in people's minds.

But review time is only one facet of an effective center. People are now bringing up drug development times: the time it takes from a chemical's discovery in the laboratory, to its testing in animals, to its testing in people, to its review by FDA, which is necessary before marketing. People are saying that the drug development time is too long, and that maybe FDA has a part in that.

I think there are some things FDA can do to shorten the drug development times. What FDA does in drug development is to set certain standards. Clearly, if we did away with all the laws we have now, drug development time could be very short. A person could make a chemical, say, in their basement, and then they could put it on sale. That's going too far.



What we can do is evaluate our standards to make sure that all the information we require is absolutely necessary, and there are no extras. And we must be very clear about what information is required at each stage of drug development. The clearer we are, and the more the standards are universal, the easier drug development will be.

About a year ago, we streamlined what's called the IND process. That is, we provided some guidance on the minimum amount of animal chemistry information necessary to start the drug development milestone of testing in humans.

Also, over the last few years, FDA, Japan, and the European Union have been negotiating to standardize technical requirements under the International Conference on Harmonization (ICH). Then, companies won't have to repeat things unnecessarily.

What the harmonization among countries means is that data that a drug company collected to submit to, say, Japanese authorities will be the same or similar data as that required for FDA. It means reducing the amount of testing, but

each country would still make its own decision about whether to approve a drug.

So far under the ICH, major progress has been made toward standardizing the information that is filed about side effects to help us detect unexpected side effects earlier, and standardizing the kinds of safety testing in humans that is required.

But to say FDA alone should decrease development times would be a big stretch. Because pharmaceutical companies develop the drugs, not FDA, much of the burden for shortening development times and decreasing development costs lies with them.

I think manufacturers are very interested in shortening drug development times. We know it can be done. For example, with the AIDS drugs, where people put in a full-court press on developing drugs, they were developed very rapidly, from the test tube to the clinic to marketing.

CDER's mission involves not only assuring that safe and effective drugs are available to the public, but that unsafe or ineffective drugs are kept off the market.

It's an interesting balance, and even consumer groups disagree about what the right balance is. Some groups are very risk-averse, and they don't believe FDA should approve any drug that has harmful effects. Well, most drugs have harmful effects, and you have to make sure that the drug's benefits outweigh its harmful effects.

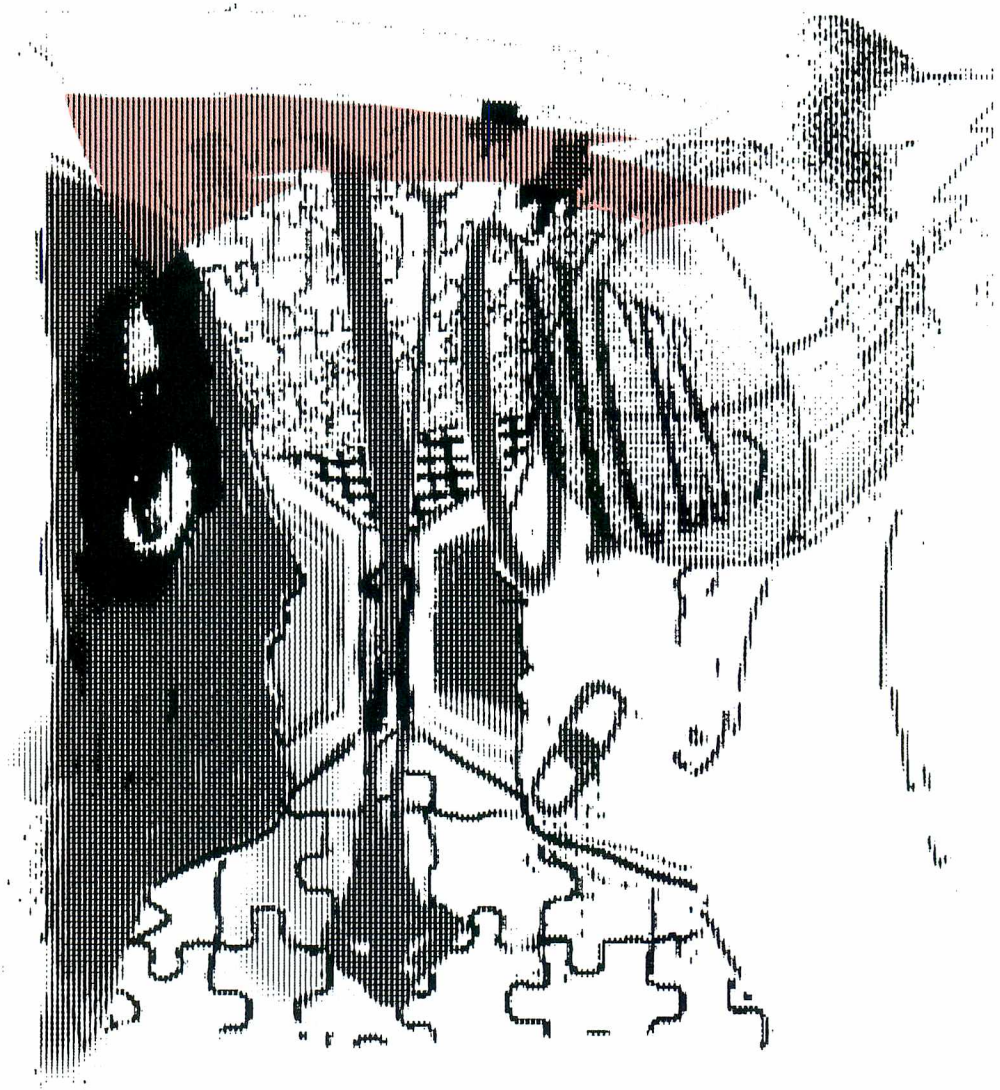
We at CDER think we've achieved the proper balance, given all the different parties and their different interests. While there will never be complete agreement, most people seem to agree on one thing: FDA should keep drugs off the market that ultimately will harm or kill people and have to be withdrawn. ■

Tamar Nordenberg is a staff writer for FDA Consumer.

Real Lives, Imaginary Terror

Schizophrenia

**Drugs,
Therapy
Can
Turn Life
Around
For Some**



by Margie Patlak

"The visions are extremely vivid. Paving stones transform into demonic faces, shattering in front of my petrified eyes. When I am in contact with people, they can become grotesquely deformed, their skin peeling away to reveal decomposing inner muscles and organs. Buildings and rooms spin and weave and their walls close in as I look on, paralyzed by fear. ... The voices either ramble in alien tongues or scream orders to carry out violent acts. They also persecute me by way of unwavering commentary and ridicule to deceive, derange, and force me into a world of crippling paranoia."

—Robert Bayley, a schizophrenia sufferer, in *Schizophrenia Bulletin*, No. 4,

1996, published by the National Institute of Mental Health (NIMH).

More than 300,000 adults in this country are like Bayley, unable to distinguish their imaginations from reality. These people have schizophrenia, a

sity of California in Los Angeles.

Because the drugs that effectively treat schizophrenia affect the functioning of the chemical messengers in the brain known as neurotransmitters, some experts hypothesize that the disorder stems

uting to this hampered logic is an inability to sort out relevant from peripheral information in a situation.

Another frequent symptom of schizophrenia is deadened emotional expression, indicated by a monotonous tone of

More than 300,000 adults in this country are unable to distinguish their imaginations from reality.

mental illness whose hallmarks are visual and auditory hallucinations. Fortunately the living hell Bayley describes can often be alleviated with a number of antipsychotic drugs, including the relatively new drugs clozapine (Clozaril) and risperidone (Risperdal), which don't seem to have some of the limiting side effects of more traditional drugs, as well as the newcomer known as olanzapine (Zyprexa), which came on the market in the fall of 1996. The Food and Drug Administration is responsible for ensuring the safety and effectiveness of the drugs used to treat schizophrenia.

About one out of a hundred people in this country develops schizophrenia during his or her lifetime, according to NIMH. Usually, it first surfaces in the teens or 20s in men and in the 20s or early 30s for women. Schizophrenia rarely develops in children, and many schizophrenics appeared perfectly normal during childhood.

Although research has turned up some intriguing clues, the puzzle of what causes schizophrenia has yet to be solved. Some people may inherit susceptibility to the condition. A person with a parent or sibling who is schizophrenic has about a 10 percent risk of developing the condition, and half of all identical twins of schizophrenics also succumb to the mental illness.

Anatomy studies suggest the condition is not caused by damage to the brain, but rather due to faulty brain development. Studies show that exposure to viral infections during the second trimester and birth complications can boost the risk of developing schizophrenia, because the normal development of the brain may be altered, according to Stephen Marder, M.D., of the Univer-

sity of California in Los Angeles.

In some patients, schizophrenia is persistent, while others have remissions and exacerbations. Full recovery rarely occurs. Suicide rates among paranoid schizophrenics can be as high as 10 percent, according to study by Thomas McGlashan, M.D., of the Yale Psychiatric Institute, published in the February 1997 *American Journal of Psychiatry*.

Voices No One Else Can Hear

Schizophrenia is one of the most complex, puzzling and disabling of the major mental illnesses. People who suffer from this condition can have a number of different symptoms, the most prominent being hallucinations, delusions, disordered thinking and behavior, and abnormal expression of emotions. Hearing voices that other people don't is the most common type of hallucination in schizophrenia. Such voices may describe the patient's activities, carry on a conversation, warn of impending dangers, or tell the person what to do.

Another common symptom of schizophrenia is delusions of persecution or grandeur. As cited in an issue of *Schizophrenia Bulletin*, one schizophrenic, who was a computer programmer, imagined that the end of the world was coming and he determined which of his colleagues would survive in the afterlife by the keys he punched on the computer. Another patient, cited in an NIMH brochure, thought a neighbor was controlling his behavior with magnetic waves.

Schizophrenics often are not able to complete a line of thought. Their thoughts come and go so rapidly it is not possible to "catch them." Fragmented thinking and conversing results. Contrib-

uting to this hampered logic is an inability to sort out relevant from peripheral information in a situation. Another frequent symptom of schizophrenia is deadened emotional expression, indicated by a monotonous tone of

voice and flat facial expressions. "Her face was a solemn mask, and she could neither give nor receive affection," wrote Evelyn Smith of her schizophrenic daughter in *Schizophrenia Bulletin*, No. 4, 1991. Schizophrenics also may show inappropriate emotions—a laugh in response to a tragic situation, for example. Some schizophrenics exhibit bizarre behavior, such as excessive activity that is apparently purposeless and not influenced by what is happening around them. In contrast, some schizophrenics may lapse into a catatonic state in which they are immobile and unresponsive.

To be diagnosed as schizophrenic, a patient needs to have two or more of any of these symptoms during a one-month period. However, some symptoms are more characteristic of schizophrenia and aid in more definitive diagnosis. For example, it is rare for people with other disorders to hear a voice commenting on their behavior or to hear two or more voices conversing with each other. Also key to the diagnosis of schizophrenia, is a significantly hampered ability to work or socialize for at least six months.

Before providing a firm diagnosis of schizophrenia, doctors need to rule out drugs as the cause. A number of illegal drugs, such as PCP (phencyclidine hydrochloride), or chronic use of high doses of amphetamines can cause some of the disorder's symptoms.

Treatment Revolutionized By Antipsychotics

A dismal outlook for schizophrenia was dramatically changed in the 1950s with the development of the

first antipsychotic drug, chlorpromazine (Thorazine). Since then, more than a dozen other similar-acting antipsychotic medications have been developed, including haloperidol (Haldol), thioridazine (Mellaril), loxapine (Loxatane), and molindone (Moban). These drugs work by blocking binding sites of the neurotransmitter dopamine. They are equally effective at stemming the delusions and hallucinations and bizarre behavior and speech experienced by schizophrenics, according to NIMH. What effects these older antipsychotic medications have on other symptoms of schizophrenia, such as flat-

studies show these drugs don't work in a little over one-quarter of schizophrenics who do take them, according to Lisa Dixon, M.D., of the University of Maryland in Baltimore. However, three drugs have come on the market during this decade that counter some of these problems.

New Drugs

Clozapine, which can only be used to treat patients who do not respond to other antipsychotic medications, can effectively treat about one-third to one-half of those non-responders, according to UCLA's Marder.

prone to seizures, and about 1 to 2 percent develop a paucity of infection-fighting white blood cells. This condition, known as agranulocytosis, can be fatal if not diagnosed and treated immediately. If detected and promptly treated, however, this condition is completely reversible. To detect agranulocytosis, patients who take clozapine must have weekly blood tests.

Unlike the older antipsychotics, studies suggest clozapine, risperidone and olanzapine work by affecting the action of the neurotransmitter serotonin, as well as dopamine. Some studies suggest that in addition to effectively stemming the hallu-

Although research has turned up some intriguing clues, the puzzle of what causes schizophrenia has yet to be solved.

tened emotions and apathy, is not as well documented. They also foster significant side effects that can limit their use.

When patients first start taking these antipsychotic drugs, they may be troubled by such side effects as drowsiness, restlessness, cramps, muscle spasms, dizziness, stiffness of the limbs, tremors, dry mouth, impotence, menstrual irregularities, or blurring of vision. Most of these can be corrected by lowering the dosage or can be controlled by other medications.

More problematic with the long-term use of older antipsychotic drugs is the development of a disorder known as tardive dyskinesia (TD), a disorder that causes involuntary movements. Patients with TD may frequently grimace, frown, smirk, or experience facial tics. They may also flick or jerk their trunk, pelvis, arms, or legs. The risk of developing TD increases with the length of drug treatment and occurs in more than one-quarter of patients who have been receiving antipsychotic drugs for more than five years. In some patients, symptoms of TD may be reversed or reduced by altering the dosage of antipsychotic medication or by treating them with a different antipsychotic.

Because of the side effects, many patients do not comply with taking older antipsychotic medications. In addition,

Although it can make patients more prone to seizures, clozapine appears to cause less cramping, tremor, muscle stiffness, and restlessness than some of the older antipsychotics, and it has been suggested that clozapine may be less likely to produce TD, although the evidence on the latter is not yet definitive. However, it can make patients more

inclined to seizures, and about 1 to 2 percent develop a paucity of infection-fighting white blood cells. This condition, known as agranulocytosis, can be fatal if not diagnosed and treated immediately. If detected and promptly treated, however, this condition is completely reversible. To detect agranulocytosis, patients who take clozapine must have weekly blood tests.



One of Vincent Van Gogh's most famous paintings is "The Starry Night," above. Many medical scholars believe that one source of Van Gogh's psychiatric problems may have been schizophrenia.

psychotic medications on these symptoms has not been well characterized, it is not clear whether the newer drugs have an advantage over the older ones in relieving them. "There's not sufficient evidence to conclude that risperidone or olanzapine are superior to older antipsychotics regarding negative symptoms," he said.

He added that studies with both risperidone and olanzapine suggest that they are no more likely than placebo to cause muscle stiffness, cramps, restlessness, and tremors, especially at the lower recommended doses. However, there are not sufficient data to conclude definitively that either of these newer drugs is superior to the older antipsychotic drugs in regards to these immediate side effects or the more chronic development of TD. There are a number of side effects associated with both the older and newer drugs, including sleepi-

and 20 percent of schizophrenic patients experience a relapse in any one year despite continued medication, according to John Kane, M.D., of the Albert Einstein College of Medicine in the Bronx.

Although there are injectable forms of antipsychotics, patients usually take these drugs orally. There is insufficient evidence to know whether they are associated with birth defects. Because these drugs can be passed to a baby via breast milk, schizophrenic mothers are usually discouraged from breast-feeding.

Other Treatments

Because some patients receive only partial relief of their symptoms from antipsychotic medications, doctors may prescribe additional medications. Studies suggest the addition of anti-anxiety medications such as lorazepam (Ativan) or alprazolam (Xanax) helps about half of schizophrenics, according to James

many patients find the addition of individual, family or group psychotherapy to be helpful. According to Jack Scott, M.D., of the Maryland Psychiatric Research Center in Baltimore, recent studies indicate that supportive reality-oriented therapy aimed at developing practical interpersonal skills is generally of more benefit to schizophrenics than more probing psychoanalytic or insight-oriented psychotherapy. Rehabilitation programs that emphasize job counseling and training, problem-solving and money management skills, use of public transportation, and social skills training are often essential.

Although there currently is no cure for schizophrenia, the present array of drugs available often can effectively control many of the disorder's symptoms and enable patients to lead more satisfactory lives. A review of the life histories of almost 2,000 patients diag-

Schizophrenia is one of the most complex, puzzling and disabling of the major mental illnesses.

ness, weight gain, and sexual problems.

To minimize side effects, psychiatrists usually treat schizophrenics with the lowest dose of an antipsychotic drug that diminishes symptoms during an episode of worsening symptoms. After that episode subsides, the doctor usually will taper the dosage slowly to the lowest possible level to keep symptoms at bay. In a few circumstances, especially when symptoms are mild and patients are particularly resistant to taking medication, treatment may be discontinued.

Several studies indicate that schizophrenics who are not receiving maintenance treatment with an antipsychotic drug following an acute episode are at much greater risk of experiencing a relapse, according to Dixon. Consequently, many schizophrenic patients continue taking antipsychotic medication for the rest of their lives. Some may be able to take very low doses except when symptoms are severe. Between 15

Thompson, M.D., of the University of Maryland in Baltimore. He noted that a smaller percentage of patients also appear to receive some benefit from lithium and carbamazepine, which are also used to treat manic depression. Some studies cited by Thompson also suggest that antidepressants such as fluvoxamine may help diminish the depression, emotional blunting, and inability to speak some schizophrenic patients experience. However, since no pharmaceutical companies have sought FDA approval for antipsychotic claims for these drugs, FDA has not evaluated whatever data support such claims and, consequently, has not approved their use for schizophrenics.

Shocking patients with electricity, called electroconvulsive therapy, one of the earliest treatments of schizophrenia, is rarely used today because the benefits have not been definitively shown.

Once antipsychotic medications have helped stem schizophrenia's symptoms,

nosed with schizophrenia suggests that one-quarter achieve full remission, half recover at least partially, and one-quarter require long-term care, according to NIMH. It is unknown whether better results might be garnered with the newer antipsychotic drugs now on the market.

With appropriate treatment, many schizophrenics have been able to turn their imaginary hells into less terrifying and more fertile grounds. Bayley, for example, has transformed many of his bizarre visions into oil paintings and musical compositions. He notes that much can be gained by "tapping into a mind experiencing the truly extraordinary." He also advocates greater compassion for schizophrenics. "It is often forgotten that there is a person behind the condition, with a fundamental need to be understood," he wrote. ■

Margie Patlak is a writer in Elkins Park, Pa.

Bone Builders

Support Your Bones with Healthy Habits

by Dixie Farley

Unearthed skeletons from ancient times testify to the durability of bone long after other bodily tissue turns to dust. Living bone in the body, however, can lose mineral and fracture easily if neglected—a disorder called osteoporosis, or porous bones. One in two women and one in eight men over 50 suffer such fractures, including sometimes life-threatening hip fractures.

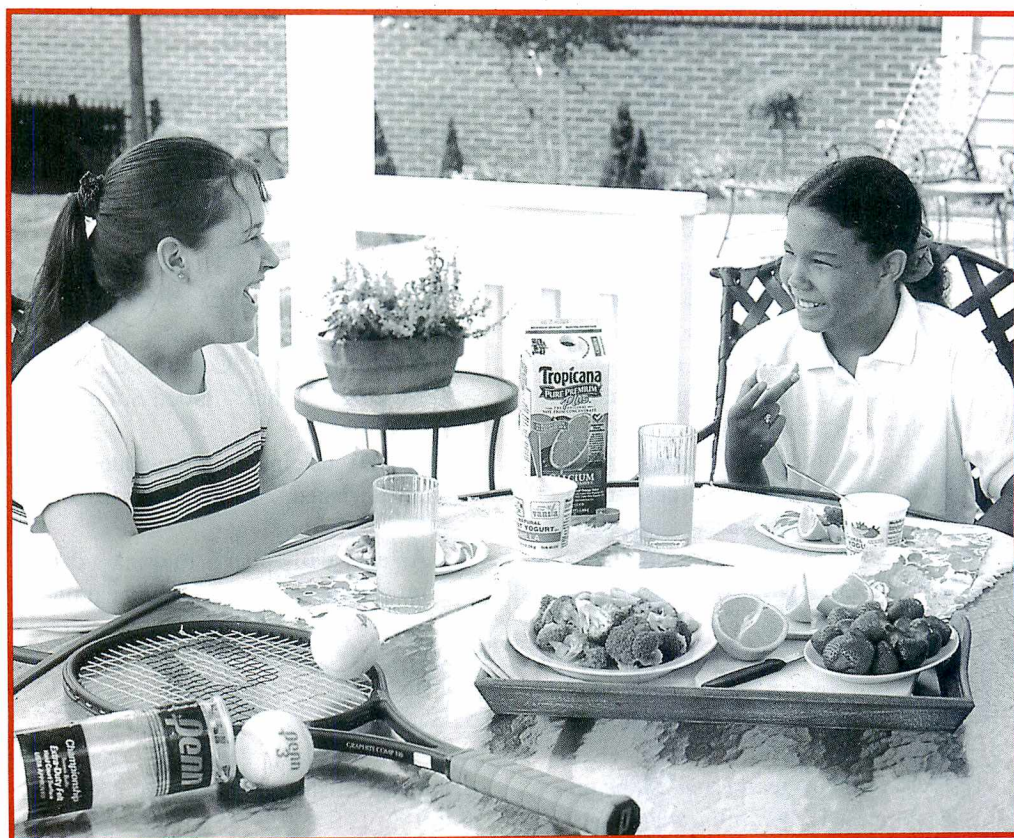
But during your preteen and teenage years, you can reduce your risk of fractured bones later in life with calcium-rich foods and physical activity.

Bone Behavior

Your body's 206 living bones continually undergo a buildup, breakdown process called remodeling.

The body starts to form most of its bone mass before puberty, the beginning of sexual development, building 75 to 85 percent of the skeleton during adolescence. Women reach their peak bone mass by around age 25 to 30, while men build bone until about age 30 to 35. The amount of peak bone mass you reach depends largely on your genes. Then gradually, with age, the breakdown outpaces the buildup, and in late middle age bone density lessens when needed calcium is withdrawn from bone for such tasks as blood clotting and muscle contractions, including beating by the heart.

"You can't do anything about the genes you're dealt," says Mona Calvo, Ph.D., a calcium expert for the Food and Drug Administration. "As a teenager, though, you can make the most of things you do control that can build your bones and help reduce the risk of fractures when you are older."



Supporting the skeleton with healthful habits now so it can support you later in life is especially important if you have an increased risk of osteoporosis—for example, if you're female or have a thin, small-boned frame. These habits are proper diet, exercise, and avoiding bone risks—lifestyle choices that are bad for bone, like smoking.

Eat Your Way to Strong Bones

The main mineral in bones is calcium, one of whose functions is to add strength and stiffness to bones, which they need to support the body. To lengthen long bones during growth, the

An afternoon of tennis followed by a snack of foods that contain calcium is a fun and easy way to build and strengthen your bones.

body builds a scaffold of protein and fills this in with calcium-rich mineral. From the time you're 11 until you're 24, you need about 1,200 milligrams (mg) of calcium each day.

Adolescent bodies are tailor-made to "bone up" on calcium. Calvo says that with the start of puberty, "your body is at a higher capacity to absorb and retain calcium."

Bone also needs vitamin D, to move calcium from the intestine to the bloodstream and into bone. You can get vitamin D from short, normal day-to-day exposure of your arms and legs to sun and from foods fortified with the vitamin. Also needed are vitamin A, vitamin C, magnesium and zinc, as well as protein for the growing bone scaffold.

Mother Nature provides many foods with these nutrients. One stands out, however, as "almost a perfect package," according to Calvo. "Milk is rich in calcium and high-quality protein. Nearly all U.S. milk has vitamins D and A added. And it has magnesium and zinc."

Still, as excellent as milk is for bones, it and other dairy products are not the only foods that contain calcium. All groups in the Food Guide Pyramid, in fact, offer calcium sources—from the pyramid's grain-based foods that you need the most of, to the produce and high-protein groups in the middle, and

even to the fats and sweets "use sparingly" group at the top. (See illustration, page 29.) The importance of choosing calcium sources from the different food groups is that each group offers its unique package of other nutrients as well.

To learn how much calcium is in a food, you can read the food label's Nutrition Facts panel. Look for the "percent Daily Value" (%DV) set by FDA for calcium. The calcium DV is 1,000 mg. But if you are 11 to 24 years old, your growing bones need more—the recommended 1,200 mg. So, each day's calcium %DVs in the foods you eat should add up to 120 percent.

Because many foods are now fortified with calcium, your investigation of labels may turn up surprising sources. To identify foods with at least 10%DV of calcium per serving, FDA allows these terms on their labels:

- 20%DV or more: "High in Calcium," "Rich in Calcium," "Excellent Source of Calcium"
- 10% to 19%DV: "Contains Calcium," "Provides Calcium," "Good Source of Calcium"
- 10%DV calcium or more added: "Calcium-Enriched," "Calcium-Fortified," "More Calcium."

An easy daily plan is to drink a calcium source at every meal and eat one

"Calcium! Do You Get It?"

Unlike boys, growing girls typically have low calcium intakes. Concerned about the low intakes, the Food and Drug Administration recently developed a pilot education program, funded by the agency's Office of Women's Health, just for girls ages 11 to 14. "Calcium! Do You Get It?" encourages girls to get enough calcium and exercise for healthy bones and to carry these healthy behaviors throughout life. This article includes much of the information in the program. ■

calcium food as a snack, says Ruth Welch, a registered dietitian with FDA.

If the lactose sugar in dairy products causes problems like gas, bloating or diarrhea, try lactose-reduced or lactose-free milk. When fortified, these products can have up to 50%DV for calcium in one serving. Also available are lactase drops and tablets, which can help you digest dairy products like ice milk, yogurt, and cheese.

Get Enough Weight-Bearing Exercise

Growing bone is especially sensitive to the impact of weight and pull of muscle during exercise, and responds by building stronger, denser bones. That's why it's especially important when you're growing a lot to be physically active on a regular basis.

And as far as bone is concerned, Calvo says impact activity like jumping up and down appears to be the best. "But the important thing is to get off the couch and get moving at some activity. It really is a matter of 'Use it now, or lose it later'."

Such activities include sports and exercise, including football, basketball, baseball, jogging, dancing, jumping rope, inline skating, skateboarding, bicycling, ballet, hiking, skiing, karate, swimming, rowing a canoe, bowling, and weight-training. (See "The Activity Pyramid.") And when your parents make you mow the lawn, rake leaves, or wash and wax the car, they're doing your muscles and bones a favor.

Girls Don't Get Enough Calcium

Between the ages 11 and 24, people need at least 1,200 milligrams (mg) of calcium every day. A 1995 survey by the U.S. Department of Agriculture, however, found that girls and young women 12 to 19 got only 777 mg of the mineral daily, overall. Intake by boys and young men in the same age group was 1,176 mg daily.

Daily calcium intake by preteen girls was far short of the recommended level also in 1990–1992 and fell with age, wrote Ann Albertson, M.S., R.D., and others recently in the *Journal of Adolescent Health*. Calcium consumption was only 781 mg at ages 11 to 12, 751 at ages 13 to 14, and a mere 602 mg—

barely half what it should be—at ages 15 to 18.

Why is calcium intake in girls and young women so low?

USDA's *Agricultural Economic Report No. 746* gives some clues. Compared with other children, female adolescents:

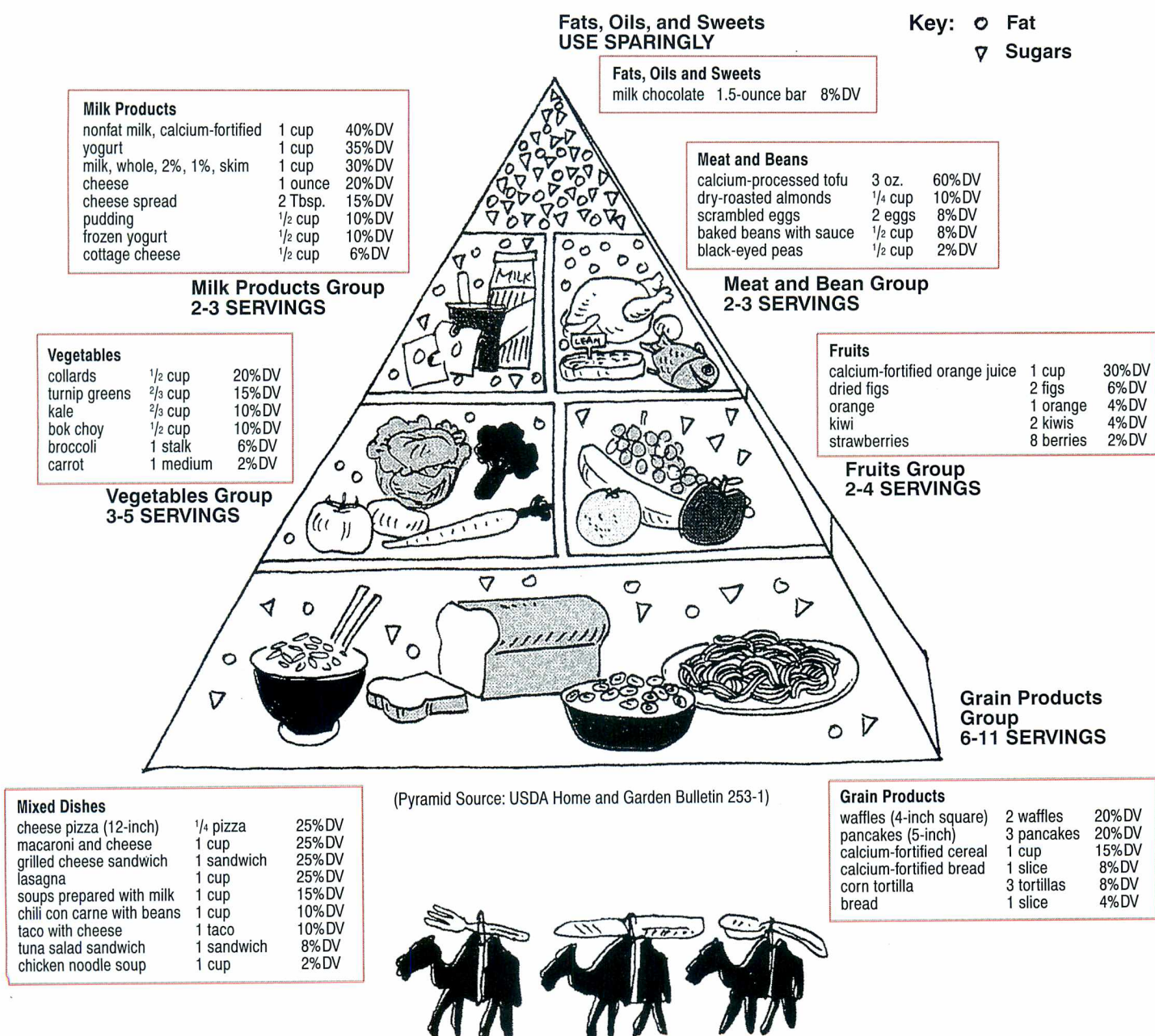
- drink the least amount of fluid milk
- have the highest tendency to skip morning meals, which offer the most calcium because of milk and cereals
- have the highest share of calories from fast-food places, which have a calcium density much lower than foods prepared at home, schools or restaurants. ■

—D.F.

Eat Enough Calcium And A Balanced Diet, Too

To get enough calcium for growing bones, each day you need to eat foods whose %Daily Value for calcium adds up to 120 percent. Because the amount of calcium in foods can vary, read the food label and check the %DV for calcium in what you eat.

So your body will have all the other nutrients it needs, too, be sure to eat the recommended number of servings from each group in the Food Guide Pyramid below. As this drawing shows, each group includes foods that provide calcium. The food examples are listed by their serving size and %DV for calcium.



The Activity Pyramid

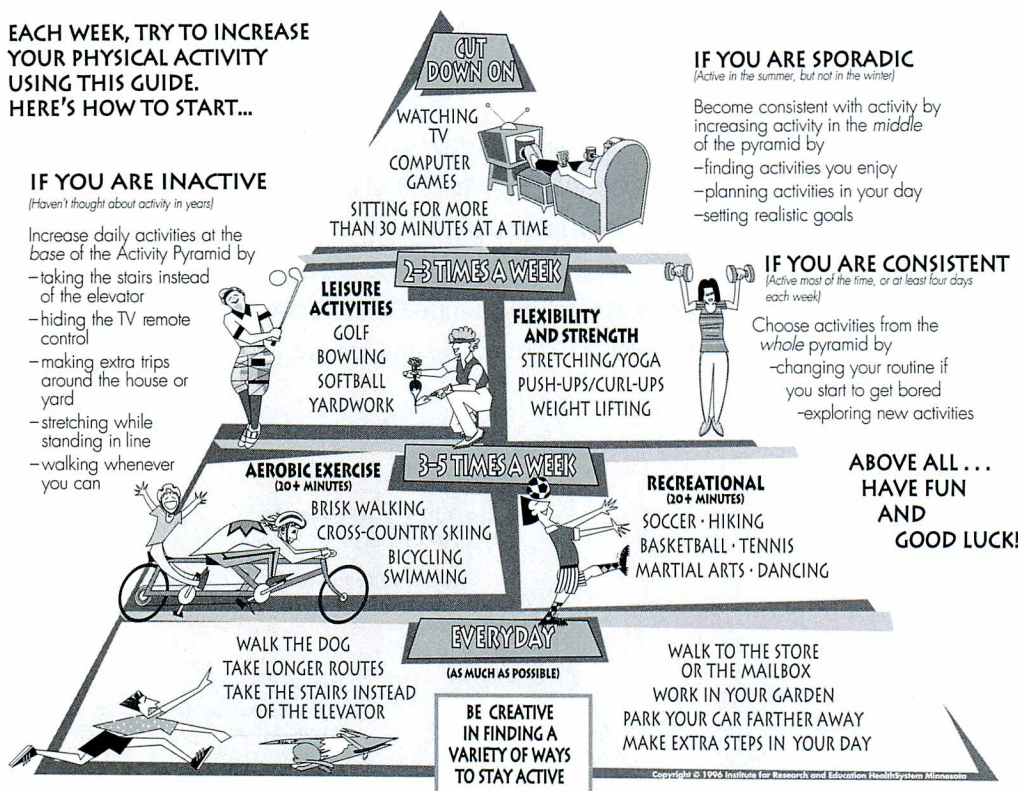
EACH WEEK, TRY TO INCREASE YOUR PHYSICAL ACTIVITY USING THIS GUIDE. HERE'S HOW TO START...

IF YOU ARE INACTIVE

(Haven't thought about activity in years)

Increase daily activities at the base of the Activity Pyramid by

- taking the stairs instead of the elevator
- hiding the TV remote control
- making extra trips around the house or yard
- stretching while standing in line
- walking whenever you can



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FDA's Welch adds, "Day-to-day activities that start in the teen years, like walking the dog or using stairs instead of elevators, can become life-long habits for healthy bones."

Avoid Bone Risks

Some habits in the teenage years can steal calcium from your bones or increase the need for it, weakening the skeleton for life.

Skipping meals is risky for bone, Welch says. In our three-meal-a-day so-

ciety, skipping a meal may reduce by a third your chance of getting your 120% DV for calcium—simply by eliminating one occasion to eat.

Replacing milk with nondairy drinks like soda pop or fruit-flavored teas or drinks is another eating habit that prevents bones from getting the calcium and other nutrients they need.

In a survey comparing 1994 daily beverage intakes with those in the late 1970s, the U.S. Department of Agriculture found a switch from milk to other drinks among young people:

- Milk drinkers among teenagers dropped from three-fourths to little more than half.
- Two to three times more children and teenagers drank non-citrus fruit juices.
- Teenage boys nearly tripled their intake of soft drinks, three-fourths of them drinking about 34 ounces; two-thirds of teenage girls drank 23 ounces.

Alcohol abuse and cigarette smoking can hurt bone. Calvo says, "Alcohol abuse can cause loss of calcium, magnesium and zinc in the urine. Many who abuse alcohol also have poor diets and malnourished, weaker bones." Cigarette smoke is also toxic to bone and can in-

fluence how much exercise you get because it affects your stamina, she says.

Eating disorders can weaken bone. The repeated vomiting in bulimia and extreme dieting in the appetite disorder anorexia can upset the body's balance of calcium and important hormones like bone-protective estrogen, decreasing bone density. And extreme exercising by young women with or without eating disorders can postpone or stop menstruation, when blood levels of estrogen are reduced.

Small Changes for Big Benefits

As a disorder of aging, osteoporosis may seem far away for worry when you're 15. But, small changes today for better bones tomorrow may be more important than you might guess.

Laura Bacharach, M.D., of Stanford University, wrote in *Nutrition & the M.D.* last year that adolescents who make "even a 5 percent gain in bone mass can reduce the risk of osteoporosis by 40 percent." And this is in addition to "immediate benefits of feeling stronger and more fit now with these changes!" ■

Dixie Farley is a staff writer for FDA Consumer.

Want More Information?

Dairy Council of California
1101 National Drive, Suite B
Sacramento, CA 95834
<http://www.dairycouncilofca.org/>

National Osteoporosis Foundation
P.O. Box 96616
Washington, DC 20077-7456
<http://www.nof.org/>

Osteoporosis and Related Bone Diseases
National Resource Center
(1-800) 624-BONE
TDD: (202) 223-0344



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

■ **Women who are obese** or who gain more than 44 pounds after age 18 are about 2½ times more likely to suffer the most common type of stroke than lean women whose weight remains fairly steady, according to research at Brigham and Women's Hospital, in Boston.

(*Journal of the American Medical Association*, May 21)

■ **Free consumer publications about childhood immunizations** are available from the National Centers for Disease Control and Prevention. For single copies of *Guide to Contraindications for Childhood Vaccinations*, *Standards for Pediatric Immunization Practices*, or *Vaccine Information Sheets*, write to the National Immunization Program, CDC, 1600 Clifton Road, N.E., Mail Stop E34, Atlanta, GA 30333.

■ **Edible vaccines contained in bananas?** Genetically altered bananas that can incorporate a desired vaccine may

be reality in the near future, say scientists who are developing such products. Bananas are ideal for this use, the scientists say, because they are grown in almost all tropical and subtropical developing countries (where vaccines are badly needed) and are eaten widely by infants and children. See *The Jordan Report*, available free from Philip J. Baker, Division of Microbiology and Infectious Disease, NIH, Solar Building, Room 3A05, MS 7630, Bethesda, MD 20892-7630.

■ **Water balloons launched by slingshots** can pose "a serious threat to vision" and inflict life-threatening injuries, according to a study at Wright State University School of Medicine, in Dayton, Ohio. In one experiment, a balloon launched at a watermelon 20 feet away caused the watermelon to explode on impact. Study authors said the maximum kinetic energy of these balloons is comparable to "a variety of objects well known to cause serious [eye] injury, including some rifle bullets." (*Ophthalmology*, May 1997)

■ FDA is extending to Oct. 6 the comment period for its **proposal to improve labeling on over-the-counter drugs**. Submit written comments to the Dockets Management Branch, HFA-305, FDA, 12420 Parklawn Drive, Room 1-23, Rockville, MD 20857. (FR June 19)

■ **Asthma among children** in U.S. inner-city areas is partly linked to cockroach allergy. Researchers in a study supported by the National Institute of Allergy and Infectious Diseases report that reducing exposure to cockroaches through patient education, roach traps, and child-safe insecticides "may be a cost-effective way of reducing the bur-

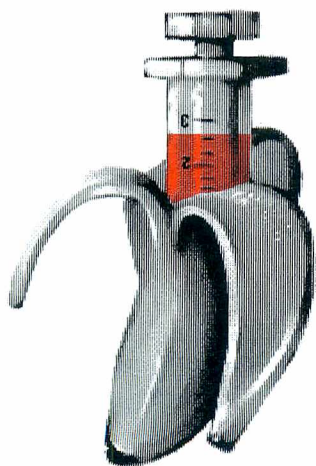
den of this serious disease." (*The New England Journal of Medicine*, May 8)

■ **Medhaden oil** is generally recognized as safe as a food ingredient with specific limitations, under an FDA final rule. The fish-derived oil may be used in cakes, fruit pies, cookies, cereals, breads, and other foods—but only in concentrations specified in the rule. (FR June 5)

■ **Oral potassium intake** can significantly reduce blood pressure, report researchers at the Johns Hopkins University School of Hygiene and Public Health, in Baltimore. The researchers combined results of 33 previous trials with data on 2,609 participants in a study where potassium supplementation was the only difference between intervention and control conditions. They concluded that even a small amount of potassium intake may help delay high blood pressure. (*JAMA* May 28)

■ **MEDLINE**, the world's largest source of published medical information, is now available free on the National Library of Medicine's World Wide Web site at <http://www.nlm.nih.gov/>

■ **Children risk strangulation** from cords that control venetian blinds and other window treatments. Officials at the Consumer Product Safety Commission and the Oregon Health Sciences University report 183 fatal window-cord strangulations between 1981 and 1995. Ninety-nine percent of victims were 3 or younger. Suggested preventive measures include using tie-down devices and moving cribs or beds away from windows with the cords. (*JAMA* June 4)





Seizers Keepers, Criminals Weepers

by Tamar Nordenberg



The maker of unapproved new drugs promoted for the treatment of cancer, heart disease, diabetes, and other serious conditions lost its fight for the return of \$600,000 worth of illegal products seized at FDA's request.

In a March 1997 order, Judge Lloyd George of the U.S. District Court for the District of Nevada ruled that International Nutrition Inc. of Las Vegas was not entitled to the return of the products sold under the Hans Nieper label, even if the company intended to relabel the products and remove the unsupported drug claims. The judge agreed with FDA that the return of the goods would allow the company and its president, Gene Sylvester Oden, to profit from their past illegal activities.

International Nutrition and Oden said they wanted the products back so they could relabel them and sell them as dietary supplements. But FDA stated in its brief to the court that the company "can-

not plausibly argue that a mere change in the labeling today will undo the effects of several years of unsubstantiated therapeutic claims."

The products were mostly orotates, which are made up of orotic acid and various minerals, such as calcium, magnesium, zinc, potassium, and lithium.

"Oden said that orotates were the best thing ever discovered for cancer and other serious diseases," says FDA investigator Luis Chavarria of the agency's Las Vegas resident post. "He said their unique transporter system could carry nutrients through the cell wall faster than anything available on the market."

FDA received no reports of injuries from the Hans Nieper products made by Oden. But, as Chavarria points out, the heavy promotion—and subsequent use—of these products for serious ailments could endanger the public health.

"For example, you could have a

diabetic substituting these unproven products for the insulin their body depends on," he says.

FDA began looking into Oden's business practices after receiving reports in 1992 and early 1993 from consumers and drug manufacturers about the sale of unapproved Hans Nieper products in the United States.

Since 1987, FDA had been aware of fraudulently promoted products manufactured in Europe by German physician Hans Nieper and sometimes shipped into the United States. But FDA knew of no U.S.-manufactured Hans Nieper products until FDA's Orlando district office traced some products seen during a plant inspection to a manufacturing facility in Pahrump, Nev. Based on this lead, Chavarria inspected Oden-owned Ramona Manufacturing Inc. in Pahrump in March 1993.

"When I confronted Oden about the illegal manufacture of orotates, he totally denied making them at his plant," Chavarria says.

But two Ramona employees who were present during the inspection secretly phoned Chavarria later and told him the plant did manufacture orotates. The informants also told Chavarria that while he was inspecting the plant, one employee ran out the plant's back door carrying boxes of orotates, while another ran into the women's bathroom and hid the products' labels behind a paper towel machine.

On April 30, 1993, an investigator with FDA's Minneapolis district office placed an anonymous order for Hans Nieper products with International Nutrition. Within two days, the district office received shark cartilage and cola-

mine phosphate drugs from International Nutrition, as well as promotional literature with unsubstantiated medical claims sent by another company owned by Oden, Papillon Botanicals Inc.

"To try to circumvent FDA's regulations," Chavarria says, "Oden had set up several companies besides International Nutrition to distribute the literature with the medical claims."

From June to August 1993, FDA investigators and U.S. marshals searched seven Oden-owned facilities, including Ramona, Papillon, and International Nutrition, and seized the unapproved drugs.

Both Oden and International Nutrition pleaded guilty in June 1995 to selling

unapproved new drugs across state lines. Oden was sentenced to five years' probation and fined \$5,000, and his company received five years' probation and a \$60,000 fine.

Almost two years later, FDA was in court with International Nutrition again, this time opposing the company's bid to get back its seized products. "Based on Oden's track record, we were very concerned that if he got the seized items back, he would turn around and continue the criminal enterprise he had been involved in," Chavarria says.

The court, sharing FDA's concern, stated in its order denying return of the products, "International Nutrition's request ... is akin to the creator of a seized

pipe bomb asking for the return of the pipe with the promise that the pipe will be used for plumbing, or the manufacturer of seized illegal firearms asking for the return of the metal with the promise that it will manufacture the metal into legal firearms."

The seized drugs will be crushed at a landfill, Chavarria says. To FDA's knowledge, Oden has stopped manufacturing the illegal Hans Nieper products. He still owns International Nutrition Inc., which he has relocated to a town near El Paso, Texas.

Tamar Nordenberg is a staff writer for FDA Consumer.

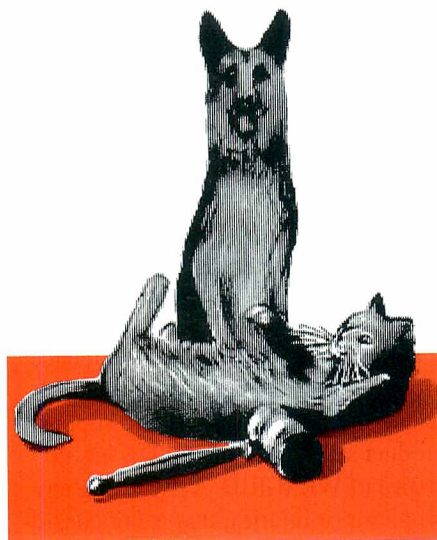
Get Rid of Worm Ridder, District Judge Rules

Because Bingman Laboratories Inc., of Sarahsville, Ohio, had made and sold WRM-RID Dog Wormer since 1955, company president W.D. Semple believed the product had the government's tacit approval. FDA believed differently.

On March 31, Judge Joseph Kinneary, of the U.S. District Court for the Southern District of Ohio, granted FDA's motion for summary judgment and ordered the destruction of almost \$26,000 worth of WRM-RID, previously seized by the government. The court agreed with FDA that the product was illegal because the company never submitted data to show safety or effectiveness of the product as required by federal law. The company had argued that its product was legal because it had been on the market before effectiveness data became a requirement for approval of new animal drugs.

Semple promoted WRM-RID for parasitic tapeworm, hookworm and roundworm infestations in dogs and cats. These infestations can cause vomiting, diarrhea, loss of appetite, weight loss, anemia, and death.

The two active ingredients in WRM-RID are piperazine phosphate and arecoline hydrobromide. Piperazine



phosphate is approved for roundworm infestation in dogs and cats. Arecoline hydrobromide is not approved at all.

The combination of the two drugs in one product is not approved "nor is it recognized by the veterinary profession for any use," Susan Homire, D.V.M., an FDA veterinarian, told the court. She added that an extensive scientific literature search produced no published studies on the safety or effectiveness of WRM-RID or any product with the same combination of active ingredients for the uses recommended in the product labeling.

FDA has inspected Bingman Laboratories periodically since it began marketing WRM-RID in the 1950s but did not cite the company for any deficiencies until April 9, 1991, when FDA's Cincinnati district office informed Semple by letter that the agency considered WRM-RID an unapproved new animal drug. FDA based its decision on, among other things, the fact that there was no new animal drug application on file with respect to the product's use or intended use.

Semple responded in letters dated April 17 and Aug. 26, that WRM-RID was not subject to the requirement for a new animal drug application because it had been on the market before an Oct. 10, 1962, amendment to the 1938 Federal Food, Drug, and Cosmetic Act added a requirement for effectiveness for all drugs.

Although discussions with staff from FDA's Center for Veterinary Medicine did not convince Semple that WRM-RID was a new animal drug, he told agency investigators during inspections in August and November 1992 that he would stop making the drug until the issue was resolved.

Members of the center's division of compliance and surveillance met with Semple again in April 1993 to discuss

the need for a new animal drug application for WRM-RID, but no progress was made in changing Semple's mind.

During an inspection in March 1994, Diane McDaniel, an investigator with FDA's Columbus resident post found that the company was still making WRM-RID. When McDaniel asked for production records, the plant manager said he would first have to talk to Semple, who conducted business from his home in Florida.

Semple called McDaniel the next day and told her that he kept all production records at his home and would send her current labeling and production records for the most recent batch of WRM-RID. McDaniel returned to the plant to collect a sample.

Within a week, McDaniel received a letter from Semple, but the labels and production records he said he would send were not included. Instead, Semple wrote, "For your information, there has been no change in the WRM-RID formula, manufacturing process, label claims and dosage directions since 1955."

In April 1994, Evelyn Forney, a compliance officer with FDA's Cincinnati district office recommended that the agency seek seizure of the product because Semple continued to deny that WRM-RID was covered under the 1962 amendment.

The Center for Veterinary Medicine agreed with Forney's recommendation, and in August, the U.S. Department of Justice, at FDA's request, filed a complaint for forfeiture and condemnation. On Sept. 12, U.S. marshals seized 154 kilograms (339 pounds) of WRM-RID, as well as labels and packaging for the product, at the Sarahsville plant.

Semple filed a claim for ownership Sept. 22, and on Oct. 13, he filed an answer to the government's complaint. He continued to assert that WRM-RID was on the market before the 1962 amendment and therefore exempt from FDA approval under a "grandfather clause."

For Semple's assertion to be true un-

der the 1962 amendment he had to prove that the current WRM-RID was:

- chemically identical to the drug in existence on Oct. 9, 1962, the day before the 1962 amendment took effect
- commercially available on Oct. 9, 1962
- generally recognized as safe on that date
- not covered by a new drug application on that date
- labeled exactly the same as it was before the 1962 amendment took effect.

Semple insisted that "there has been no change in the WRM-RID formula, manufacturing process, label claims and dosage directions since 1955." But when asked to submit to FDA documentation to back up these claims, he never did.

In addition, the grandfather clause could be considered only if the documentation submitted to FDA or available in the scientific literature showed that WRM-RID was considered safe before the date of the 1962 amendment. Safety has been a requirement for all drugs since the 1938 Food, Drug, and Cosmetic Act.

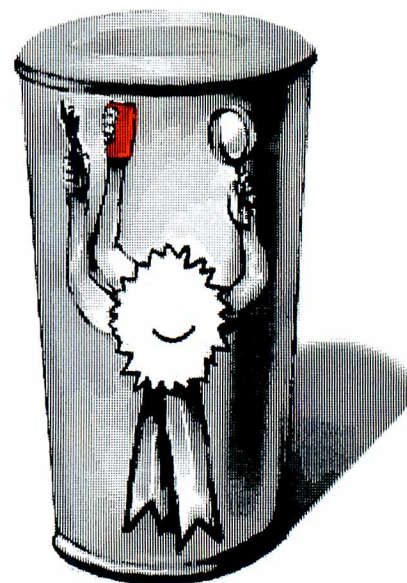
Semple did not submit any evidence proving safety, and an FDA literature search did not find any data to support product safety. Although FDA has no record of WRM-RID ever causing any problems or injuries, that is not considered documentation.

On April 23, 1997, Semple filed an appeal to prevent destruction of the seized product. At press time in July, the appeal was pending.

—Isadora Stehlin

Sixth-Grader Opens Lid For FDA Investigation

When 13-year-old Cason Schmit of Oakland, Calif., began work on his sixth-grade science project, his main goal was to win a blue ribbon. But he got much more, including national exposure, a job for his college-age brother, and a chance to protect public health by



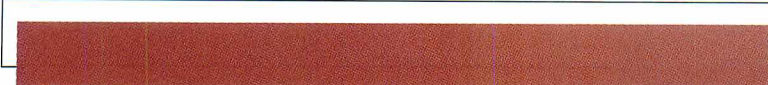
sparking an FDA investigation.

Earlier this year, investigators with FDA's San Francisco district office confirmed Schmit's findings of lead-soldered canned food on some area retail shelves, even though FDA had banned the cans for food use two years ago and required their removal from commerce by June 1996.

Most of the San Francisco-area stores found with illegal lead-soldered cans, imported mainly from southeastern Asia, were small ethnic groceries specializing in imported foods. Almost all of the cans have since been removed from store shelves, according to Richard Jacobs, Ph.D., a research chemist and metal specialist in FDA's San Francisco district office who participated in the inspections.

Lead is a known metabolic poison that can damage the kidneys and liver and the nervous, reproductive, cardiovascular, immune, and gastrointestinal systems. It is particularly damaging in children, where, among other things, it can impede intellectual development. Extremely high levels of lead in the body can cause death.

Lead-soldered cans pose a risk because the lead seeps into the food. Until November 1991, when U.S. manufacturers voluntarily stopped producing lead-



soldered cans, 14 to 45 percent of lead in food came from these types of cans. In 1995, FDA imposed a mandatory ban that covered not only U.S.-produced canned goods but imported canned food, as well. Many countries still make lead-soldered cans for food use.

Schmit's sixth-grade project got its start during his fourth-grade year, when he came across a news story about FDA's impending ban. For his fourth-grade science project, he decided to see whether he could find lead-soldered cans on Oakland store shelves. He scouted four stores looking for suspect cans with thick wide seams and, sometimes, solder smears.

He ended up buying six suspect cans from two stores. At home, he tested them, using one of several commercial home lead test kits modeled after a lead test developed by FDA, and found that the cans were indeed lead soldered.

His sixth-grade science project updated and expanded the earlier one. Last January, he revisited the two stores where he had previously found lead-soldered canned food. He did not find any lead-soldered cans at one of the stores but found 10 lead-soldered cans—six more than he had found two years earlier—on the shelves of the other store.

With help from his mother, Schmit arranged for a private laboratory to help him test samples of food from the lead-soldered cans. The food samples tested positive for lead.

These findings prompted Schmit in February to contact county and state health authorities, as well as FDA. "I [wanted] to get as many people aware of this health hazard [as possible]," he said. "I had a responsibility to let people know."

Impressed with the quality of Schmit's research and concerned about his findings, FDA, in March, sent four teams of investigators to check out smaller stores specializing in imported foods in Oakland, Berkeley, South San Francisco, and San Francisco. These cities have large ethnic populations

served by a number of what Jacobs referred to as "mom-and-pop operations."

The teams visited 24 stores, most of which sold Chinese, Vietnamese, Philippine, or Korean foods. A few specialized in Central and Eastern European food.

The investigators examined thousands of different canned products. All but one proprietor willingly handed over suspect cans for FDA laboratory analysis. The remaining proprietor told investigators they would have to pay for the cans, which they did.

According to Jacobs, the four teams collected "thousands" of suspect products, 64 of which tested positive for lead in the side seam. The Oakland team, which visited five stores, examined 818 cans, 47 (6 percent) of which tested positive for lead-soldered seams.

"Except for a few cases, most of the canned goods that tested positive for lead appeared to be quite old, perhaps manufactured substantially before the prohibition [on lead-soldered cans]," Jacobs said.

According to the labels, most of the canned goods came from China and Taiwan. Other countries of origin included Thailand, India, Japan, Mexico, Chile, Peru, and Canada.

During the search for lead-soldered cans, investigators also came across a number of swollen, leaky cans and spotted rodent droppings, urine stains, and other signs of filth around the cans. "There were really some outrageous conditions," Jacobs said. "I almost got sick in the store."

FDA investigators brought their findings to store owners' attention. In many cases, Jacobs said, store owners were not aware of the ban on lead-soldered cans. Most agreed to remove and destroy illegal products, Jacobs said.

Many of the store owners also appeared unfamiliar with the thick wide seams and solder smears that indicate a can is soldered shut with lead. So investigators instructed store owners on what to look for.

The investigators forwarded their findings to the county and state health departments for follow-up. FDA's San Francisco metals' team plans to rein-spect stores found with illegal canned goods, as well.

In addition, FDA's San Francisco and Los Angeles district offices joined together to prepare educational materials on the hazards of lead-soldered cans.

Seventh-grader Schmit helped with educational efforts, too. He appeared on a one-hour Chinese-language San Francisco TV program. Also, his school project was the focus of several local print and broadcast news stories. He was interviewed by National Public Radio and, according to Jacobs, *Scholastic News*.

His brother, a science major at Northwestern University in Evanston, Ill., got a job with FDA's San Francisco district laboratory this past summer, a feat that the younger Schmit attributed to his involvement with FDA.

Science seems to be his calling, too, he said, citing medicine or laboratory work as possible future fields he will enter. He may even decide to join FDA some day. "That's a consideration," he said.

Jacobs' comments during the NPR interview indicated he wouldn't mind hiring him: "Too bad he [is] too young to make an inspector because I would really liked to have had him doing some of our work. ... He had a very great interest in this project, and it went beyond just a science project."

A blue-ribbon-winning science project at that.

—Paula Kurtzweil

Unapproved Drugs End Up At Hazardous Waste Site

A manufacturer of over-the-counter antiseptics who developed his active ingredient in a so-called "chemical nuclear reactor" asserted the products were not only effective but out of the realm of FDA regulation. FDA investi-

gation, however, found that the drugs were unapproved and dangerous as well, causing at least two cases of skin burns. At the agency's request, the drugs were recalled and seized during the past three years. The last batch of seized products was finally destroyed late last year at a hazardous waste disposal site.

The drugs were made by Magna-Bon Corp., of Okeechobee, Fla. Magna-Bon president, Kenneth Sorber, developed an antiseptic ingredient he called "Sorber Acid," a combination of sulfuric acid and ammonium sulphate mixed together in what Sorber termed a chemical nuclear reactor using electricity and high heat. He claimed the resultant Sorber Acid was nontoxic, with a pH range of 0 to 0.5. (The pH scale represents the degree of acidity, where a pH less than 1 is very acidic and a pH greater than 13 is very basic.)

But analysis of the samples by FDA's Southeast Regional Laboratory in Atlanta revealed a pH ranging from 0.7 to 1.24. The agency concluded that the drugs were so harmful they posed a Class I health hazard—a reasonable probability of causing serious illness or death.

The products' approval status and safety were first questioned in 1992 by Gary Beers, president of Low Pharmaceuticals Inc., of Wallingford, Conn. Low was Magna-Bon's main distributor. Beers relayed his concerns to Magna-Bon's president.

Dissatisfied with Sorber's response, Beers contacted Victor Spanioli, an investigator with FDA's Miami resident post, in 1992. Sorber's response to Beers' concerns, Spanioli learned, was that the Magna-Bon products were generally recognized as safe and so didn't need FDA approval. Sorber also had advised Beers to distribute the products without delay.

To look into the matter, Lynn Albinson, an investigator with FDA's Florida district office in Orlando, inspected Magna-Bon in December 1992. She learned that the company began business in Okeechobee in December

1990, registering there with FDA in April 1991. Shortly afterward, the company moved to Port St. Lucie, Fla. It moved back to Okeechobee in September 1992 but never re-registered with FDA, according to her inspection report.

Albinson found Magna-Bon to be in violation of FDA's drug good manufacturing practices. In describing Sorber Acid to Albinson, Sorber said that because the acid kills off all bacteria, molds and viruses, he was not concerned with dust and bacteriological controls during the manufacturing process. Also, he kept no written records or procedures, he told her, because of "industrial espionage."

Albinson collected samples and presented her findings to Sorber. "Management stated that they would need an 'exemption' from FDA and could not comply with most of the findings," she recalled.

Based on laboratory analysis of the samples and the inspection report, FDA issued a warning letter to Magna-Bon on March 1, 1993, asking the company to recall its antiseptic cream, antiseptic spray for burns, and facial cream. FDA also asked Magna-Bon to stop distributing the drugs immediately, recall them, and respond to the agency or face possible legal sanction.

FDA concluded that use of the products as labeled could lead to permanent injury and scarring from skin burns, particularly in children with diaper rash involving broken skin. Further, if any of these products got into the eye, they would be expected to cause pain and possibly corneal damage, FDA said.

FDA also told Magna-Bon that the products were:

- illegal because they were being sold without FDA new drug approval
- new drugs because FDA knew of no substantial scientific evidence that showed the products were generally recognized as safe and effective for the labeled uses
- misbranded because their labels did not give proper directions or name their active ingredients.

On March 12, Magna-Bon began recalling and destroying the drugs.

However, on May 28, FDA's Florida district recall coordinator, Philip Delisle, notified the agency's New England district office that the distribution company Low hadn't returned its products, worth about \$430,830.

In September 1993, Magna-Bon regulations' manager informed Delisle that all products returned to the company and any under a "stop-sale" order had been destroyed the day before at a landfill.

In November, John Hollings, an investigator with FDA's Hartford, Conn., resident post, went to Low for a final inventory of Magna-Bon products and found the company "closed, locked up and lights out," he said. A note on the door gave a telephone number and the message, "For info call Larry Zarrella." Hollings called but couldn't reach Zarrella. He finally did get hold of another employee and, with fellow investigator Stephen Souza, met her there on Dec. 6. The drugs were still at Low's.

FDA proceeded to have the warehoused products seized, and on May 19, 1994, a Verified Complaint was filed in the U.S. District Court for the District of Connecticut, New Haven. U.S. marshals seized the inventory in June 1994.

On June 6, 1994, Magna-Bon's lawyer informed FDA that the company had no objection to the destruction of the warehoused products. Four days later, FDA's Hollings accompanied Deputy U.S. Marshal Patricia Henshaw to the warehouse, where the Magna-Bon antiseptic products were seized and then shipped to Hamden, Conn., for storage until U.S. marshals could locate a suitable disposal site.

—Dixie Farley

Summaries of Court Actions will not appear in this issue of FDA Consumer, but will return in the November–December issue.

Food Safety On The Home Front

What comes to mind when you think of a clean kitchen? Shiny waxed floors? Spotless counters and neatly arranged cupboards?

These things are important, but a truly “clean” kitchen—that is, one that ensures safe food—relies on more than just looks: It also depends on safe food practices.

Some safe food basics are:

- Wash hands with warm water and soap for at least 20 seconds before handling all food. Wash hands—and utensils—after handling raw meat, poultry and seafood.
- Don't let raw foods such as meat, poultry and seafood touch ready-to-eat foods such as raw vegetables and already cooked dishes.
- Use a meat thermometer to see if cooked meat, fish and poultry have reached a safe temperature.
- Refrigerate perishables and cooked foods within two hours—the sooner, the better.



FOOD AND DRUG ADMINISTRATION

National Food Safety Education Month/September 1997