

# FDA *Consumer*

The Magazine of the U.S. Food and Drug Administration

September–October 2003 • Vol. 37 No. 5



**REVEALING  
TRANS FATS**







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*FDA Consumer* (ISSN 0362-1332) is published bimonthly by the Food and Drug Administration (HFI-40), 5600 Fishers Lane, Rockville, MD 20857, U.S. Public Health Service, Department of Health and Human Services.

#### Editorial Matters

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# U.S. Department Of Health And Human Services

# FDA Consumer

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◀ **Inside Cover:** A new FDA regulation designed to make generic drugs more accessible took effect on Aug. 18, 2003. For more on this story, see page 12.



## OBSERVATIONS

Until recently, about the only way you could determine if artery-clogging *trans* fats were part of your diet was to look carefully at the ingredient list on the food package. If the words "hydrogenated" or "partially hydrogenated" were among the ingredients, *trans* fat was part of your diet.

Most *trans* fats in food are formed when oils are put through a process called hydrogenation. The chemical makeup of fatty acids is altered during hydrogenation, and hydrogenated liquid oils act more like their saturated fat counterparts.

Hydrogenated oils last longer without turning rancid, and can be used to make products such as shortenings and hard stick margarine.

Unfortunately, hydrogenation has a downside.

Research done over the past decade has indicated that *trans* fat acts much like saturated fat in the cardiovascular system. It raises low-density lipoprotein (LDL) cholesterol, the "bad" kind of cholesterol, and lowers high-density lipoprotein (HDL) cholesterol, the "good" type of cholesterol.

In July, the FDA announced that it would begin requiring manufacturers to include the amount of *trans* fat in the labeling of their products. Under the labeling rule, the amount of *trans* fat contained in a food will be required to appear just under the amount of saturated fat on the Nutrition Facts



label. Some manufacturers are already providing this information voluntarily. For more on *trans* fat and the steps the FDA is taking to ensure that consumers can make healthy choices when it comes to their nutrition needs, see our cover story, "Revealing *Trans* Fats," beginning on page 20.

Generic drugs are copies of brand-name drugs and available in both prescription and over-the-counter forms. At roughly one-third the cost of brand-name medications, generics can mean big savings for consumers.

Generic medications must pass FDA review before they are marketed. And FDA experts say that generics have an important role to play in the health care arena. For more on generic medications and their impact on health care costs, see our feature story titled "Greater Access to Generic Drugs" on page 12.

Clinical trials—the testing of new products and treatments on people—are an integral part of new product development. The FDA requires such trials and reviews the results before approving new products for marketing. The FDA is committed to protecting those who participate in the trials, which often provide the answers on whether a potential treatment should be approved for wider use. For more on clinical trials and the safeguards in place to protect participants, see our feature story "Inside Clinical Trials: Testing Medical Products in People," beginning on page 30.

Ray Formanek Jr.  
Editor

## TO THE EDITOR

### Does Punishment Fit the Crime?

In prior issues of *FDA Consumer* you have illustrated the various investigations of lawbreakers your organization has undertaken, and the fines and sentences given to the perpetrators.

I have noticed there is usually quite a lag time between all these actions, and that the sentences given never seem to fit the severity of the crimes committed. One gets the impression that many of your efforts may have ended in futility for the time and expense involved.

Is there some way to speed up the process and get a better percentage of convictions?

I certainly in no way am impugning your efforts, which are greatly appreci-

ated by the public, only suggesting some way to improve your image.

Thank you for a very informative and well-designed publication. I would love to see your circulation improved dramatically.

Edward Kaplan  
West Palm Beach, Fla.

*A reply from the FDA's Office of Criminal Investigations:*

The federal criminal offenses investigated by special agents assigned to the FDA's Office of Criminal Investigations (OCI) are usually extremely complex and often occur in a number of judicial districts within the United States.

In addition, many cases have international aspects, which can further impact the OCI's ability to investigate and gather evidence. Ultimately, a U.S. Attorney with jurisdiction must review the evidence and present the case to a federal grand jury before a felony indictment can be brought. Then the defendants are brought before the District Court and the case proceeds in accordance with the Federal Rules of Criminal Procedure. All of this can take significant time depending on the circumstances in each case. ■

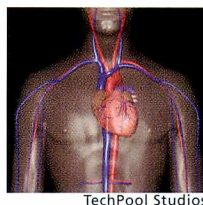


## Lower-Cost Defibrillator

A new, lower-cost heart device implanted into the chest of people at risk of dying from sudden cardiac arrest has been approved by the FDA. The Cardiac Airbag implantable cardioverter defibrillator (ICD) system from Biotronik of Lake Oswego, Ore., monitors the heart's function and automatically delivers an electrical shock when needed to restore normal heart rhythms.

The Biotronik defibrillator has fewer features than other ICDs on the market. It is priced at \$10,000—about half the price of standard ICDs—and is easier to program and use than stan-

dard models. The device provides high-energy shock therapy, but does not use lower-energy pacing therapies, which are sometimes used to bring the heart back into normal rhythm. The FDA approved the Cardiac Airbag ICD in May, about two months after the firm submitted its marketing application. The agency is requiring that Biotronik conduct a two-year post-approval study of the 370 people in whom the device is implanted.



TechPool Studios

## AstraZeneca to Pay \$355 Million Fine

AstraZeneca Pharmaceuticals LP of Wilmington, Del., has agreed to pay a \$355 million fine to resolve criminal charges and civil liabilities stemming from an illegal marketing and pricing scheme involving a drug to treat prostate cancer. The massive conspiracy involving the drug Zoladex (goserelin acetate) caused multimillion-dollar losses for federally and state-funded insurance programs and patients.

The FDA's Office of Criminal Investigations (OCI) discovered that AstraZeneca employees were using illegal methods to stimulate the demand for Zoladex by enabling physicians to reap illicit profits.

In one of these schemes, AstraZeneca provided thousands of free samples to physicians, knowing they would charge their patients and insurance programs for them. Another illegal inducement used by the firm involved inflating the price of Zoladex reported to Medicare as the basis for reimbursement, while deeply discounting the actual price charged to physicians. AstraZeneca also misreported and underpaid the Medicaid rebates it owed to the states for the use of Zoladex.

"FDA will not tolerate criminal conduct that exploits patients, plunders the national treasury, and adds to the cost of health care," says FDA Commissioner Mark B. McClellan, M.D., Ph.D. The FDA's OCI was joined by representatives of the U.S. Attorney's Office for the District of Delaware, the Department of Health and Human Services, and the Defense Criminal Investigative Service in announcing the guilty plea in June. The Federal Bureau of Investigation was also involved with the case.

The investigation resulted in charges against three physicians of conspiring with AstraZeneca to bill patients and third-party payers for free Zoladex samples.

## Preventing Monkeypox

Health and Human Services Secretary Tommy G. Thompson has ordered a halt to the importation of all rodents from Africa due to their potential to spread monkeypox to other animals and humans. Monkeypox is a rare viral disease found mainly in central and western Africa. June 2003 marked the first monkeypox outbreak in the United States, according to the Centers for

Disease Control and Prevention (CDC). Most of the people got sick after having contact with pet prairie dogs that had monkeypox.

In addition to the ban, announced June 11, 2003, Thompson also stopped the distribution, sale, and transport within the United States of prairie dogs and six specific African rodent species implicated in the monkeypox outbreak: tree squirrels, rope squirrels, dormice, Gambian giant pouched rats,



USDA

brush-tailed porcupines, and striped mice.

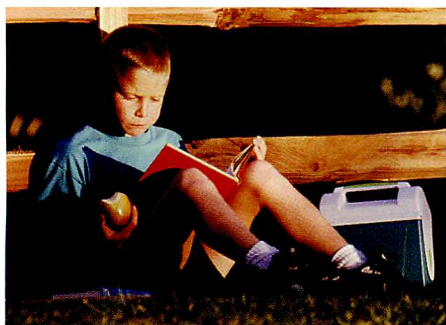
The ban does not apply to people who transport the listed animals to veterinarians, animal control officials, or other entities recommended by federal, state, or local government authorities.

HHS also is advising that people who acquired an animal named in the ban since April 15 should carefully monitor their health and the health of the animal. People showing symptoms such as a rash with a fever, cough, or aches should immediately contact a physician. If an animal becomes ill, immediately contact a veterinarian, contain the animal in an appropriate carrier, and transport it to the veterinarian without other people or pets in the vehicle. Under no circumstances should such animals be intentionally released into the wild.

For more information on monkeypox from the CDC, see [www.cdc.gov/ncidod/monkeypox/](http://www.cdc.gov/ncidod/monkeypox/).



## Concerns About Paxil for Children



Photodisc

After reviewing reports of a possible increased risk of suicidal thinking in children being treated with the antidepressant Paxil (paroxetine), the FDA is recommending that Paxil not be used in children and adolescents for the treatment of major depressive disorder (MDD). Currently, there is no evidence that Paxil is effective in children or adolescents with MDD, and the antidepressant is not approved for such use.

sant is not approved for such use.

Paxil is approved for use in adults for the treatment of obsessive-compulsive disorder, MDD, panic disorder, social anxiety disorder, generalized anxiety disorder, and post-traumatic stress disorder. There is no evidence that Paxil is associated with an increased risk of suicidal thinking in adults.

Despite the new possible safety concerns about children and Paxil, the FDA advises that caretakers of children already receiving treatment with Paxil for MDD talk to their doctors before stopping use of the drug. Patients should not discontinue using Paxil without first consulting their physicians, and it is important that Paxil not be abruptly discontinued.

More information about these concerns is available at [www.fda.gov/cder/drug/infopage/paxil/](http://www.fda.gov/cder/drug/infopage/paxil/).

## Deceptive Marketing Practices for Dietary Supplements Halted

The Federal Trade Commission (FTC) has charged two dietary supplement marketers and their companies with making false and unsubstantiated health and medical claims. This enforcement action is part of a series of initiatives by the FDA and the FTC to cut down on deceptive marketing.

Kevin Trudeau and Robert Barefoot, the marketers of Coral Calcium Supreme Dietary Supplement, violated the FTC Act by claiming, falsely and without substantiation, that the supplement can treat or cure cancer and other diseases, investigators say. In a separate action, the FTC charged Trudeau with violating a previous court order by claiming that a pain-relief product called Biotape provides significant or permanent relief from severe pain.

The FDA and the FTC are sending strong warning letters to Web site operators who are marketing coral calcium products and claiming it is an effective treatment or cure, notifying them that they will take legal action against violators. Neither agency is aware of any reliable scientific evidence supporting the marketers' claims.

## CORRECTION

The chart on page 32 of the July–August issue contained erroneous information concerning when problems with medical devices need to be reported. Here is the corrected version.

Summary of FDA's Medical Device Reporting Requirements				
	Within 5 days	Within 10 days	Within 30 days	Annually
User Facility		Deaths (also report to manufacturer) Serious injuries (report to manufacturer or FDA if manufacturer unknown)		Summary of reported deaths and serious injuries to FDA (January 1)
Importer			Deaths and serious injuries to FDA and manufacturer Malfunctions (report to manufacturer or FDA if manufacturer unknown)	
Manufacturer	5-day report on events requiring immediate remedial action and other designated events		30-day report of deaths, serious injuries and malfunctions Baseline report to provide specific data on each reported device	

Source: FDA Center for Devices and Radiological Health

## First Once-Daily Protease Inhibitor

A protease inhibitor formulated to be taken once a day has been approved by the FDA. Reyataz (atazanavir sulfate) is to be used in combination with other anti-retroviral agents for the treatment of patients with HIV infection. As with other anti-retroviral agents, Reyataz does not cure and does not prevent transmission of HIV infection or AIDS.

Protease inhibitors work at the final stages of viral replication and attempt to prevent HIV from making new copies of itself by interfering with the HIV protease enzyme. Currently there are six other protease inhibitors approved by the FDA for the treatment of HIV infection.

Reyataz is manufactured by Bristol-Myers Squibb Co. of Princeton, N.J.



## First Biologic for Allergy-Related Asthma

People with allergy-related asthma now have a bioengineered treatment option.

Asthma caused by allergies results from the immune system's over-reaction to inhaled allergens such as dust mites or animal dander. The body forms antibodies in response to the allergen, and this immune system reaction prompts inflammation that causes airway narrowing and other symptoms. Xolair (omalizumab) is a genetically engineered protein that blocks this immune response. The treatment, given as an injection under the skin, gained FDA approval in June.

Only people who have asthma caused by allergies can benefit from this treatment. The product's labeling indicates that this type of asthma should be established by skin or blood test before treatment. Xolair has been shown to be safe and effective in people ages 12 and older who have moderate to severe allergy-related asthma that hasn't been adequately controlled with inhaled steroid treatments. Xolair is a second-line treatment, recommended only after the first-line treatments have failed. The drug has been shown to decrease the number of episodes of airway narrowing that result in wheezing, breathlessness, and coughing.

In clinical trials of more than 1,000 adolescents and adults, about 85 percent of patients had no exacerbation of their symptoms, compared with about 75 percent of patients treated with a placebo. More patients treated with Xolair developed a new or recurrent cancer (0.5 percent) compared to control patients (0.2 percent). Long-term studies will investigate whether there is a relationship between Xolair treatment and cancer. The other major safety concern identified in clinical trials was severe allergic reaction (anaphylaxis).

Xolair is manufactured by Genentech Inc. of South San Francisco, Calif. Genentech will jointly market the product with Novartis Pharmaceuticals Corp. of East Hanover, N.J.

## Combination Diabetes Device

A new device for diabetes that combines a glucose meter and an insulin pump with a dose calculator could be the first step in the development of a fully automated glucose monitoring and insulin delivery system. The device, which is made by Medtronic MiniMed Inc. of Northridge, Calif., and Becton, Dickinson, and Co. (BD) of Franklin Lakes, N.J., was cleared by the FDA in July.

The product combines the Medtronic MiniMed Paradigm insulin pump with a BD glucose monitor. It has circuitry and software modifications that allow it to transmit glucose values to the insulin pump and to transfer data between the insulin pump and a personal computer running the appropriate Medtronic MiniMed communications software.

Because the glucose meter calculates and transmits information to the insulin pump automatically, it prevents the errors that sometimes can result when people input this data manually. Use of the integrated system is expected to make it more convenient for people to manage their diabetes.

## Barr Laboratories Recalls Nortrel Contraceptive

Barr Laboratories voluntarily has recalled three lots of its Nortrel 7/7/7-28 day oral contraceptive (norethindrone and ethinyl estradiol tablets, USP) due to packaging errors that could lead to increased pregnancy risk. The recall involves lot numbers 290122001, 290122002, and 290122003, distributed between January and April 2003. Nortrel is a generic form of Ortho-Novum 7/7/7.

Nortrel 7/7/7-28 is packaged in a blister card containing four horizontal rows of seven tablets each. Colored tablets, which contain the active hormonal ingredients, should be in the first three rows. The fourth (bottom) row should contain the white tablets—placebos that contain no active

ingredient. Barr Laboratories reported that out of about 470,000 packages that are subject to the recall, it has received two reports in which tablets in the blister pack are reversed, causing the white placebo to be in the first row (for the first week) labeled "start" rather than in the last row labeled "Week 4." Also, the lot number and expiration date were not visible on the back of these two blister cards.

Any woman who has taken pills from a blister card with tablets in the wrong color sequence could be at increased risk of pregnancy, and changes to the menstrual cycle may occur. These could include delayed bleeding, irregular bleeding, or spotting.

For more information, call the Barr

Laboratories Inc. drug information line at 1-800-222-0190. Report any adverse reactions experienced with the use of this product to the FDA's MedWatch program by phone at 1-800-FDA-1088, by fax at 1-800-FDA-0178, by mail at MedWatch, FDA, 5600 Fishers Lane, Rockville, MD 20852-9787, or on the MedWatch Web site at [www.accessdata.fda.gov/scripts/medwatch/](http://www.accessdata.fda.gov/scripts/medwatch/). ■



## FDA Announces Initiative to Curb Counterfeit Drugs



FDA/Michael Ermarth

The FDA has announced a major new initiative to more aggressively protect consumers from counterfeit drugs. An internal task force will be created to explore the use of technologies, stronger enforcement, and other measures that will make counterfeiting more difficult. The FDA also plans to coordinate more closely with other

Although drug counterfeiting in the United States is relatively rare, the agency has recently seen an increase in counterfeiting activities. The FDA's counterfeit drug investigations have increased to more than 20 per year since 2000, after averaging only about 5 per year through the late 1990s.

The FDA believes the increase has occurred for a number of reasons, including more sophisticated counterfeiting technology, better organized criminal groups, the online sale of prescription drugs by unlicensed pharmacies and foreign Web sites, and weak spots in the domestic wholesale distribution chain.

Consumers can protect themselves from counterfeit drugs by purchasing medications from licensed domestic pharmacies, and by contacting their pharmacist or doctor if they notice anything unusual about their medication such as with packaging, taste, or unfamiliar side effects.

federal agencies, state and local governments, and members of Congress.

Commissioner of Food and Drugs Mark B. McClellan, M.D., Ph.D., says, "At the forefront of this effort will be the special agents of our Office of Criminal Investigations. Their record and dedication are impressive. Working together, I am confident we will defeat the criminal element engaged in counterfeit drug activity."

**We're eager to hear what you like and what you don't like. We also want to know the subjects you'd like to see covered.**

To contact *FDA Consumer*:

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**General FDA questions:** E-mail [webmail@oc.fda.gov](mailto:webmail@oc.fda.gov).

**Mailing address:** Food and Drug Administration (HFI-40), 5600 Fishers Lane, Rockville, MD 20857

## New Test Predicts Heart Risk

A new blood test will help doctors predict the risk of coronary heart disease (CHD), the No. 1 killer of men and women in the United States.

The FDA has cleared PLAC, a lab test that measures an enzyme called lipoprotein-associated phospholipase A2. This enzyme is made by a type of white blood cell called a macrophage. Macrophages make more of this enzyme and release it into the blood when a person has CHD.

The FDA cleared the test based on results of a study of more than 1,348 people. They were free of CHD at the start of the study and were followed for the development of disease for nine years. The greatest increased risk was found in subjects with the highest PLAC test results and LDL cholesterol levels lower than 130 mg/dL. The study was part of a large multicenter study sponsored by the National Heart, Lung, and Blood Institute.

The PLAC test is not a stand-alone test for predicting CHD. An elevated PLAC test result with an LDL cholesterol level of less than 130 mg/dL gives doctors increased confidence that patients have two to three times the risk of having CHD, compared with patients having lower PLAC test results. CHD, the most common form of heart disease, is caused by a narrowing of the coronary arteries that feed the heart. Each year, more than 500,000 Americans die of heart attacks caused by CHD.

The PLAC test is manufactured by diaDexus Inc. of San Francisco.



## Consumer Guide for Malaria Drug

A new medication guide provides better information to consumers about the risks and benefits of Lariam (mefloquine hydrochloride), a drug that helps to prevent malaria.

Janet Woodcock, M.D., director of the FDA's Center for Drug Evaluation and Research, says, "Lariam can work in certain areas where malaria is resistant to other drugs, and it offers several other advantages, including its once weekly dosing, the ability to use it in children, and the fact that it does not sensitize people to sunlight."

But in rare instances, Lariam has been associated with serious psychiatric problems. The Lariam medication guide instructs people who experience a sudden onset of certain adverse events—anxiety, depression, restlessness, or confusion—to contact a doctor or other health care provider because it may be necessary to stop tak-

ing Lariam and use another malaria prevention medicine. Sometimes these adverse events may persist even after stopping the medication. Rare reports have claimed that some Lariam users think about killing themselves. There have been rarer reports of suicides, but the FDA does not know if Lariam use was related to these suicides.

The medication guide highlights the risks of malaria and provides information on how to recognize psychiatric risks. It also gives other important facts, including how the drug should be taken and a list of the most common side effects, such as bad dreams, difficulty sleeping, nausea, and vomiting.

The FDA and Lariam's manufacturer, Roche Pharmaceuticals of Nutley, N.J., developed the medication guide, which should be given with each Lariam prescription filled.

## FDA Approves New Drug for Treatment of Erectile Dysfunction in Men

A second oral medication to treat impotence in men (erectile dysfunction) has been approved by the FDA. The drug, Levitra (vardenafil) acts by relaxing blood vessels and muscles in the penis, allowing increased blood flow into the penis to produce an erection.

Erectile dysfunction affects millions of men in the United States.

Levitra was evaluated in randomized, placebo-controlled trials involving more than 2,000 men with erectile dysfunction. In two of the trials, men had erectile dysfunction associated with diabetes mellitus or following radical prostatectomy for prostate cancer.

The drug's effectiveness was assessed using a sexual function questionnaire. In addition, patients were asked to report if they were able to achieve an erection adequate for intercourse and whether the erection was maintained to allow completion of intercourse. In all of the trials, Levitra improved patients' ability to achieve and maintain a penile erection.

The recommended dose is 10 milligrams taken 1 hour before sexual activity. A higher dose of 20 milligrams is available for patients whose response to the 10-milligram dose is not adequate. Two lower doses (2.5 mg and 5

mg) are also available and may be necessary for patients who are taking other medicines or have medical conditions that may decrease the body's ability to metabolize vardenafil. Levitra should not be used more than once a day.

Levitra should not be used with nitrates (such as nitroglycerin tablets or patches) or with alpha-blockers (medicines used to treat benign prostatic hyperplasia and/or high blood pressure such as tamsulosin, terazosin, doxazosin, and alfuzosin) because the combination may significantly lower blood pressure and lead to fainting in some men. Currently there is no information available to support the safety of even the lower doses of Levitra taken together with alpha-blockers. In addition, Levitra should not be used in patients who have a rare heart condition known as "prolongation of the QT interval" because of the possibility of producing abnormal heart rhythm.

Because some drugs may affect the metabolism of Levitra, patients should inform their doctors that they are taking Levitra and they should not begin taking new medicines without informing their doctor. For example, patients taking erythromycin should not take more than a 5-milligram dose of

Levitra. The maximum recommended dose for patients who are taking ritonavir is 2.5 milligrams of Levitra once every 72 hours.

Levitra should not be taken by men in whom sexual activity is inadvisable because of their underlying cardiovascular status (heart condition). Patients should inform their doctor about any heart problems they have experienced before taking Levitra.

Levitra is not recommended in patients who have suffered a heart attack or stroke within the last six months, or patients who have significantly low blood pressure, uncontrolled high blood pressure, unstable angina, severe liver impairment, end-stage renal disease requiring dialysis, or retinitis pigmentosa (an eye disorder).

The most common side effects reported in clinical trials included headache, flushing, rhinitis, and indigestion. Dizziness was reported in about 2 percent of patients. A small number of patients taking Levitra also reported abnormal vision.

Levitra is manufactured by Bayer Corporation in Germany and will be distributed by GlaxoSmithKline of Research Triangle Park, N.C. The drug is currently available in Europe. ■



## Severe Childhood ADHD May Predict Alcohol, Substance Use in Teen Years

Scientists tracking the progress of children diagnosed with attention-deficit/hyperactivity disorder (ADHD) as they became teen-agers have shed new light on the link between ADHD and the risk of developing alcohol and substance use problems. The researchers found that individuals with severe problems of inattention as children were more likely than their peers to report alcohol-related problems, a greater frequency of getting drunk, and heavier and earlier use of tobacco and other drugs.

The findings, published in the August issue of the *Journal of Abnormal Psychology*, indicate that childhood ADHD

with the National Institute on Drug Abuse, the National Institute of Mental Health, and the National Institute of Environmental Health Sciences, all components of the Department of Health and Human Services' National Institutes of Health.

Brooke Molina, Ph.D., at the University of Pittsburgh School of Medicine and University of Pittsburgh Medical Center, and William Pelham Jr., Ph.D., at the State University of New York at Buffalo conducted the research. The scientists recruited 142 teens between 13 and 18 years old who had received treatment for childhood ADHD an

once; however, the ADHD group was three times more likely to have tried some other illegal drug besides marijuana. The teens with childhood ADHD also reported having used tobacco and having tried an illegal drug other than marijuana at younger ages than their non-ADHD peers. Additionally, about 11 percent of the teens diagnosed with ADHD reported having used two or more different illegal drugs more often, compared with 3 percent of the control group.

The researchers analyzed distinctions within the ADHD group, focusing on responses from youngsters with more

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*ADHD is one of the most commonly diagnosed pediatric mental health disorders.*

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may be as important for the risk of later substance use problems as having a history of family members with alcoholism and other substance use disorders.

ADHD is one of the most commonly diagnosed pediatric mental health disorders. It occurs in 3 percent to 5 percent of school-age children. While previous research has indicated that ADHD together with a variety of other childhood behavior disorders may predispose children to drug, alcohol, and tobacco use earlier than children without ADHD, this study explores more closely specific aspects of that association.

"This is one of the first studies to focus on the severity of inattention problems in childhood ADHD as distinct from impulsivity and hyperactivity," says Ting-Kai Li, M.D., director of the National Institute on Alcohol Abuse and Alcoholism (NIAAA). "It demonstrates the usefulness of distinguishing ADHD's effects from the effects of childhood behavior disorders, such as aggression and defiance."

NIAAA supported the study together

with the National Institute on Drug Abuse, the National Institute of Mental Health, and the National Institute of Environmental Health Sciences, all components of the Department of Health and Human Services' National Institutes of Health.

Brooke Molina, Ph.D., at the University of Pittsburgh School of Medicine and University of Pittsburgh Medical Center, and William Pelham Jr., Ph.D., at the State University of New York at Buffalo conducted the research. The scientists recruited 142 teens between 13 and 18 years old who had received treatment for childhood ADHD an

average of 5 years earlier at the Attention Deficit Disorder Clinic at the University of Pittsburgh School of Medicine. The researchers interviewed the teens along with their parents and teachers.

The scientists also recruited a control group of 100 similar teens not diagnosed with childhood ADHD. They asked both groups about their alcohol and substance use, including whether they had ever tried a substance during their lifetime, how old they were when they first tried tobacco, alcohol, or drugs, and the type, frequency, and quantity of substances used during the past six months.

Both groups gave similar responses when asked if they had ever tried alcohol, cigarettes, or marijuana at least

once; however, the ADHD group was three times more likely to have tried some other illegal drug besides marijuana. The teens with childhood ADHD also reported having used tobacco and having tried an illegal drug other than marijuana at younger ages than their non-ADHD peers. Additionally, about 11 percent of the teens diagnosed with ADHD reported having used two or more different illegal drugs more often, compared with 3 percent of the control group.

The researchers analyzed distinctions within the ADHD group, focusing on responses from youngsters with more severe symptoms of inattention in childhood, something not routinely done previously.

The researchers found that the teenagers who reported more frequent episodes of drunkenness, higher alcohol problem scores, and a greater likelihood of substance abuse were those diagnosed with more severe inattention problems in childhood. The youngsters with severe inattention were about 5 times more likely than others to use an illegal drug other than alcohol and marijuana at an early age.

Although impulsivity-hyperactivity was not associated with teenage substance abuse, the authors say that better measurement of this behavior in future studies will be important. "The presence of ADHD during childhood appears to be as strong a risk factor for substance use and abuse as having a positive family history of substance use disorder. It is not specific to only one substance but cuts across alcohol, marijuana, and other drugs," says Molina. ■



# HHS, FDA Implement Food Security Research Program

A new \$5 million research program will help the Food and Drug Administration develop technologies and strategies to minimize potential threats to the safety and security of the nation's food supply.

"Americans need to feel secure that the food they eat is safe and healthy," Health and Human Services Secretary Tommy G. Thompson said in announcing the program in July. "We are investing unprecedented time, energy and resources to make sure the food that goes from our nation's ports and food facilities to our families' dinner tables is safe."

Announcement of the research program coincided with the release of an FDA report highlighting the progress made toward enhancing the safety and security of the roughly 80 percent of the nation's food supply under its jurisdiction.

The new report, submitted to Thompson by FDA Commissioner Mark B. McClellan, M.D., Ph.D., discusses the agency's progress in making the food supply more secure in 10 critical areas.

For example, during fiscal year 2003, the FDA has done five times the number of imported food examinations it conducted during fiscal year 2001—62,000 inspections completed so far this year, compared with 12,000 in all of fiscal 2001.

The increase in inspections reflects a steep increase in the number of U.S. ports of entry with FDA staff, from 40 to 90. Also figuring into the increase were the FDA's intense efforts during a period of heightened security alert earlier this year, and collaboration with other government agencies to protect the food supply more efficiently.

This progress stems in large measure from the \$96 million increase in the agency's food-security budget during fiscal years 2002 and 2003. The additional resources allowed the FDA to hire 655 new field personnel that work almost ex-

## FDA's 10-Point Food Security Program

1. **Build a Stronger FDA:** Hire and train skilled scientific, investigational staff
2. **Strategic Approach to Imports:** Increase coverage and gain flexibility to monitor imported foods
3. **Implement the Bioterrorism Act:** Institute rules for efficient monitoring of domestic, imported foods
4. **Preventive Measures:** Guidance to improve industry's threat awareness and prevention
5. **Vulnerability and Threat Assessments:** Focus resources, priorities on greatest risks

6. **Operation Liberty Shield:** Respond to heightened threat with greater surveillance, intergovernmental cooperation

7. **Emergency Preparedness and Response:** Crisis management and planning

8. **Laboratory Enhancements:** Develop analytical methods and response network

9. **Research:** Develop detection, prevention, and intervention technologies

10. **Foster Interagency Communication and Collaboration:** Increase cooperation with federal, state and local governments. ■

clusively on food security and food safety.

"We will continue to maximize our efforts to give Americans the most protection possible from deliberate or accidental food risks," McClellan says. "That includes not only using the best ideas that science has to offer, but seeking out still better ideas and methods."

The \$5 million in new research funding is being made available from a post-9/11 emergency response fund, allocated by the Office of Management and Budget. The FDA will use the money for food security research, including efforts to develop new technologies and to improve the ability to detect contamination of foods by chemical, biological and radiological agents.

The FDA's strategy focuses on improvements in five key areas:

- **Awareness**—Developing increased awareness among federal, state, local

and tribal governments and the private sector by collecting, analyzing and disseminating information and knowledge to reduce vulnerabilities

- **Prevention**—Developing capacity for rapid identification of a specific threat or attack on the food supply if one occurs

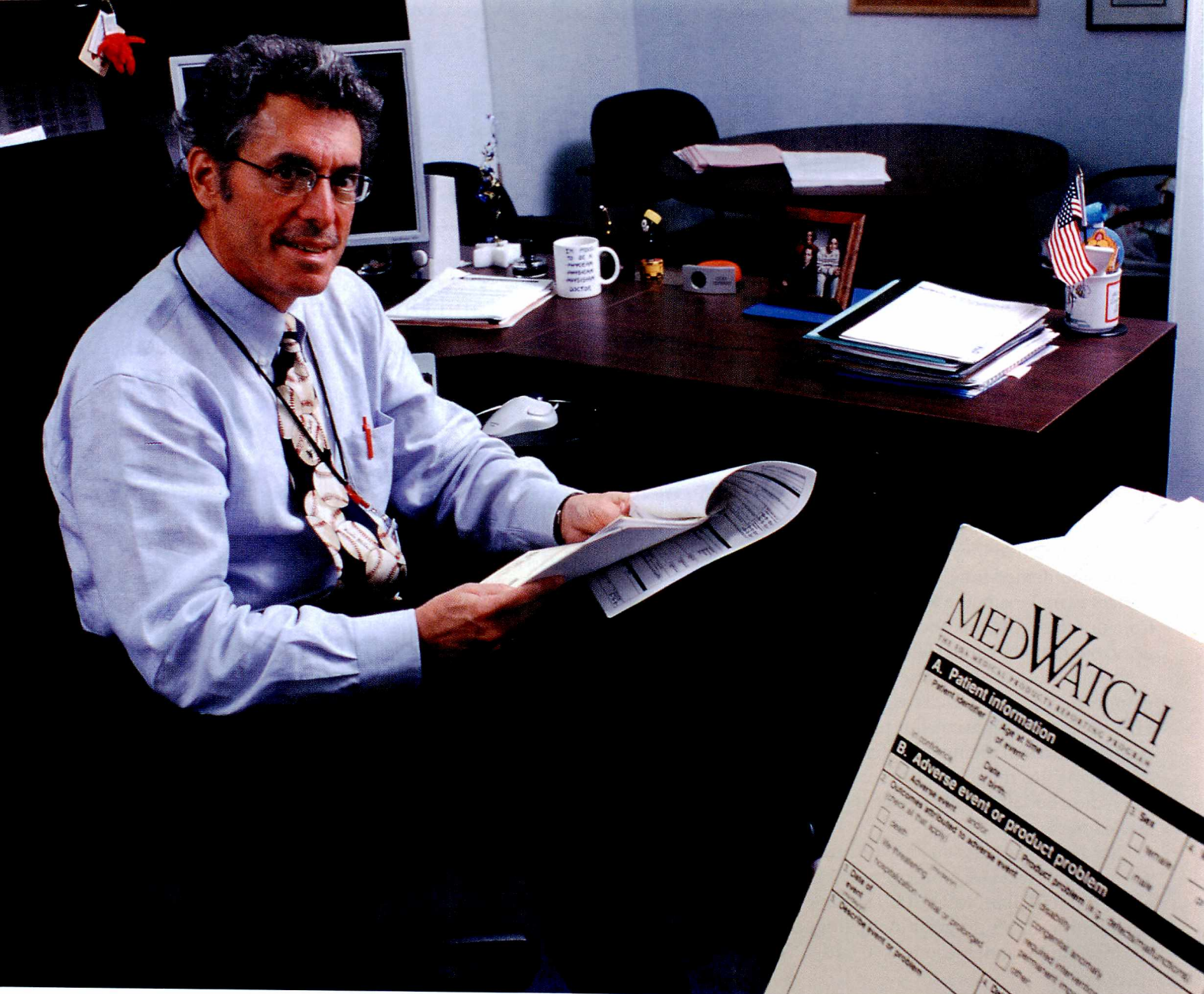
- **Preparedness**—Developing effective protection strategies to "shield" the food supply from terrorist threats

- **Response**—Developing capacity for rapid, coordinated response to a foodborne terrorist attack, including "surge capacity" and the ability to contain the attack quickly

- **Recovery**—Developing capacity for rapid, coordinated recovery from a foodborne terrorist attack.

The full progress report is at [www.fda.gov/oc/initiatives/foodsecurity/](http://www.fda.gov/oc/initiatives/foodsecurity/). ■





Black Star/Dennis Brack

**Norman Marks, M.D., director of the FDA's MedWatch program, reviews voluntary reports of adverse events and product quality problems.**

*By Michelle Meadows*

**W**hen the Food and Drug Administration approves a medical product, it means the agency has determined that the benefits of the product outweigh the risks. "But every product the FDA approves carries some risk," says Norman Marks, M.D., director of the FDA's MedWatch program. "And sometimes there are risks that only come to light after a product gets on the market and is used in larger numbers of patients who differ from those studied before approval. They may differ in the complexity of their health

problems or other medications that they use, for example."

That's where MedWatch comes in.

MedWatch, the FDA's safety information and adverse event reporting program, plays a critical role in the agency's postmarketing surveillance—the process of following the safety profile of medical products after they've begun to be used by consumers. Through MedWatch, a voluntary program, health professionals report serious adverse reactions and problems related to drugs, biologics, medical devices, dietary supplements, cosmetics, and infant formulas.

"Consumers can also send in reports, but we encourage them to work with a health professional to submit because we'll get a much richer report," Marks says. "Health professionals have clinical information that will help us better evaluate the report."

Marks adds, "What we mean by 'serious' adverse reactions is death and disability, life-threatening problems, hospitalization, congenital anomalies, and other problems that aren't listed on the label as known side effects." MedWatch also accepts reports of product quality problems with drugs or devices, suspected product tampering or counter-



# MedWatch:

## Managing Risks at the FDA

feit drugs, medication errors due to packaging problems or name confusion, and any other unexpected problems with the product that could pose a safety risk.

Once the FDA receives early signals of possible safety issues, the agency can rapidly identify problems and take appropriate actions, including broadcasting new safety information as "MedWatch alerts."

MedWatch alerts in 2003 include:

- **Viga Tablets:** The FDA announced a voluntary recall of Viga tablets by Best Life International of Clarkston, Wash. The tablets were sold as a dietary supplement with claims to increase sexual performance. The FDA warned consumers against using the product, which was found to contain the prescription drug sildenafil, even though the ingredient is not listed on the drug's label. Sildenafil is the active ingredient contained in Viagra, a drug available by prescription for treatment of erectile dysfunction. People who are taking nitrates for heart disease should not take sildenafil. An unsuspecting user of Viga tablets could develop life-threatening lowering of blood pressure.
- **Gynecare Intergel Adhesion Prevention Solution:** Gynecare Worldwide, a division of Ethicon Inc. of Somerville, N.J., voluntarily withdrew this product and urged customers to immediately stop using the device. The product is intended to be used in gynecological surgery to reduce post-surgical adhesions. There were postmarket reports of several serious problems, including postoperative pain and the need for repeat surgeries.
- **Risperdal (risperidone):** Janssen Pharmaceutica Products L.P. of Titusville, N.J., announced important changes to Risperdal (risperidone), a treatment for schizophrenia. The labeling was updated to include a warning of cerebrovascular problems, including

stroke, in elderly people with dementia. The update is based on data from four clinical trials. The company also reminded health professionals that, like other antipsychotic drugs, Risperdal is not indicated to treat dementia.

"The FDA's MedWatch program has two main goals," Marks says. "We want to facilitate the reporting of problems in to the agency and we want to get safety information out to the public." MedWatch receives about 22,000 reports each year. The agency has a number of ways to alert the public about important information. The MedWatch Web site pulls as much safety information together as possible to make it easier for the public to find. MedWatch sends e-mail notification of all safety alerts and monthly safety labeling changes for drugs to a growing e-mail list of both health care professionals and consumers. By 2003, the number of subscribers to the MedWatch e-mail list jumped to 32,000, from the 5,000 people who signed up in 2000. People on the list receive safety alert summaries by e-mail, with a hyperlink that directs them to more detailed information. Names and e-mail addresses of MedWatch subscribers are not shared with other organizations.

MedWatch also works with 161 "MedWatch partner" organizations to widely disseminate new safety information. For example, the American Pharmacists Association receives e-mail notification of MedWatch safety alerts and includes this information in its own weekly e-mail bulletin, sent to over 64,000 pharmacists nationwide. FDA alerts also appear on a Web site called *Pharmacist.com*, a joint project of the American Pharmacists Association and the National Association of Boards of Pharmacy.

The MedWatch program is also explor-

ing opportunities to work with large health care systems that are already collecting adverse event and medication error reports. "This will facilitate the receipt of these reports by the FDA," Marks says. "We also work with partners like the American Association of Nurse Anesthetists to encourage their members to report to the FDA. It can be hard to get busy health professionals to report, but what we hope is that they see the whole process working—reports coming in from them and the resulting new safety information going back to them in order to make their work easier and their patients safer."

After the FDA evaluates reports, the result may be safety alerts, letters to health care professionals, labeling changes, product withdrawals, or further postmarketing research. When the FDA receives a MedWatch report, it is entered into a powerful database that allows a safety evaluator to compare it to similar reports. As few as a handful of signals, sent in from locations as diverse as Idaho, Arizona, Florida, and Vermont, may trigger a careful investigation by the FDA and a manufacturer.

"We want the public to know that we depend on their reports," Marks says. "They could prompt important actions that improve the public health." ■

### How to Report to MedWatch

Log onto the MedWatch site at [www.fda.gov/medwatch](http://www.fda.gov/medwatch) to download the reporting form. You can:

- Submit a report electronically
- Call 800-FDA-1088 to report by phone
- Fax a report to 800-FDA-0178
- Mail a report to MedWatch, FDA, 5600 Fishers Lane, Rockville, MD 20852-9787. ■



# *Greater Access to*





## *New FDA initiatives to improve drug reviews and reduce legal loopholes*

# Generic Drugs

*By Michelle Meadows*

**Y**ou might think that lower cost means lower quality, but that's not the case with prescription drugs, says Gary Buehler, R.Ph., director of the Food and Drug Administration's Office of Generic Drugs. "The FDA ensures a rigorous review of all drugs, and consumers can be assured that generic drugs are as safe and effective as brand-name drug products," he says.

Generic drugs are copies of brand-name drugs and are available in both over-the-counter (OTC) and prescription form. For example, ibuprofen is the generic version of the OTC pain medicine Advil. Last year, the FDA approved the first generic of the prescription diabetes drug Glucophage (metformin). Generics have the same quality, safety, and strength as branded medicines. But for an average brand-name drug that costs \$72, the generic version costs about \$17.

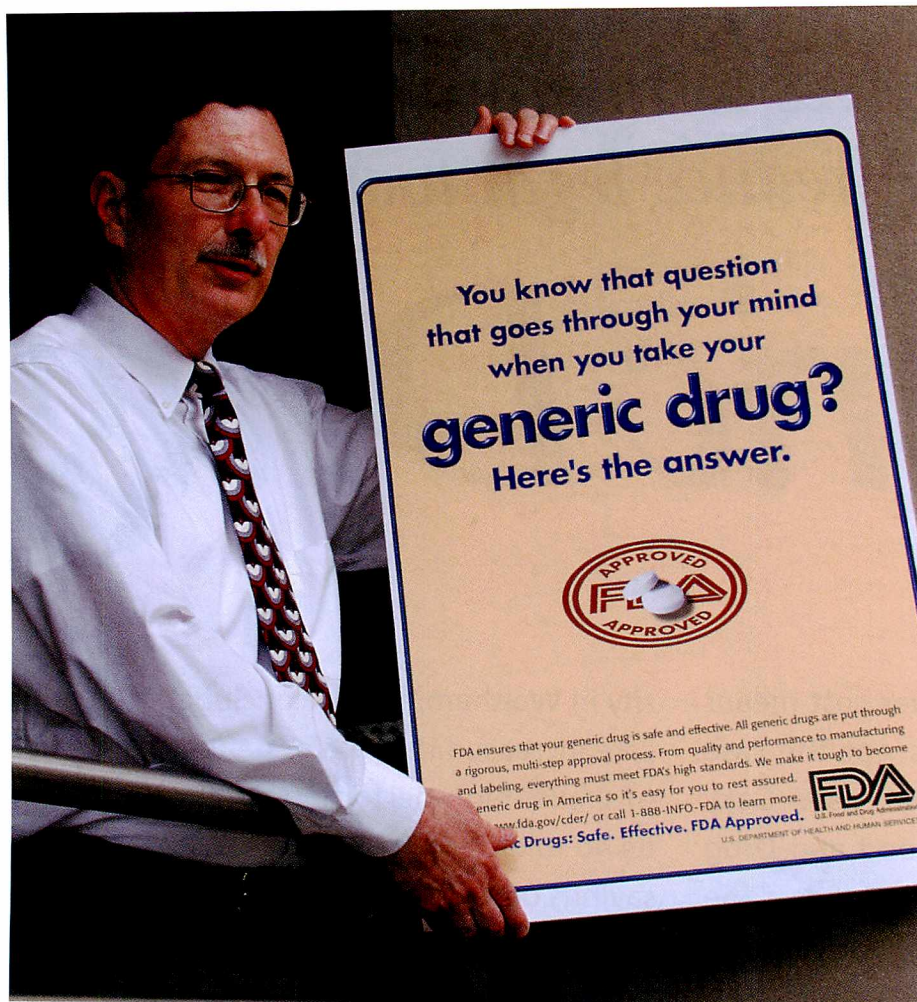
At roughly one-third the price of brand-name medications, generics can bring consumers significant savings. A 2002 study by the Schneider Institute for Health Policy at Brandeis Univer-

sity in Waltham, Mass., concluded that if Medicare increased the rate of generic usage to that of similar high-performing private sector plans, its 40 million beneficiaries could see potential savings of \$14 billion in 2003.

Because generic drugs play a key role in making health care more affordable, FDA Commissioner Mark B. McClellan, M.D., Ph.D., has made it a priority to encourage their availability. FDA experts say there is no question that brand-name drugs are also essential.

"Generic drugs are possible only as a result of the development of new innovative drugs, and this innovation requires significant investment," McClellan says. "Without fair compensation from meaningful patent protection, drug research and development would slow or stop." According to the Boston-based Tufts Center for the Study of Drug Development, the cost to develop a new drug averages \$897 million. The Pharmaceutical Research and Manufacturers of America (PhRMA) reports that its member companies invested about \$32 billion in 2002 in discovering and developing new medicines.





FDA/Michael ErmARTH

**Gary Buehler, R.Ph., director of the FDA's Office of Generic Drugs, leads the agency's efforts to educate consumers on the quality of generic drugs.**

A brand-name company submits information to the FDA on patents it holds on a drug and their expiration dates. Then the agency lists patents on new drugs in the publication *Approved Drug Products with Therapeutic Equiva-*

*lence*, also known as the Orange Book. Patent protection gives brand-name companies, also known as "innovator" companies, the sole right to sell a drug for a certain period of time. This allows them to fairly recoup their investment costs. Patent protection for drugs typically lasts an average of 11 years. A ge-

neric drug can only enter the market after the brand-name patent or other marketing exclusivities have expired and FDA approval is granted. But rising drug costs remain a major challenge for consumers, especially

aimed at streamlining the process for improving access to generic drugs. The move is expected to save consumers \$35 billion over 10 years, as well as lower costs for state Medicaid programs and employer-provided coverage.

To supplement the regulation, the FDA also launched an initiative called "Improving Access to Generic Drugs." The initiative involves revamping the FDA's review process to put generic drugs into consumers' hands more quickly. President Bush's fiscal year 2004 budget request increases funding for the FDA's generic drug program by \$13 million, the largest ever for that program. The additional funds would go toward speeding up generic drug reviews. This funding request would increase the 2003 generic drug budget of \$45 million by roughly one-third. According to McClellan, "All of these generic drug reforms are important for the protection of public health in this country."

#### **How Generics Get on the Market**

The main reason generic drug companies can market their drugs at lower prices is that they don't face the same development costs as brand-name companies. Under the Drug Price Competition and Patent Term Restoration Act of 1984, also known as the Hatch-Waxman Act, generic drug companies don't have to repeat expensive clinical trials.

"The Hatch-Waxman Act essentially created the generic drug industry," says Buehler. Roughly two decades ago, ge-

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*'... generic drug reforms are important for the protection of public health ...'*

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*lence*, also known as the Orange Book. Patent protection gives brand-name companies, also known as "innovator" companies, the sole right to sell a drug for a certain period of time. This allows them to fairly recoup their investment costs. Patent protection for drugs typically lasts an average of 11 years. A ge-

neric drug can only enter the market after the brand-name patent or other marketing exclusivities have expired and FDA approval is granted. But rising drug costs remain a major challenge for consumers, especially

older Americans. "This is where generics play an essential role," McClellan says. "Once the appropriate patent protection has expired, generic medicines give patients an alternative." On June 12, 2003, the FDA, along with HHS Secretary Tommy G. Thompson, announced new FDA regulations

nerics made up only 12 percent of all prescriptions. Now, generics represent almost 51 percent of all prescriptions in the United States, according to the Generic Pharmaceutical Association (GPhA). "The law paved the way for many more generic drugs because rather than repeating research, generic



drug companies instead must show the FDA that their drugs are bioequivalent to the brand-name drug," Buehler says.

When a drug is "bioequivalent" to another, it means that its active ingredient works in the same way and in the same amount of time as the brand-name drug. Scientists measure a generic drug's bioavailability—the amount of the generic drug in the bloodstream and how long it takes to get there. Then

sues. This may occur after a generic applicant certifies that an innovator's patent will not be infringed. Unless the innovator sues within 45 days after such notice, there is no 30-month stay. The innovator can still sue, but no 30-month stay results.

A stay is the term for the delay in generic approval that occurs when a brand-name company files a patent infringement lawsuit. This delay is

several brand-name drugs between 1994 and 2000 in which repeated 30-month stays delayed access to generic drugs.

Access to generic drugs has sometimes been delayed from four to 44 months when drug companies have used various methods to get repeated 30-month stays. Examples of delaying tactics include submitting patent information on the color of the pill bottle,

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## *The FDA's new rule seeks to close legal loopholes that delay generic drug approval.*

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they compare that measurement to the brand-name drug. While innovator companies submit full new drug applications, generic companies submit what are known as abbreviated new drug applications (ANDAs). Along with showing that a generic drug has the same bioavailability as the brand-name drug, generic companies must prove that their products have the same active ingredient, follow the same quality manufacturing standards, and have similar labeling. (See "FDA Requirements for Generic Drugs.")

The competition encouraged by the Hatch-Waxman Act helps to keep drug costs down and also spurs innovator firms to develop more new drugs, Buehler says. "The law aims to protect the intellectual property rights of innovator companies, while also encouraging the development of generic drugs," he says. As an incentive for generic drug firms to submit ANDAs to the FDA, the first generic challenger of patents is awarded a period of marketing exclusivity.

### **Reducing Legal Barriers**

The FDA's generic drug rule, which went into effect on Aug. 18, seeks to close legal loopholes in the Hatch-Waxman Act that delay generic drug approval. For example, only one 30-month "stay" is allowed under the new regulation if an innovator company sues a generic company over patent is-

sues. This may occur after a generic applicant certifies that an innovator's patent will not be infringed. Unless the innovator sues within 45 days after such notice, there is no 30-month stay. The innovator can still sue, but no 30-month stay results.

A limit of one 30-month stay is in line with recommendations from the Federal Trade Commission (FTC). According to an FTC study released July 30, 2002, there were cases involving

ingredient combinations, and other minor matters that don't affect the drug's effectiveness or safety.

Such strategies have been seen only in a minority of drug firms. And, according to PhRMA, stays are rare. But the FTC concluded that multiple stays can have substantial financial impact and are "harmful to consumers." When President Bush first announced the pro-

### **FDA Requirements for Generic Drugs**

- Generic drugs must have the same active ingredients and the same labeled strength as the brand-name product.
- Generic drugs must have the same dosage form (for example, tablets, liquids) and must be administered in the same way.
- Generic drug manufacturers must show that a generic drug is bioequivalent to the brand-name drug, which means the generic version delivers the same amount of active ingredients into a patient's bloodstream in the same amount of time as the brand-name drug.
- Generic drug labeling must be essentially the same as the labeling of the brand-name drug.
- Generic drug manufacturers must fully document the generic drug's chemistry, manufacturing steps, and quality control measures.
- Firms must assure the FDA that the raw materials and finished product meet specifications of the U.S. Pharmacopoeia, the organization that sets standards for drug purity in the United States.
- Firms must show that a generic drug will remain potent and unchanged until the expiration date on the label before it can be sold.
- Firms must comply with federal regulations for good manufacturing practices and provide the FDA a full description of facilities they use to manufacture, process, test, package, and label the drug. The FDA inspects manufacturing facilities to ensure compliance. ■



posals for these regulations last year, he said, "Our message to brand-name manufacturers is clear: You deserve the fair rewards of your research and development; you do not have the right to keep generic drugs off the market for frivolous reasons."

The new regulation also implements another FTC recommendation to

ceuticals Act, a bill that amends the Hatch-Waxman Act and has passed the U.S. Senate and House of Representatives. Both the Senate and the House have added generic drug access provisions to the Medicare Prescription Drug and Modernization Act of 2003. As of mid-August, the Senate and House versions of the bill were in conference—a

Hatch-Waxman Act of 1984 is achieving its purpose of speeding market entry of generic drugs."

Kuhlik pointed out that since the law was enacted, the generic share of the drug market has soared, and so has the expense of developing new drugs. "Our patent laws and regulations provide a key incentive for continued innovation in medicines," Kuhlik said. "Better treatments and new cures can come only from pharmaceutical research companies, and only if patent incentives are maintained."

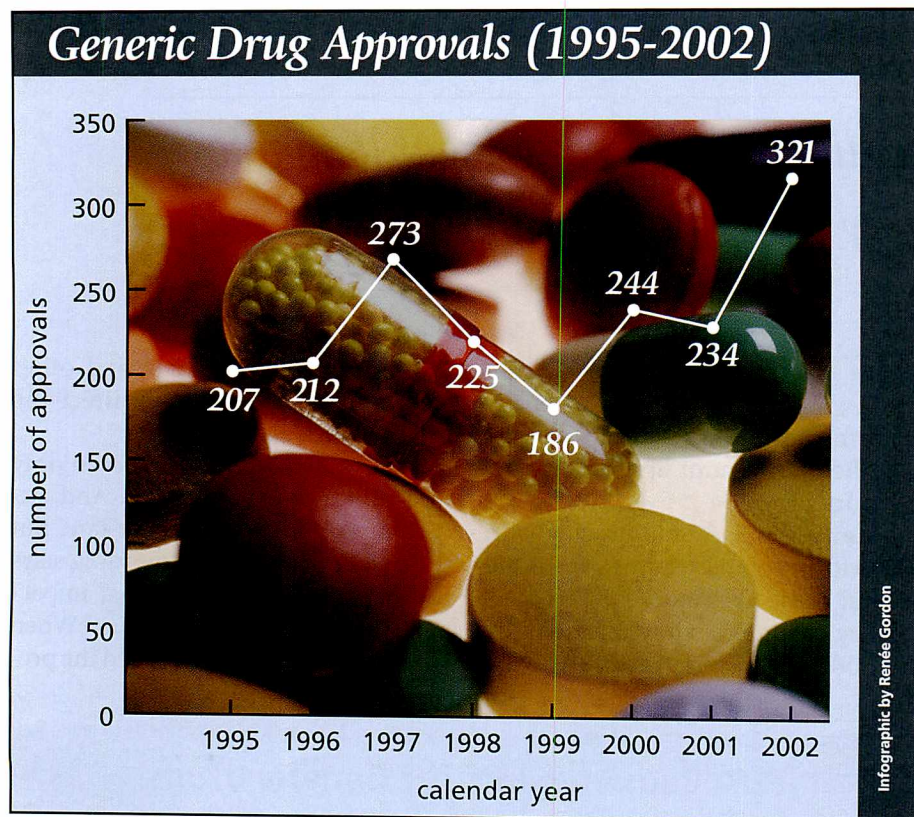
### More Efficient Reviews

In 2002, the FDA approved 321 generic drugs, up from 207 in 1995. Of those, 80 were first-time generics. The agency also issued 63 "tentative approvals" and 20 "approvables" of generic drugs. A tentative approval indicates that final approval of the application is delayed due to patent or exclusivity issues. Approvable applications are reviewed and ready for full approval pending a labeling issue, also typically dealing with legal matters.

It takes more than 20 months on average for a new generic drug to be approved by the FDA, and it usually involves multiple review cycles. Only about 7 percent of applications are approved on the first cycle and about a third are approved on the second cycle. Sometimes multiple review cycles can't be avoided, but the FDA has identified the lack of early communication between generic drug companies and the FDA as one cause for multiple review cycles. With the proposed increases for the generics budget, the FDA plans to increase resources that would make earlier communications possible.

The agency plans to hire 40 more experts to help speed up the review of generic drug applications so that review time can be reduced by at least two months. The goal is to provide guidance that improves the quality of applications the first time they are submitted, rather than going through multiple review cycles because of problems. "Each round of review means six months or more delay in approval," McClellan says.

The new resources, along with other improvements, are expected to reduce



tighten the patent submission and listing process so that only appropriate patents are submitted to the FDA. To help prevent unfair competition, the final rule clarifies the types of patents that must be submitted to the FDA. Companies must submit patent information on active ingredients, drug formulations and compositions, and approved uses of a drug. Certain patents, such as those for packaging claims, are among those that cannot be submitted. More detailed information will now be required on patent submissions, and false statements could lead to criminal charges.

Kathleen Jaeger, GPhA president and chief executive officer, praised the announcement of the generic drug regulation and said it complements the Greater Access to Affordable Pharma-

time during which differences in the two versions are discussed.

"GPhA strongly believes that the Administration's initiatives, coupled with substantial legislative measures in the compromise legislation, will ensure that American health care becomes more affordable," Jaeger said in a statement. The legislation, which also aims to eliminate practices that delay access to low-cost drugs, overlaps with the FDA's regulation in one area in that it would also prevent multiple 30-month stays in the approval of generic drugs.

In testimony before the Senate Judiciary Committee on June 17, 2003, Bruce N. Kuhlik, PhRMA's senior vice president and general counsel, cautioned against changes that could "undermine incentives for continued pharmaceutical innovation." He said, "The



the total time to approval for most new generic drugs by three months or more over the next three to five years. One new approach will be to develop an FDA standard for giving generic companies initial feedback on obvious minor deficiencies within 10 days after the

magazines and journals. Posters and brochures are being distributed at major pharmacies throughout the country. Advertisements rolled around on buses in Chicago, Los Angeles, and New York, and have appeared on billboards in Michigan.

pany and the customers, Cole says.

Blue Cross Blue Shield challenged pharmacies to develop in-store campaigns and tracked generic dispensing rates. More than 1,000 Michigan pharmacies competed. The prize for the stores with the highest rates: featured

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## *'Consumers saw it as our job to tell them about generic drug options.'*

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first review cycle is completed. Applicants will have an opportunity to respond and amend an application to try to avoid a whole new review cycle. The Office of Generic Drugs will issue guidance in 2004 on various policy changes related to earlier communication with drug companies.

"It won't be enough for FDA just to improve its review cycle time," McClellan adds. "Generic manufactur-

ers want lower-cost options for drugs, according to AARP, a non-profit organization that addresses the needs of people ages 50 and older. In a recent AARP survey of 1,046 people ages 45 and up, 84 percent said generic drugs are important for controlling drug costs. Most also said they usually choose generics over brand names when generics are available. And 24 percent reported not being able to afford a prescription drug when no generic was available.

Richard Cole, senior vice president of corporate communications at Blue Cross Blue Shield of Michigan, says in a statewide survey he conducted in the summer of 2001, most people said

they believe generic drugs are equivalent to brand-name drugs. "In the past, the conventional wisdom was that if we increased education about generic drugs, it would look like our only motives were to save money for the company," Cole says. "But consumers reported that they saw it as our job to tell them about generic drug options."

In the fall of 2001, Blue Cross Blue Shield invited all Michigan pharmacies to participate in a competition to increase generic dispensing rates. The goal was to increase generic use among Michigan Blues members by one percentage point, which would result in a \$17 million savings for both the com-

spots in a \$1 million advertising campaign with the slogan "Generic Drugs—The Unadvertised Brand." Rite Aid won for the retail chain category and Grand Value Drugs of Detroit won for the independent pharmacy category. Cole estimates that the annual savings for Michigan Blues members was more than \$30 million.

"People don't want a less expensive drug if they think the quality isn't good," Cole says. "When you or a member of your family gets sick, you don't want second best. But you don't have to worry about that with generic drugs."

The FDA's Center for Drug Evaluation and Research would like to hear from organizations interested in partnering with the FDA on its generic drug education program. For more information about a potential partnership, call 301-827-7503. ■

### **For More Information**

FDA's Office of Generic Drugs  
[www.fda.gov/cder/ogd/](http://www.fda.gov/cder/ogd/)

Generic drugs final rule  
[www.fda.gov/oc/initiatives/generics](http://www.fda.gov/oc/initiatives/generics)

### **Approvals for 2002**

Examples of recent first-time generic equivalent approvals for brand-name drugs:

- loratadine (Claritin), for allergies
- isotretinoin (Accutane), for severe acne
- metformin (Glucophage), for diabetes
- cefuroxime axetil (Ceftin), for infections

ers must improve the quality of their initial applications. The FDA and generic manufacturers all need to try harder to get it right the first time around."

### **Getting the Word Out**

"Generic Drugs: Safe. Effective. FDA Approved." That's one of the slogans featured in an FDA consumer education program to promote consumer confidence in generic drugs. The FDA messages have been featured in newspaper articles, posters, and brochures highlighting the safety and effectiveness of generic drugs. Public service announcements have appeared in major



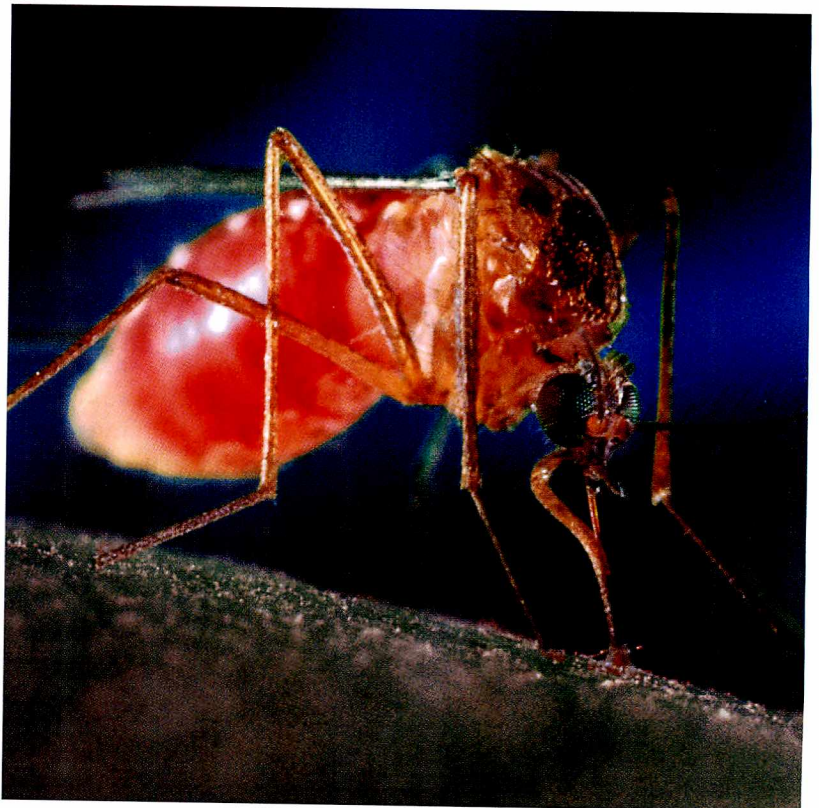
# First Test Approved to Help Detect West Nile Virus

By Carol Rados

**T**he Food and Drug Administration has cleared the first test that will help physicians diagnose cases of potentially deadly West Nile virus earlier than with current methods.

The West Nile Virus IgM Capture ELISA test is intended to be used in people who have symptoms of viral encephalitis or meningitis, which are serious inflammatory conditions of the brain or spinal cord that may occur in people infected with the virus.

"The rapid review and approval of this blood test, which uses antibody levels to identify persons who were recently exposed to West Nile virus, reflects FDA's commitment to making safe and effective medical products available promptly," says FDA Commissioner Mark B. McClellan, M.D., Ph.D. The new test works by detecting the levels of IgM, a particular type of antibody to West Nile virus, in blood serum. It is manufactured by PanBio Ltd. of Windsor, Australia.



Mosquitoes play a key role in the transmission of West Nile virus.

CDC



West Nile virus is a mosquito-borne virus first detected in the United States in 1999. While it often causes a mild infection that clears without further treatment, some people, especially those over 50, develop severe infections resulting in neurological disease and even death. The virus is most prevalent during peak mosquito season, beginning in July and ending in October.

By 2002, West Nile virus had spread to most of the continental United States. The CDC reported this season's first human case of West Nile virus in the United States in early July. As of early August, three deaths in Texas and Alabama had been attributed to the virus. The CDC says that West Nile virus activity detected in humans began a "significant uptick" in early August 2003.

The new diagnostic test is a significant breakthrough in the detection of West Nile virus. However, it's important to know that it is not a donor screening test, but is one of several tools used by the physician to determine if the patient is infected. Results from the IgM Capture ELISA must be confirmed with other laboratory tests as part of a comprehensive evaluation. The test is designed to be used in cases when someone has symptoms of West Nile encephalitis or meningitis—headache, high fever, neck stiffness, stupor, disorientation, coma, tremors, convulsions, muscle weakness, and paralysis.

In addition to its usefulness for diag-

## Reduce the Risk of West Nile Virus

### 1) Avoid mosquito bites

- Cover up. Wear long-sleeved shirts, long pants and socks sprayed with repellent while outdoors.
- Avoid mosquitoes, which often bite between dusk and dawn.
- Limit time outdoors during these hours.
- Spray insect repellent containing DEET (look for N, N-diethyl-m-toluamide) on exposed skin outdoors.
- Spray clothing with repellents containing DEET or permethrin.
- Don't spray repellent on skin under clothing.
- Don't use permethrin on skin.
- Use repellent carefully.
- Don't put repellent on kids' hands because it may get into their mouths or eyes.

### 2) Mosquito-proof your home

- Install or fix window and door screens.

- Drain standing water, where mosquitoes like to breed.
- Look around every week for possible mosquito breeding places.
- Empty water from buckets, cans, pool covers, flowerpots, and other items.
- Throw away or cover up stored tires and other items not being used.
- Clean outdoor pet water bowls weekly.
- Check to see if rain gutters are clogged.

### 3) Help your community

- Dead birds help health departments track West Nile virus.
- Check with your local or state health department to find out their policy for reporting dead birds. ■

Source: CDC

ments on procedures to protect the blood supply. The FDA updated this guidance in May 2003, based on experience with the 2002 outbreak.

Additionally, the agency is working with manufacturers to expedite development of necessary medical products, such as screening tests and additional diagnostic methods. Experimental do-

at the virus as it replicates in animals, humans, and mosquitoes. In the area of prevention, the NIH is supporting three different approaches to vaccines, including a live vaccine made by mixing West Nile virus with the already established yellow fever vaccine. Through its grants and contracts, the NIH is the largest supporter of infectious disease

## The new diagnostic test is a significant breakthrough.

nosing individuals with the infection, the test has the potential to help monitor the scope and spread of the disease.

The FDA has established guidance and procedures to avoid collection and use of blood that might be at risk for transmitting West Nile virus. The agency is cooperating with the country's blood organizations, both in the laboratory and in epidemiological investigations of the virus. In August 2002, prior to any actual report of transmission, the FDA alerted the blood industry to be vigilant in excluding symptomatic donors and then later that year provided guidance to blood establish-

ment nor screening tests have been put into place and have been available nationwide since July 1, 2003. These tests add a measure of safety and will prevent contaminated blood from entering the nation's blood supply.

Other federal efforts are ongoing to combat West Nile virus. The National Institutes of Health (NIH) is supporting ongoing research at universities and companies nationwide aimed at developing the public health tools to help fight the infection. Currently the NIH is funding four areas of research for West Nile virus: diagnosis, prevention, therapy, and basic research that looks

research in the United States.

For now, the CDC, the FDA and the NIH all agree that the most important message about the virus is that people need to be prepared and take the steps necessary to prevent mosquito bites and avoid exposure, especially until treatment or vaccines are available to add additional layers of protection. ■

### For More Information

See "West Nile Virus: Reducing the Risk" in the January–February 2003 issue of *FDA Consumer*.

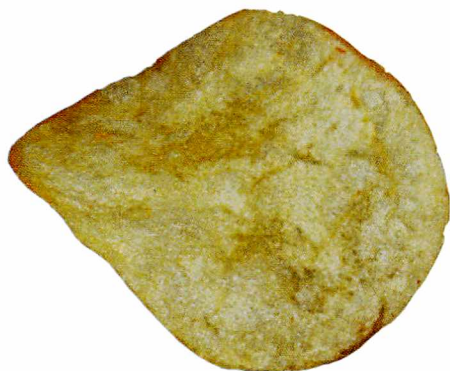


# REVEALING

**S**cientific evidence shows that consumption of saturated fat, *trans* fat, and dietary cholesterol raises low-density lipoprotein (LDL), or “bad” cholesterol, levels that increase the risk of coronary heart disease (CHD).

According to the National Heart, Lung, and Blood Institute of the National Institutes of Health, more than 12.5 million Americans have CHD, and more than 500,000 die each year. That makes CHD one of the leading causes of death in the United States.

The Food and Drug Administration has required that saturated fat and dietary cholesterol be listed on food labels since 1993. By adding *trans* fat on the Nutrition Facts panel, you will know for the first time how much of all three—saturated fat, *trans* fat, and cholesterol—are in the foods you choose. Identifying saturated fat, *trans* fat, and cholesterol on the food label gives you information you need to make food choices that help reduce the risk of CHD. This revised label will be of particular interest to people concerned about high blood cholesterol and heart disease.



Photos: Digital Stock



# TRANS FATS



However, everyone should be aware of the risk posed by consuming too much saturated fat, *trans* fat, and cholesterol. But what is *trans* fat, and how can you limit the amount of this fat in your diet?

## What is *Trans* Fat?

Basically, *trans* fat is made when manufacturers add hydrogen to vegetable oil—a process called hydrogenation. Hydrogenation increases the shelf life and flavor stability of foods containing these fats.

*Trans* fat can be found in vegetable shortenings, some margarines, crackers, cookies, snack foods, and other foods made with or fried in partially hydrogenated oils. Unlike other fats, the majority of *trans* fat is formed when food manufacturers turn liquid oils into solid fats like shortening and hard margarine. A small amount of *trans* fat is found naturally, primarily in dairy products, some meat, and other animal-based foods.





*Trans* fat, like saturated fat and dietary cholesterol, raises the LDL cholesterol that increases your risk for CHD. Americans consume on average 4 to 5 times as much saturated fat as *trans* fat in their diets.

Although saturated fat is the main dietary culprit that raises LDL, *trans* fat and dietary cholesterol also contribute significantly.

### Are All Fats the Same?

Simply put: No. Fat is a major source of energy for the body and aids in the absorption of vitamins A, D, E, and K, and carotenoids. Both animal- and plant-derived food products contain fat, and when eaten in moderation, fat is important for proper growth, development, and maintenance of good health. As a food ingredient, fat provides taste, consistency, and stability and helps you feel full. In addition, parents should be aware that fats are an especially important source of calories and nutrients for in-



The Glad Products Co.

with the lower amounts of saturated fat, *trans* fat, and cholesterol. Health experts recommend that you keep your intake of saturated fat, *trans* fat, and cholesterol as low as possible while consuming a nutritionally adequate diet. However, these experts recognize that eliminating these three components entirely from your diet is not practical because they are unavoidable in ordinary diets.

### Where Can You Find *Trans* Fat on the Food Label?

Although some food products already have *trans* fat on the label, food manufacturers have until January 2006 to list it on all their products.

You will find *trans* fat listed on the Nutrition Facts panel directly under the line for saturated fat.

### How Do Your Choices Stack Up?

With the addition of *trans* fat to the Nutrition Facts panel, you can review your food choices and see how they stack up. The table on page 26 illustrates total fat, saturated fat, *trans* fat, and cholesterol con-

nants and toddlers (up to 2 years of age), who have the highest energy needs per unit of body weight of any age group.

While unsaturated fats (monounsaturated and polyunsaturated) are beneficial when consumed in moderation, saturated and *trans* fats are not. Saturated fat and *trans* fat raise LDL cholesterol levels in the blood. Dietary cholesterol also raises LDL cholesterol and may contribute to heart disease even without raising LDL. Therefore, it is advisable to choose foods low in saturated fat, *trans* fat, and cholesterol as part of a healthful diet.

### What Can You Do About Saturated Fat, *Trans* Fat, and Cholesterol?

When comparing foods, look at the Nutrition Facts panel, and choose the food





tent per serving for selected food products.

Don't assume similar products are the same. Be sure to check the Nutrition Facts panel because even similar foods can vary in calories, ingredients, nutrients, and the size and number of servings in a package.

### How Can You Use the Label to Make Heart-Healthy Food Choices?

The Nutrition Facts panel can help you choose foods lower in saturated fat, *trans* fat, and cholesterol. Compare similar foods and choose the food with the lower com-

bined saturated and *trans* fats and the lower amount of cholesterol.

Although the updated Nutrition Facts panel will list the amount of *trans* fat in a product, it will not show a Percent Daily Value (%DV). While scientific reports have confirmed the relationship between *trans* fat and an increased risk of CHD, none has provided a reference value for *trans* fat or any other information that the FDA believes is sufficient to establish a Daily Reference Value or a %DV.

Saturated fat and cholesterol, however, do have a %DV. To choose foods low in saturated fat and cholesterol, use the general rule of thumb that 5 percent of the Daily Value or less is low and 20 percent or more is high.

You can also use the %DV to make dietary trade-offs with other foods throughout the day. You don't have to give up a favorite food to eat a healthy diet. When a food

**bag size, date, price and numbers  
found below price for each package.**

## Nutrition Facts

Serving Size 1 oz. (28g/About 20 chips)  
Servings Per Container 12

### Amount Per Serving

**Calories** 150      Calories from Fat 90

% Daily Value\*

**Total Fat** 10g      **15%**

Saturated Fat 3g      **15%**

Trans Fat 0g

**Cholesterol** 0mg      **0%**

**Sodium** 180mg      **8%**

**Total Carbohydrate** 15g      **5%**

Dietary Fiber 1g      **4%**

Sugars 0g

**Protein** 2g

Vitamin A 0%      •      Vitamin C 10%

Calcium 0%      •      Iron 0%

Vitamin E 6%      •      Thiamin 4%

Niacin 6%      •      Vitamin B<sub>6</sub> 4%

Phosphorus 4%      •      Zinc 2%

\* Percent Daily Values are based on a 2,000 calorie diet. Your daily values may be higher or lower depending on your calorie needs:

	Calories:	2,000	2,500
Total Fat	Less than	65g	80g
Sat Fat	Less than	20g	25g
Cholesterol	Less than	300mg	300mg
Sodium	Less than	2,400mg	2,400mg
Total Carbohydrate		300g	375g
Dietary Fiber		25g	30g

Calories per gram:

Fat 9 • Carbohydrate 4 • Protein 4

**Ingredients:** Potatoes, Corn and/or Cottonseed Oil, and Salt.

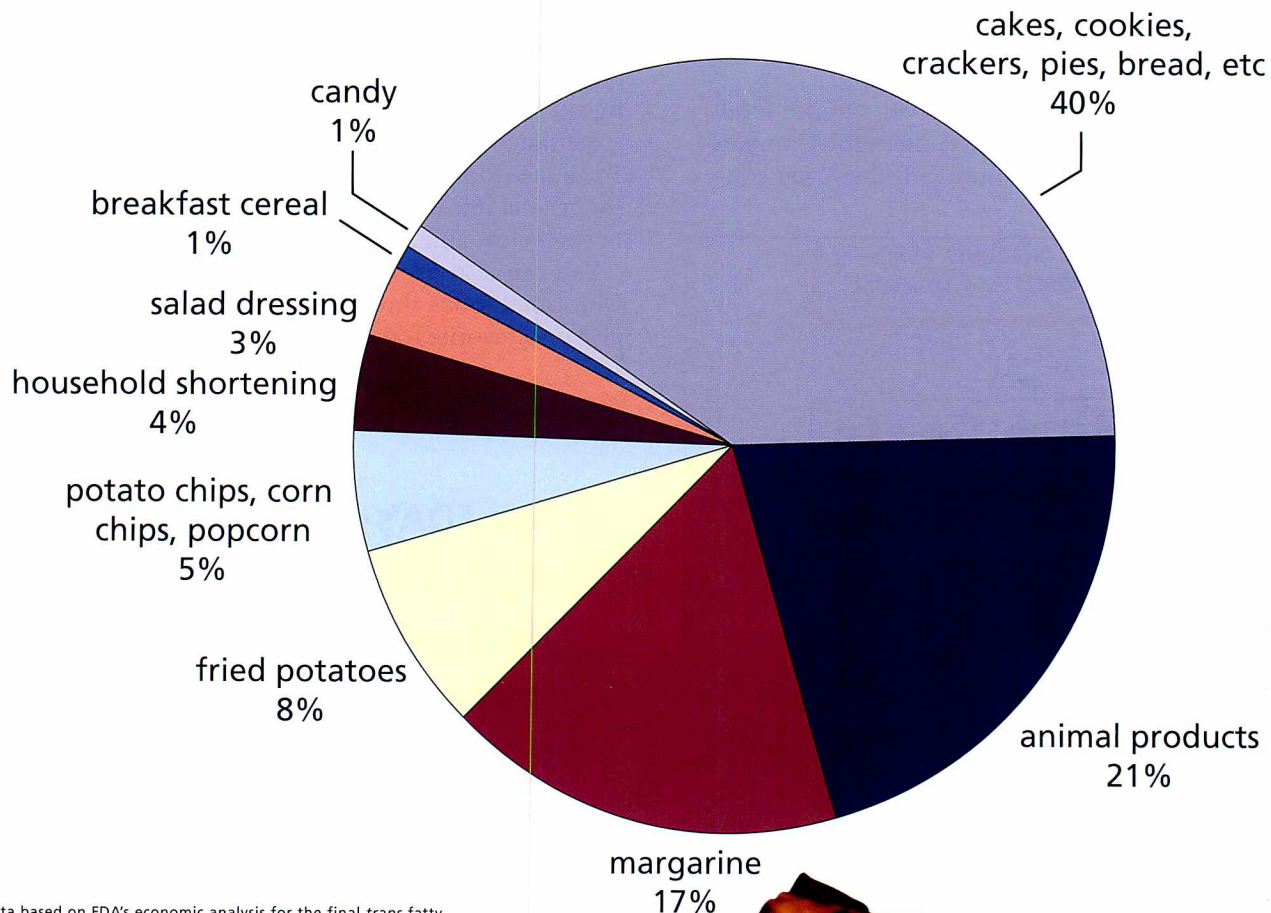
No Preservatives.

The FDA's *trans* fat labeling regulations don't take effect until Jan. 1, 2006, but some manufacturers are already listing the amount of *trans* fat in their products.

FDA/Michael ErmARTH



## Major Food Sources of Trans Fat for American Adults (Average Daily Trans Fat Intake is 5.8 Grams or 2.6 Percent of Calories)

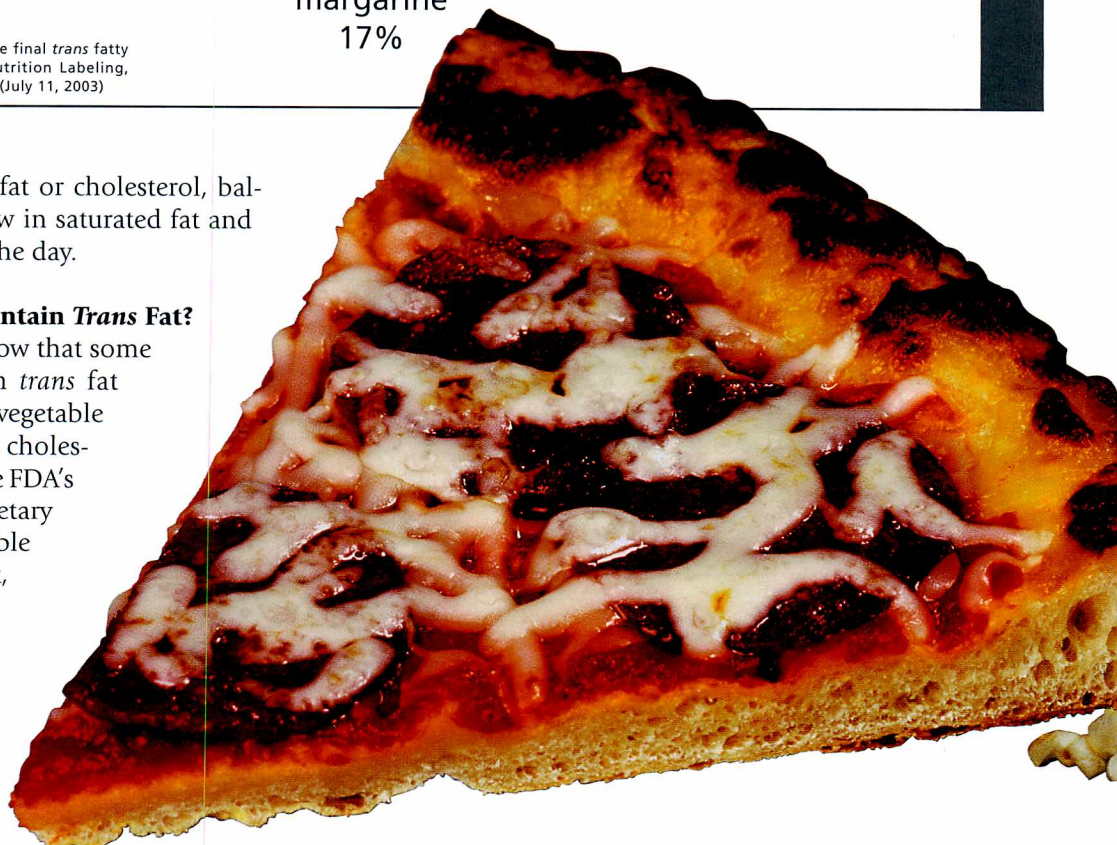


Data based on FDA's economic analysis for the final *trans* fatty acid labeling rule, "*Trans* Fatty Acids in Nutrition Labeling, Nutrient Content Claims, and Health Claims" (July 11, 2003)

you like is high in saturated fat or cholesterol, balance it with foods that are low in saturated fat and cholesterol at other times of the day.

### Do Dietary Supplements Contain *Trans* Fat?

Would it surprise you to know that some dietary supplements contain *trans* fat from partially hydrogenated vegetable oil as well as saturated fat or cholesterol? It's true. As a result of the FDA's new label requirement, if a dietary supplement contains a reportable amount of *trans* or saturated fat, which is 0.5 gram or more, dietary supplement manufacturers must list the amounts on the Supplement Facts panel. Some dietary supplements that may contain saturated





fat, *trans* fat, and cholesterol include energy and nutrition bars.

### Fat Tips

Here are some practical tips you can use every day to keep your consumption of saturated fat, *trans* fat, and cholesterol low while consuming a nutritionally adequate diet.

- **Check the Nutrition Facts panel** to compare foods because the serving sizes are generally consistent in similar types of foods. Choose foods lower in saturated fat, *trans*



## Highlights of the Final Rule on *Trans* Fat

- Manufacturers of conventional foods and some dietary supplements will be required to list *trans* fat on a separate line, immediately under saturated fat on the nutrition label.
- Food manufacturers have until Jan. 1, 2006, to list *trans* fat on the nutrition label. The phase-in period minimizes the need for multiple labeling changes, allows small businesses to use current label inventories, and provides economic savings.
- FDA's regulatory chemical definition for *trans* fatty acids is all unsaturated fatty acids that contain one or more isolated (i.e., nonconjugated) double bonds in a *trans* configuration. Under the Agency's definition, conjugated linoleic acid would be excluded from the definition of *trans* fat.
- Dietary supplement manufacturers must also list *trans* fat on the Supplement Facts panel when their products contain reportable amounts (0.5 gram or more) of *trans* fat. Examples of dietary supplements with *trans* fat are energy and nutrition bars. ■

fat, and cholesterol. For saturated fat and cholesterol, keep in mind that 5 percent of the daily value (%DV) or less is low and 20 percent or more is high. (There is no %DV for *trans* fat.)

- **Choose alternative fats.** Replace saturated and *trans* fats in your diet with monounsaturated and polyunsaturated fats. These fats do not raise LDL cholesterol levels and have health benefits when eaten in moderation. Sources of monounsaturated fats include olive and canola oils. Sources of polyunsaturated fats include soybean oil, corn oil, sunflower oil and foods like nuts and fish.
- **Choose vegetable oils** (except coconut and palm kernel oils) and soft margarines (liquid, tub, or spray) more often because the amounts of saturated fat, *trans* fat, and cholesterol are lower than the amounts in solid shortenings, hard margarines, and animal fats, including butter.
- **Consider fish.** Most fish are lower in saturated fat than meat. Some fish, such as mackerel, sardines, and salmon, contain omega-3 fatty acids that are being studied to determine if they offer protection against heart disease.
- **Ask before you order when eating out.** A good tip to remember is to ask which fats are being used in the preparation of your food when eating or ordering out.
- **Watch calories.** Don't be fooled! Fats are high in calories. All sources of fat contain 9 calories per gram, making fat the most concentrated source of calories. By comparison, carbohydrates and protein have only 4 calories per gram.



## Total Fat, Saturated Fat, Trans Fat, and Cholesterol Content per Serving\*

Product	Common Serving Size	Total Fat g	Sat. Fat g	%DV for Sat. Fat	Trans Fat g	Combined Sat. & Trans Fat g	Chol. mg	%DV for Chol.
French Fried Potatoes± (Fast Food)	Medium (147 g)	27	7	35%	8	15	0	0%
Butter**	1 tbsp	11	7	35%	0	7	30	10%
Margarine, stick†	1 tbsp	11	2	10%	3	5	0	0%
Margarine, tub†	1 tbsp	7	1	5%	0.5	1.5	0	0%
Mayonnaise†† (Soybean Oil)	1 tbsp	11	1.5	8%	0	1.5	5	2%
Shortening±	1 tbsp	13	3.5	18%	4	7.5	0	0%
Potato Chips±	Small bag (42.5 g)	11	2	10%	3	5	0	0%
Milk, whole±	1 cup	7	4.5	23%	0	4.5	35	12%
Milk, skim†	1 cup	0	0	0%	0	0	5	2%
Doughnut±	1	18	4.5	23%	5	9.5	25	8%
Cookies± (Cream Filled)	3 (30 g)	6	1	5%	2	3	0	0%
Candy Bar±	1 (40 g)	10	4	20%	3	7	<5	1%
Cake, pound±	1 slice (80 g)	16	3.5	18%	4.5	8	0	0%

\*Nutrient values rounded based on FDA's nutrition labeling regulations. \*\*Butter values from FDA Table of Trans Values, 1/30/95. †Values derived from 2002 USDA National Nutrient Database for Standard Reference, Release 15. ††Prerelease values derived from 2003 USDA National Nutrient Database for Standard Reference, Release 16. ±1995 USDA Composition Data.

To keep your intake of saturated fat, *trans* fat, and cholesterol low:

- Look at the Nutrition Facts panel when comparing products. Choose foods low in the combined amount of saturated fat and *trans* fat and low in cholesterol as part of a nutritionally adequate diet.

- Substitute alternative fats that are higher in mono- and polyunsaturated fats like olive oil, canola oil, soybean oil, corn oil, and sunflower oil. ■

### For More Information

Questions and Answers on the *Trans* Fat Final Rule  
[www.cfsan.fda.gov/~dms/qatrans2.html](http://www.cfsan.fda.gov/~dms/qatrans2.html)

#### Backgrounder

[www.fda.gov/oc/initiatives/transfat/backgrounder.html](http://www.fda.gov/oc/initiatives/transfat/backgrounder.html)

Guidance on How to Understand and Use the Nutrition Facts Panel on Food Labels

[www.cfsan.fda.gov/~dms/foodlab.html](http://www.cfsan.fda.gov/~dms/foodlab.html)

Federal Register Final Rule: *Trans* Fatty Acids in Nutrition Labeling, Nutrient Content Claims, and Health Claims

[www.cfsan.fda.gov/~lrd/fr03711a.html](http://www.cfsan.fda.gov/~lrd/fr03711a.html)

Advance Notice of Proposed Rulemaking to solicit information on *trans* fat nutrient and health claims

[www.cfsan.fda.gov/~lrd/fr03711b.html](http://www.cfsan.fda.gov/~lrd/fr03711b.html)

"What's New on the Nutrition Facts Label? *Trans* Fat Now Listed with Saturated Fat and Cholesterol."

[www.cfsan.fda.gov/~dms/lab-cat.html#transfat](http://www.cfsan.fda.gov/~dms/lab-cat.html#transfat)



# Nasal Flu Vaccine Approved



MedImmune Vaccines Inc.

By Michelle Meadows

**V**accination is the best way to fight the flu virus, and many people will have an alternative to getting a shot this fall. The FDA has approved the first nasally administered flu vaccine to be marketed in the United States. The needle-free vaccine may be good news for children and others who are reluctant to get a shot.

Experts say FluMist also gives a welcome boost to the flu vaccine supply. "This new vaccine provides another option for protection against influenza and will potentially increase the availability of the injected killed virus vaccine for those people at highest risk," says FDA Commissioner Mark B. McClellan, M.D., Ph.D.

Like the injected flu vaccine, each FluMist dose contains the three influenza strains recommended for the 2003–2004 season. FluMist is the first

live virus influenza vaccine to be approved in the United States. The strains of live virus are modified so they don't grow efficiently at body temperature, but replicate enough to produce immunity.

"Because it is live, it can grow in the nose and some people get flu symptoms, though usually milder than natural influenza," says ChrisAnna Mink, M.D., a medical officer in the FDA's Center for Biologics Evaluation and Research. The most common side effects associated with FluMist are nasal congestion, runny nose, sore throat, and cough.

"So far, the vaccine seems to be very safe in the healthy people we've tested," says Paul Glezen, M.D., a professor of molecular virology and microbiology at Baylor College of Medicine in Houston, who has run FluMist clinical trials. "But we haven't tested the vaccine in people who are immunocompromised."

As with other live virus vaccines, FluMist should not be given to people with immune suppression, such as people with AIDS or cancer. The vaccine also shouldn't be given to pregnant women, people with a history of asthma or other reactive airway diseases, people age 50 and over, or to children under 5. People who have ever had an allergic reaction to eggs or to a previous dose of the flu vaccine shouldn't take any kind of flu vaccine.

Flu symptoms include fever, headache, extreme fatigue, dry cough, sore throat, runny or stuffy nose, and muscle

ache. "Flu is generally more likely to have sudden onset than colds, which tend to come on gradually," Glezen says. Flu also has more severe symptoms and complications than colds. "The most common flu complications are middle ear infections, sinusitis, and bronchitis. Rarer complications—but ones that are more serious—include pneumonia and dehydration."

According to the Centers for Disease Control and Prevention (CDC), about 10 percent to 20 percent of U.S. residents come down with the flu each year. About 114,000 people are hospitalized for flu-related complications, and there is an annual average of 36,000 deaths. Most people get vaccinated in October and November, but the flu vaccine can still provide protection when used in December and January. The CDC recommends that people in high-risk groups and people who come into contact with high-risk groups get a flu vaccine every year. Rates of flu infection are highest in children ages 5 to 14, and the most severe illnesses and deaths occur in people with underlying medical conditions, children under 2, and people over age 65. Because the safety of FluMist has not been established in high-risk individuals, they should get the injected killed virus flu vaccine. ■

## For More Information

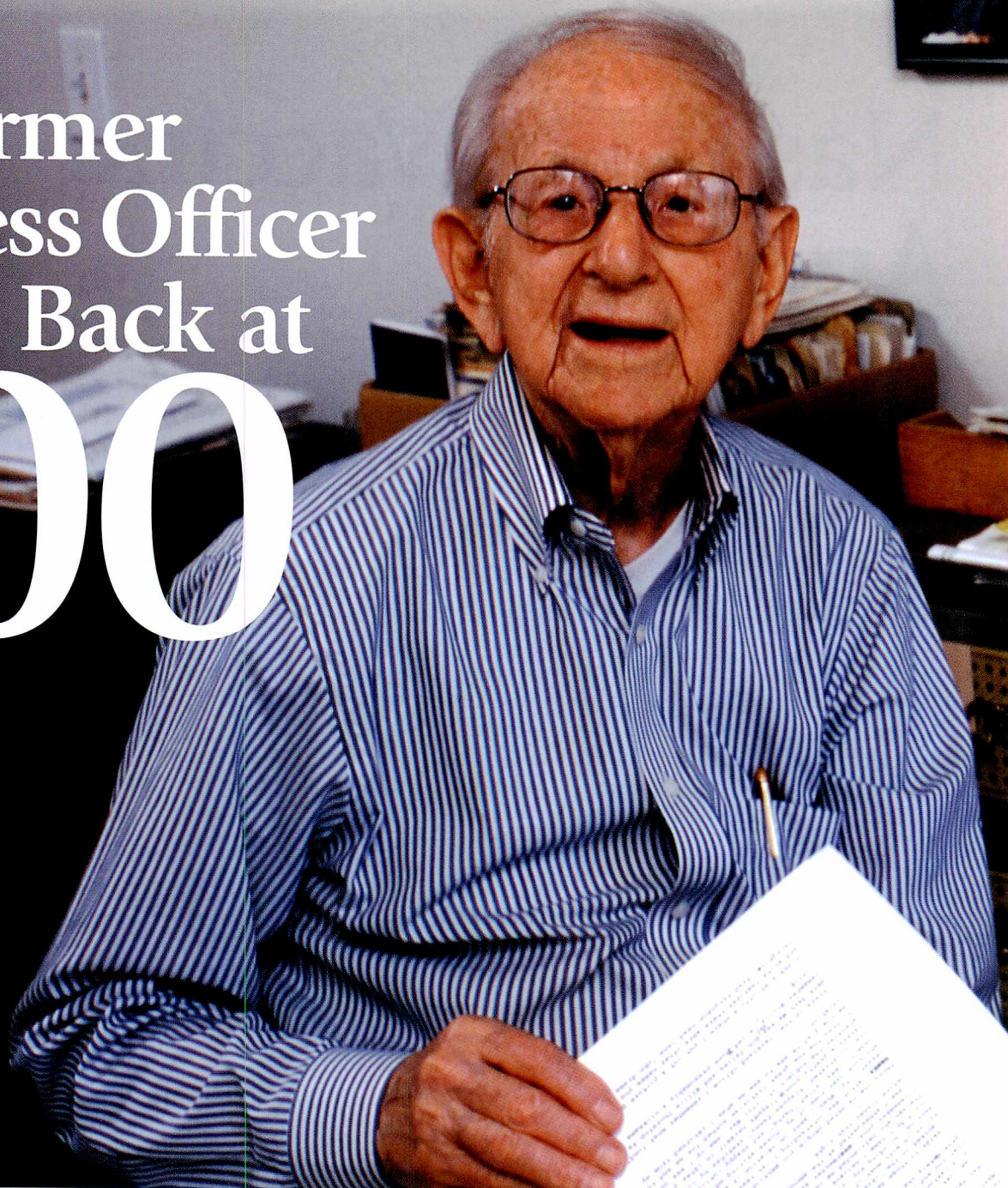
[www.cdc.gov/ncidod/diseases/flu/fluvirus.htm](http://www.cdc.gov/ncidod/diseases/flu/fluvirus.htm)

## About FluMist

FluMist (Influenza Virus Vaccine Live, Intranasal), which is sprayed into both nostrils, is approved to prevent disease caused by influenza viruses in healthy children and adolescents ages 5 to 17 and in healthy adults ages 18 to 49. People ages 9 to 49 need one dose, and children ages 5 to 8 need two doses at least six weeks apart the first year they get the vaccine. In clinical trials, FluMist was tested in roughly 20,000 people, including more than 10,000 healthy children 5 to 17 years of age. The vaccine is manufactured by MedImmune Vaccines Inc. of Gaithersburg, Md., and will be marketed by MedImmune and by Wyeth Vaccines of Philadelphia. ■



# Former FDA Press Officer Looks Back at 100



Black Star/Dennis Brack

By Carol Rados

**E**mil Corwin has sampled sea slugs, picked over pigeon eggs, and applied “tiger balm” to his temples after contracting a particularly hardy strain of Asian virus. He’s no stranger to spider eggs in bubble gum, rat poison in toothpaste, or earthworms in hamburgers. He’s fielded questions on everything from food irradiation and the banning of aerosols to the unsuccessful bid for approval of a sweetener called “dulcin,” named for Don Quixote’s lady friend, Dulcinea. Corwin has even walked among “barefoot doctors”—all in the interest of public health.

After becoming a public affairs officer at the Food and Drug Administration—at age 70—Corwin traveled extensively, delivered speeches, wrote copy and answered inquiries from a public health perspective. Often the inquiries were off-beat calls related to irradiated food glowing in the dark, the government’s decision to ban saccharin (which caused cancer in rats) but not tobacco (which causes cancer in people), and how such vermin as earthworms got into hamburgers in the first place.

With regard to the agency’s food irradiation proposal, some 400 callers in only 10 days were assured by employ-



ees like Corwin that the proposed radiation would not make their food radioactive. And Congress responded to the public outcry about saccharin—fueled in part by media reports that the test rats were fed the equivalent of as many as 800 diet sodas a day—by passing the Saccharin Study and Labeling Act. This law placed a moratorium on any ban of the sweetener while additional safety studies were conducted and required that the sweetener carry a warning label.

audiences numbered in the millions.” Misstatements, says Corwin, are not retrievable.

Toward the end of his FDA career, Corwin says he noticed that the role of press officer had changed. Much of the difference involved process: While press officers still had access to agency experts, much of the information passed on to newspapers, magazines, and other media outlets was coming directly from FDA experts. With the magnitude and volume of complex, scientific issues fac-

smoking campaign, he remembers, was “to get after the airlines.” While that, too, took many years to catch on, Corwin believes that the efforts of such campaigns had a significant impact on the smoking ban in 1990 on all U.S. flights.

In 1978, when the FDA planned to ban aerosol sprays with fluorocarbons, Corwin says press officers were asked “how propellants in hair sprays, deodorants, shaving cream and perfumes could seep out of the bathroom, travel 10 to 40 miles up into the stratosphere

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## *‘I lost sleep many a night over the interviews I gave.’*

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As for the earthworms, Corwin says they were one of those “criminals” that in this business often prove elusive, and whose origin would always be hunted.

Corwin kept up his hectic pace until 1999, when he retired at age 96. “I felt reasonably prepared to deal with such questions from the public,” he says. Judging by his age when he was hired, the FDA agreed. Corwin attempted to retire—and was talked out of it—a couple of times during his FDA career. His sons, he says, “retired before I did!”

After turning 100 years “young” in April, Corwin reminisced with *FDA Consumer* and compared the work of today’s public affairs specialists with the duties of yesterday’s public information officers.

“Times have changed,” he says. “You didn’t have to worry as much about what you said since you knew the subject matter well enough.” Corwin fondly remembers the hundreds of agency experts—chemists, nutritionists, microbiologists, and physicists—whom he and other members of the public affairs staff depended on for quick answers and relevant details. “In those days, we had very good access to the people who had all the information,” he says.

Nevertheless, Corwin remembers, “I lost sleep many a night over the interviews I gave. I don’t remember saying anything I regretted,” he adds, “but on those occasions you prayed for a clear head and a sure grasp of facts to communicate with communicators whose

ing the agency, Corwin remembers that during his last few years at the FDA, “It was a matter of referring such issues to a higher authority.”

Prior to working at the FDA, Corwin spent many years as a reporter and editor with the *Springfield* (Mass.) *Republican*, the United Press, and the Newspaper Enterprise Association. He later did public relations at NBC for conductor Arturo Toscanini, and then for the United Nations. During the mid-1950s, Corwin served as the American Cancer Society’s director of public information. In 1964, he became an information officer for the U.S. Department of Health, Education and Welfare’s National Clearinghouse for Smoking and Health. When that office relocated to Atlanta in 1974, Corwin was not interested in leaving Maryland and instead, he says, “I walked across the street and applied for a job at the FDA.” He got it and at 70, he was still going strong.

In his lengthy stint with the tobacco issue, both at the Clearinghouse and then at the FDA, Corwin was involved in public health campaigns to educate people about the Surgeon General’s first report on the risks of cigarettes. “Once the correlation between lung cancer and cigarette smoking was made,” Corwin says, “it became front-page news and Washington took this seriously.”

Did these campaigns pay off? “I think so,” says Corwin. “There’s enough evidence to show that change is taking place.” One agenda item of the cigarette

and destroy the ozone layer that protects people from ultraviolet radiation.” Science, Corwin told people, “shows this does happen.” The FDA, Environmental Protection Agency, and Consumer Product Safety Commission worked together to phase out non-essential uses of fluorocarbons in 1978.

The aerosol problem faced by the FDA in Corwin’s day dramatizes the range of the agency concerns even today—from hazards in the sky to harmful substances so tiny they are measured in parts per trillion. (Just for the record, Corwin says, “One part per billion is like one person in all of China; one part per trillion would be equal to a grain of salt in an Olympic-sized swimming pool.”)

Corwin also remembers, albeit not so fondly, angry outbursts and a write-in assault on the agency over an FDA proposal to revise regulations on the safety and labeling of vitamins and minerals decades ago. The proposal was called “idiotic, tyrannical and socialistic” by opponents. People wanted the federal government to let the consumer make his or her own choice. What’s interesting, Corwin notes, is that none of the thousands of protests about the regulations had practical suggestions for improving the proposal. One even read: “Please thump the Commissioner on the head; we suspect there is an empty space there.” ■



# Inside Clinical Trials:

## Testing Medical Products in People

By Carol Rados

**C**arolyn Meritt was preparing to undergo a stem cell transplant in 2001 to treat mantle cell lymphoma—a rare cancer of the lymph nodes—when her doctor told her about a clinical trial being conducted by the National Institutes of Health (NIH). He suggested that she consider becoming a participant.



Carolyn Meritt receives a vaccine treatment as part of an NIH clinical trial investigating mantle cell lymphoma.

Family photo



"I didn't even know what a clinical trial was," Meritt says. That was only one of many questions she would need answered before she could decide whether or not to enroll.

But Meritt's white blood counts were rising. She would need treatment soon. She could proceed with the stem cell transplant—the only existing therapy—or, as long as she felt well enough, she could hold out hope and participate in

an integral part of new product discovery and development, and are required by the FDA before a new product can be brought to the market.

The FDA is committed to protecting the participants of clinical trials, as well as providing reliable information to those interested in participating. Recently, unethical behavior on the part of some researchers has shaken the public trust and prompted the federal government to es-

help advance medical knowledge. Others have tried all available treatments for their condition without success.

In a spring 2000 Harris Poll of cancer clinical trial participants, 76 percent of the respondents said they participated because they believed that the trial offered the best quality of care for their disease. Helping other people and receiving more and better attention for their own specific disease were other

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## *'Clinical trials test potential treatments in human volunteers ...'*

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the clinical trial, an option open to her only if she had no prior treatment. But how would she decide?

Predicaments like Meritt's are not uncommon. "We get this kind of call just about every day," says Theresa Toigo, director of the Food and Drug Administration's Office of Special Health Issues (OSHI). "The patients have serious and life-threatening diseases. They're afraid. They want some options, but they're not sure where to go. We try to provide the information patients and their families need to make important decisions in such difficult situations."

### **What Is A Clinical Trial?**

A common thread linking such calls, says Toigo, is clinical trials. Clinical trials, also known as clinical studies, test potential treatments in human volunteers to see if they should be approved for wider use in the general population. A treatment could be a drug, medical device, or biologic, such as a vaccine, blood product, or gene therapy. Potential treatments, however, must be studied in laboratory animals first to determine potential toxicity before they can be tried in people. Treatments having acceptable safety profiles and showing the most promise are then moved into clinical trials.

Although "new" may imply "better," it is not known whether the potential medical treatment offers benefit to patients until clinical research on that treatment is complete. Clinical trials are

establish regulations and guidelines for clinical research to protect participants from unreasonable risks.

Although efforts are made to control risks to clinical trial participants, some risk may be unavoidable because of the

reasons cited.

"I was going ahead with the stem cell transplant because I thought I had no other options," Meritt admits. "Part of the reason I decided to do this study was so that maybe what they learned

### **Institutional Review Boards**

Clinical trial procedures are reviewed by Institutional Review Boards (IRBs). These boards are composed of at least five members that include scientists, doctors and lay people, and they must approve every clinical trial taking place within their jurisdiction—usually a hospital. The purpose of an IRB review is to ensure that appropriate steps are taken to protect the rights and welfare of participants as subjects of research. If the risks to participants are found to be too great, the IRB will not approve the research or it will specify changes that must be made before the research can be done.

IRBs also review participant inclusion and exclusion requirements to be sure that appropriate people have been identified as eligible for the trial. They often look at how and where recruitment for clinical trials will occur. IRBs review the adequacy of the informed consent document to ensure that it includes all the elements required by law, and that it is at an appropriate reading level and understandable to study participants. ■

uncertainty inherent in clinical research involving new medical products. It's important, therefore, that people make their decision to participate in a clinical trial only after they have a full understanding of the entire process and the risks that may be involved.

### **Why Participate in a Clinical Trial?**

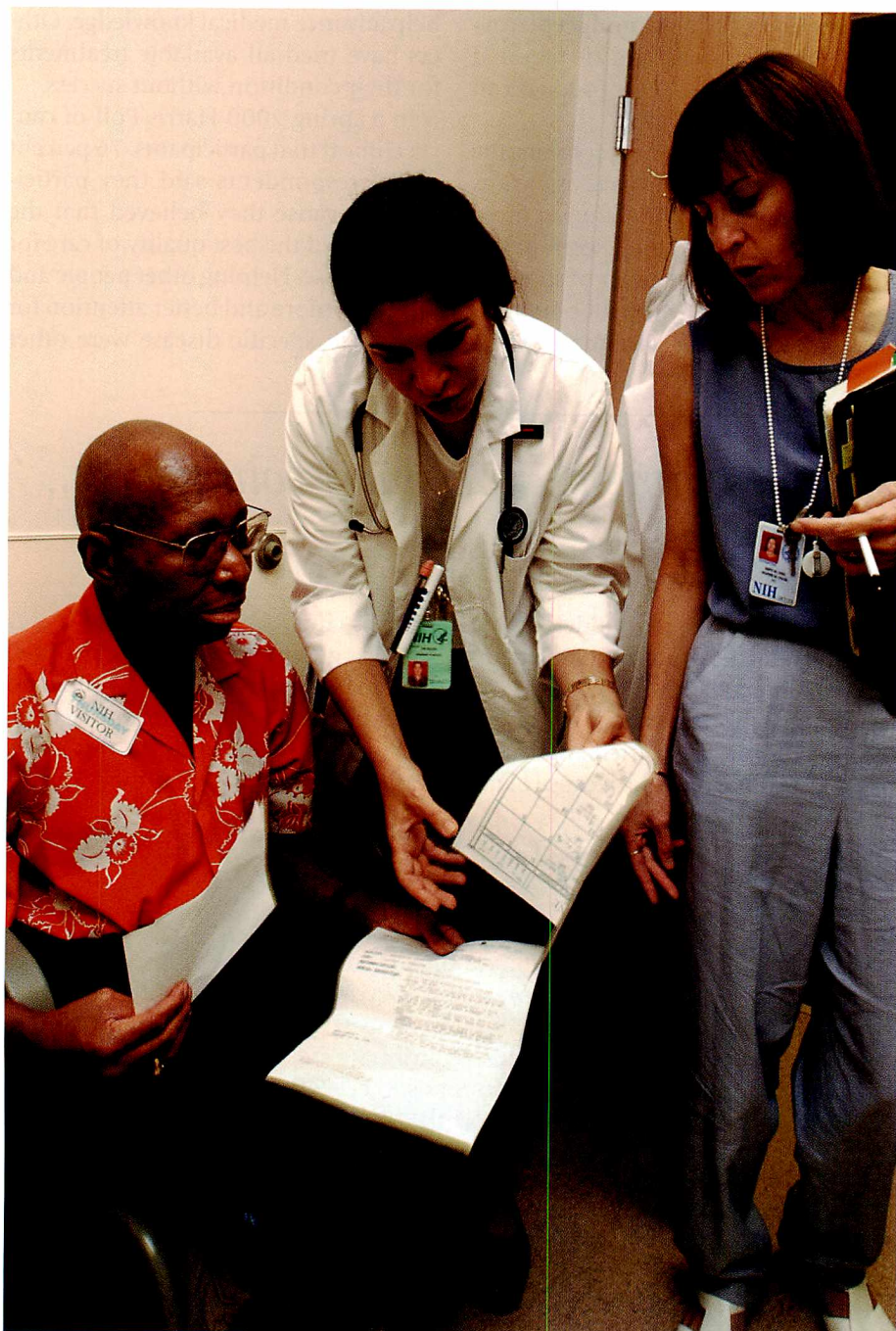
People volunteer to participate in clinical trials for different reasons. Some volunteer because they want to

through me would help other people with mantle cell lymphoma." Others enter clinical trials in hopes of finding a potential treatment, after traditional therapies fail.

People should not, however, be tempted to enroll in a clinical trial simply because a potential treatment is being offered free during a study, or because of the promise of money, says David Banks, an FDA pharmacist.

"People lured by compensation may





NCI

**A researcher and other members of the team prepare a participant for an upcoming clinical trial. Ensuring that participants understand their rights and the risks involved are important steps in the clinical trial process.**

overlook the known risks," Banks says. "Or [they may fail] to adequately appreciate the potential for discovery of serious new side effects during clinical testing of a new treatment." Banks also says that clinical trials "are generally not a means for patients to receive long-term treatment for their chronic disease." Still, he adds, "clinical trials often represent an option to seriously consider."

### **Who Can Participate?**

It's important to test medical products in the people they are meant to help. In the past, most new drug testing had been done on white men. Groups such as women, African-Americans, and Hispanics often were not adequately represented. It's important to test medical products in a wide variety of people because drugs can work differently in people of various ages, races, ethnicity,

and gender. The FDA seeks to ensure that people from many different groups are included in clinical trials.

Trial guidelines, or eligibility requirements, are developed by the researchers and usually include criteria for age, sex, type and stage of disease, previous treatment history, and other medical conditions. Some trials involve people with a particular illness or condition to be studied, while others seek healthy volunteers. Inclusion or exclusion criteria—medical or social standards used to determine whether a person may or may not be allowed to enter a clinical trial—help identify appropriate participants and help to exclude those who may be put at risk by participating in a trial.

Volunteering for a clinical trial is no guarantee of acceptance. Similarly, there's no guarantee that an individual in a clinical trial will receive the drug or medical product being studied.

### **What Happens in a Clinical Trial?**

Every clinical trial is carefully designed to answer certain research questions. A trial plan called a "protocol" maps out what study procedures will be done, by whom, and why. Products are often tested to see how they compare to standard treatments or to no treatment. The FDA often provides extensive technical assistance to researchers conducting clinical trials, helping them design better trials that can characterize effects of a new product more efficiently, while reducing risks to those participating in the trials.

The clinical trial team includes doctors and nurses as well as other health care professionals. This team checks the health of the participant at the beginning of the trial and assesses whether that person is eligible to participate. Those found to be eligible—and who agree to participate—are given specific instructions, and then monitored and carefully assessed during the trial and after it is completed.

Done at hospitals and research centers around the country, clinical trials are conducted in phases. Phase 1 trials try to determine dosing, document how a drug is metabolized and excreted, and identify acute side effects. Usually, a small number of healthy volunteers (between 20 and 80) are used in Phase 1 trials.



Phase 2 trials include more participants (about 100-300) who have the disease or condition that the product potentially could treat. In Phase 2 trials, researchers seek to gather further safety data and preliminary evidence of the drug's beneficial effects (efficacy),

placebos, particularly if an effective treatment is available. Withholding treatment (even for a short time) would subject research participants to unreasonable risks.

The treatment each trial participant receives is often decided by a process

that treatment selection will be free of any preference a physician may have. Randomization increases the likelihood that the groups of people receiving the test drug or control are comparable at the start of the trial, enabling comparisons in health status between

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## *Clinical trials are an integral part of new product discovery and development, and are required by the FDA.*

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and they develop and refine research methods for future trials with this drug. If the Phase 2 trials indicate that the drug may be effective—and the risks are considered acceptable, given the observed efficacy and the severity of the disease—the drug moves to Phase 3.

In Phase 3 trials, the drug is studied in a larger number of people with the disease (approximately 1,000-3,000). This phase further tests the product's effectiveness, monitors side effects, and, in some cases, compares the product's effects to a standard treatment, if one is already available. As more and more participants are tested over longer periods of time, the less common side effects are more likely to be revealed.

Sometimes, Phase 4 trials are conducted after a product is already approved and on the market to find out more about the treatment's long-term risks, benefits, and optimal use, or to test the product in different populations of people, such as children.

Phase 2 and Phase 3 clinical trials generally involve a "control" standard. In many studies, one group of volunteers will be given an experimental or "test" drug or treatment, while the control group is given either a standard treatment for the illness or an inactive pill, liquid or powder that has no treatment value (placebo). This control group provides a basis for comparison for assessing effects of the test treatment. In some studies, the control group will receive a placebo instead of an active drug or treatment. In other cases, it is considered unethical to use

called "randomization." This process can be compared to a coin toss that is done by computer. During clinical trials, no one likely knows which therapy is better, and randomization assures

groups of patients who participated in the trial.

In conjunction with randomization, a feature known as "blinding" helps ensure that bias doesn't distort the con-



### **VOLUNTEERS NEEDED FOR STUDY ON UV TANNING OPTIMIZATION FOOD AND DRUG ADMINISTRATION**

The FDA recently ran this ad seeking participants for an ongoing study that will allow the agency to revise recommendations for sunlamp exposure schedules. The goal of the study is to limit the negative side effects of chronic exposure to ultraviolet radiation.



duct of a trial or the interpretation of its results. Single-blinding means the participant does not know whether he or she is receiving the experimental drug, an established treatment for that disease, or a placebo. In a single-blinded trial, the research team does know what the participant is receiving.

A double-blind trial means that neither the participant nor the research team knows during the trial which participants receive the experimental drug. The patient will usually find out what he or she received at a pre-specified time in the trial.

ied and the health of the people participating in the trial. All known risks must be fully explained by the researchers before the trial begins. If new risk information becomes available during the trial, participants must be informed.

"I didn't tolerate the drugs well," says Leslie Garelick of Olney, Md., referring to the two rounds of experimental chemotherapy she received as a participant in a clinical trial of a breast cancer treatment. Because her white blood cell counts were dangerously low, she was forced to skip some of the scheduled

tion of human research participants, and oversees human protection in HHS-funded research.

"It's important that we have the rapport with the public that allows them to trust us with this program," says Bernard A. Schwetz, D.V.M., Ph.D., acting director of the OHRP. He adds, "Without people willing to participate, there won't be any clinical trials."

The FDA has authority over clinical trials for drug, biologic and medical device products regulated by the agency. This authority includes studies that are HHS-funded (with joint oversight by the FDA and the OHRP), as well as studies that are solely funded by industry or by private parties. Many clinical trials are not subject to FDA regulation but are monitored by the institution sponsoring the trial, such as a hospital. (See "Institutional Review Boards," page 31.)

To help protect the rights and welfare of volunteers and verify the quality and integrity of data submitted for review, the FDA performs inspections of clinical trial study sites and anyone involved in the research, says David A. Lepay, M.D., Ph.D., director of the FDA's Good Clinical Practice Program. Lepay says that the quality of clinical trials has improved markedly since the agency started inspecting them back in 1977.

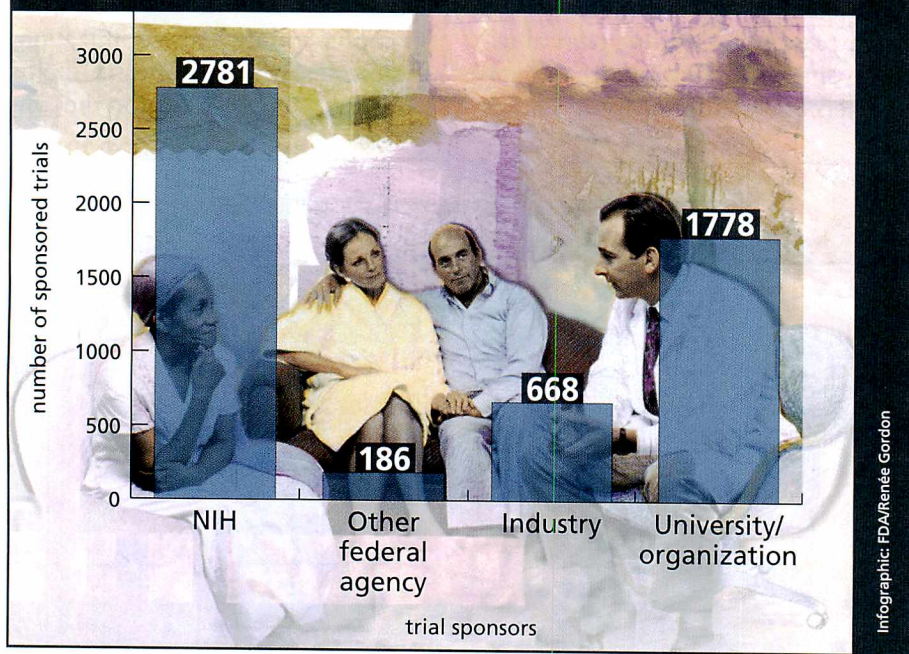
"Between FDA, the help of other government agencies, the review by Institutional Review Boards, the required monitoring of studies by industry or private sponsors, and the required oversight and reporting by investigators and their staff," Lepay says, "a lot of people are looking out for the research subject's safety."

### What Is Informed Consent?

The FDA requires that potential participants be given complete information about the study. This process is known as "informed consent," and it must be in writing. (See "Information Required for Informed Consent," page 35.)

The informed consent process provides an opportunity for the researcher and patient to exchange information and ask questions. Patients invited to enter a trial are not obligated to join, but can consent to participate if they

## Sponsored Clinical Trials (2003)



Meritt participated in an NIH study of a vaccine and chemotherapy combination in previously untreated mantle cell lymphoma. Following more than a year of medical treatment through the study, her cancer went into remission.

### What Are the Risks?

Some treatments being studied can have unpleasant, or even serious, side effects. Often these are temporary and end when the treatment is stopped. Others, however, can be permanent. Some side effects appear during treatment, and others may not show up until after the study is over. The risks depend on the treatment being stud-

trial treatments. On the advice of her doctor, the 30-year-old mother of two withdrew from the trial and received standard treatment for breast cancer. Even though she quit the study, Garelick's experience gave the research team information about tolerance to the drug being tested.

### How Are People Protected?

Most clinical trials are federally regulated with built-in safeguards to protect participants. Today, the Office for Human Research Protections (OHRP) in the Department of Health and Human Services (HHS) leads the department's programs for the protec-



## Information Required for Informed Consent

The FDA requires that people be told:

- That the study involves research of an unproven drug, biologic (such as a vaccine, blood product, or gene therapy) or device
- The purpose of the research
- How long the participant will be expected to participate in the study
- What will happen in the study and which parts of the study are experimental
- Possible risks or discomforts to the participant
- Possible benefits to the participant
- Other procedures or treatments that might be advantageous to the participant instead of the treatment being studied
- That the FDA may look at study records, but the records will be kept confidential
- Whether any compensation and medical treatments, if any, are available if the participant is injured, what those treatments are, where they can be found, and who will pay for the treatment
- The person to contact with questions about the study, participants' rights, or if the participant gets hurt
- That participation is voluntary and that he or she can quit the study at any time without penalty or loss of benefits to which the participant is otherwise entitled. ■

find the potential risks and benefits acceptable. A consent form must be signed by the participant prior to enrollment and before any study procedures can be performed.

Participants also have the right to leave a study at any time. At the same time, people need to know that circumstances may arise under which their participation may be terminated by the researcher, without their consent.

For example, Schwetz says that sometimes it becomes evident early on that

a trial is not working and researchers know they are not going to get enough meaningful information to make continuation worthwhile. In addition, if an unexpected change occurs in the health status of a participant, such as toxic effects or sudden kidney problems that may have developed, it "would not be in the best interest of the patient to continue, and certainly not consistent with what the investigator is trying to study," he says. In any case, the circumstances must be described in the consent document.

### Where To Get Information on Clinical Trials

It is often difficult for patients to learn about opportunities to participate in clinical trials. Doctors and patient advocacy groups can be valuable resources for patients in search of clinical trial information. Newspapers, particularly in large cities, often carry clinical trial recruitment advertisements. A call to the relevant department at nearby university medical centers can lead to information about clinical trials currently recruiting patients.

The Web site *ClinicalTrials.gov* also provides patients, family members, health care professionals, and members of the public easy access to information on clinical trials for a wide range of diseases and conditions. The NIH, through its National Library of Medicine, has developed this site in collaboration with all NIH institutes and the FDA.

The site currently contains information on about 8,200 clinical studies sponsored by the NIH, other federal agencies, and the pharmaceutical industry in over 99,000 locations worldwide. Studies listed in the database are conducted primarily in the United States and Canada, but include locations in about 90 countries. *ClinicalTrials.gov* gives information about a trial's purpose, who may participate, locations, and phone numbers for more details. In addition, a glossary is available that will help people become familiar with the most common clinical trial terms.

### The Bottom Line

While it's true that clinical trials offer no guarantees, when standard treat-

ments fail, or none exist, clinical research trials sometimes can offer hope. People can reduce the confusion and uncertainty that often comes with deciding whether or not to participate in a clinical trial by obtaining all the information available on various Web sites, through phone calls, within FDA, HHS, and NIH offices, and from patient advocacy organizations.

The bottom line: Know and understand the different types of trials, which questions to ask, and your rights as a trial participant. Find out what risks there may be, and determine what level of risk you are willing to accept before you agree to enroll in a clinical trial for medical research. ■

### For More Information

FDA's Office of Special Health Issues  
301-827-4460 or 888-INFO-FDA (1-888-463-6332), select 3 for directory information and ask to be connected to the Office of Special Health Issues  
[www.fda.gov/oashi/home.html](http://www.fda.gov/oashi/home.html)

Cancer Information Service  
1-800-4-CANCER (1-800-422-6237)  
[www.cancer.gov/clinical\\_trials](http://www.cancer.gov/clinical_trials)

AIDS and HIV trials  
1-800-874-2572  
[www.aidsinfo.nih.gov](http://www.aidsinfo.nih.gov)

Patient advocacy groups  
[www.cancer.gov/cancerinfo/make-a-difference](http://www.cancer.gov/cancerinfo/make-a-difference)





Photodisc

# Daily Aspirin Therapy

**IN RECENT YEARS, YOU MAY HAVE SEEN TELEVISION ADS** promoting aspirin's ability to reduce the risk of heart attack and stroke in certain groups of people. You should know that deciding to take an aspirin a day is not as simple as it may seem. The FDA's Center for Drug Evaluation and Research (CDER) has launched a public education campaign to remind consumers that aspirin is not without risk; the decision to use aspirin to prevent a heart attack and stroke is safest when made in consultation with a health professional.

It's been about 100 years since aspirin was created. And in that time, it has played a major role in treating headaches, fever, and minor aches and pains for millions. Now there are studies showing that aspirin is helpful in lowering the chance of a heart attack and clot-related stroke.

Still, most health professionals agree that long-term aspirin use to prevent a heart attack or stroke in healthy people is unnecessary. If you are using aspirin to lower the risk of heart attack and stroke and you haven't talked with a health professional about it, you may be putting your health at risk.

Aspirin can help prevent a heart attack or clot-related stroke by lowering the clotting action of the blood's platelets. But the same properties that make aspirin work in stopping blood from clotting may also cause unwanted side effects, such as stomach bleeding, bleeding in the brain, kidney failure, and other kinds of strokes. There may be a benefit to daily aspirin use if you have some kind of heart or blood vessel disease, or if you have evidence of poor blood flow to the brain. But only a doctor can tell you whether the risks of long-term aspirin use may be greater than the benefits.

If your health professional agrees to your use of daily aspirin treatment,

you'll need his or her medical knowledge and guidance to help prevent unwanted side effects. Before deciding if daily aspirin use is right for you, your health professional will consider such factors as your medical and family history, your use of other medicines, your allergies and sensitivities, and what side effects you may experience.

Some medical conditions, such as pregnancy, high blood pressure, bleeding disorders, asthma, stomach ulcers, and liver and kidney disease, could make aspirin a bad choice for you. Aspirin is also a drug that can mix badly with other medicines (prescription and over-the-counter), vitamins, herbals, or dietary supplements. People who are already using a prescribed medicine to thin the blood should talk to a health professional before using aspirin, even occasionally. It's important to discuss the use of all medicines, vitamins and dietary supplements with your health professional before using aspirin daily.

You should also discuss the different forms of aspirin products that might be best suited for you. Not all over-the-counter pain relievers have aspirin, so it's important to read the label carefully. Some drug products combine aspirin with other pain relievers or with certain other ingredients and should not be used as long-term aspirin treatment.

There are no directions on the label for using aspirin to reduce the risk of heart attack or clot-related stroke. Your health professional can provide the dose and directions that will give you the most benefit with the fewest side effects. Whether you are using aspirin daily to lower the risk of a heart attack or a clot-related stroke, or for any other purpose not listed on the aspirin's label, the dose does matter. It's important that the dose you use and the frequency with which you use it are right for you. ■

## For More Information

[www.fda.gov/cder/consumerinfo/dailyaspirin\\_brochure.htm](http://www.fda.gov/cder/consumerinfo/dailyaspirin_brochure.htm)

For a free brochure and fact sheet on aspirin and the heart, call 301-827-1243 or e-mail [dpapubs@cderr.fda.gov](mailto:dpapubs@cderr.fda.gov).



By John Henkel

## Take the Physical Fitness Challenge

Several government studies dating from the mid-1990s report that our reliance on technology has discouraged physical activity and led to more sedentary lifestyles. This has helped fuel an alarming rise in weight-related problems: Nearly two-thirds of all American adults and 15 percent of children are overweight or obese, setting the stage for diabetes, heart disease, and other serious maladies.

To help counteract this trend, the President's Council on Physical Fitness and Sports (PCPFS) has launched the President's Challenge, an interactive Web site that aims to get people of all ages on their feet and engaged in physical activity. The site offers a free and easy-to-use tool to track progress toward becoming fit. The site also gives awards for reaching fitness milestones.

Here's how it works:

- Log onto [www.presidentschallenge.org](http://www.presidentschallenge.org)
- Pick an age category (kids, teens, adults, or seniors)
- Choose from over 100 physical activities and start tracking daily efforts in a private log

Any participant can work toward a Presidential Active Lifestyle Award by engaging in physical activity five days a week for six weeks (adults should be active at least 30 minutes a day, and children for at least 60 minutes).

Though the awards are given for short-term fitness progress, the program is intended to last much longer. "It can help people be healthy, active and fit for the rest of their lives," says Lynn Swann, former Pittsburgh Steeler and chairman of the PCPFS.

## Food for Thought—On Video

Want to learn more about food-related topics such as labeling, allergies and safety of fresh produce? The FDA's Center for Food Safety and Applied Nutrition offers an easy way through its online video library. Using a free downloadable plug-in, you can view short productions that explain, for example, how to avoid foodborne illness by preventing contamination of foods in your kitchen. Other longer videos explain FDA programs such as measures the agency is taking to protect the food supply as part of recent bioterrorism legislation. Some of the videos are available in multiple languages.

The site, at [www.cfsan.fda.gov/~comm/videos.html](http://www.cfsan.fda.gov/~comm/videos.html), also links to a library of videos from other federal agencies on subjects such as using a food thermometer to ensure thorough cooking and washing hands frequently to avoid contamination.

## What's In Those Household Products?

Brake fluid. Air fresheners. Insect repellent. Bleach. Sure, you use these things all the time. But do you ever wonder what's in these products or what the potential health effects of exposure to them are? The National Library of Medicine has the answers in its online Household Products Database. Browse or search specific brand-name products in categories such as auto products, landscape/yard, home maintenance, and hobbies/crafts.

If, for example, you want to know more about the anti-perspirant you use, just click on that category and a list of dozens of brand names will appear, each with detailed safety and manufacturing information.

But suppose you only have the name of a product ingredient. No problem. The site allows searching or browsing through a chemical registry for background on the ingredient. You also can search for information about health effects such as dizziness or headache.

To check out your household products, go to <http://householdproducts.nlm.nih.gov/>.

## Useful Publications on Alcohol Abuse

Nearly half of adolescents have had at least one alcoholic drink by the time they're in eighth grade, and over 20 percent report having been drunk, according to the National Institute on Alcohol Abuse and Alcoholism (NIAAA). About 30 percent of 12th graders report drinking on three or more occasions per month, and about 20 percent have had at least five drinks on more than one occasion within the past two weeks.

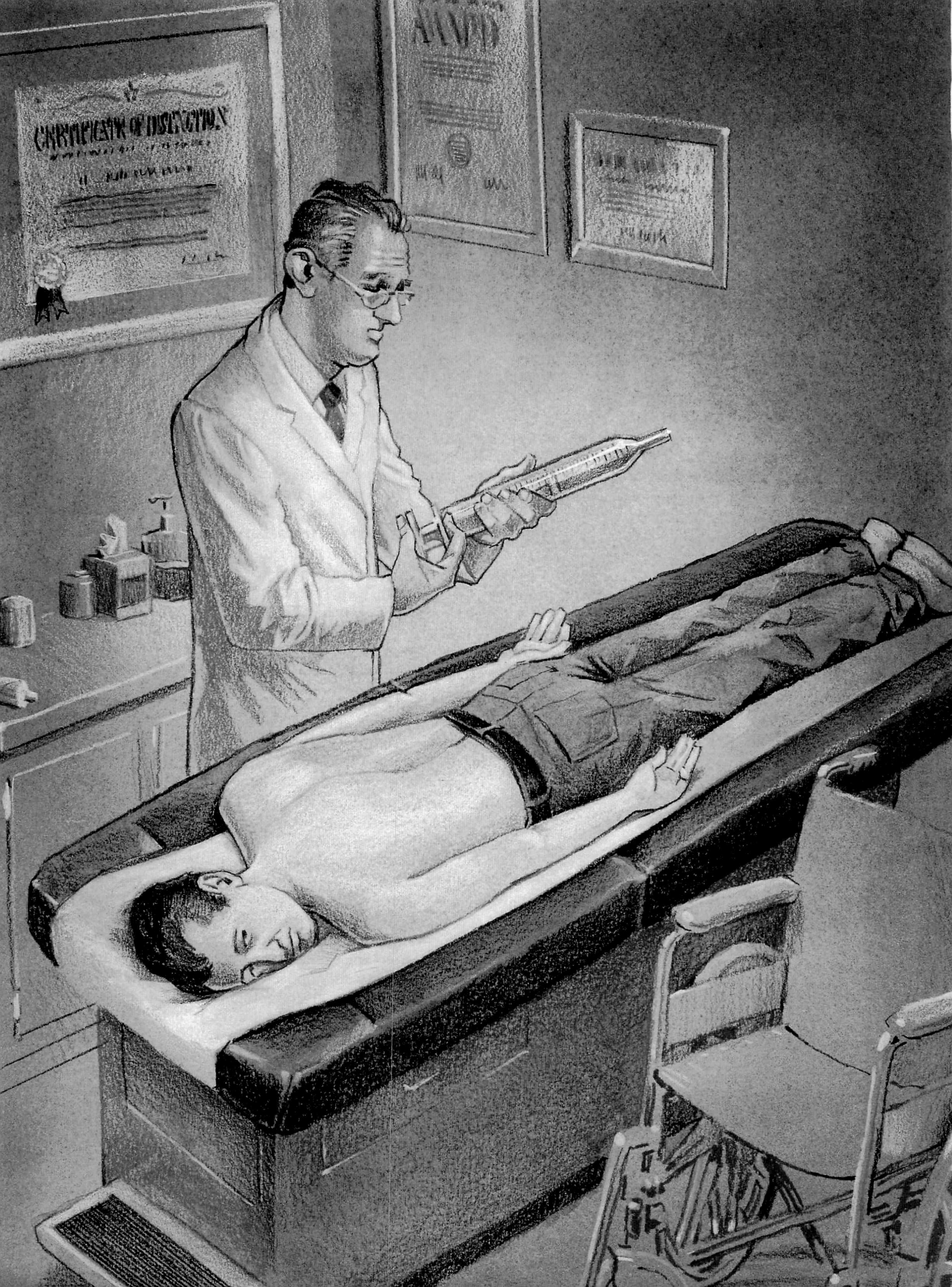
These disturbing statistics, a proposal for reversing them, and other information on underage drinking can be found in the latest issue of "Alcohol Alert," a free newsletter found on the NIAAA's Web site ([www.niaaa.nih.gov/publications/publications.htm](http://www.niaaa.nih.gov/publications/publications.htm)). The site includes back issues of the newsletter, covering topics such as fetal alcohol exposure, alcohol and the workplace, and advances in alcohol treatment.

Several other useful publications are on the site, including *NIAAA Newsletter*, which spotlights the institute's activities and events; the scientific journal *Alcohol Research & Health*; a thesaurus defining more than 10,000 alcohol and drug terms; and numerous brochures covering a wide range of alcohol-related topics.

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*John Henkel is a member of the FDA's Website Management Staff.*







# Idaho Woman Sentenced for Touting Bogus Medical Cure

By Carol Rados

Steve Crowder of San Diego sat in his wheelchair while a doctor tugged on his skin and applied beads of liquid through a dental syringe onto parts of his body. A quadriplegic, Crowder came to the Alternative Medicine and Biophysics Research Institute in Nampa, Idaho, believing he might walk again, or at least find some relief from chronic pain and spasticity. Crowder paid a hefty price for believing in such miracles. According to investigators from the Food and Drug Administration and the FBI, all he got for his \$10,000 was a useless vial of colored liquid.

Between April 1997 and June 2000, Beverly and Thomas Vigil of Meridian, Idaho, touted a product called Neuralyn on the Web and elsewhere as a highly effective treatment for spinal cord injuries and other ailments. The couple claimed that Neuralyn was an all-natural substance made up of B vitamins, amino acids, and extracts of plants from the Yucatan Peninsula. According to Thomas Vigil, Neuralyn was created "from a dream."

In fact, the Vigils teamed up with pharmacist David Taylor and concocted Neuralyn using a number of homeopathic ingredients as well as the topical anesthetics lidocaine and procaine.

According to Assistant U.S. Attorney Wendy Olson, more than 100 people, most of them paraplegics or quadriplegics, paid up to \$10,000 each to come to clinics in Idaho, Utah and Colorado for treatment. These people were told that Neuralyn treatments had been 85 percent to 95 percent successful, and that the product would enable spinal cord injury patients to move, stand on their own, or walk again by regrowing nerve cells. Many of these claims were

made on the Vigils' Web site.

Following an investigation, the Vigils were charged with conspiracy to use the Internet to commit wire fraud and introducing a misbranded drug in interstate commerce with intent to defraud.

During and after treatments, the Vigils falsely told spinal cord injury patients that even slight body movements were a result of the Neuralyn treatment. In truth, investigators say, any such movement was either due to involuntary spasms—caused, in some cases, by Thomas Vigil or his employees putting pressure on the patient's tendons or nerves—or movements the patient could do prior to being treated with the product.

Vials of Neuralyn for home treatment cost up to \$500. The Vigils claimed that the high price was justified by the costs of the ingredients, production process, and costs of research and patent applications. In fact, as Taylor and Beverly Vigil later admitted, a vial of Neuralyn actually cost only a few dollars to make.

Crowder obtained a sample of Neuralyn and had it analyzed. When it proved not to be the "all natural" product the Vigils had promoted, he contacted the U.S. Attorney's Office in San Diego. Because the case involved a questionable drug, FBI Special Agent Mary Martin, who was investigating the case, contacted the FDA for assistance. Investigators from the two agencies eventually determined that the Neuralyn sample was identical to the formula for a product called "Trigeminol" used by a Mexican dentist to treat various ailments at his clinic in Cancun. The Vigils, it turned out, also copied and used Trigeminol promotional materials to tout Neuralyn.

By introducing a misbranded drug in

interstate commerce with the intent to defraud, the Vigils violated the Federal Food, Drug, and Cosmetic Act. Under the act, it is illegal to market a drug for treatment of specific illnesses if it is not approved by the FDA.

Not only did the couple mislead their patients about the bogus treatment, but they also misrepresented Mr. Vigil as a physician who trained at Harvard Medical School. Vigil held nothing more than a mail-order certificate for a 27-day biochemistry course he took at a "diploma mill" university that is no longer operating.

In addition, the couple falsely claimed that Neuralyn had undergone clinical studies, and that both a patent application and FDA approval were pending. "They were all actors," says Crowder. "Down to the certificates on Vigil's wall, it was all a staged event."

In June 2003, the U.S. District Court for the District of Idaho sentenced Beverly Vigil to 33 months in prison and ordered her to pay nearly \$800,000 in restitution to people taken in by the scam. She also was sentenced to three years of supervised release following her imprisonment. Her ex-husband, Thomas Vigil, was indicted on similar charges. He remains a fugitive and has not been arrested.

Taylor pleaded guilty to conspiracy to deliver a misbranded drug in interstate commerce with intent to defraud. He cooperated with investigators and was sentenced to five years probation. Taylor also paid restitution of nearly \$37,000 to those who paid for the phony treatments. ■



# Trans Fatty Acids: Better Decisions or Information Overload?

By Cindy Moore, M.S., R.D.



Information about *trans* fatty acids (aka *trans* fats) in our foods will soon be available on our food labels. The disclosure will prompt food manufacturers to re-examine the healthfulness of their ingredients, and possibly reformulate their recipes. Whether through changes in consumers' food selections or changes in ingredients and food manufacturing practices, consumers' health should benefit from these changes.

Once this information is readily available, consumers will begin to realize the full extent of *trans* fats in our food supply and will be able to make better-informed decisions. Currently, snack foods such as crackers, chips, cookies, baked goods, and candies; frozen convenience items such as frozen entrees, chicken nuggets, and pizza; as well as fried foods, salad dressings and puddings all contain *trans* fatty acids. Is it any wonder that the National Academy of Sciences' report recommended that *trans* fatty acid consumption be "as low as possible while consuming a nutritionally adequate diet," since our current food supply makes a diet free of *trans* fats nearly impossible?

Consumers will need to change their eating habits to limit the amounts of *trans* fat consumed in foods that are not reformulated. The latter option will mean a shift back to cooking from scratch, using oils and soft tub margarines, and eating more fruits, vegetables, whole grains, low-fat dairy and lean sources of protein.

As a registered dietitian, I find that most people follow lifelong patterns when it comes to their eating habits. Most of us prefer to eat certain foods during meals and snacks and find it difficult to change. For those of us whose diets regularly include highly processed foods, many will find it challenging to reduce their *trans* fat consumption unless they change their food choices. This may be the impetus that some need to include more healthful and unprocessed forms of foods in their diets. For example, energy bars, snack chips, crackers, and cookies can be replaced with fresh fruit, nuts, seeds, and whole grain breads. Fat-free dairy products or comparable products made from soy or rice also can be easily incorporated. Since animal products naturally contain a small amount of *trans* fats, select fat-free milk, yogurt, and sorbet in place of higher-fat counterparts such as premium ice cream and high-fat cheese.

For people willing to forgo convenience, a variety of lean meats, fish, poultry, legumes, and eggs prepared using vegetable oils or soft tub spreads can help reduce the amounts of saturated and *trans* fats. When vegetables are on the menu, people can select fresh, frozen or canned products that don't contain added fat from sauces, dressings or other ingredients. Frequent meals and snacks throughout the day can fit into a healthful lifestyle. However, some may need to redefine "snack" as healthful foods eaten between meals in moderate amounts rather than high-calorie, high-fat, and highly processed foods in unlimited quantities.

Just as consumers will need to adapt their habits, savvy food manufacturers will recognize the advantages of reformulating their products with an eye toward more healthful ingredients and cooking methods.

Changes are already evident. Manufacturers already are taking steps to reformulate products, changing the types of fat used in processing to ones that contain little or no *trans* and saturated fats. Products with "*trans* fat-free" on the label are already appearing on supermarket shelves. But use caution: Consumers need to realize that the relatively small amount of *trans* fat commonly eaten by Americans has serious health ramifications. The average intake of *trans* fat is only 5.8 grams per day, but the recommendation from scientific reports is to lower that amount closer to zero. Because manufacturers will be permitted to indicate zero grams of *trans* fats if the product has less than 0.5 grams per serving, consumers may see labels that indicate "*trans* fat-free," but won't necessarily know if the product contains some *trans* fats—less than 0.5 grams per serving—or none at all. Someone who eats multiple servings of a "*trans* fat-free" labeled product that does contain some *trans* fats could still ingest a considerable amount of *trans* fatty acids without being aware of it.

Consumers should take advantage of this new label information to make informed decisions when purchasing foods. Continue to limit foods high in fat, saturated fat and cholesterol. Become aware of *trans* fats in the foods you eat. Enjoy a variety of foods including fruits, vegetables, whole grains, low-fat dairy and lean sources of protein.

To your health! ■

*Cindy Moore is a registered dietitian and director of nutrition therapy at The Cleveland Clinic Foundation in Ohio. She also serves as spokeswoman for the American Dietetic Association*



I'm Prized.  
I'm Immunized.



Fully Immunize Your Child By Age Two

CDC National Immunization Information Hot Line  
English 800-232-2522 Español 800-232-0233  
[www.cdc.gov/nip](http://www.cdc.gov/nip)

