

FDA CONSUMER

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BOTTLED WATER New Trends, New Rules





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FDA Licenses Combination Childhood Vaccine

A combination vaccine that requires only four injections instead of the current eight was licensed by FDA last March 30 to prevent four serious childhood illnesses.

The new vaccine, Tetramune, is recommended for use at 2, 4, 6, and 15 months of age to immunize against diphtheria, tetanus, whooping cough (pertussis), and Haemophilus influenza type b, the leading cause of meningitis.

Clinical trials have shown that a series of four injections of the vaccine—a combination of diphtheria toxoids, tetanus toxoid, and pertussis vaccine adsorbed (DTP) and Haemophilus b conjugate vaccine—is as effective as the eight injections of DTP and Haemophilus b conjugate vaccines that have been used for almost a decade.

The clinical trials included 6,793 children immunized with the combination product and 4,232 children immunized separately but simultaneously with the two older vaccines. The results showed no significant difference in antibody response between the two groups or in the frequency and types of adverse reactions reported. The most common adverse reactions were fever, redness and inflammation at the injection site, and irritability.

Most children are vaccinated by the time they enter school. But because many infectious diseases are particularly dangerous in very small children, public health officials have sought a method to immunize before age 2.

To be appropriately immunized by age

2, children often have three of four shots—DTP, Haemophilus influenza type b, hepatitis B, and measles-mumps-rubella vaccine—at the same time (when they are 2, 4, 6, and 15 months of age).

Combining Haemophilus influenza type b in a single vaccine with DTP could reduce the shots to as few as two at each session so that children won't need as many injections.

The new combination vaccine is manufactured by Lederle Laboratories and Praxis Biologics, Inc., subsidiaries of American Cyanamid Co. of New York City.

Gender Guideline For Clinical Tests

A new guideline for studying gender differences in responses to drugs and biologics was announced by FDA late last March.

The guideline will require manufacturers to provide information from clinical studies about any significant differences between women and men in responses to these products. It also removes a 1977 restriction excluding women capable of becoming pregnant from participating in early clinical trials.

The reason given previously for this exclusion was to protect any fetus a woman might be carrying from unnecessary exposure to potentially toxic agents.

Women do not metabolize (process) drugs the same way as men due to differences in weight, proportion of body fat, the menstrual cycle, and menopause. The restriction on women in early trials meant that data would not show gender-related variations in the effects of new drugs and biologics. In addition, some people said the restrictive policy was overprotective of

women and denied them the opportunity to decide for themselves what risks to take.

The new FDA guideline reflects the agency's conclusion that the fetus can be protected by measures short of excluding women from early trials. The recommended precautions include pre-enrollment pregnancy testing, use of contraception, and informed consent that includes all available information about dangers to the fetus.

The new guideline encourages manufacturers to include women in adequate numbers in all phases of clinical trials and requires the manufacturers to analyze the results for gender-related differences. If any significant differences are identified, sponsors will be expected to characterize them in additional studies.

FDA believes that earlier participation of women in trials will advance the selection of doses and monitoring procedures in the final testing phase and will result in better labeling information for prescribing physicians.

Children's Tea Sets Recalled

Eight brands of children's china (ceramic) tea sets, found by FDA to contain excessive levels of leachable lead, are being voluntarily recalled nationwide by the products' distributors. The recalled sets are:

- Chilton Toys 12-piece tea set
- Barbie china 12-piece tea set, and 16-piece dinner set
- Holly Hobbie china 12-piece tea set, and 16-piece dinner set

- Cabbage Patch Kids china 13-piece set
- Campbell's 9- and 15-piece "Soup Time" china sets
- Friendly Home Parties porcelain 13-piece tea set
- Lillian Vernon Catalog porcelain 17-piece tea set for children
- McCrory children's china 13-piece tea set.



FDA analyses found that liquid placed in the tea sets could leach lead at levels ranging from 1.8 parts per million (ppm) to 31.5 ppm. (FDA guidelines for ceramic ware allow no more than 0.5 ppm leachable lead in cups, mugs and pitchers, and no more than 3 ppm in plates, saucers, and other flatware.) FDA considers the products no more than a limited to moderate hazard to health because the sets most likely are not used for regular food serving or storage.

Nevertheless, parents who suspect their children may have had long periods of direct exposure to lead through eating or drinking foods placed in these products (for example, by repeatedly drinking tea or juice from teacups) should consult their doctors.

All the sets were manufactured in China. They were distributed by Chilton-Globe, Inc., Manitowoc, Wis.; Friendly Home Parties, Inc., Albany, N.Y.; McCrory Corp., York, Pa.; and Lillian Vernon Corp., Mount Vernon, N.Y.

The distributors have notified retailers of the recall and asked them to remove the products from their shelves. Individuals who purchased these products are urged to return them to the place of purchase for a full refund.

(For additional advice to consumers concerning lead, see "Lead Threat Lessens, But Mugs Pose Problem" *FDA Consumer*, April 1993.)

Magna-Bon Products Recalled

At FDA's request, Magna-Bon Company of Okeechobee, Fla., recalled six over-the-counter topical drug products last March because they pose a risk of burns to the skin, possibly causing permanent injury and scarring. Consumers should stop using them immediately.

The products are Magna-Bon Antiseptic Cream, Magna-Bon Facial Cream, Magna-Bon Burn Spray, Magna-Bon Magnum Strength, Magna-Bon Medium Strength, and Magna-Bon Mild Strength. They had been distributed in California, Colorado, Connecticut, Florida, Georgia, Kentucky, Maryland, Michigan, Pennsylvania, Texas, and Virginia.

Consumers with questions may call Magna-Bon at (1-800) 845-1357.

Two Studies Yield New Data On Breast Implants

Two recent studies of laboratory rats may help provide a scientific rationale for the possible link between silicone gel-filled breast implants and autoimmune-like disorders. On the basis of these studies, FDA is requiring breast implant manufacturers to update information about the possible connection between the implants and immune-related disorders in the informed consent documents for women receiving these breast implants under clinical studies.

The animal studies do not, however, establish the connection with certainty, particularly since they were designed to intentionally stimulate an antibody response by mixing a known antigen with the silicone. More research, some now under way, is needed to determine the relevance of the studies to women with the implants.

In the two studies—one conducted in New York state by John Naim, Ph.D., and his colleagues and the other by Dow Corning Corporation, a supplier of silicone gel for implants—silicone gel was blended with liquid silicone and a known antigen (bovine albumin) and injected into the rats. Under these test conditions, the antigen alone would not have been expected to produce an immune response. In the presence of silicone gel or another antibody adjuvant (a substance that stimulates antibody production), however, it produced a strong antibody response. Naim's study appeared in the March 22 issue of *Immunological Investigations*.

FDA continues to advise women with silicone gel-filled implants to be alert to

symptoms of autoimmune disorders and consult a doctor if the symptoms do not subside. They include:

- pain and swelling of joints
- tightness, redness or swelling of the skin
- swollen glands or lymph nodes
- unusual and unexplained fatigue
- swelling of the hands and feet
- unusual hair loss.

Many women—with or without implants—may experience such symptoms from time to time. But people with immune-related disorders, which are relatively rare, generally experience a combination of these and other symptoms that don't go away.

Habitrol Manufacturer Agrees to Balance Info

In a multi-state court settlement last March, the manufacturer of the Habitrol nicotine patch agreed to provide balanced information about its product to the public. CIBA-Geigy Corporation of Summit, N.J., also agreed to provide \$550,000 to 11 states for costs, attorney fees, or consumer education activities.

Minnesota Attorney General Hubert Humphrey III charged that CIBA-Geigy

engaged in false advertising and deceptive trade practices by failing to disclose important information about the effectiveness and potential risks of its nicotine patch in consumer advertisements.

Under the settlement, CIBA-Geigy must disclose the following facts in direct-to-consumer advertisements and in a written disclosure statement:

- Habitrol is only an aid to help people quit smoking by reducing nicotine withdrawal symptoms. It has only been shown effective when used as part of a comprehensive smoking cessation program that includes counseling.
- Habitrol won't work for everyone. Effectiveness studies have been limited to three months.
- Habitrol should not be used for more than three months.
- Pregnant women and nursing mothers should talk to their doctors about alternative ways to quit smoking, because nicotine in the patches could harm their babies.
- Consumers with certain health conditions (such as cardiovascular disease), who take other prescription drugs, or who are under a doctor's care should first talk with their doctors about potential risks of nicotine patches.
- Nicotine patch users should not smoke or use other nicotine-containing products while using the patch.
- Habitrol hasn't been studied for use by children or adolescents.
- Habitrol is available by prescription only.

Joining Humphrey in the multi-state settlement were the attorneys general of Arizona, California, Illinois, Iowa, Massachusetts, Missouri, New Mexico, New York, North Carolina, and Texas. The settlement, called an Assurance of Voluntary Compliance, is not an admission of

wrongdoing, but is a legally enforceable court order.

(See also "Prescriptions to Help Smokers Quit" in the December 1992 *FDA Consumer*.)

First OTC Test Kit For Blood Cholesterol

The first over-the-counter kit to test at home for blood cholesterol was cleared for marketing by FDA last March 2. Elevated blood cholesterol is a risk factor for heart disease. Previous cholesterol tests had to be administered by medical professionals.

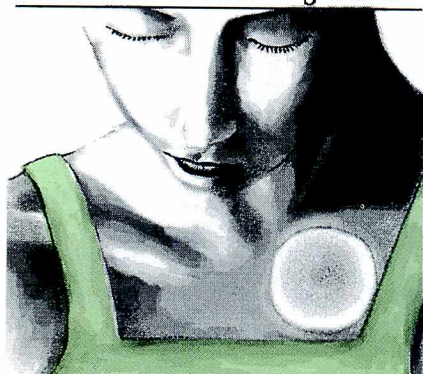
FDA based its decision to clear the Accumeter Cholesterol Self-Test kit for consumer use on results of a multi-center clinical trial involving nearly 500 adults. The study showed the home-use test was as accurate as cholesterol tests used by doctors and medical laboratories.

"Accuracy is crucial," said David A. Kessler, M.D., commissioner of the Food and Drug Administration. "It is also important, as the study showed, that participants were able to . . . understand the instructions and perform the test without assistance."

To perform the test, the user pricks a finger, squeezes blood into a cassette containing a test strip, and then waits 10 to 15 minutes. The strip changes color as the cholesterol rises on it. When the time is up, the user compares the color with an accompanying conversion chart to get the reading.

The test measures total cholesterol. A reading of less than 200 is desirable; 200 to 239 is borderline high; and 240 or above is high, which may mean an increased risk. People with readings of borderline or high should see a doctor.

APRIL MAY JUNE



The National Institutes of Health's National Cholesterol Education Program advises people with readings in the desirable range to have tests every five years and those with higher readings to ask their doctors how often to test.

Hemophiliacs and people taking medicine to thin the blood should not use this test because they may bleed excessively from the finger prick. They should only have their cholesterol checked by their doctors.

Besides giving detailed instructions for use, the package labeling includes information on cholesterol, heart disease, diet, and exercise. It also lists this toll-free number for additional information: (1-800) 927-7776. The new test is made by Chem Trak Inc. of Sunnyvale, Calif.

Multiple Sclerosis Treatment Being Considered

An FDA advisory committee of outside experts last March 19 recommended approval of the first product reviewed for the treatment of multiple sclerosis, a chronic, often debilitating disease of the central nervous system.

The Peripheral and Central Nervous System Drugs Advisory Committee recommended that FDA approve recombinant human interferon beta for patients with exacerbating-relapsing multiple sclerosis. (Advisory committee recommendations are not binding on FDA.)

The committee based its recommendation on data from a study of 338 patients with this form of multiple sclerosis, which affects nearly 30 percent of all patients with the disease. In such patients, flare-ups of symptoms are followed by total or partial

remissions that can last for months, often years. The U.S. and Canadian patients injected themselves with beta interferon every other day for two years.

The clinical trial provided evidence that beta interferon decreases the frequency of flare-ups. Adverse reactions to recombinant human interferon beta included inflammation and pain at the injection site, flu-like symptoms, and malaise.

Multiple sclerosis occurs when a protective sheath surrounding the nerve fibers of the central nervous system breaks down. In some cases, "sclerotic" or hardened patches of tissue develop in "multiple" places within the central nervous system.

Multiple sclerosis affects twice as many women as men and between 250,000 and 350,000 Americans. In two-thirds of patients, symptoms first occur between the ages of 20 and 40.

Beta interferon is manufactured by Chiron Corporation and Berlex Laboratories.

Precautions Urged For Two Blood-Borne Viruses

People infected with the viruses HTLV-I or HTLV-II should take precautions against infecting others similar to those taken by people infected with HIV, the virus that causes AIDS.

The national Centers for Disease Control and Prevention recommends that carriers:

- tell their doctors they are infected
- avoid donating blood, semen, body organs, or other tissues
- avoid sharing needles or syringes
- avoid breast-feeding (unless other infant nutrition sources are unavailable)
- use latex condoms to prevent sexual transmission.

Reporting a CDC study in the March 15, 1993, *Annals of Internal Medicine*, Rima Khabbaz, M.D., and colleagues said infection with HTLV-I or HTLV-II, two retroviruses different from HIV, is uncommon in most of the United States, but has become established in some U.S. cities and other countries. These viruses do not cause AIDS.

CDC estimates that 16 of every 100,000 U.S. blood donors carry HTLV-I or HTLV-II, with cases about equally divided. Blood banks use FDA-licensed tests to screen donated blood for HTLV. They destroy donations found to be infected and inform the donors they are infected and may no longer give blood.

HTLV-I causes a quickly fatal leukemia and a progressive nerve disease. It is found in the United States among clusters of African Americans in the Southeast and among people in Brooklyn, N.Y., who once lived in areas of the world with widely infected populations, such as southwestern Japan, the Caribbean, Melanesia, and parts of Africa.

HTLV-II is not clearly associated with any disease. It mainly occurs in the United States among intravenous drug users and some groups of American Indians in Florida and New Mexico.

Retroviral Tests Don't Identify Chronic Fatigue Syndrome

No scientific basis exists for using retroviral tests to diagnose chronic fatigue syndrome (CFS), according to a study published by the national Centers for Disease Control and Prevention in its March 19 *Morbidity and Mortality Weekly Report*.

This study supports other recent studies

that were unable to find evidence supporting claims that CFS is caused by a retrovirus or spumavirus, a retrovirus sub-family.

Chronic fatigue syndrome is characterized by prolonged, debilitating fatigue.

For the study, blood samples were obtained from 68 confirmed CFS patients in four geographic areas—Charlotte, N.C., Lyndonville, N.Y., and two areas in northern New Jersey. In addition, blood samples were collected from healthy individuals from the same areas and of similar age, sex and race for each case patient.

The samples were then sent to two laboratories that had developed retroviral tests they claimed could identify CFS. The study found that these retroviral tests could not distinguish between healthy individuals and those with CFS.

CFS is primarily diagnosed by identifying specific symptoms reported by the patient and by excluding other potential causes of prolonged fatigue.

Hearing Screening Recommended for Newborns

All newborns should be screened for hearing impairment before leaving the hospital, a panel convened by the National Institutes of Health recently recommended. The panel was sponsored by the National Institute on Deafness and Other Communication Disorders.

In the United States nearly 1 of every 1,000 children is born deaf and many more are born with hearing problems. Without infant screening, most hearing

impairments are not detected until a child is 1 to 3 years old. Because children develop speech and language skills during the first three years of life, hearing impairments can interfere with this development, as well as affect a child's social and emotional growth.

The panel recommended universal screening of infants with a test that measures otoacoustic emissions—inaudible sounds produced by the inner ear. Those who fail this test should then be screened with auditory brainstem response audiometry, which measures the function of the inner ear hearing nerve and parts of the brain involved in hearing.

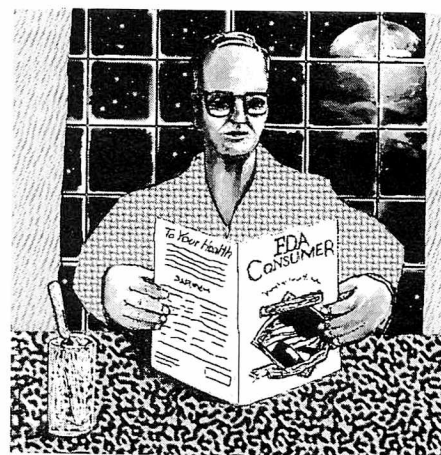
Auditory brainstem response testing has been the screening method for high-risk infants for nearly 15 years, but its cost, testing time, and technical difficulties have discouraged its use for screening large populations. The recently developed otoacoustic emissions test is fast, inexpensive and noninvasive.

The only infants screened now are those identified with one or more high-risk factors for hearing impairment, such as low birth weight or family history of hearing impairments. However, these criteria fail to identify 50 to 70 percent of children with hearing impairments.

While the best opportunity to perform universal hearing screening is before infants are discharged from newborn nurseries, the panel urged that it be done at least within the first three months of life.

Special Issue on Food Labeling

In-depth but easy-to-understand information about the new food label has been compiled into a single source: an *FDA Consumer* special issue on food labeling.



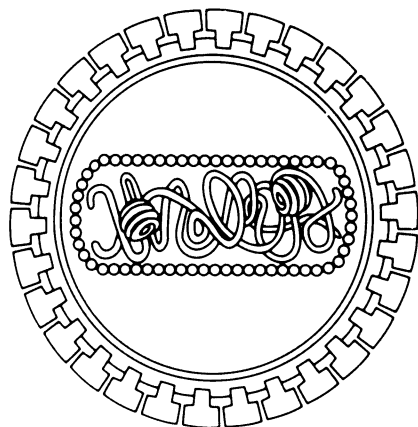
The special issue features recent *FDA Consumer* articles on food labeling, as well as some newly published material. Subjects covered include health claims, nutrient content descriptors, nutrition panel format and content, and Daily Values.

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



CDC Advises Hospitals to Test Patients for HIV

Hospitals in areas that have significant numbers of patients with HIV infection or AIDS should offer routine counseling and HIV testing to all patients, the national Centers for Disease Control and Prevention has advised.

CDC, a branch of the U.S. Public Health Service, recommends that hospitals anonymously test patients to see whether 1 percent or more are infected with HIV (human immunodeficiency virus), which

causes AIDS. If so, hospitals should routinely offer counseling and testing to all patients.

Experts estimate that about two-thirds of HIV-infected people don't realize they are infected. Testing and proper counseling can help such people to get early life-prolonging treatment and prevent them from transmitting the virus to others.

In addition, PHS has established a nationwide consultation service for doctors treating HIV infections and AIDS and has begun clinical testing of an AIDS vaccine.

The consultation service is staffed by the PHS Health Resources and Services Administration. Health professionals can call (1-800) 933-3413 between 10:30 a.m. and 8 p.m. Eastern time, Monday through Friday. Other people who want information should call the AIDS hot line, (1-800) 342-AIDS.

For information about the AIDS vaccine clinical trials, some of which will involve children and mothers infected with HIV, call (1-800) TRIALS-A.

Lancet Letter Discusses Early Retrovir Treatment

Partial results of a European study of the clinical benefits of early treatment with Retrovir (zidovudine, also known as AZT) were reported in a letter in the April 3, 1993, issue of the British medical journal *The Lancet*.

Researchers in what is known as the Concorde trial wrote that they found no difference in clinical outcomes between

HIV-infected people without symptoms who received Retrovir early in the disease and those treated initially with a placebo followed by Retrovir treatment when AIDS symptoms appeared.

The authors also said they found no connection between the increases in CD4 cell counts and the condition of the patients after three years. (Previous studies showed that Retrovir provides clinical benefits for 12 to 18 months, but that the drug's benefits may decrease substantially in patients treated for longer periods.)

The partial results of the Concorde trial do not call into question the clinical importance of Retrovir in treating HIV-infected persons who have symptoms. Neither do they contradict the relevance of early CD4 cell count changes in predicting the short-term benefits of drugs like Retrovir.

When this issue of *FDA Consumer* went to press, FDA had not reviewed the data mentioned in the letter to *The Lancet*. The agency believes this letter shows the need for continued studies of Retrovir and other AIDS therapies to explore the usefulness of the products, and to delineate what factors, such as viral resistance, may be responsible for decreases in benefits of drugs over time.



BOTTLED WATER

NEW TRENDS, NEW RULES

by Victor Lambert

It's practically everywhere. In the workplace. Beside exercise stations in health clubs. At athletic events. In backpacks hanging from the shoulders of students. Even on tables at conferences and workshops. Bottled water, once considered the refreshment of the affluent, has become the liquid icon of today's active, health-conscious consumer.

In 1984, Americans consumed an average of 4 gallons of bottled water per person. By 1991, that number had doubled, according to data collected by the International Bottled Water Association (IBWA).

More than 700 different brands of bottled water are available in the United States. Seventy-five of those brands are made from imported waters. The average retail price of a 1-gallon bottle of domestic drinking water is 90 cents, \$5.29 for a 5-gallon bottle that is delivered.

Taste is the number one reason why people say they prefer bottled water, according to consumer attitude and usage surveys conducted by IBWA, the trade association for the \$2 billion bottled water industry.

The final disinfectant agent used by most of the nation's 430 bottling facilities is ozone, a form of oxygen. But, unlike the chlorine used to disinfect tap water, ozone leaves no chemical residual after-taste or smell.

The second reason more people today

are choosing bottled water has to do with the notion that it's purer and healthier. Because low levels of lead or chlorination byproducts are sometimes found in tap water, most bottled water drinkers believe the bottled variety is healthier than water from the tap. But is it?

Making Bottled Water Safe

Bottled water quality standards were originally adopted in 1973 and were based on the 1962 U.S. Public Health Service standards for drinking water.

In 1974, the Safe Drinking Water Act made the Environmental Protection Agency responsible for ensuring the safety of municipal water systems, which includes setting maximum limits for chemical, bacteriological and radioactive contaminants and physical contaminants that affect odor, taste and color. In 1986, amendments to the Safe Drinking Water Act required EPA to set additional standards. When EPA adds or amends a contaminant standard, the Food and Drug Administration must set an acceptable level for it in bottled water or publish in the *Federal Register* its reasons for not doing so.

Since 1975, under the "misbranded products" provision of the Federal Food, Drug, and Cosmetic Act, FDA has been responsible for ensuring that the quality standards for bottled water are compatible with EPA standards for quality and safety of tap water. In 1978, FDA broadened the

bottled water standards to include maximum allowable contaminant levels for pesticides, mercury and radioactive matter.

In carrying out its mission to ensure the safety of bottled water, FDA also inspects bottled water facilities on a regular basis. Like other foods, bottled water must be processed, packaged, shipped, and stored in a safe and sanitary manner, and be truthfully and accurately labeled.

According to Terry Troxell, Ph.D., director of FDA's division of programs and enforcement policy in the Office of Plant and Dairy Foods and Beverages, "If we [FDA] find a problem during an inspection, we make that company a priority and FDA field personnel inspect it more frequently. For example, after the Perrier 'mineral' water incident in 1990 [when the carcinogen benzene was found in Perrier], we did a follow-up survey to analyze the water's quality."

State agencies, some under contract to FDA, and industry also conduct regular inspections of bottled water facilities in an effort to ensure that only safe products are distributed.

"We're interested in making sure bottled water companies produce safe products and that they're truthfully labeled," Troxell said.

The terms "spring," "well," "artesian," "distilled," "purified," and "mineral" have appeared on bottled water labels for years. But recently, there have been an increas-

APPROXIMATELY 75 PERCENT OF BOTTLED WATER COMES FROM PROTECTED SPRINGS AND WELLS. THE OTHER 25 PERCENT IS DERIVED FROM MUNICIPAL WATER SYSTEMS.



(Photo courtesy of International Bottled Water Association)

ing number of companies whose labels didn't match their products.

At the same time, variations in how states define the different types of bottled water have been an issue. In North Carolina, for example, "spring" water refers only to water that has been collected from the natural orifice in the earth's surface. In other states, it can be both water that has been collected from the natural orifice or from a bore hole that taps the spring and is located near where the spring emerges.

As a result, FDA, last Jan. 5, announced proposed regulations that would establish standard definitions for all bottled water products, and set new limits for approximately 50 chemical and other contaminants that may be present in bottled water. FDA has already established quality standards for 31 contaminants.

The regulations would also apply the quality standard requirements for bottled water to mineral water.

IBWA petitioned FDA to establish stricter guidelines for bottled water in 1988.

After studying the situation, FDA proposed standard definitions because the terms provided by the "misbranded products" provision of the Food, Drug, and Cosmetic Act were not specific enough for use in identifying components of such a diverse group of bottled water products.

"The bottled water industry has grown too much over the last few years to continue handling violations on a case-by-case basis," Troxell said. "We need revised bottled water regulations that are broad based."

Revising the Regulations

Under the proposed regulations, "artesian" water would be considered bottled

UNDER THE STRICTER RESTRICTIONS IN THE PROPOSED REGULATIONS, THE BOTTLED WATER LABEL WOULD HAVE TO STATE IF THE WATER COMES FROM A MUNICIPAL SOURCE.

water that is drawn from a well that taps a confined aquifer (a water-bearing rock, rock formation, or group of rocks) in which the water level stands above the natural water table.

"Distilled" water would be bottled water that has been produced by a process of distillation—vaporizing water, then condensing it in a way that leaves it free of dissolved minerals.

"Purified" water would be water that is produced by distillation, deionization (passing water through resins that remove most of the dissolved minerals), reverse osmosis (the use of membrane filters to remove dissolved solids), or other suitable processes, and that meets the U.S. Pharmacopeia's most recent definition of "purified" water. The U.S. Pharmacopeia establishes the standard for "purified" water because it is commonly used in laboratories and for medical purposes.

"Spring" water would be bottled water obtained from an underground formation from which water flows naturally to the surface, or would if it were not collected underground through a bore hole where a spring emerges.

Bottled water that comes from a hole bored, drilled, or otherwise constructed in the ground to tap an aquifer would be called "well" water.

"Mineral" water, which was previously exempt from bottled water quality standards, would be water that comes from a source tapped at one or more bore holes or springs originating from a geologically and physically protected underground water source. " 'Mineral' water was exempt until now because it was only consumed in very small amounts," Troxell said. "It was considered a different product."

In addition to including "mineral" water

in the proposed regulations, the water ingredient in certain types of flavored bottled waters have to comply with the same maximum allowable contaminant levels required of other bottled waters.

The proposed regulations, however, would continue to exclude products labeled as "carbonated" water, "seltzer" water, "soda" water, and "tonic" water, because they are considered soft drinks.

"We think the proposed regulations are well done and we're completely supportive," said Ronald Davis, president of IBWA and chairman of the Greenwich, Conn.-based Perrier Group of America. "They provide the basis to have bottled water regulated in an intelligent yet thorough way."

And what about bottled water that actually comes from municipal water systems? All products fitting this description, under the proposed regulations, would have to be clearly labeled as such. The requirement would be dropped, however, if the water has been taken from municipal water supplies and then processed and treated in a way that would enable it to be labeled "distilled" or "purified."

Approximately 75 percent of bottled water comes from protected springs and wells. The other 25 percent is derived from municipal water systems that meet federal and state requirements established by the 1974 Safe Drinking Water Act.

Under the stricter restrictions in the proposed regulations, the bottled water label would have to state if the water comes from a municipal source.

The proposed regulations also require specific labeling on bottled waters marketed for infants. Labels on this type of water would have to indicate if the water is not sterile and that it should only be

used as directed by a physician or according to infant formula preparation instructions.

Besides addressing labeling issues, the proposed regulations would set maximum limits for many contaminants found in bottled water.

Reducing Contaminants

Under a final rule published in the Jan. 3, 1993, *Federal Register*, the allowable levels for seven synthetic volatile organic chemicals were amended to comply with maximum contaminant levels set by EPA. The seven chemicals are: benzene, carbon tetrachloride, 1,2-dichloroethane, 1,1-dichloroethylene, 1,1,1-trichloroethane, trichloroethylene, and vinyl chloride.

Proposed regulations would also revise or affirm maximum levels for inorganic substances such as lead, copper, mercury, barium, and cadmium.

The proposed regulations would also establish or modify permitted levels for 28 synthetic organic chemicals, including 10 synthetic volatile organic chemicals, 17 pesticides, and polychlorinated biphenyls.

In all, the proposed regulations would establish 27 new chemical levels and amend the existing allowable levels of many others.

"The new regulations mean a lot to us for two reasons," IBWA's Davis said. "They'll help ensure that bottled water is as good as tap water, and they'll make labeling consistent from state to state. But we're pleased with the new regulations and look forward to implementing them." ■

Victor Lambert, now with Howard University, Washington, D.C., wrote this article while on the staff of FDA Consumer. Judith Levine Willis also contributed to this article.

“Low fat.” “No cholesterol.” “High in oat bran.” “Light.” And don’t forget “lite.”

Until now, many of these claims have been nothing more than advertising hype. The public has been misled with products like the “light” vegetable oil that was just light in color and the “lite” cheesecake that was just light in texture.

But with the publication of new food labeling regulations in January 1993, the Food and Drug Administration and the U.S. Department of Agriculture’s Food Safety and Inspection Service (FSIS) address the problem of misleading nutrition claims and help reestablish the credibility of the food label. The regulations spell out which nutrient content claims are allowed and under what circumstances they can be used.

There are 11 core terms:

- free
- low
- lean
- extra lean
- high
- good source
- reduced
- less
- light
- fewer
- more

Free

The new regulations allow manufacturers the option to use the following synonyms for the term “free”:

- without
- trivial source of
- negligible source of
- dietarily insignificant source of
- no
- zero

Whatever term the manufacturer chooses, the product must either be absolutely free of the nutrient in question or, if the nutrient is in the food, the amount must be dietetically trivial or physiologically insignificant.

For example, zero fat cannot be required

because it is impossible to measure below a certain amount. So, the regulation will allow a fat-free claim on foods with less than 0.5 grams (g) of fat per serving, an amount that is physiologically insignificant even if a person eats several servings.

Foods that don’t contain a certain nutrient naturally must be labeled to indicate that all foods of that type meet the claim. For example, a fat-free claim on applesauce would have to read “applesauce, a fat-free food.”

“Free” also can be used in reference to saturated fat, cholesterol, sodium, sugars, and calories.

Low

A food meets the definition for “low” if a person can eat a large amount of the food without exceeding the Daily Value for the nutrient. (See “‘Daily Values’ Encourage Healthy Diet” in the May 1993 *FDA Consumer*.)

The synonyms allowed for “low” are:

- little
- few
- contains a small amount of
- low source of

“Low” claims can be made in reference to total fat, saturated fat, cholesterol, sodium, and calories.

A Little 'LITE' Reading

by Dori Stehlin

A claim of “very low” can be made only about sodium.

Lean and Extra Lean

“Lean” and “extra lean” can be used to describe the fat content of meat, poultry, seafood, and game meats. (FSIS regulates meat and poultry products; FDA oversees seafood and game meats.)

“Lean” means the food has less than 10 g of fat, less than 4 g of saturated fat, and less than 95 milligrams (mg) of cholesterol per serving and per 100 g. An example of a serving is 55 g (2 oz.) for fish, shellfish or game meat. Some “lean” foods are Spanish mackerel, bluefin tuna, and domesticated rabbit.

“Extra lean” means the food has less than 5 g of fat, less than 2 g of saturated fat, and less than 95 mg of cholesterol per serving and per 100 g. Examples of “extra lean” foods are haddock, swordfish, clams, and deer.

Percent Fat Free

FDA and FSIS believe that this claim implies, and consumers expect, that products bearing “percent fat free” claims contain relatively small amounts of fat and are useful in maintaining a low-fat diet. Therefore, products with these claims must meet the definitions for low fat.

In addition, the claim must accurately reflect the amount of fat present in 100 g of the food. For example, if a food contains 2.5 g of fat per 50 g, the claim must be “95 percent fat free.”

Good Source and High

“High” and “good source” focus on nutrients for which higher levels are desirable. To qualify for the “high” claim, the food must contain 20 percent or more of the Daily Value for that nutrient in a serving. Approved synonyms for high are “rich in” or “excellent source.”

“Good source” means a serving contains 10 to 19 percent of the Daily Value for the nutrient.



By 1994, claims about the nutrient content of a food, such as “low cholesterol,” “light,” and others on these food packages, will have to mean the same on every product on which they appear.

Special Situations

"Standards of identity" define a food's composition and specify the ingredients it must contain. The government originally developed these standards to protect consumers from economic deception.

But some standards of identity require high amounts of nutrients that many consumers would like to avoid. For example, the standard for sour cream requires that the food contain 18 percent fat and the standard for mozzarella cheese requires it to be 45 percent fat. Before the new regulations, "reduced-fat" sour cream or mozzarella cheese were required to have their

own standards of identity or be called "imitation" or "substitute," names that consumers may perceive as negative.

The new regulations allow manufacturers to reduce the fat content of such products and call them "low fat" or "light," as appropriate, as long as the food is still nutritionally equivalent to the regular version. For example, sour cream can be called "light" as long as its fat content is reduced to 9 percent and it has vitamin A added to replace the amount lost when the fat was removed. If the company decides not to add the vitamin A, it must call the product "imitation light sour cream."

FDA is not allowing nutrient content claims on foods for infants and children

under 2, unless explicit permission has been given.

FDA allows manufacturers to use the terms "unsweetened" and "unsalted" on these foods because these claims are considered to be about taste rather than nutrient content. However, current dietary guidelines do not call for limiting salt or sugar in the diets of children under 2. Therefore, FDA will not allow phrases that imply low or reduced amounts of sodium and calories, such as "no salt added" and "no sugar added," on these types of foods. ■

—D.S.

Comparison Claims

Manufacturers who want to compare a nutritionally altered product with the regular product may make a relative claim—that is, "reduced," "less," "fewer," "more," or "light." The regular products, or reference foods, may be either an individual food or a group of foods representative of the type of food—for example, an average of three market leaders.

Restrictions on these claims and the reference foods include:

- A relative claim must include the percent difference and the identity of the reference food.
- "Reduced," "less" and "light" claims can't be made on products whose nutrient level in the reference food already meets the requirement for a "low" claim.
- Reference foods for "light" and "reduced" claims must be similar to the product bearing the claim—for example, reduced fat potato chips compared with regular potato chips.
- Reference foods for "less" and, in the

case of calories, "fewer" may use dissimilar products within a product category—for example, pretzels with 25 percent less fat than potato chips.

At the other end of the spectrum, a serving of a food carrying a "more" claim (or claims of fortified, enriched or added) must have at least 10 percent more of the Daily Value for a particular nutrient (that is, dietary fiber, potassium, protein, or an essential vitamin or mineral) than the reference food that it resembles.

Light/Lite

"Light" or "lite" can mean one of two things:

First, that a nutritionally altered product contains one-third fewer calories or half the fat of the reference food. If the food derives 50 percent or more of its calories from fat, the reduction must be 50 percent of the fat.

Second, that the sodium content of a low-calorie, low-fat food has been reduced by 50 percent.

The term "light in sodium" is allowed if the food has at least 50 percent less sodium than a reference food. If the food

still does not meet the definition for "low sodium," the label must include the disclaimer "not a low-sodium food."

"Light" will be allowed to describe color or texture, provided qualifying information is included. However, names that have a long history of use, such as "light brown sugar," can still be used without qualifying information.

Meals and Main Dishes

Any product represented as or in a form commonly understood to be breakfast, lunch or dinner is subject to the special rules for meal products. Examples include frozen dinners, some pizzas, and shelf-stable items.

Under FDA rules, a main dish must weigh at least 6 ounces and contain at least two different foods from at least two of four specified food groups. (While FDA endorses the five food groups recommended in current dietary guidelines, the agency believes treating fruits and vegetables as separate groups in this situation would allow the inappropriate classi-

Getting Specific

Here are examples of the meanings of some descriptive words for specific nutrients:



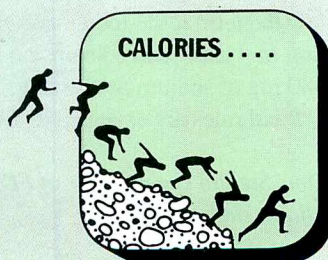
Sugar

Sugar free: less than 0.5 grams (g) per serving

No added sugar, Without added sugar, No sugar added:

- No sugars added during processing or packing, including ingredients that contain sugars (for example, fruit juices, apple-sauce, or dried fruit).
- Processing does not increase the sugar content above the amount naturally present in the ingredients. (A functionally insignificant increase in sugars is acceptable from processes used for purposes other than increasing sugar content.)
- The food that it resembles and for which it substitutes normally contains added sugars.
- If the food doesn't meet the requirements for a low- or reduced-calorie food, the product bears a statement that the food is not low-calorie or calorie-reduced and directs consumers' attention to the nutrition panel for further information on sugars and calorie content.

Reduced sugar: at least 25 percent less sugar per serving than reference food

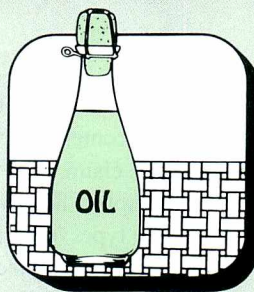


Calories

Calorie free: fewer than 5 calories per serving

Low calorie: 40 calories or less per serving and if the serving is 30 g or less or 2 tablespoons or less, per 50 g of the food

Reduced or Fewer calories: at least 25 percent fewer calories per serving than reference food



Fat

Fat free: less than 0.5 g of fat per serving

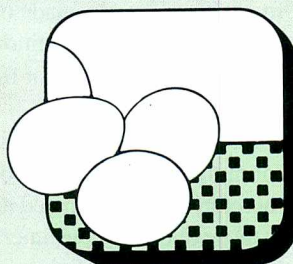
Saturated fat free: less than 0.5 g per serving and the level of trans fatty acids does not exceed 1 percent of total fat

Low fat: 3 g or less per serving, and if the serving is 30 g or less or 2 tablespoons or less, per 50 g of the food

Low saturated fat: 1 g or less per serving and not more than 15 percent of calories from saturated fatty acids

Reduced or Less fat: at least 25 percent less per serving than reference food

Reduced or Less saturated fat: at least 25 percent less per serving than reference food



Cholesterol

Cholesterol free: less than 2 milligrams (mg) of cholesterol and 2 g or less of saturated fat per serving

Low cholesterol: 20 mg or less and 2 g or less of saturated fat per serving and, if the

serving is 30 g or less or 2 tablespoons or less, per 50 g of the food

Reduced or Less cholesterol: at least 25 percent less and 2 g or less of saturated fat per serving than reference food



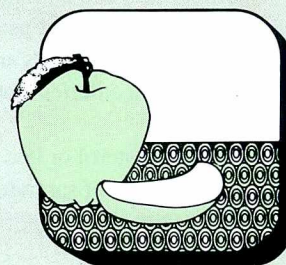
Sodium

Sodium free: less than 5 mg per serving

Low sodium: 140 mg or less per serving and, if the serving is 30 g or less or 2 tablespoons or less, per 50 g of the food

Very low sodium: 35 mg or less per serving and, if the serving is 30 g or less or 2 tablespoons or less, per 50 g of the food

Reduced or Less sodium: at least 25 percent less per serving than reference food



Fiber

High fiber: 5 g or more per serving. (Foods making high-fiber claims must meet the definition for low fat, or the level of total fat must appear next to the high-fiber claim.)

Good source of fiber: 2.5 g to 4.9 g per serving

More or Added fiber: at least 2.5 g more per serving than reference food

A serving of a food carrying a “more” claim (or claims of fortified, enriched or added) must have at least 10 percent more of the Daily Value for a particular nutrient (that is, dietary fiber, potassium, protein, or an essential vitamin or mineral) than the reference food that it resembles.

fication of a fruit and a vegetable product as a main dish.)

FDA requires a “meal” to weigh at least 10 ounces and have at least three different foods from at least two of the four specified food groups.

USDA defines a meal-type product as one weighing between 6 and 12 ounces per serving and containing ingredients from two or more of four specified food groups.

Claims that a meal or main dish is “free” of a nutrient, such as sodium or cholesterol, must meet the same requirements as those for individual foods.

“Low” claims can be made if the main dish or meal has:

- 120 calories or less per 100 g
- 140 mg sodium or less per 100 g
- 3 g fat or less and no more than 30 percent of calories from fat per 100 g
- 1 g saturated fat or less and no more than 10 percent calories from saturated fat per 100 g **or**
- 20 mg cholesterol or less per 100 g and no more than 2 g of saturated fat per 100 g.

Implied Claims

“Made with oat bran” and “no tropical oils” are examples of statements that may be implied nutrient content claims. Such claims are prohibited when they wrongfully imply that a food contains or does not contain a meaningful level of a nutrient. They are allowed if the food’s nutrient

content meets the definition for appropriate nutrient content descriptors that are implied by the claim.

For example, FDA considers statements about some types of oil as an ingredient, such as “made with canola oil” or “contains corn oil,” to imply that the oil in the product is low in saturated fat. Therefore, to carry that claim, a food would have to meet the definition of “low saturated fat.”

The statement “made only with vegetable oil” implies that because vegetable oil is used instead of animal fat, the oil component contributes no cholesterol and is low in saturated fat. In this case, the claim could be used only if the food meets the definition of “cholesterol free” and “low saturated fat.”

And the statement “contains no oil” implies that the product contains no fat and thus is fat free. Such a claim on a product that contained another source of fat, such as animal fat, would be misleading. Therefore, this statement would be allowed only if the food is truly fat free.

Claims that imply a product contains a particular amount of fiber, such as “high in oat bran,” can be made only if the food actually meets the definition for “high” fiber or “good source” of fiber, whichever is appropriate.

Statements that don’t fall under the rules for nutrient content implied claims and therefore are still allowed are:

- those that help consumers avoid certain foods because of religious beliefs or dietary practices—for example, a “milk-free” claim
- those about nonnutritive ingredients, such as “no preservatives” or “no artificial colors”
- those about ingredients that provide added value, such as “contains real fruit”

- statements of identity, such as “Colombian coffee” and “100 percent corn oil”

Fresh

Although not mandated by the Nutrition Labeling and Education Act of 1990, as regulations for the other nutrient content claims are, FDA has issued a regulation for the term “fresh.” Under this regulation, “fresh” can be used only on a food that is raw, has never been frozen or heated, and contains no preservatives. (Irradiation at low levels is allowed.) “Fresh frozen,” “frozen fresh,” and “freshly frozen” can be used for foods that are quickly frozen while still fresh. Blanching (brief scalding before freezing to prevent nutrient breakdown) is allowed.

Other uses of the term “fresh,” such as in “fresh milk” or “freshly baked bread,” are not affected.

Healthy

Along with the final rule on nutrient content claims published last January, FDA and FSIS published proposed rules that would allow manufacturers to make a “healthy” claim on the label. Under FDA’s proposal, “healthy” could be used if the food is low in fat and saturated fat and a serving does not contain more than 480 mg of sodium or more than 60 mg of cholesterol. USDA’s proposal would allow the term if the food meets the definition for “lean” and contains no more than 480 mg of sodium per serving.

Final rules are expected in 1993. ■

Dori Stehlin is a member of FDA’s public affairs staff.

The Food Pyramid—Food Label Connection

by Etta Saltos, Ph.D., R.D.

What foods fit in a healthy diet? How can you compare the nutritional values of food? Can the new food label help you answer these questions?

It can, if you use the label information to follow the Dietary Guidelines for Americans. (See accompanying article.)

Food Pyramid

The Food Guide Pyramid can help you put the Dietary Guidelines into action. The pyramid illustrates the research-based food guidance developed by the U.S. Department of Agriculture and supported by the Department of Health and Human Services. It is based on USDA's research on what foods Americans eat, what nutrients are in these foods, and how to make the best food choices to promote good health. It outlines what to eat each day, but it is not a rigid prescription. You can use it as a general guide in choosing a healthful diet that is right for you. The pyramid calls for eating a variety of foods to get the nutrients you need, and, at the same time, the right amount of calories to maintain a healthy weight. It also focuses on fat because most American diets are too high in fat, especially saturated fat.

You don't have to avoid foods that are high in fat, saturated fat, cholesterol, and sodium completely. It's your average intake over a few days, not in a single food or even a single meal, that's important. If you eat a high-fat food or meal, balance your intake by choosing low-fat foods the rest of the day or the next day. The new food label can help you "budget" your intake of fat, saturated fat, cholesterol, and sodium over several days.

The new food label also can help you identify good sources of fiber and vitamins and minerals.

Look to the Label

How does it do this? First, descriptors such as "free," "low" or "reduced" on the front of the package can signal that a food is low in a certain dietary component, such as calories, fat, saturated fat, or sodium. Eating those foods can then help you moderate your intake of these and other nutrients.

Descriptors such as "good source" and "high" can help you identify foods that contain significant amounts of dietary fiber, vitamins, and minerals. (See "A Little 'Lite' Reading" on page 12.)

Claims about the relationship between a nutrient or a food and the risk of a disease or health-related condition also may show up on the front of the package of FDA-regulated products. These are called health claims, and FDA has authorized seven of them. They can help you identify foods with certain nutritional qualities that are of



"Here's your problem . . . You've been reading the Food Pyramid upside down!"

(Reprinted by permission of A.A. McCourt)

Food Guide Pyramid

A Guide to Daily Food Choices

KEY

■ Fat (naturally occurring and added) ■ Sugars (added)
These symbols show that fat and added sugars come mostly from fats, oils and sweets, but can be part of or added to foods from the other food groups as well.

Fats, Oils, & Sweets
USE SPARINGLY

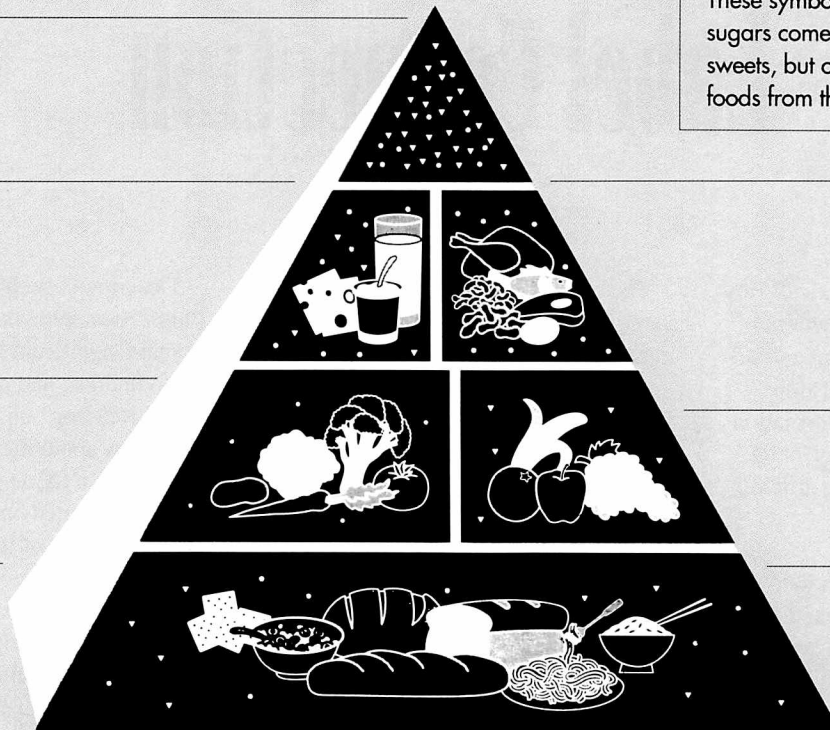
Milk, Yogurt, & Cheese Group
2-3 SERVINGS

Vegetable Group
3-5 SERVINGS

Meat, Poultry, Fish, Dry Beans, Eggs, & Nuts Group
2-3 SERVINGS

Fruit Group
2-4 SERVINGS

Bread, Cereal, Rice, & Pasta Group
6-11 SERVINGS



(Source: U.S. Department of Agriculture/U.S. Department of Health and Human Services)

How to Use the Daily Food Guide

What Counts as One Serving?

Breads, Cereals, Rice, and Pasta

- 1 slice of bread
- 1/2 cup of cooked rice or pasta
- 1/2 cup of cooked cereal
- 1 ounce of ready-to-eat cereal

Vegetables

- 1/2 cup of chopped raw or cooked vegetables
- 1 cup of leafy raw vegetables

Fruits

- 1 piece of fruit or melon wedge
- 3/4 cup of juice
- 1/2 cup of canned fruit
- 1/4 cup of dried fruit

Milk, Yogurt, and Cheese

- 1 cup of milk or yogurt
- 1 1/2 to 2 ounces of cheese

Meat, Poultry, Fish, Dry Beans, Eggs, and Nuts

- 2 1/2 to 3 ounces of cooked lean meat, poultry or fish
- Count 1/2 cup of cooked beans, or 1 egg, or 2 tablespoons of peanut butter as 1 ounce of lean meat (about 1/3 serving)

Fats, Oils, and Sweets

Limit calories from these, especially if you need to lose weight

The amount you eat may be more than one serving. For example, a dinner portion of spaghetti would count as two or three servings of pasta.



A daily diet of 2,000 calories—the basis for the “% Daily Value” on food labels—is about right for women who engage in moderate activity, such as an occasional tennis game. It is also the target calorie level for teenage girls and sedentary men.

Find Your Fat Limit

Recommended upper limits of total fat and saturated fat intake at different calorie levels:

	Calories			
	1,600	2,000	2,500	2,800
Total Fat (grams)	53	65	80	93
Saturated Fat (grams)	18	20	25	31

Descriptors such as “free,” “low” or “reduced” on the front of the package can signal that a food is low in a certain dietary component, such as calories, fat, saturated fat, or sodium.

interest to you. (See “Starting This Month: Look for ‘Legit’ Health Claims on Foods” in the May 1993 *FDA Consumer*.)

However, you don’t have to select only foods with descriptors or health claims on the label to follow the Dietary Guidelines. In moderation, all foods can fit into a healthy diet.

Second, look at the nutrition panel, now titled “Nutrition Facts.” With a few exceptions, the nutrition panel will list calories, calories from fat, and the amount of nutrients of greatest public health concern contained per serving of the food. (See “‘Nutrition Facts’ to Help Consumers Eat Smart” in the May 1993 *FDA Consumer*.) Similar information also will be available voluntarily for some raw foods. (See “Nutrition Info Available for Raw Fruits, Vegetables, Fish” in the January–February 1993 *FDA Consumer*.)

On the nutrition panel, nutrient content will be expressed not only as an amount by weight but also as a percent of the Daily Value, or DV—a new label reference value. (See “‘Daily Values’ Encourage Healthy Diet” in the May 1993 *FDA Consumer*.)

These percentages can help you decide whether a food contributes a lot or a little of a particular nutrient. Lower percentages indicate the food contributes less of the nutrient, and higher percentages indicate that it contributes more of the nutrient.

Look to see whether the nutrients you would like to get more of (such as carbohydrate, dietary fiber, and vitamins and minerals) have high percentages and the



Teenage boys are among those who may need 2,500 calories a day.

Daily values for that calorie level are required on the labels of larger food packages.

nutrients you may need to limit (such as fat, cholesterol and sodium) have low percentages. The percent Daily Values, while based on a 2,000-calorie diet, will indicate in a relative way the nutritional contributions of a food to your diet regardless of your calorie intake.

Also, because serving sizes are now more uniform across product lines, comparing the nutritional content of foods is easier.

However, the amount of food you eat may be different from the stated serving size. For example, the serving size for ice cream is a half cup, so if you usually eat one cup of ice cream, you would have to double the number of calories and the percentages of the Daily Values listed to learn the nutrient content of the portion you eat.

Figuring Fat

While the food label provides a reliable general guide for most people, you may want to use the information on it to make more personal choices.



Men and women engaged in heavy manual labor or heavy activity, such as daily running or team sports, may need at least 2,800 calories a day to maintain an appropriate weight. Although this figure is not on the food labels, people in this category can use the percent Daily Values to guide them.

You may be concerned about fat, for example. The Dietary Guidelines suggest that you eat a diet that provides 30 percent or less of calories from fat and less than 10 percent of calories from saturated fat. Thus, the recommended upper limit on the grams of fat and saturated fat in your diet depends on the calories you need (see chart on page 19). The percent DVs for fat and saturated fat are based on a 2,000-calorie diet, which is about right for moderately active women, teenage girls, and sedentary men.

Some people keep a running total of the amount of fat and saturated fat they eat in a day and compare this to their target level. If you eat about 2,000 calories a day, you can simply monitor the percent DV information from the foods you eat so that the total is close to or less than 100 percent over the day.

If you eat fewer than or more than 2,000 calories a day, you can keep a total of the actual amount of fat and saturated fat contained in the foods you eat. This informa-

tion is listed immediately after the nutrient name (for example, "Total Fat 13 g").

Daily values based on an intake of 2,500 calories a day are listed in a footnote, at least on the nutrition panels of larger packages. These values can be used as a target level for many men, teenage boys, and active women.

The chart on page 19 lists recommended upper limits of fat and saturated fat intakes for other calorie levels. Many older adults, children, and sedentary women need fewer than 2,000 calories a day and may want to select target levels based on 1,600 calories a day. Some active men and teenage boys and very active women may want to select target levels based on 2,800 calories per day.

Sugars and Others

The percent DV column also can be used to help you moderate your intake of sodium and cholesterol. The Daily Values for sodium and cholesterol are the same for everyone, regardless of total calories

Dietary Guidelines

The Dietary Guidelines, developed by the Department of Health and Human Services and the U.S. Department of Agriculture, represent the best, most current advice for healthy Americans 2 years and older. They reflect recommendations of health and nutrition experts, who agree that enough is known about the effect of diet on health to encourage certain eating practices. The seven Dietary Guidelines are:

- **Eat a variety of foods** to get the energy (calories), protein, vitamins, minerals, and fiber you need for good health.
- **Maintain a healthy weight** to reduce your chances of having high blood pressure, heart disease, a stroke, certain cancers, and the most common kind of diabetes.
- **Choose a diet low in fat, saturated fat, and cholesterol** to reduce your risk of heart disease and certain types of cancer. Because fat contains more than twice the calories of an equal amount of carbohydrates or protein, a diet low in fat can help you maintain a healthy weight.
- **Choose a diet with plenty of vegetables, fruits, and grain products** that provide needed vitamins, minerals, fiber, and complex carbohydrates. They are generally lower in fat.
- **Use sugars only in moderation.** A diet with lots of sugars has too many calories and too few nutrients for most people and can contribute to tooth decay.
- **Use salt and other forms of sodium only in moderation** to help reduce your risk of high blood pressure.
- **If you drink alcoholic beverages, do so in moderation.** Alcoholic beverages supply calories, but little or no nutrients. Drinking alcohol is also the cause of many health problems and accidents and can lead to addiction. ■



Children are among those people needing fewer calories than the target levels for adults. Persons older than 3 also can use the percent Daily Values to help them select appropriate nutrient intakes.

consumed, so you do not have to make adjustments based on your caloric needs.

Food labels also can be helpful if you're trying to moderate your sugar intake. The nutrition panel lists the amount of sugars in grams (4 grams is equivalent to 1 teaspoon) in a serving of the food.

Note that this amount includes sugars that are present *naturally* in the food (such as lactose in milk and fructose in fruit), as well as sugars *added* to the food during processing. If you're interested in finding out whether a sweetener has been added to a food, check the ingredient listing. Terms such as "sugar (sucrose)," "fructose," "maltose," "lactose," "honey," "syrup," "corn syrup," "high-fructose corn syrup," "molasses," and "fruit juice concentrate" are used to describe sweeteners added to foods.

If one of these terms appears first or second in the list of ingredients, or if several of them appear, the food is likely to be high in added sugars. A percent DV is not given for sugars because there is no target

quantity of sugars to aim for each day.

Labeling of the alcohol content of beverages is regulated by the Bureau of Alcohol, Tobacco, and Firearms. Alcohol content (in percentage by volume) appears on the front panel of some alcoholic beverage labels. Alcohol content of foods and beverages is not required to be listed on the nutrition panel. However, some alcoholic beverages, such as light beers and wine coolers, provide information about the amount of calories, carbohydrate, protein, and fat they contain. You may find this information useful if you're counting calories because alcoholic beverages are generally rich in calories and poor in nutrients.

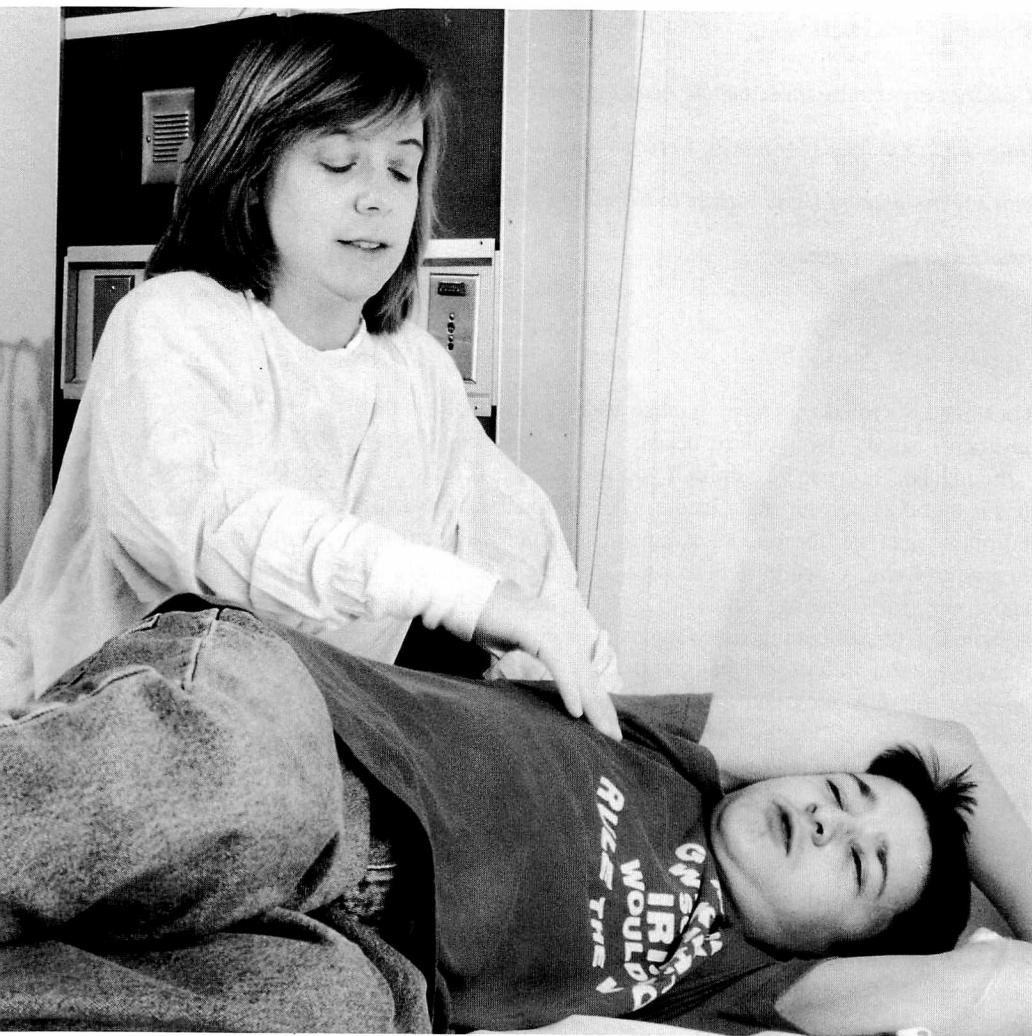
You'll find lots of information on food labels. So take the time to read them. The information can help you plan a healthful diet that meets the recommendations of the Dietary Guidelines. ■

Etta Saltos is a nutritionist with USDA's Human Nutrition Information Service.

Cystic Fibrosis

Tests, Treatments Improve Survival

by Ricki Lewis, Ph.D.



Physical therapist Katherine Parker administers chest therapy with postural drainage to T. James O'Neill, 20, a cystic fibrosis patient, at Children's Hospital National Medical Center in Washington, D.C.

Alex Deford had been ill almost from the moment of her birth on Oct. 30, 1971. Her frequent colds and ear infections coupled with her small size, despite a healthy appetite, prompted doctors to vaguely diagnose "failure to thrive." When Alex developed double pneumonia at 4 months, it was clear that something was very wrong.

That something turned out to be cystic fibrosis, the most common inherited illness among white people of Northern and Western European ancestry, although it is seen in all ethnic groups. Symptoms include thick, sticky mucus clogging the lungs, impairing breathing and attracting infection; a blocked pancreas that cannot release digestive enzymes, causing pain after eating; stubbed fingers from poor circulation; infertility; salty sweat; and other problems. Patients may have any or all of these symptoms—Alex had quite a list.

When she was diagnosed at Boston Children's Hospital early in 1972, Alex was so ill that she was expected to live only days. She survived eight years, but not easily.

Alex began each day by inhaling a decongestant. Then her parents took turns providing "postural drainage," a 30- to 60-minute pounding and pressing on each of 11 segments of the lungs, to loosen the mucus, which she coughed up. Alex would then take drugs—antibiotics to prevent lung infection and powdered digestive enzymes mixed into applesauce.

Despite this daily regimen, Alex died in

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January 1980. Her father, sportswriter and commentator Frank Deford, tells her story in his book, *Alex, the Life of a Child*.

Cystic fibrosis (CF) is inherited and affects 30,000 Americans. In 1989, scientists discovered the gene that causes cystic fibrosis (see accompanying article.) This discovery is enabling researchers to develop new diagnostic tests that will help identify those who can benefit from traditional as well as several new treatment approaches being evaluated by FDA.

How CF Is Inherited

CF is typically passed from parents who each carry the gene, to children of either sex. Carriers have one faulty copy of the gene, which is responsible for the illness, plus one normal copy, which prevents symptoms. Each child of carrier parents has a 1 in 4 chance of inheriting CF; a 1 in 4 chance of being completely free of the mutant gene; and a chance of 1 in 2 of being a carrier, like the parents.

Couples usually learn that they carry CF when they have an affected child. By 1985, individuals who had a sibling with CF could find out if they carried the gene by taking a "genetic marker" (linkage analysis) test that spots a particular family's CF-carrying chromosome, but not the gene itself. Finding the CF gene makes it possible to detect most carriers, even if there are no affected relatives.

The Office of Technology Assessment estimates that 100 million to 200 million people in the United States might want to

take a CF carrier test. About 8 million people in the United States, or 1 in 25 whites, may be carriers.

Diagnosing CF

The same gene discovery that has led to developing carrier tests is expected to help more quickly diagnose CF, whose symptoms resemble those of other illnesses.

The most widely used and best-known CF test is the electrolyte sweat test. It detects the excess sodium, potassium and chloride (charged chemicals called electrolytes) found on the skin of many people with CF. A physician would perform a sweat test in a child with unexplained failure to gain weight, or with very frequent respiratory infections.

The sweat test evolved from the observations made by a physician, Dr. Paul di Sant'Agnese, during a 1953 heat wave in New York City. He was curious why so many children with CF were being brought to Babies and Children's Hospital, where he worked, with heat prostration. The youngsters were unable to cope with the heat because too much salt exited their bodies in sweat. The fact that the sweat of a person with CF contains two to six times as much salt as normal sweat gave him the idea for the sweat test.

The sweat test became widely used by the mid-1950s, and is the only CF test cleared by FDA for marketing. (A forerunner of the sweat test was the observation that a child's brow was salty when kissed. At the turn of the century, this is

how midwives identified babies with cystic fibrosis.)

Although the sweat test is a critical part of a CF diagnostic work-up, salty sweat can indicate any of several disorders.

Other tests help focus the diagnosis. Some of these tests are based on methodologies developed by reference laboratories, which perform medical tests and send the results to physicians. According to Freda Yoder of FDA's Center for Devices and Radiological Health, methodologies developed in-house have not traditionally been regulated by the agency.

Explains Tom Tsakeris, director of the division of clinical laboratory devices at FDA, "FDA regulates products, not laboratories. As long as they are not marketing the test itself, we do not regulate the lab." However, he adds, the Clinical Laboratory Improvement Act, signed into law in 1988 but not yet fully implemented, will regulate reference laboratories.

One test developed by reference labs measures the amount of the protein trypsinogen in a newborn's blood. Trypsinogen is manufactured by the pancreas and sent to the intestine, where it is snipped to a shorter form, trypsin, which helps digest proteins. If the pancreas is clogged by the sticky mucus of CF, trypsinogen levels are elevated, because the longer protein cannot be cut down to size.

In one study conducted by researchers at the University of Colorado School of Medicine and Children's Hospital in Den-

Cheek Brush Test



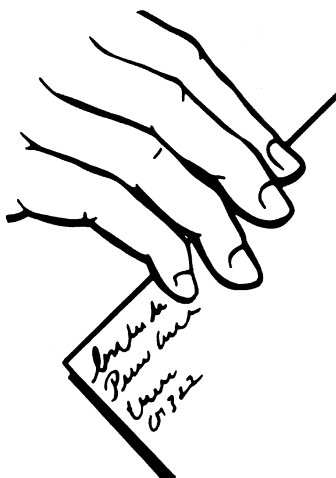
The health professional twists a tube containing a cheek brush and pulls it open, removing the cheek brush from the tube.



The cheek brush is inserted into the patient's mouth and twisted vigorously against the inside of the cheek for at least 30 seconds to collect cells containing DNA.



The professional then carefully places the cheek brush back into the original tube and replaces the cap.



The cheek brush in its tube is mailed to the manufacturer for analysis.

ver, the trypsinogen test identified 95.2 percent of infants with CF who did not have the earliest sign, a greenish discharge called meconium ileus indicating intestinal blockage. But in the study there were many false positives—of 96 infants who tested high for trypsinogen on two tests, only 31 had CF. So, although the trypsinogen test alone is not perfect, combined with a sweat test and observing symptoms, it can begin to paint a portrait of CF.

Another test detects the level of certain fetal intestinal enzymes in the amniotic fluid (the liquid surrounding the fetus). Amniotic fluid is collected for testing by a procedure called amniocentesis (see "Genetic Screening: Fetal Signposts on a Journey of Discovery" in the December 1990 *FDA Consumer*). In a fetus with CF, these enzymes are decreased. Again, however, other disorders besides CF can produce this finding, and therefore it is not a specific disease marker. Researchers have turned to the genetic material to develop a definitive CF test.

Enter Genetic Testing

Developing a test to detect the gene that causes CF would provide a definitive diagnosis, because this mutant gene is the only cause of the disorder. The first step was to find out where the gene behind CF lies among the 23 pairs of chromosomes.

By 1985, several research teams had narrowed the search to a part of chromosome 7 (the seventh largest chromosome). Until the CF gene itself was isolated and characterized in 1989, relatives of patients could take an indirect test that uses linkage analysis. Because of the complexity of test interpretation, these tests are primarily performed at academic centers.

A genetic linkage test tracks a known

(Artwork courtesy of Genzyme Corp., Cambridge, Mass.)

*Checking for an
errant CF gene may be
easy, but interpreting
the results may not be.*

DNA sequence (a genetic marker) that, within a family, always occurs in people with CF, and never in those who do not have the illness. A genetic marker and the gene responsible for the disorder behave like two inseparable friends. If you see one at a party, you know the other is nearby. Genetic linkage testing is based on the observation that genes carried close together on the same chromosome tend to be inherited together.

Ray White at the Howard Hughes Medical Institute at the University of Utah in Salt Lake City and Robert Williamson of St. Mary's Hospital Medical School in London each found a marker, one on either side of the CF gene. Using these two markers, a couple who already had a child with CF could have fetal chromosomes tested in a subsequent pregnancy. If the two markers on the two chromosome 7's in the fetus matched those of the affected child, then it, too, has likely inherited the disease.

A major limitation of linkage tests is that they only work on families known to have CF. Because people can carry CF without having symptoms, a disease-causing gene can be in a family without anyone in recent memory being ill. Finding the CF gene itself, however, may make possible a test useful on anyone, so that carriers could be detected in families where no one has CF.

Like other genetic tests, CF tests can be performed on any type of tissue, because all human cells (except red blood cells) contain two copies of all of the genes, and sperm and egg have one copy of each. The first CF tests used white blood cells. Then Williamson's group in London came up with a pleasanter alternative—a mouthwash! After swishing a saltwater solution

in the mouth, the person spits into a bottle. The CF gene can be spotted in cells dislodged from the inside of the cheek.

Taking a cue from London, Genzyme Corp. (Cambridge, Mass.) developed a cheekbrush test for CF, which is investigational. A patient swabs cheek cells onto a brush, and the physician sends the sample to Genzyme. The presence of both normal and mutant CF genes indicates carrier status. If only mutant genes are there, CF is indicated.

To Test or Not To Test?

A carrier test provides information to couples who are not ill but whose children are at high risk of inheriting the condition.

Many experts predict that the day of universal CF screening is approaching, with several companies developing CF tests that simultaneously screen for several CF mutations.

Two factors contribute to the sensitivity of a CF carrier test. The first is the number of mutations that can be detected. The more mutations tested for, the more carriers will be spotted.

Ethnic background is the other important factor, says Marisa Ladoulis, a genetic counselor at Collaborative Diagnostic Services in Waltham, Mass. For example, a 12-mutation test that spots 84 percent of whites with a Northern or Western European background will detect 92 to 95 percent of Ashkenazi Jews, and the 16-mutation test finds 96 to 98 percent of them.

All CF Mutations Are Not Equal

Checking for an errant CF gene may be easy, but interpreting the results may not be. Researchers are finding that different CF mutations cause different degrees of sickness. Alex Deford probably had two

copies of delta F508, the most common and one of the more serious mutations that can cause CF. But a researcher in the laboratory of Francis Collins, the co-discoverer of the CF gene, has a milder case of CF because he inherited the delta F508 mutation as well as a different one.

This young man must perform postural drainage on himself and take antibiotics and digestive enzymes, but he also plays the trumpet, bikes, and sings. Still, a respiratory infection can send him to the hospital for a week or longer. Clinicians are finding that some people who have frequent bouts of pneumonia and other respiratory infections actually have CF.

Some people with CF may not even have lung or digestive symptoms. Aubrey Milunsky, D.Sc., Director of the Center for Human Genetics at the Boston University School of Medicine, found that some men who were referred to him because they were having difficulty fathering a child actually had CF. In examining x-rays that had been taken as part of a standard fertility work-up, Milunsky noticed the men lacked the vas deferens, the paired tubes that deliver sperm from the body. Knowing this is a symptom in 90 percent of men with CF, Milunsky tested their genes and found they had inherited CF.

"Cystic fibrosis is not a simple single mutation to look for," says Margaret Wallace, Ph.D., assistant professor in the division of genetics in the department of pediatrics at the University of Florida in Gainesville. "There will be a lot of problems in doing the diagnosis and giving an idea of what it means," she adds.

Treating CF

CF symptoms are controlled with a number of drugs. Antibiotic drugs combat

Advances and Stumbling Blocks

The symptoms of CF were first described in medical journals in 1938. The malady was attributed to a defect in the channels leading from certain glands—a remarkably accurate description, it would turn out. But the disorder was recognized before it was given a name, as illustrated by the 17th century English saying, “A child that is salty to taste will die shortly after birth.”

In 1960, a CF patient rarely lived past the age of 12. By 1970, only half lived to see their 18th birthdays. In the 1970s, when postural drainage began to be implemented and FDA approved enzyme replacement and antibiotic therapy, the average lifespan began to creep upwards. Today, it is 29 years, according to the Cystic Fibrosis Foundation. New, more targeted therapies may raise survival age higher.

Cystic fibrosis researchers marked a medical milestone on Oct. 8, 1989, when *Science* magazine published a report by Francis Collins and his co-workers at the University of Michigan at Ann Arbor and Lap-chee Tsui at the Hospital for Sick Children in Toronto on precisely how a specific gene disrupts a certain protein to cause CF.

The researchers named the protein the “cystic fibrosis transmembrane conductance regulator,” or CFTR for short. CFTR is normally manufactured inside cells lining glands in the respiratory passages, small intestine, pancreas, and sweat glands. The protein travels to the cell’s surface, where it controls the flow of salt in and out of the cell like a gateway in the cell membrane.

In the disorder, CFTR protein is abnormal in a way that prevents it from reaching the cell’s surface. Without the gateway in the membrane, salt is trapped inside cells. Following a natural chemical ten-

dency to try to dilute the salty interiors of cells, moisture is drawn inside them through other gateways. This dries out the surrounding secretions, causing symptoms. In most people with CF, the protein is missing just one amino acid building block out of 1,480—a tiny, but devastating, glitch.

Almost as soon as Collins and Tsui described the mutation that causes CF, dubbed delta F508, a difficulty arose. Delta F508 was not the only way that the gene could be altered. (A gene consists of sequences of four types of building blocks. Just as a sentence can have an error in any of its letters, a gene can be altered in many ways. A person with CF inherits two abnormal forms.)

But within days of the publication of the *Science* report, several biotechnology firms were already devising carrier tests for delta F508. A test for the disease-causing gene variant became available on an investigational basis by November 1989. But on Feb. 1, 1990, Collins, Tsui, and several others reported in *The New England Journal of Medicine* that only 75.9 percent of white CF patients of Northern and Western European backgrounds had the delta F508 variant. How useful would a test for delta F508 be, researchers worried, if this wasn’t the only variant responsible for CF? At current count, more than 200 variants of the gene are known.

The multiple guises of the CF gene meant that a test to spot delta F508 would miss about 24 percent of Northern or Western European descended whites in the United States who do carry a CF gene. This, in turn, meant that the test would find only about half the couples in the United States who risk passing CF to a child (this figure is derived by multiplying the chances of each parent having delta F508). But it would be too costly to develop a test for more than 200 different mutations, when only a few of them are common.

Adding to the complexity is that different populations have different proportions of the CF gene variants. For example, delta F508 occurs in only 35 percent of African-Americans and Jews of Central and Eastern European ancestry (called Ashkenazi) who carry CF, making the test for this mutation even less valuable than it is for non-Jewish whites. For Hispanics and Italians, the frequency of delta F508 is 50 percent.

The potential powder keg of a carrier test for a common genetic disease that would, at best, only work three-quarters of the time set off a flurry of statements by professional medical organizations. On Nov. 13, 1989, the American Society of Human Genetics urged caution in carrier testing until a greater percentage of the CF-carrying population could be identified, calling for pilot programs to test the tests. Meanwhile, they suggested the test only for those with a close affected relative.

In early March 1990, a panel of physicians, geneticists, genetic counselors, and attorneys met at the National Institutes of Health in Bethesda, Md., to develop guidelines for CF carrier testing. This group echoed the earlier call for pilot programs, adding that widespread testing should wait until tests could detect 90 to 95 percent of carriers.

In December 1992, the American Society of Human Genetics reevaluated their 1989 statement, in light of the ability to detect many CF mutations. Their advice remains unchanged—for now, CF testing should be offered only to those with a relative who has the disorder. The organization also calls for informed consent and genetic counseling, confidentiality of results, and quality control of the laboratory performing the test. ■

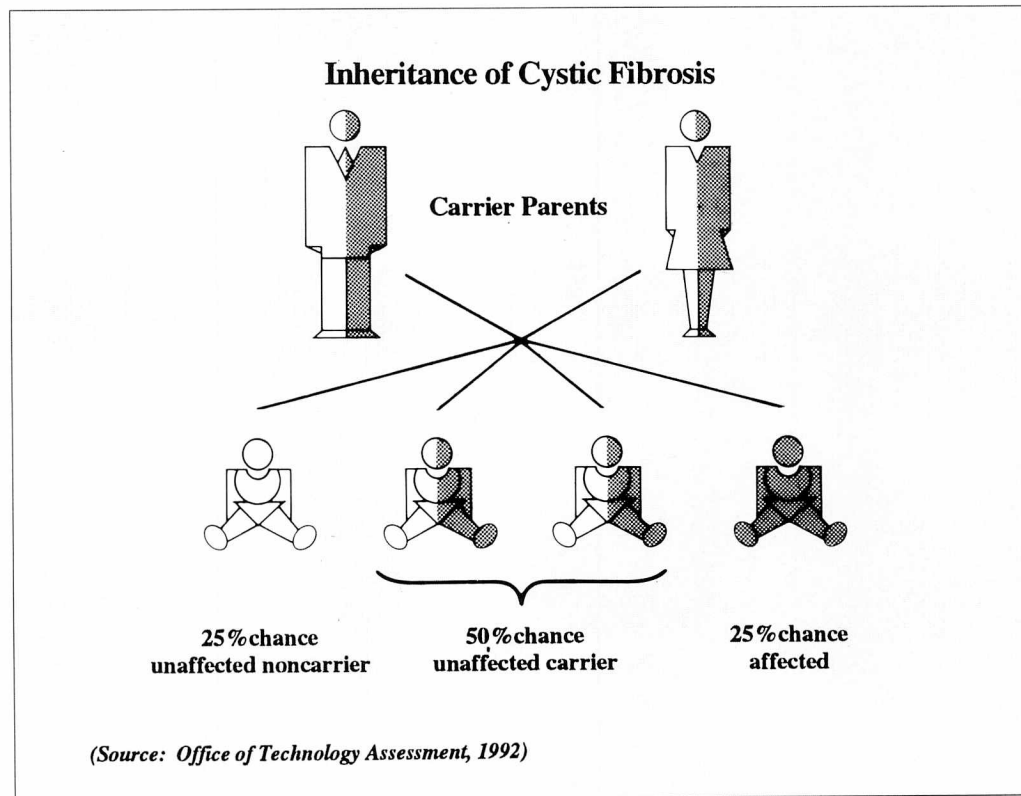
—R.L.

infections to which CF patients are prone, including *Pseudomonas aeruginosa* bacteria, a type of microbe that is attracted to the sticky mucus in the lungs. The combination of animal enzymes, called Viokase, that Alex Deford took regularly is still used today by CF patients. It is approved as a prescription digestive aid for CF patients and others with pancreatic insufficiencies. Combined with a high-calorie diet, this enzyme preparation aids digestion, helping the patient to maintain weight.

Many patients also take anti-inflammatory prescription drugs, such as ibuprofen (Motrin and others), prednisone (Deltasone, Winpred, Orason, and others), and naproxen (Anaprox, Naprosyn and others).

The drug amiloride (Midamor, Moduretic), introduced in 1967 and approved as an adjunct to treatment with some diuretic drugs, is now being tested as a treatment for CF. Scientists believe amiloride thins lung secretions by blocking sodium uptake by lung cells. Clinical studies are under way to assess amiloride as a CF treatment alone, and in combination with the biological products adenosine triphosphate (ATP) and uridine triphosphate (UTP). (ATP and UTP are components of the nucleic acids DNA and RNA.)

Other investigational products are aimed at tempering the body's immune response to lung infection, which can be excessive. One such product is deoxyribo-



nuclease. The March 19, 1992, *New England Journal of Medicine* reported that in a pilot study, this protein biologic given in an aerosol helped clear the lungs of 16 adult CF patients. It is being tested in 900 CF patients at 50 medical centers in the United States.

Gene Therapy

FDA has designated recombinant cystic fibrosis transmembrane conductance regulator (the gene's protein product, abbreviated CFTR) as well as gene therapy as orphan products. This gives their sponsors special incentives because they are developing products for a condition affecting relatively few people.

The first human gene therapy study of CF got under way last April 17 at the National Heart, Lung, and Blood Institute after FDA gave the go-ahead the previous day. An engineered cold virus (adenovirus) was introduced into the cells lining the nose and airways of a 23-year-old man with CF. The virus was altered to carry the normal CFTR gene and lacks the genes to cause a cold and to replicate.

The research was the first use of gene

therapy for a common genetic disorder and the first use of a cold virus to transport genes. The study includes 10 patients 21 or older who have mild to moderate CF symptoms.

Previous experiments in rats indicated that replacing the CF genes in just 10 percent of the lung lining cells improves lung function. However, because the genes go to the patients' lungs but not their sex cells, CF can still be passed to the patients' children.

New knowledge of CF is coming so fast that the goals of carrier screening may change even before the tests are cleared for marketing.

Soon, detecting the gene for CF may be a way of finding who needs treatment, as early as possible, just as is presently done for high blood pressure and elevated blood cholesterol. Says Wallace, "CF research is moving so quickly, with a lot of hope for treatment in the near future. It will be treatable, and possibly easily." ■

Ricki Lewis is a genetic counselor and is the author of textbooks on biology and human genetics.

For more information, contact:

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FDA Reports On PESTICIDES IN FOODS

by Judith E. Foulke

Pesticide residues on infant foods and adult foods that infants and children eat are almost always well below tolerances (the highest levels legally allowed) set by the Environmental Protection Agency. This was the conclusion of a recent Food and Drug Administration report based on the agency's monitoring of these types of foods over the last seven years.

The FDA report, "Monitoring of Pesticide Residues in Infant Foods and Adult Foods Eaten by Infants and Children," was published in the May-June 1993 issue of the *Journal of the Association of Official Analytical Chemists International*.

The authors, consumer safety officer Norma Yess and chemists Ellis Gunderson and Ronald Roy of the Center for Food Safety and Applied Nutrition, based their findings on food samples from the three approaches FDA uses to monitor pesticides: regulatory, incidence and level, and Total Diet Study.

Through the regulatory approach, FDA checks foods close to the point of production for levels of residues and, if they are violative, considers enforcement action. Incidence and level is a study approach that analyzes selected samples of certain foods. Total Diet Study is an approach that uses data from supermarket shopping.

Of more than 10,000 food samples re-

ported from regulatory monitoring, fewer than 50 were violative. No residues over EPA or FDA action levels were found in samples from the incidence and level studies. In the Total Diet Study, no residues were found in infant formulas, and no residues over FDA or EPA allowed levels were found.

Shared Responsibility

The responsibility for ensuring that residues of pesticides in foods are not present at levels that will pose a danger to health is shared by FDA, EPA, and the Food Safety and Inspection Service of the U.S. Department of Agriculture. Pesticides of concern include insecticides, fungicides, herbicides, and other agricultural chemicals.

EPA reviews the scientific data on all pesticide products before they can be registered (or licensed) for use. If a product is intended for use on food crops, EPA also establishes a tolerance.

FDA is responsible for enforcing these tolerances on all foods except meat, poultry, and certain egg products, which are monitored by USDA. In addition, FDA works with EPA to set "action levels"—enforcement guidelines for residues of pesticides, such as DDT, that may remain in the environment after their use is dis-

continued. The guidelines are set at levels that protect public health.

Regulatory Monitoring

In its regulatory monitoring to enforce EPA-set tolerances, FDA checks foods for pesticide residues as close to production of the commodity as possible—at distributors, at food processors, or, if imported, at entry into the country. If illegal residues are found in domestic samples, FDA can take regulatory action, such as seizure or injunction. For imports, FDA can stop shipments at ports of entry.

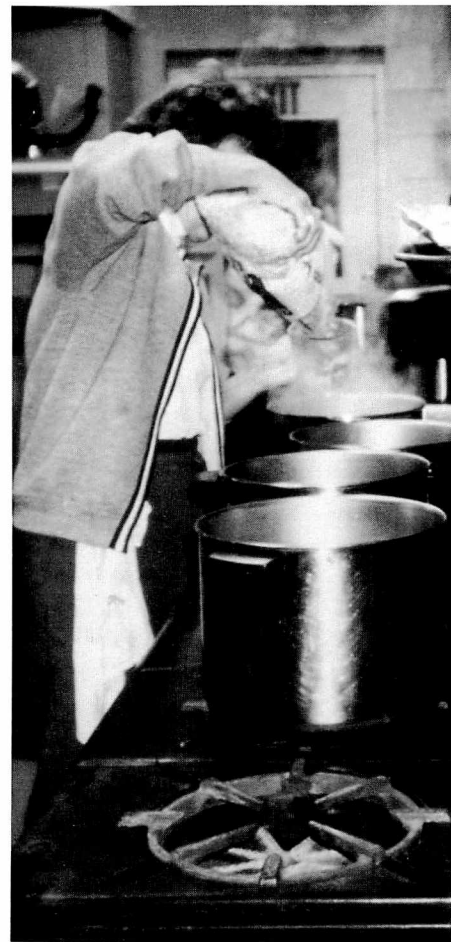
The FDA report used data from FDA regulatory monitoring between 1985 and 1991. The authors chose eight foods that infants and children eat in relatively large quantities—apples, bananas, oranges, and pears; apple, grape and orange juices; and milk.

FDA found 50 violative samples, representing only 0.3 percent of domestic products and 0.6 percent of imports reported under the regulatory monitoring approach.

All foods sampled in regulatory monitoring are analyzed unwashed and unpeeled—even bananas. Yess explains that because food processors, and most consumers, wash or peel produce before eating or using it in food products, many of the violative samples reported in the



Preparing food for analysis as part of FDA's Total Diet Study (above), workers cut up peppers for use in an FDA-supplied stuffed pepper recipe. At right, a worker in an FDA-contracted church kitchen near Kansas City measures the correct portion of instant mashed potatoes before putting it into a pot of boiling water, following package instructions. The prepared foods will be analyzed for more than 200 pesticides and industrial chemical residues.



FDA study showed higher residues than the actual amount people are exposed to. Studies have shown that residues of many pesticides can be washed off fresh produce, a good practice for anyone fixing a salad or snacking on grapes (see accompanying article).

Of the 50 violative samples, nearly all were pesticide residues for which there were no tolerances or EPA "approval for use" on the specific food sampled. Since pesticides are registered for specific crops, residues on crops for which the pesticide has not been registered are illegal.

A few samples had residues higher than EPA tolerances or FDA action levels in effect at the time; a number of tolerances were revised between 1985 and 1991. The revisions for daminozide (Alar), for example, reflect that it has not been used in agriculture since 1989.

Some domestic milk samples showed small amounts of chlorinated pesticide residues. The registration for food use for these compounds expired more than 20 years ago, but because they persist in the environment, residues are still found at low levels.

Incidence and Level Studies

When FDA wants to know more about specific pesticides, commodities, or pesticide-commodity combinations, the agency supplements its regulatory monitoring by analyzing selected samples of certain foods in incidence and level monitoring.

For the pesticide residue report, the authors used the results of two studies. One study targeted five specific commodity-pesticide combinations for infant foods and other foods commonly eaten by infants and children. The analyses for this study were directed by FDA and completed in 1990 through a cooperative agreement with a USDA laboratory in Gulfport, Miss. The other study, also in 1990, analyzed whole pasteurized milk samples through an FDA-supported contract.

Both studies included results of analyses of several pesticides and pesticide-commodity combinations that have been the focus of public attention within the last five years. No residues over EPA tolerances or FDA action levels were found in samples from either of the two studies.

The first study involved five tasks. In

the first, about 900 samples of commercially prepared infant foods and formulas were collected and analyzed for residues of the following pesticides:

- benomyl-thiabendazole (fungicides)
- daminozide (sprayed on apple trees to prevent premature drop, no longer used by growers)
- ethylenethiourea (ETU, a breakdown product of a fungicide)
- aldicarb (an insecticide, acaricide against snails, and nematocide against worms)
- the organochlorine group of pesticides (older, more persistent pesticides, including those no longer used in foods).

The other four tasks were analyses of adult foods eaten by infants and children:

- apples, bananas, oranges, and pears for benomyl-thiabendazole
- apple and grape juices, applesauce, and canned pears for daminozide
- grape juice for ETU
- bananas, oranges, and orange juice for aldicarb.

Three-quarters of the samples collected for all tasks were from large retail grocery stores in six states—Massachusetts, Illi-

NAS Evaluation Expected

The National Research Council of the National Academy of Sciences (NAS) is expected to issue a report this summer on its evaluation of the methods the government uses to estimate the health risks to infants and children from dietary exposures to pesticide residues. At issue is whether federal pesticide risk assessments, on which Environmental Protection Agency tolerances are based, adequately protect special segments of the population, particularly infants and children.

Tolerance levels reflect both the toxicity of a chemical and anticipated dietary exposure. Risks are calculated from two types of exposure estimates:

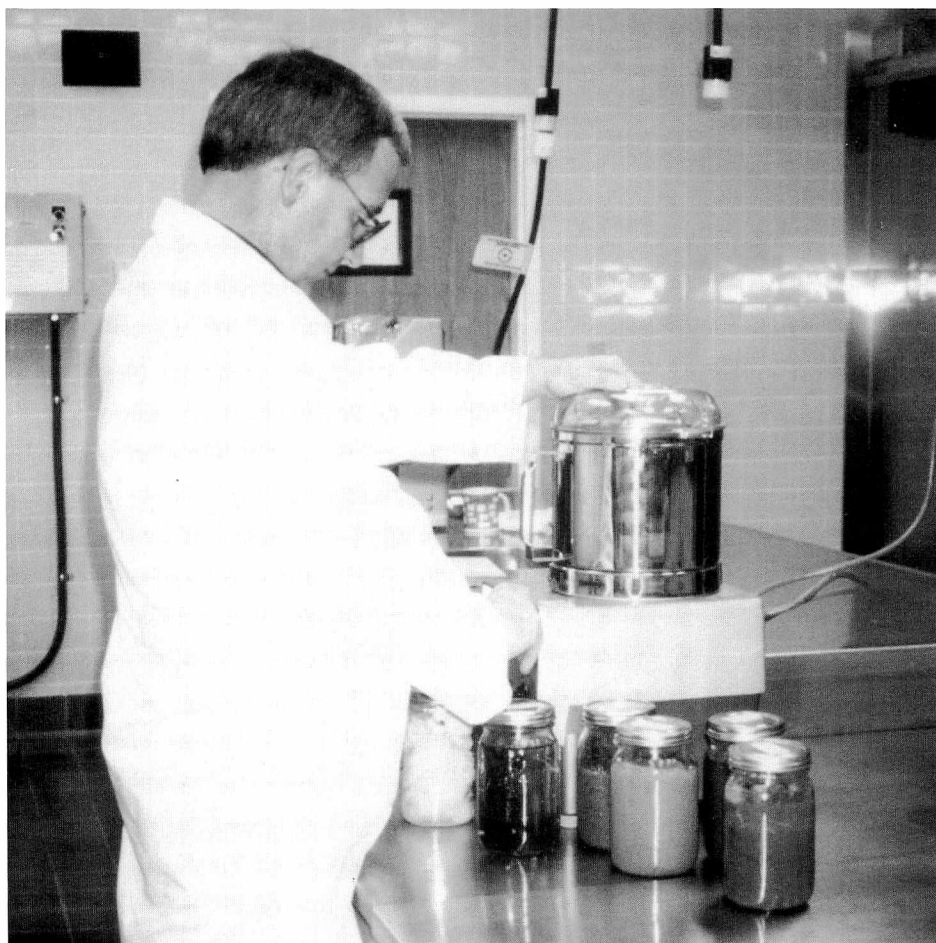
- the potential risk from a one-time exposure
- a composite average lifetime risk, which includes a proportionately greater exposure in childhood.

FDA and U.S. Department of Agriculture monitoring for pesticide residues consistently show that levels rarely exceed or approach established tolerances. Estimated dietary intakes of pesticides by children and adults in the United States are also well below Acceptable Daily Intakes (ADI) established by the Food and Agriculture Organization and the World Health Organization, seldom exceeding 1 percent of the ADI.

In response to a request from Congress in 1988, NAS convened a 14-person committee representing academia, medicine, state governments, industry, USDA, and Canada's health agencies. EPA asked the committee to address:

- the ways in which children are more or less susceptible to the toxicity of pesticides in their diets
- diets of various age groups
- pesticide use patterns on crops likely to contain residues that cause concern
- improvements EPA could make in its toxicological testing requirements and methods of estimating risk to improve protection for infants and children. ■

—J.E.F.



nois, Michigan, Wisconsin, Minnesota, and Washington. The remaining samples were collected in the Gulfport, Miss., area (the home of USDA's National Monitoring and Residue Analysis Laboratory, where the FDA-directed study was done). The prepared infant foods and formula samples were selected mostly from the major manufacturers.

The second study showed the results of sampling for residues of the organochlorine group of pesticides in whole pasteurized milk. Organochlorine pesticide residues—mostly DDT, DDE and dieldrin—were found in 398 of the 806 milk samples, but all were well below EPA tolerances or FDA action levels.

Samples for the milk study came from monthly collections at 63 sampling stations that are a part of EPA's Environmental Radiation Ambient Monitoring System, located in large metropolitan areas throughout the United States. At each sampling station, milk from selected sources was combined to represent the milk routinely consumed in that area. Portions of the milk were sent to an FDA contract laboratory for analysis.

FDA analyst Pat Hudnall uses a food processor to prepare table-ready entrées for laboratory analysis as part of the Total Diet Study.

Total Diet Study

For its report, FDA also used data from the Total Diet Study, which is used to monitor a number of nutritional concerns, including pesticides. As part of the Total Diet Study, FDA staffers shop in supermarkets or grocery stores four times a year, once in each of four geographical regions of the country. Shopping in three cities from each region, they buy the same 234 foods (including meat), selected from nationwide dietary survey data to typify the American diet. The purchased foods are called "market baskets."

Foods from the market baskets are then prepared as a consumer would prepare them. For example, beef and vegetable

Wash Before Eating



Washing fresh produce before eating is a healthful habit. You can reduce and often eliminate residues if they are present on fresh fruits and vegetables by following these simple tips:

- Wash produce with large amounts of cold or warm tap water, and scrub with a brush when appropriate; do not use soap.
- Throw away the outer leaves of leafy vegetables such as lettuce and cabbage.
- Trim fat from meat, and fat and skin from poultry and fish. Residues of some pesticides concentrate in animal fat.

Supermarkets, as a rule, don't wash produce before putting it out, but many stores mist it while it's on display. Misting keeps the produce from drying, but surface resi-

dues drain off also, in much the same way as from a light wash under the kitchen faucet.

A 1990 report in the *EPA Journal* by three chemists from that agency, Joel

Garbus, Susan Hummel, and Stephanie Willet, summarized four studies of fresh tomatoes treated with a fungicide, which were tested at harvest, at the packing house, and at point of sale to the consumer. The studies showed that more than 99 percent of the residues were washed off at the packing house by the food processor.

A 1989 study reported by Edgar Elkins in the *Journal of the Association of Official Analytical Chemists* showed the effects of peeling, blanching and processing on a number of fruits and vegetables. For example, in the case of benomyl, 83 percent of the residues found on fresh apples were removed during processing into applesauce, 98 percent of residues from oranges processed to juice were removed, and 86 percent of residues from fresh tomatoes processed to juice were removed. Another study in 1991 by Gary Eilrich, reported in an *American Chemical Society Symposium*, showed similar results. ■

—J.E.F.

stew is made from the collected ingredients, using a standard recipe. The prepared foods are analyzed for pesticide residues, and the results, together with USDA consumption studies, are used to estimate the dietary intakes of pesticide residues for eight age-sex groups ranging from infants to senior citizens.

For their report, the FDA researchers included results from 27 market baskets collected and analyzed between 1985 and 1991. Included were 33 different infant foods (both strained and junior), 10 adult foods eaten by infants and children, and four types of milk. The infant foods included cereals, combination meat and poultry dinners, vegetables, desserts, fruits and fruit juices, and infant formulas. The adult foods included apples, oranges, pears, and bananas; apple, grape and or-

ange juices; applesauce; grape jelly; and peanut butter. Milks were chocolate, evaporated, low-fat (2 percent), and whole.

No residues were found in the infant formulas, and no residues over EPA tolerances or FDA action levels were found in any of the Total Diet Study foods. Low levels of malathion were found in some cereals because malathion is widely used both before and after harvest on grains. Low levels of thiabendazole, a post-harvest fungicide used on many fruits, were found on some of the fruits and fruit products.

The low levels of pesticide residues found in the Total Diet Study and incidence-level monitoring samples show how processing foods or otherwise preparing them for consumption at the table can re-

duce residue levels. Washing at home removes much of the residues. But commercial food processing steps, such as peeling and blanching, can further reduce residues. For example, the highest finding of thiabendazole in raw apples was 2 parts per million (EPA tolerance is 10 ppm), 0.08 in apple juice, and 0.06 in applesauce.

Also, agricultural specialists from major infant food manufacturers work with their contract growers to minimize pesticide applications and to ensure that only those pesticides specified in the contract are applied. Therefore, when pesticide residues are found on infant foods, they are usually well below EPA tolerances. ■

Judith E. Foulke is a staff writer for FDA Consumer. Judith Levine Willis also contributed to this article.

PREVENTING STDs

by Judith Levine Willis

This article is part of a series with important health information for teenagers. Unlike previous articles, however, it contains sexually explicit material in an effort to reduce the incidence of STDs among teens. Parents and teachers may want to review the article before giving it to teenagers.



It's important to read the information printed on the package to make sure a condom's made of latex and labeled for disease prevention. The label may also give an expiration date and tell you if there is added spermicide or lubricant.

You don't have to be a genius to figure out that the only sure way to avoid getting sexually transmitted diseases (STDs) is to not have sex.

But in today's age of AIDS, it's smart to also know ways to lower the risk of getting STDs, including HIV, the virus that causes AIDS.

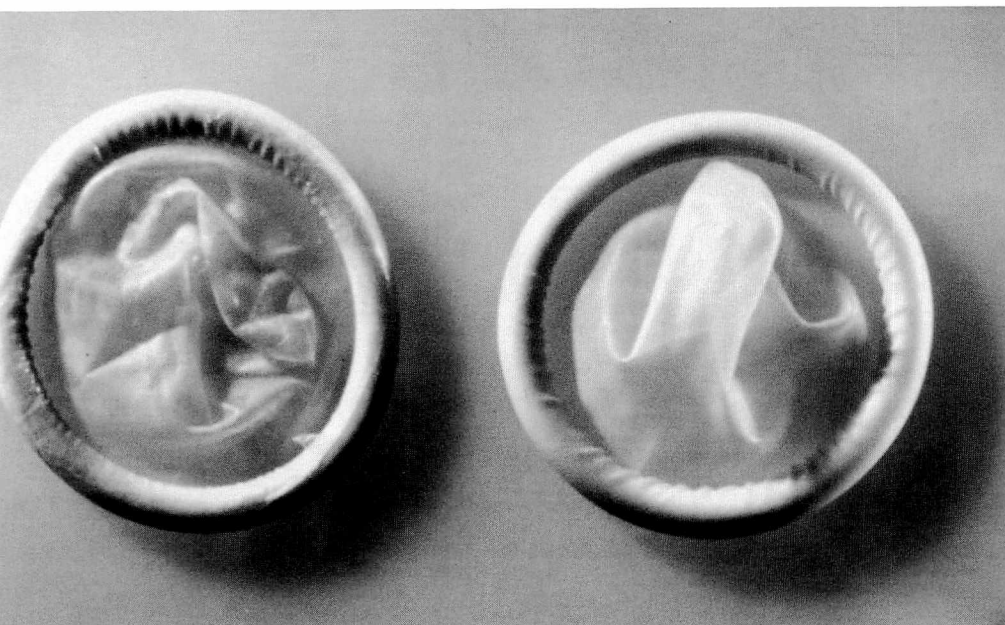
Infection with HIV, which stands for human immunodeficiency virus, is spreading among teenagers. From 1990 to 1992, the number of teens diagnosed with AIDS nearly doubled, according to the national Centers for Disease Control and Prevention. Today, people in their 20s account for 1 out of every 5 AIDS cases in the United States. Because HIV infection can take many years to develop into AIDS, many of these people were infected when they were teenagers.

You may have heard that birth control can also help prevent AIDS and other STDs. This is only partly true. The whole story is that *only one form of birth control—latex condoms* (thin rubber sheaths used to cover the penis)—is highly effective in reducing the transmission (spread) of HIV and many other STDs.

(When this *FDA Consumer* went to press, the Food and Drug Administration was preparing to approve Reality Female Condom, a form of birth control made of polyurethane. It may give limited protection against STDs, but it is not as effective as male latex condoms.)

So people who use other kinds of birth control, such as the pill, sponge, diaphragm, Norplant, Depo-Provera, cervical cap, or IUD, also need to use condoms to help prevent STDs.

Here's why: Latex condoms work against STDs by keeping blood, a man's semen, and a woman's vaginal fluids—all of which can carry bacteria and viruses—from passing from one person to another. For many years, scientists have known that male condoms (also called safes, rubbers, or prophylactics) can help prevent STDs transmitted by bacteria, such as syphilis and gonorrhea, because the bacteria can't get through the condom. More recently, researchers discovered that latex condoms can also reduce



If a condom is sticking to itself, as is the one on the left, it's damaged and should not be used. The one on the right is undamaged and okay to use.

NEW INFORMATION ON LABELS

Information about whether a birth control product also helps protect against sexually transmitted diseases (STDs), including HIV infection, is being given added emphasis on the labeling of these products.

"In spite of educational efforts, many adolescents and young adults, in particular, are continuing to engage in high-risk sexual behavior," said FDA Commissioner David A. Kessler, M.D., in announcing the label strengthening last April. "A product that is highly effective in preventing pregnancy will not necessarily protect against sexually transmitted diseases."

Labels on birth control pills, implants such as Norplant, injectable contraceptives such as Depo Provera, intrauterine devices (IUDs), and natural skin condoms will state that the products are intended to prevent pregnancy and do not protect against STDs, including HIV infection (which leads to AIDS). Labeling of natural skin condoms will also state that consumers should use a latex condom to help reduce risk of many STDs, including HIV infection.

Labeling for latex condoms, the only product currently allowed to make a claim of effectiveness against STDs, will state that if used properly, latex condoms help reduce risk of HIV transmission and many other STDs. This statement, a modification from previous labeling, will now appear on individual condom wrappers, on the box, and in consumer information.

Besides highlighting statements concerning sexually transmitted diseases and AIDS on the consumer packaging, manufacturers will add a similar statement to patient and physician leaflets provided with the products.

Consumers can expect to see the new labels by next fall. Some products already include this information in their labeling voluntarily. FDA may take action against any products that don't carry the new information.

FDA is currently reviewing whether similar action is necessary for the labeling of spermicide, cervical caps, diaphragms, and the Today brand contraceptive sponge. ■

the risk of getting STDs caused by viruses, such as HIV, herpes, and hepatitis B, even though viruses are much smaller than bacteria or sperm.

After this discovery, FDA, which regulates condoms as medical devices, worked with manufacturers to develop labeling for latex condoms. The labeling tells consumers that although latex condoms cannot entirely eliminate the risk of STDs, when used properly and consistently they are highly effective in preventing STDs. FDA also provided a sample set of instructions and requested that all condoms include adequate instructions.

Make Sure It's Latex

Male condoms sold in the United States are made either of latex (rubber) or natural membrane, commonly called "lambskin" (but actually made of sheep intestine). Scientists found that natural skin condoms are not as effective as latex condoms in reducing the risk of STDs because natural skin condoms have naturally occurring tiny holes or pores that viruses may be able to get through. Only latex condoms labeled for protection against STDs should be used for disease protection.

Some condoms have lubricants added and some have spermicide (a chemical that kills sperm) added. The package labeling tells whether either of these has been added to the condom.

Lubricants may help prevent condoms from breaking and may help prevent irritation. But lubricants do not give any added disease protection. If an unlubricated condom is used, a water-based lubricant (such as K-Y Jelly), available over-the-

Looking At A Condom Label

Like other drugs and medical devices, FDA requires condom packages to contain certain labeling information. When buying condoms, look on the package label to make sure the condoms are:

- made of latex
- labeled for disease prevention
- not past their expiration date (EXP followed by the date). ■

STD FACTS

counter (without prescription) in drug stores, can be used but is not required for the proper use of the condom. Do *not* use petroleum-based jelly (such as Vaseline), baby oil, lotions, cooking oils, or cold creams because these products can weaken latex and cause the condom to tear easily.

Condoms with added spermicide give added birth control protection. An active chemical in spermicides, nonoxynol-9, kills sperm. Although it has not been scientifically proven, it's possible that spermicides may reduce the transmission of HIV and other STDs. But spermicides alone (as sold in creams and jellies over-the-counter in drugstores) and spermicides used with the diaphragm or cervical cap do not give adequate protection against AIDS and other STDs. For the best disease protection, a latex condom should be used from start to finish every time a person has sex.

FDA requires condoms with spermicide to be labeled with an expiration date. Some condoms have an expiration date even though they don't contain spermicide. Condoms should not be used after the expiration date, usually abbreviated EXP and followed by the date.

Condoms are available in almost all drugstores, many supermarkets, and other stores. They are also available from vending machines. When purchasing condoms from vending machines, as from any source, be sure they are latex, labeled for disease prevention, and are not past their expiration date. Don't buy a condom from a vending machine located where it may be exposed to extreme heat or cold or to direct sunlight.

Condoms should be stored in a cool, dry place out of direct sunlight. Closets and drawers usually make good storage places. Because of possible exposure to extreme heat and cold, glove compartments of cars are *not* a good place to store condoms. For the same reason, condoms shouldn't be kept in a pocket, wallet or purse for more than a few hours at a time.

How to Use a Condom

- Use a new condom for every act of vaginal, anal and oral (penis-mouth contact) sex. Do not unroll the condom before placing it on the penis.
- Put the condom on after the penis is erect and before *any* contact is made be-

- Sexually transmitted diseases affect more than 12 million Americans each year, many of whom are teenagers or young adults.
- Using drugs and alcohol increases your chances of getting STDs because these substances can interfere with your judgment and your ability to use a condom properly.
- Intravenous drug use puts a person at higher risk for HIV and hepatitis B because IV drug users usually share needles.
- The more partners you have, the higher your chance of being exposed to HIV or other STDs. This is because it is difficult to know whether a person is infected, or has had sex with people who are more likely to be infected due to intravenous drug use or other risk factors.
- Sometimes, early in infection, there may be no symptoms, or symptoms may be confused with other illnesses.
- You cannot tell by looking at someone whether he or she is infected with HIV or another STD.

STDs can cause:

- pelvic inflammatory disease (PID), which can damage a woman's fallopian tubes and result in pelvic pain and sterility
- tubal pregnancies (where the fetus grows in the fallopian tube instead of the womb), sometimes fatal to the mother and always fatal to the fetus
- cancer of the cervix in women
- sterility—the inability to have children—in both men and women
- damage to major organs, such as the heart, kidney and brain, if STDs go untreated
- death, especially with HIV infection.

See a doctor if you have any of these STD symptoms:

- discharge from vagina, penis or rectum
- pain or burning during urination or intercourse
- pain in the abdomen (women), testicles (men), or buttocks and legs (both)
- blisters, open sores, warts, rash, or swelling in the genital or anal areas or mouth
- persistent flu-like symptoms—including fever, headache, aching muscles, or swollen glands—which may precede STD symptoms. ■

tween the penis and any part of the partner's body.

- If the condom does not have a reservoir top, pinch the tip enough to leave a half-inch space for semen to collect. Always make sure to eliminate any air in the tip to help keep the condom from breaking.
- Holding the condom rim (and pinching a half inch space if necessary), place the condom on the top of the penis. Then, continuing to hold it by the rim, unroll it all the way to the base of the penis. If you are also using water-based lubricant, you can put more on the outside of the condom.
- If you feel the condom break, stop immediately, withdraw, and put on a new condom.
- After ejaculation and before the penis gets soft, grip the rim of the condom and carefully withdraw.
- To remove the condom, gently pull it

off the penis, being careful that semen doesn't spill out.

- Wrap the condom in a tissue and throw it in the trash where others won't handle it. (Don't flush condoms down the toilet because they may cause sewer problems.) Afterwards, wash your hands with soap and water.

Latex condoms are the only form of contraception now available that human studies have shown to be highly effective in protecting against the transmission of HIV and other STDs. They give good disease protection for vaginal sex and should also reduce the risk of disease transmission in oral and anal sex. But latex condoms may not be 100 percent effective, and a lot depends on knowing the right way to buy, store and use them. ■

Judith Levine Willis is editor of FDA Consumer.



The Notebook: a potpourri of items of interest fathered 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.

■ **An orphan products list** is available from FDA. All drugs or biologics that have been granted orphan status through Dec. 31, 1992, are included in the list, which is updated monthly. Free copies of the list are available from the Dockets Management Branch (HFA-305), Food and Drug Administration, Room 1-23, 12420 Parklawn Drive, Rockville, MD 20857. (FR March 2)

■ **Cholesterol screening** in young adults may do more harm than good, according to a study by Stephen B. Hulley, University of California, San Francisco, and colleagues. They recommend limiting screening to young adults with coronary heart disease (CHD) or other factors placing them at high risk. (*Journal of the American Medical Association*, March 16)

■ **Chronic disease evaluation** is one topic to be discussed at the Eighth National Conference on Chronic Disease Prevention and Control, Nov. 17 to 19, in Kansas City, Mo. Other topics include chronic disease epidemiology, interventions, and intervention assessment. For more information, contact the National Center for Chronic Disease Prevention and Health Promotion, Mailstop K-43, 4770 Buford Highway, NE, Atlanta, GA 30341-3724; telephone (404) 488-5390; facsimile (404) 488-5962. (*Morbidity and Mortality Weekly Report*, Feb. 26)

■ **Bicycle helmets** substantially reduce the risk of head injuries during crashes, but many cyclists still don't wear them. Cyclists who don't use helmets face a 3.9 to 6.7 times greater risk for head injuries than those who wear helmets. However, fewer than 2 percent of U.S. children riding bicycles and 10 percent of all bicyclists wear helmets. (*MMWR* March 26)

■ **More than 2.5 million cigarette lighters** by Marlboro, called "Party Lighter" and "Night Lighter," have been recalled by Philip Morris after Connecticut fire officials implicated a lighter in a fire started by children. Philip Morris is offering \$5 for each lighter. For information, call (800) 241-9005. (*JAMA* March 16)

■ **Confidentiality is crucial to teens** seeking health care, according to a study by Tina L. Cheng, University of Massachusetts Medical Center, and colleagues. The study reports on 1,295 ninth- through 12th-grade students at three Massachusetts public schools. It found that 58 percent of the students had health concerns they wished to keep private from their parents,

and 69 percent from friends and classmates; 25 percent reported they would not seek care in some situations if their parents might find out. (*JAMA* March 16)

■ **Veterinary information** that includes a veterinary biological products and establishment licenses list is available free from the Animal and Plant Health Inspection Service (APHIS). Contact: Maxine Kitto, Veterinary Biologics, Biotechnology, Biologics, and Environmental Protection, APHIS, Room 838, Federal Building, 6505 Belcrest Rd., Hyattsville, MD 20782; telephone (301) 436-8245. (FR March 23)

■ **The Green Pages**, the first listing of U.S. suppliers of environmental technology and services, published by the Commerce Department and Environmental Protection Agency, is available from local Commerce Department district offices. (FR March 12)

■ **Minors can easily purchase cigarettes** despite warnings posted in businesses that sell tobacco products, two studies published by CDC found. In addition, CDC reports, smoking among high school seniors had not substantially decreased from 1981 through 1991. (*MMWR* Feb. 26)





Court Orders Dairy to Stop Illegal Use of Drugs in Cows

by Judith E. Foulke

A California dairy, warned repeatedly that cull cows it was selling for slaughter for human food contained veterinary drug residues, was ordered by preliminary injunction to correct its animal husbandry practices or stop selling all cattle until the conditions set by the court are met. (Cull cows are animals that are removed from the herd for reasons such as lowered milk production or inability to breed.)

The preliminary injunction, filed on Jan. 5, 1993, in the U.S. District Court for the Northern District of California, against the Mulas Dairy Company in Sonoma, Calif., is based on seven illegal residue violations between 1988 and 1991, reported to FDA by the Food Safety and Inspection Service (FSIS) of the U.S. Department of Agriculture. The firm milks approximately 900 cows and markets about 400 cull cows and a like number of calves for slaughter each year.

FSIS inspectors, stationed at slaughterhouses, check the meat for various problems, including the presence of illegal levels of drug residues. FDA sets and enforces allowable levels, and when FSIS finds a violation, it informs FDA for follow-up regulatory action.

In June 1989, FSIS notified FDA's San Francisco district office that gentamicin sulfate, a drug not approved for use in cattle, had been found in the kidneys of two cull cows marketed by Mulas Dairy. FDA investigators inspected the dairy on Aug. 23 and found the drug there. During that inspection, Mario Mulas, one of two operators of the family-owned firm,



signed an affidavit admitting to the use of gentamicin in the dairy cows. In a letter dated Oct. 30, 1989, FDA warned Mario Mulas and his nephew, Michael Mulas, that adulterating human food with unapproved drug residues was illegal. The letter also stated that the firm had made gentamicin sulfate unsafe because the drug was being used in cattle, an unapproved use of a new animal drug. The letter asked the firm to correct the violations and advised it of possible regulatory action if corrections were not made. The letter requested a written response, but FDA did not receive one.

On Sept. 27, 1991, FSIS informed FDA that on Sept. 23, FSIS had found illegal amounts of penicillin residues in the liver

and kidney of another Mulas Dairy cull cow. FSIS records showed additional previous violations: In 1988, one cull cow from the dairy had tested positive for residues of the antibiotic tylosin, and from 1990 to 1991, two cows had tested positive for the antibiotic neomycin and two others for penicillin. The residues for tylosin and penicillin ranged from two to more than eight times above the permitted levels. FSIS had sent the dairy eight warning letters during that time.

FDA inspected the firm on Nov. 13 and 14, 1991, and found the dairy using new animal drugs contrary to the terms of the drugs' approval. During the inspection, Michael Mulas admitted that he had administered penicillin at about three times

more than the approved dose, and that he stops administering drugs to the animals 10 days before they are shipped to the slaughterhouse. This is 20 days short of the required 30-day withdrawal period.

Also during the November inspection, FDA reported inadequate record-keeping. The investigator noted, for example, that although the dairy was maintaining medication records, the disease and date of treatment were recorded on a board in the dairy, then written on paper, and a few days later entered into a computer. The computer record did not show the dates of treatment, the dates the animals were sent to slaughter, or the drugs given. The firm claimed that it uses only a certain drug for a certain disease, and therefore it would know the drug by the disease listed.

The FDA inspection report noted that although the dairy operators promised some specific steps after the inspection, they did not promise to avoid all illegal

residues. On Dec. 19, 1991, FDA's San Francisco district recommended that the dairy be enjoined from further violations of the Food, Drug, and Cosmetic Act because it had repeatedly marketed cattle with illegal antibiotic residues, despite repeated warnings.

Under the preliminary injunction, the firm:

- cannot administer any new animal drug except by written protocol given by the defendants' veterinarian
- must make a permanent record for each animal, identifying the animal medicated, the drug used, and the dates of administration
- must record the dosage, the route of administration, the person administering the drug, and the date, established in accordance with the protocol, when the withdrawal period elapses
- must tag, at the dairy, each animal to be sold with a USDA Veterinary Service-ap-

proved backtag. Each animal sent to slaughter must be accompanied by a declaration identifying the backtag number, signed by one of the defendants, verifying that the animal either has received no medication or, if the animal has been medicated, that it passed the withdrawal period established by the veterinarian. A copy of the declaration must be attached to a permanent record of all medical treatments given the animal within 90 days of the date it is delivered for slaughter.

The firm submitted a final written residue avoidance plan to FDA on Jan. 20, 1993, as required by the terms of the preliminary injunction, and had the plan in operation by Feb. 15.

As of this writing, the firm has complied with the terms of the preliminary injunction.

Judith E. Foulke is a staff writer for FDA Consumer.

Misbranded Devices Seized, Labeling Destroyed

In accordance with a court order, a Northbrook, Ill., importer destroyed the labeling for his company's computerized hearing test because of unsubstantiated medical claims that the device effectively diagnoses hearing loss.

The labels and pamphlets accompanying Communidyne, Inc.'s, Communidyne Computerized Hearing Test Machine, Model 4000, were destroyed March 5, 1993, under the terms of a consent decree signed the preceding December by the firm's president, Roger Gerber.

Federal deputy marshals, accompanied by investigators from FDA's Chicago district office, had seized 375 of the hearing test devices, which the company valued at \$375,000, and approximately 900 pamphlets titled "Facts about Hearing Loss" on July 9, 1991.

Directions for the device—a medium-sized box sitting atop a pedestal—instruct the user, "To test your hearing, deposit quarters, place your ear close to speaker cover and push the start button to begin the tone. When you can no longer hear the tone, push the stop button."

The labeling purports that the device gives a digital reading of the user's hearing ability based on the loudness of the tone, in cycles per second, at the time the user pushed the stop button, according to George Bailey, Chicago district compliance officer. In addition, promotional material claims the device rates the user's hearing as excellent, above average, average, below average, or far below average.

FDA first learned of the hearing test device when Gerber wrote FDA's device registration and listing branch Dec. 13, 1989, asking about the regulatory status of the device.

The branch responded March 29, 1990,

stating that the hearing test is considered a medical device under the Food, Drug, and Cosmetic Act and is therefore subject to registration, listing and pre-market notification with the agency. Gerber failed to comply with any of these requirements.

As a result, an FDA investigator inspected the Communidyne warehouse on Feb. 13, 1991. Gerber told the investigator that his firm had imported 425 of the devices from a manufacturer in Taiwan but he had sold only 50 since 1989. He said he planned to sell the remaining 375 devices at a reduced price.

At FDA's request, U.S. deputy marshals seized the hearing test machines July 9, 1991, to ensure no more devices were sold.

The agency charged that the devices were misbranded under the FD&C Act because the labeling contained misleading claims and did not provide adequate directions for use of the device.

According to Bailey, "Once they destroy the labeling, they're rendering it a nonmedical device by removing any and all labeling claims to testing for hearing loss."

Communi-dyne can sell the remaining devices as long as no health or medical claims are made.

—Kevin L. Ropp

Pharmacist's License Suspended For Illegal Drug Sales

A Bean Station, Tenn., drugstore owner was fined \$15,000 and had his pharmacy license suspended for four years for selling prescription drug samples, a violation of both Tennessee and federal laws.

Tennessee law prohibits the sale of prescription drug samples and adulterated, misbranded, and out-of-date drugs. In addition, the Prescription Drug Marketing Act of 1987, an amendment to the Federal Food, Drug, and Cosmetic Act, prohibits hospitals and health-care entities from selling prescription drug samples.

Investigators from the Tennessee Board of Pharmacy found 1,203 adulterated drugs and prescription drug samples at Bean Station Drug Center, owned by Joseph T. Huntsman, D.Ph., during a routine inspection of his store on Oct. 23, 1991.

The investigators photographed the drugs, then removed most of them from the shelves. Because they suspected violations of the FD&C Act, the investigators also notified FDA's Nashville district office.

On Oct. 24, the investigators, joined by Kari L. Norton of FDA's Nashville office, returned to Huntsman's store to collect the remaining drugs, but discovered they had been removed. After searching the premises, the investigators found 97 containers of drugs by a dumpster behind the store, and 36 other containers in a nearby shed. Also, a prescription drug sample that the investigators had taken off a shelf the

day before had been put back and had to be removed again.

A week later, the Tennessee Board of Pharmacy subpoenaed Huntsman's records, including invoices, prescriptions, and computer back-up tapes.

While reviewing the back-up tape for the period Jan. 1, 1988, to Oct. 31, 1991, Earl E. Davis, a computer specialist with the Nashville district office, found that Huntsman, a pharmacist, was listed as the physician on 2,448 original and refill prescriptions.

Davis and Glenn Radford, a board of pharmacy statistician, also uncovered 73 violations of Tennessee's "48-hour rule." This rule limits to 24 dosage units the maximum amount of a controlled substance that can be sold to any one purchaser within 48 hours. They also found 43 incidents of same-day, multiple prescription drug sales and 10 cases of dispensing excessive amounts of drugs to individual patients over a year's time, a violation of Tennessee law.

Records showed Huntsman had also dispensed drugs without a prescription and sold unapproved new drugs, such as "Joe's Mixture" (whiskey and rock candy) and "Dean's Mixture" (the antihistamine promethazine, the bronchodilator Ventolin, and APAP Cod, an acetaminophen with codeine combination).

On Nov. 13, 1992, Huntsman signed a Tennessee pharmacy board order that suspended his pharmacy license and outlined conditions he must meet to retain it. Huntsman must complete 15 hours of continuing education in pharmacy during 1994 and provide the board with evidence of having completed a pharmaceutical jurisprudence college course within one year.

Two and a half years of Huntsman's four-year license suspension is stayed. Upon completion of the active suspension period, Huntsman will be on probation.

—Victor Lambert

Magnetic Devices Seized

At FDA's request, the U.S. Marshals Service recently seized and destroyed magnetic devices valued at some \$42,000 because the products were being marketed illegally with unsubstantiated medical claims.

The device, known as Elekiban, was a quarter-inch magnetic disk attached to a circular adhesive patch. According to the labeling, users should place the Elekiban patch on their skin at "pressure spots," similar to acupuncture, where its magnetic force "stimulates the blood circulation and relieves the stiffness in the shoulder, neck and waist."

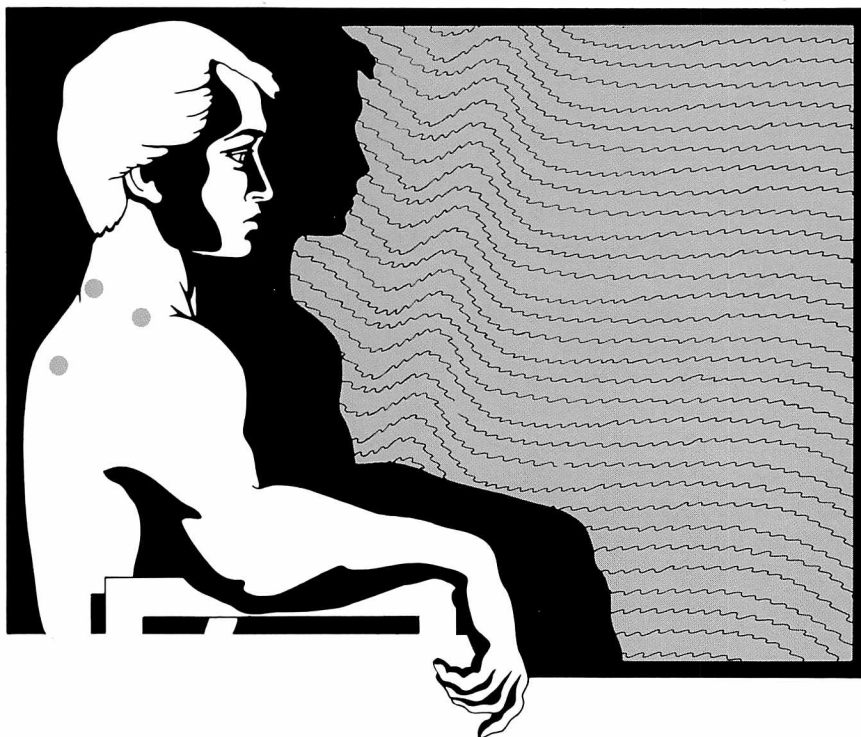
Raymond Kent, a compliance officer with FDA's Buffalo district office, which recommended the seizure, says, "The device was purported to have a beneficial effect through interaction of its own magnetic field with the magnetic field of the Earth. But the misleading claims could pose an unreasonable health hazard if use of the device caused people to postpone necessary treatment."

Claims also asserted FDA had actually approved the device, which was untrue, Kent says.

The Elekiban stock was destroyed Nov. 3, 1992.

The magnetic disks had been distributed primarily by Physio Meditec Corporation (PMC), an Amherst, N.Y., firm jointly owned by the device importer, UNIC International Corporation, of Canada, and manufacturer, PIP-Fujimoto Co., Ltd., of Japan.

Similar devices had been marketed in the mid to late 1970s as "Mag-U-Dot" with similar claims, including references to acupuncture. FDA informed the distributor at that time, Domenico International Ltd., of Akron, Ohio, that the device was subject to a March 1973 *Federal Register* notice declaring acupuncture devices investigational, which means they



couldn't be commercially marketed.

The Domenico president teamed up with other individuals to form ACU-DOT Corporation, in Akron. They changed the device's name to "ACU-DOT" and dropped acupuncture references from the labeling, but continued to market it with unproven medical claims. Mag-U-Dot and ACU-DOT had the same U.S. patent number as Elekiban, and all were made, at least in part, by PIP-Fujimoto.

At FDA's request, the U.S. Marshals Service seized ACU-DOT devices several times in 1979 and 1980. ACU-DOT contested the seizures, submitting to FDA results of a U.S. clinical study and a survey conducted in Japan. But two FDA physicians and an agency biophysicist determined the submissions were inadequate to warrant agency approval. A judge ruled the devices were misbranded because of the misleading labeling claims.

Later, PIP-Fujimoto met with FDA at headquarters several times. Agency officials explained the requirements for proof of effectiveness for labeled uses for devices FDA designates as "class III devices," which includes acupuncture instruments. FDA considers such instruments to be investigational devices.

Then, in January 1985, MNS, Ltd., of Hawaii, submitted to FDA an application

to market another similar device called Elekiban. The application was submitted under "510(k)," the section of the Federal Food, Drug, and Cosmetic Act stating that devices may be marketed without new study data if shown substantially equivalent to products sold before the Medical Device Amendments of 1976. The submission, however, did include two additional clinical studies sponsored by PIP-Fujimoto.

FDA determined that Elekiban was substantially the same as the Mag-U-Dot, a pre-Amendments device, but that the earlier device was misbranded because the claims were false and misleading. FDA also found these studies—like those submitted for ACU-DOT—to be inadequate.

According to T. Whit Athey, Ph.D., an FDA senior scientist and expert in magnetic theory, "The submitted material, at best, was misleading and vague, mixing a few well-known facts with many more unsupported assumptions. There was basically no scientific support for the mechanisms put forth."

In a letter dated April 16, 1985, the agency informed MNS that marketing its Elekiban for any medical purpose would be illegal.

Meanwhile, on June 18, 1984, MNS had petitioned FDA to reclassify Elekiban

from class III to class I (which only requires general controls, such as proper labeling and good manufacturing practices), submitting results of the same two studies. FDA replied that the evidence of effectiveness was insufficient.

On Nov. 30, 1987, FDA issued an import alert to detain at U.S. borders all magnetic support medical devices, including Elekiban and similar products.

Early in 1990, representatives of PIP-Fujimoto and Canadian importer UNIC Corp. began promoting Elekiban in the Buffalo, N.Y., area press. In a May 1990 letter to UNIC Corp., FDA advised the firm that Elekiban was misbranded and wouldn't be allowed into the United States.

In July 1990, FDA Buffalo district investigator Joseph Famiglietti visited Physio Meditec Corporation. While PMC was registered with FDA as a medical device distributor, Famiglietti learned, it had no authority to be marketing Elekiban. What's more, Famiglietti found that PMC was intentionally misinvoicing the product as "novelty items" at the time of import to avoid detection by U.S. Customs. Famiglietti warned PMC that marketing the device was against the law.

On Jan. 28, 1991, in response to letters from PMC's attorney concerning the legal status of Elekiban, FDA again warned the firm that it was an illegal device. The U.S. Marshals Service seized all of PMC's Elekiban stock and labeling on May 1, 1991. PMC filed a claim that same day to have the goods returned.

After a lengthy period of meetings, hearings, and legal communications with FDA, the firm's attorney withdrew from the case. On June 9, 1992, PMC agreed to forfeit its stock. A U.S. marshal removed the product and supervised its destruction.

—*Dixie Farley (William Defibaugh, a compliance officer with FDA's Center for Devices and Radiological Health, also contributed to this report.)*

SUMMARIES OF COURT ACTIONS



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

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

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

SEIZURE ACTIONS

Food/Contamination, Decomposition, Insanitary Handling

PRODUCT: **Crab claws, frozen**, at Roxbury, Dist. Mass.; Civil No. 92-11004-MA.

CHARGED 4-30-92: When shipped by Orion Seafood International, Portsmouth, N.H., from Cottlesville, Canada, the label of the article labeled "Packed By Breakwater Fisheries Ltd., Cottlesville, Nfld. Canada . . . CLAWS . . . 20 kg. Frozen Fish . . . Product of Canada" lacked a quantity of contents statement in terms of avoirdupois pounds and ounces—403(e)(2); and while held for sale, the article contained decomposed crab claws—402(a)(3).

DISPOSITION: Default—ordered destroyed. (F.D.C. No. 66416; S. No. 92-639-945; S.J. No. 1)

PRODUCTS: **Mung beans and Chinese Maid chow mein noodles**, at Chicago, N. Dist. Ill.; Civil No. 90-C-5029.

CHARGED 8-28-90: While held by Chinese Maid, Inc., Chicago, Ill. (who had manufactured the noodles using interstate flour), the noodles had been held under insanitary conditions—402(a)(4); and the mung beans had been held under insanitary conditions and contained rodent filth—402(a)(3), 402(a)(4).

DISPOSITION: The mung beans were claimed by the Dover Seed Co., Dover, Okla. A consent decree of condemnation authorized release of the mung beans for salvaging. A default decree of condemnation ordered the destruction of the noodles. Subsequently, an agreed order authorized the return to Chinese Maid, Inc., of two cases of noodles for the sole purpose of laboratory testing, provided, however that those noodles also be destroyed at the conclusion of the testing. (F.D.C. No. 65917; S. No. 90-575-464 et al.; S.J. No. 2)

PRODUCT: **Pollock fillets, salted**, at Barceloneta, Dist. Puerto Rico; Civil No. 92-2049(JP).

CHARGED 7-30-92: When shipped by Faros Seafoods, Inc., Tacoma, Wash., the article contained decomposed fish and was unfit for food due to rancidity—402(a)(3).

DISPOSITION: A consent decree of condemnation authorized release of the article to the dealer for destruction, since the article consisted of decomposed and rancid fish, commingled with good fish, rendering the totality of the article unfit for food. (F.D.C. No. 66483; S. No. 92-667-395 et al.; S.J. No. 3)

PRODUCTS: **Rice sticks, rice sheets, black bean garlic sauce, and Oriental-style noodles**, at Seattle, W. Dist. Wash.; Civil No. C-92-1296.

CHARGED 8-18-92: When imported, the articles (which had labels such as "Chantaboon Rice Stick . . . Royal Orchid . . . Packed for Seasia Seattle, WA . . . Product of Thailand," "Kim Tar Brand Emperor's Choice Co., Ltd. Rice Sheet . . . Product of Thailand," "Sun Luck Maifun Rice Sticks . . . Product of China," "Pangasinan . . . Salted Anchovies packed for: Newport Food and Seafood Co. . . LA, CA, USA . . . Product of the Philippines," and "Lee Kum Kee . . . Black Bean Garlic Sauce . . . Product of Hong Kong") contained human hair and/or bird, insect, rodent, or other filth—402(2)(B); and when imported an article labeled "Shirakiku Brand . . . Chuka Soba Japanese Style Alimentary Paste . . . Product of Japan" contained the artificial coloring yellow carotenoid color additive and the article's label failed to state that fact—403(k).

DISPOSITION: Default—ordered destroyed. (F.D.C. No. 66452; S. No. 92-667-308 et al.; S.J. No. 4)

Food/Economic and Labeling Violations

PRODUCT: **Lobster tails, frozen**, at Austin, Dist. Minn.; Civil No. 4-92-1086.

CHARGED 11-5-92: While held for sale, the articles labeled "Amies . . . Lobster Tails . . . 8 oz [or "5 oz"]" were short weight—403(e)(2).

DISPOSITION: Default—ordered constructively destroyed by delivering one case to FDA for use as a sample in a seafood inspection training course and by donating the remaining cases to a charitable institution. (F.D.C. No. 66631; S. No. 92-658-381/2; S.J. No. 5)

Animal Feed

PRODUCT: **Tuna chunks in water, canned**, at Norwich and North Syracuse, N. Dist. N.Y.; Civil No. 92-CV-441.

CHARGED 4-6-92: While held for sale, the article (which had been imported from Canada) contained decomposed tuna fish—402(a)(3);

the article was pet food which had been relabeled as human food—402(b)(3); and the article was offered for sale under the name of another food—403(b). (F.D.C. Nos. 66396 & 66400; S. No. 92-543-696 et al.; S.J. No. 6)

Drugs/Human Use

PRODUCT: Herbal capsules, at Vernon, C. Dist., Calif.; Civil No. 92-6405-WMB(Tx).

CHARGED 10-26-92: While held by Continental Vitamin Co., Inc. (t/a CVC Specialties), Vernon, Calif., which was distributing the article labeled “Pep ’n Energy . . . The Natural Energizer 3 Capsules . . . CVC . . . Los Angeles, CA.” with display holders reading: “Are you tired? You need Pep ’n Energy . . . physical activity and mental alertness,” the article was a new drug without an effective approved New Drug Application—505(a); the labeling of the article lacked adequate directions for use, and was not exempt due to its new drug status—502(f)(1); and the article had not been submitted for inclusion in a required list of drugs and was processed in an unregistered establishment—502(o).

DISPOSITION: Default—ordered destruction. (F.D.C. No. 66498; S. No. 92-683-392; S.J. No. 7)

PRODUCT: Oxygen, U.S.P., in cylinders, at Hicksville, E. Dist. N.Y.; Civil No. 91-3140.

CHARGED 8-21-91: While held by Respiratory Care Group, Inc., Hicksville, N.Y., the circumstances used for the articles’ manufacture, processing, packing, and holding failed to conform with current good manufacturing practice—501(a)(2)(B).

DISPOSITION: Consent—authorized release to Puritan-Bennett Corp., Lenexa, Kan., for salvaging. (F.D.C. No. 66154; S. No. 91-600-657 et al.; S.J. No. 8)

Drugs/Veterinary Use

PRODUCT: Streptomycin sulfate for injection, oxytetracycline, lincomycin HCl, B.P., and other bulk drugs for veterinary use, at Rushville, C. Dist. Ill.; Civil Nos. 86-3201 and (upon appeal) 88-1233 & 88-614.

CHARGED 7-3-86: While held by Schuyler Laboratories, Rushville, Ill., the articles lacked adequate directions for use—502(f)(1); and a number of the articles (*e.g.*, the certifiable antibiotics penicillin, amoxicillin, ampicillin, oxytetracycline, streptomycin, and lincomycin HCl) were new animal drugs and no approval of a New Animal Drug Application was in effect—501(a)(5).

DISPOSITION: *District Court*—The articles were claimed by the dealer, who denied the charges. The government served written interrogatories and a request for admissions on the claimant; and the claimant served a request for the production of documents and several sets of interrogatories on the government. The parties filed cross-motions for summary judgment. The court ruled for the claimant, holding that the drugs were not misbranded because a portion of the exempting regulation was invalid as applied to the

articles, that the bulk-drug distributors did not have the burden of proving that the drugs they sell will be used in a legal manner by their customers, and that the certifiable antibiotic drugs did not require statutory approval because such drugs were not intended for animal use while in bulk form.

The government moved for reconsideration of the district court’s order granting the claimant summary judgment. The district court denied the government’s request for an oral hearing on the motion for reconsideration and concluded that only one issue (severance of 21 *CFR* 201.122) raised by the government had not been raised at the summary judgment stage. The court addressed only that one issue.

The government argued that invalidating part of the exempting regulation meant that all of such regulation must fall; and, accordingly, the seized drugs should be condemned because the seized drugs would not qualify under any exemption. However, since there is a presumption in favor of severability if what remains is operative as law, and since the court believed that FDA would prefer a regulation after severance of the limitation to no regulation at all and severing the regulation clearly fulfilled the legislative intent of the statute, the district court denied the motion for reconsideration. The government, in order to retain the *status quo* pending appeal, applied for a stay of the district court’s orders, which otherwise would effect release of the articles to the claimant. The stay was granted and the government perfected its appeal.

Court of Appeals—Upon appeal, the American Food Animal Veterinary Medical Association filed an *amicus curiae* brief in support of the claimant’s position, and the American Feed Industry Association filed an *amicus curiae* brief in support of the government’s position. The Court of Appeals found in favor of the government and reversed the order of the district court. The Court of Appeals noted that obtaining approval of a new animal drug or feed took a long time and cost a lot of money, that few new animal drugs had been approved, and that for a number of significant animal diseases there were no effective FDA approved drugs.

In this case, the claimant was a middleman who purchased unblended ingredients from the manufacturer and resold such drugs, still in bulk, to veterinarians who would mix and administer finished drugs as professional judgment dictated. As the district court had seen things, the FDA limits on the permission to sell unlabeled bulk drugs were neither necessary nor prudent for three reasons: 1) Congress wanted to leave medical professionals free to practice as their judgment required; 2) veterinarians were not regulated in compounding drugs, implying liberty to obtain drugs to compound; and 3) the middleman could not know whether his customer had the necessary approval.

However, the Court of Appeals noted that no individual veterinarian would possess complete knowledge of the efficacy of a novel drug compound—let alone its persistence in the food chain. One needed only think of the complexities of DES litigation if courts had to trace drugs back through the food chain to find their sources. Some of the claimant’s bulk drugs were dimetridazole and nitrofurans, both of which had been found to cause cancer in animals and, inferentially, to pose a risk in humans.

[REDACTED]

The exclusion of veterinarians by Congress from several features of the regulatory system was found to mean that veterinarians might use—in compounding prescription drugs for their private practice—whatever bulk drugs they might lawfully purchase; but this did not guarantee that any particular drug would be available lawfully.

As to the middleman's claim that it was impossible to tell what would become of the bulk drugs, the Court of Appeals noted that the seller need only ask the buyer what use lies in store. Here it had been stipulated that all of the middleman's sales were to veterinarians and that no veterinarians held an approved New Animal Drug Application for any drug.

The Court of Appeals concluded as follows: that the statute essentially forbids the sale, in any form, of any drugs formulated or put to new uses after 1935, without the approval of FDA; that the claimant had not offered to show that FDA had approved the formulations and uses its customers would make of its bulk drugs; that the claimant did not come within the regulatory exemption; and that the 52 lots of seized bulk drugs were mislabeled under 502(f) and were forfeit. Subsequently, the claimant petitioned for a rehearing, but the petition was denied.

Supreme Court of the United States—The claimant filed a petition for a writ of *certiorari*. The Humane Society of the United States, Washington, D.C., upon consent of the parties, filed a brief as *amicus curiae*, in support of the petition.

Following denial of the petition for *certiorari*, a consent decree of condemnation ordered the articles destroyed. However, the district court stayed the order because the decree had been entered under the signature of an attorney who had not appeared in the case. Upon review of the filing, the district court was satisfied that the situation arose from an oversight, and another consent decree of condemnation and destruction was submitted and entered. (F.D.C. No. 64840; S. No. 85-481-445 et al.; S.J. No. 9)

CRIMINAL ACTIONS

DEFENDANT: **Tim R. Alexander**, manager of a plasmapheresis center, Las Cruces, Dist. N. Mex.; Criminal No. 89-300.

CHARGED 10-24-89: *One count*—causing the shipment in interstate commerce of adulterated and misbranded blood plasma—301(a).

DISPOSITION: Plea of guilty; sentenced to imprisonment for one year, suspended, and placed on probation for three years. (F.D.C. Misc. No. 871; S. No. 86-467-134 et al.; S.J. No. 10)

DEFENDANTS: **El Paseo Plasma, Inc.**, and **Gary D. Mays**, responsible head and part owner, Las Cruces, Dist. N. Mex.; Criminal No. 89-300-JP.

CHARGED 7-18-89 by grand jury: *Count 1*—Conspiracy with others to cover up material facts, make false statements, and impede inspection by FDA in connection with specified records and incidents involving the firm's plasmapheresis operations—18 U.S.C. 371; and *Counts 2-5*—false records were made and used (*i.e.*, false

entries concerning donor screening, false whole blood logs not accurately recording the weight of bags of whole blood taken from donors, false records to cover up a wrong red blood cell infusion, and false donor record files to conceal occasions of misconnections for infusion of a donor with the red blood cells of another donor)—18 U.S.C. 1001.

CHARGED 10-11-89 in separate criminal informations: *Two-count information* charging only the individual with causing shipments in interstate commerce of adulterated and misbranded blood plasma; and *three-count information* charging only the firm with causing shipments in interstate commerce of adulterated and misbranded blood plasma—301(a).

DISPOSITION: After the firm entered into a plea agreement to plead no contest to the three-count criminal information and have the indictment dismissed, the firm was fined \$7,125 and placed on probation for three years. All counts of the indictment of 7-18-89, except count 1, were agreed to be dismissed upon the individual's plea of guilty; and the individual also agreed to plead to the violations charged in the two-count criminal information of 10-11-89. The individual was sentenced to imprisonment for five years with the sentence suspended, except for six months to be served, and was placed on probation for five years. (F.D.C. No. Misc 871; S. No. 86-467-134 et al.; S.J. No. 11)

DEFENDANT: **William A. Patten**, assistant manager of a plasmapheresis center, Las Cruces, Dist. N. Mex.; Criminal No. 89-300.

CHARGED 10-24-89: *Two counts*—causing the shipment into interstate commerce of adulterated and misbranded blood plasma—301(a).

DISPOSITION: Plea of guilty; sentenced to imprisonment for two years, suspended, and placed on probation for three years. (Misc. No. 871; S. No. 86-467-134 et al.; S.J. No. 12)

INJUNCTION ACTIONS

DEFENDANTS: **Algon Chemical Inc.**, and **Edward Lainsky**, president, Haworth, Dist. N.J.; Civil Nos. 87-1820(JWB) and (upon appeal) 88-5478.

CHARGED 5-12-87 in a complaint for injunction: That the defendants received, sold and distributed in interstate commerce various articles of drug (*e.g.*, 13 lots of drugs stored for the defendants at Garfield, N.J.) intended for animal use. The defendants' Garfield, N.J., drugs (five lots of dimetridazole, two lots each of levamisole and nitrofurazone, and one lot each of penicillin, sulfamethoxazole, lidocaine, and oxytetracycline) were bulk drugs intended for further processing. The Garfield, N.J., drugs were under state embargo at the request of FDA; but, prior to the embargo, portions of such lots had been shipped in interstate commerce to distributors of veterinary drugs and veterinarians, and most of the remaining lots of the drugs had been ordered to be shipped to a distributor in Illinois. The labeling of all of the embargoed drugs lacked adequate directions for use (since there were no such directions on the labeling), and the

articles were not exempt from such requirements—502(f)(1). In addition, the embargoed penicillin was a new animal drug, and no approval of a New Animal Drug Application was in effect with respect to the use and intended use of such drug—501(a)(5). The defendants had been made aware that their activities were in violation of the law, and the government was informed and believed that violations would continue unless the defendants were restrained by the court.

DISPOSITION: District Court—The court issued an order to show cause why a preliminary injunction should not be entered enjoining the defendants. After oral argument, the court, finding no material issue of fact, dismissed the government's application for a preliminary injunction and *sua sponte* ordered the parties to file cross-motions for summary judgment. The district court said that it was unreasonable to require Algon to show that either the finished product is not a new drug, or, if it is a new drug, to show that a New Animal Drug Application has been secured by the veterinarian receiving the bulk drug. Therefore, the exempting regulation for bulk drugs (21 *CFR* 201.122) placed on Algon an impossible burden of demonstrating that the exemption applied to its bulk drugs and the exceptions to the basic exemption are not consistent with the statute. In order to give a reasonable meaning to the exempting regulation, the district court found that only that portion of the regulation that exempted bulk drugs from the labeling requirements of 502(f)(1) applied to bulk drugs supplied for use in the practice of veterinary medicine. The court also concluded that the new animal drug provisions did not apply to the embargoed lot of penicillin. Accordingly, the court granted the defendants' motion for summary judgment. The government appealed.

Court of Appeals—Upon appeal, Algon argued that, since Congress anticipated that veterinarians would be able to compound drugs in the course of their practice, Congress must have intended that veterinarians would have access to the bulk drugs necessary to do the compounding. However, the Court of Appeals believed that Algon misread the intent of Congress because Congress intended to authorize compounding with legally required drugs and not to create an exception to the statute's pre-market approval process. In addition, the record indicated that Algon's customers were not being deprived of their ability to compound drugs, since veterinarians might use in compounding of prescriptions for their private practice whatever bulk drugs or other pharmaceuticals they might lawfully purchase. Although Congress could have made clear that bulk drugs sold to medical practitioners were exempt from the statute's coverage, there is no such blanket exemption. The legislative history shows neither that bulk drugs purchased by veterinarians for compounding in the course of their professional practice are excluded from the statute's labeling requirements, nor that FDA's limitation

of the bulk drugs exception to holders of approved NADAs was inconsistent with the purpose of the statute.

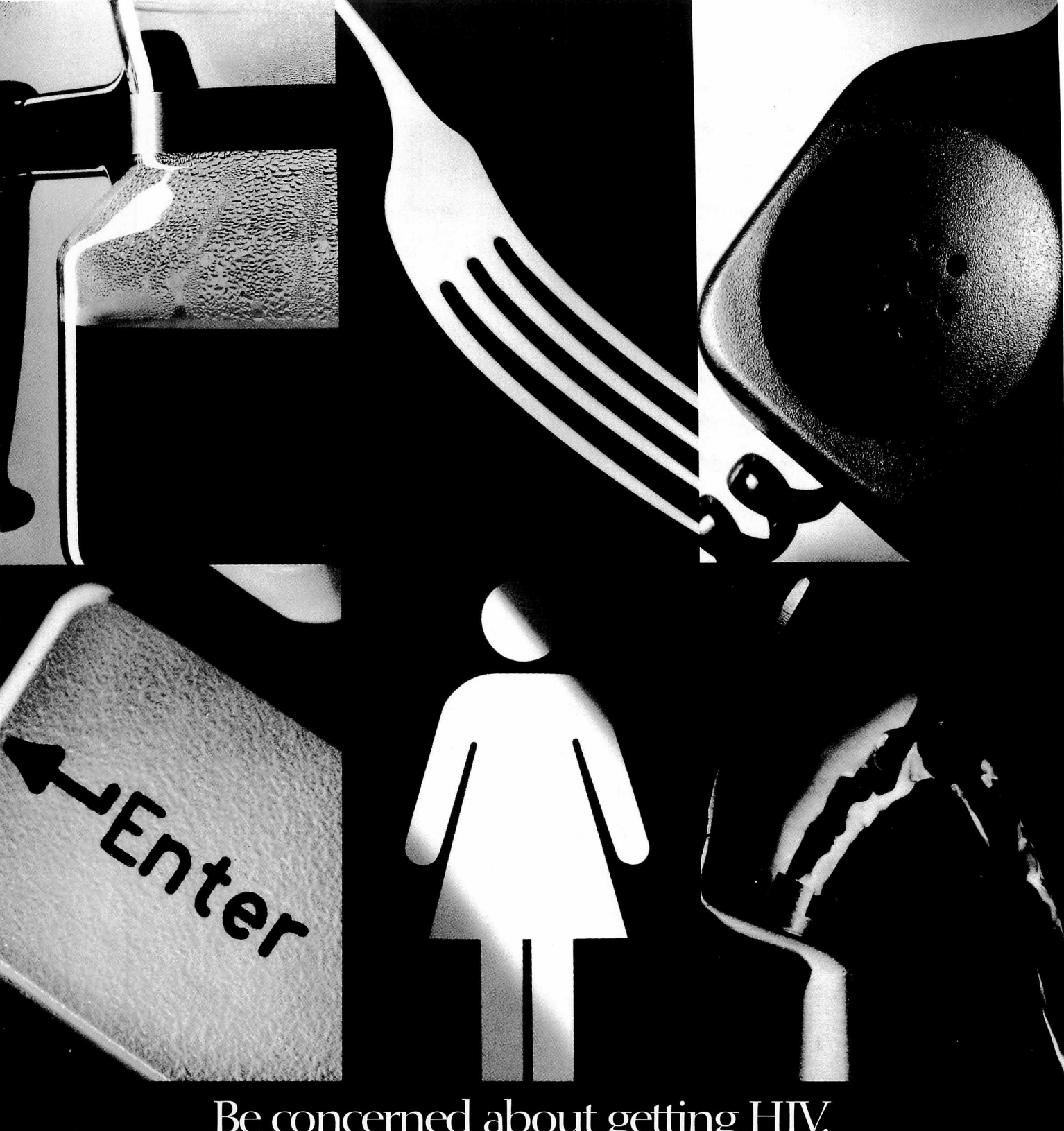
The court noted that none of the affidavits submitted by Algon for the purpose of summary judgment even suggested that bulk drugs were "*necessary* for the practice of veterinarian medicine, as opposed to merely *preferred* as the cheaper or simpler alternative to compounding with finished-form drugs." The only real objection to the government's actions in this case appeared to be an economic one; but FDA's action effecting an increase in cost of drugs to practitioners did not undermine the practice or treatment decisions of veterinarians. Accordingly, the judgment of the district court was reversed and remanded. Accordingly, the defendants were enjoined from the complained-of violations. (F.D.C. No. 65112; S. No. 86-332-443 et al.; S.J. No. 13)

DEFENDANTS: Larson Laboratories, Inc. (t/a Larson Pharmaceuticals), and Arthur Z. Berenstein, president, Erie, W. Dist. Pa.; Civil No. 88-288-Erie.

CHARGED 11-3-88 in a complaint for injunction: That the defendants manufactured, processed, packed, held for sale, and distributed various interstate drugs, such as Podiodine Solution (povidone-iodine topical solution, U.S.P.) and Podiodine Surgical Scrub (povidone-iodine cleansing solution, U.S.P.); that the strength, quality or purity of such named drugs differed from the U.S.P. standards—501(b); that a certain substance had been mixed with the defendants' Podiodine Solution so as to reduce its quality or strength or a that certain substance had been substituted in part for the article—501(d); and that the circumstances used for the manufacture, processing, packing, holding, and distribution of the defendants' drugs failed to conform with current good manufacturing practice—501(a)(2)(B).

The defendants were well aware that their conduct was in violation of the law. FDA inspections had revealed that the firm was not manufacturing drugs in conformity with current good manufacturing practice, and FDA analyses revealed that sampled drugs were subpotent. Instances of other problems were also detailed, and the government believed that, unless restrained by the court, the defendants would continue to violate the law.

DISPOSITION: A consent decree of permanent injunction was entered that enjoined the complained-of violations. In addition, the defendants were enjoined from operations involving interstate drugs unless and until a number of conditions were met, including the following: that current good manufacturing practice was established; that an expert certified that specified requirements had been met; and that all stocks of drugs on hand had been tested and, as necessary, should be destroyed or brought into compliance. (Inj. No. 1198; S. No. 88-437-901 et al.; S.J. No. 14)



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