

FDA CONSUMER

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

• VOL. 27 NO. 10

DECEMBER 1993 •

*Seeing to the Safety of
Color Additives*





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Honey Bears, Snowmen and Other Exceptions to Food Label Rules 5
Food packages shaped like honey bears, snowmen, and Santa Claus face a special challenge when trying to incorporate the new nutrition labeling, as do other small or odd-shaped packages. But FDA has found ways to deal with such problems.

Controlling 'Yeast' Infections 10
In the last few years, FDA has approved switching products for treating vaginal "yeast" from prescription to OTC status. Though quick help is a boon, repeated infections should not be taken lightly.

From Shampoo to Cereal: Seeing to the Safety of Color Additives 14
Though we may hardly notice, they're all around us—in our food, drugs, shampoos, toothpaste, contact lenses, vitamins, and more. And over the years, FDA has refined a process that keeps color additives safe.

Dental Amalgam: Filling a Need or Foiling Health? 22
Amalgam has been used in dentistry for 150 years and remains the most widely used material to fill cavities in decayed teeth. Recently, scientists have been investigating whether mercury vapor escaping from "silver fillings" poses any health problem.

Food Allergies: When Eating Is Risky 26
Allergy may be a more frequent suspect in problems that follow dining than an actual villain. But for the 2 to 8 percent of people who truly suffer from food allergies, eating—especially when the recipe is unknown—can be fraught with danger.

On the Teen Scene: A Balanced Look at the Menstrual Cycle 32
The menstrual cycle doesn't affect all women the same. Some hardly notice it, while others may have bad cramps and other symptoms. Happily, modern medicine has come up with many ways to lessen discomfort and keep life on an even keel.

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Inside Front Cover Photo: Should amalgam be used to fill this youngster's tooth? See page 22.



New Drug for Flu

A new oral drug, Flumadine (rimantadine), was approved to combat influenza A, the most serious form of the flu. FDA announced the approval last Sept. 17.

The drug can alleviate symptoms in adults, and in some situations it can be used to prevent influenza A in both children and adults. However, early vaccination remains the method of choice for preventing the flu, according to the national Centers for Disease Control and Prevention.

If taken within 48 hours after symptoms begin, Flumadine can reduce the duration of fever and other flu symptoms. The drug should be taken twice a day for at least seven days. It has not been proven safe and effective to treat symptoms in children, however, and is labeled only as a treatment for adults.

The most common side effects of Flumadine are insomnia, nausea and dizziness.

As a preventative, Flumadine, taken twice a day, can protect against influenza A in children and adults who cannot tolerate vaccines—for instance, if they are allergic to vaccine components or are taking drugs that suppress the immune system. Flumadine has not been shown to be safe to take for more than six weeks, however, and it does not protect against influenza B, the other main type of flu. Also, one study indicated that if Flumadine is used for both prevention and treatment in the same setting—such as the same household—this might result in transmission of drug-resistant strains of the virus.

Each year, 12 million to 50 million people in the United States get the flu, and some 20,000 die, 90 percent of them eld-

erly. Of the two main types of flu, influenza A causes the most severe illness and the most deaths, primarily in the elderly and in people with chronic illnesses and other health problems.

Flumadine, produced by Forest Pharmaceuticals Inc., St. Louis, Mo., is available as a 100-milligram coated tablet and as a syrup.

FDA Proposes Adding Folic Acid to Grains

To lower the risk of neural tube birth defects, FDA is proposing to require manufacturers to add folic acid, a "B" vitamin, to enriched grain products. The proposal, published in the Oct. 8, 1993, *Federal Register*, would also allow a health claim noting this beneficial effect on labels of foods and dietary supplements that are good sources of this vitamin.

Because neural tube birth defects develop before most women are aware they're pregnant, it's important for young women to consume adequate folic acid *before* becoming pregnant.

Last year, the U.S. Public Health Service recommended a daily intake of 0.4 milligrams of folic acid for women of childbearing age as a way to reduce spina bifida and anencephaly neural tube birth defects in their babies. Since then, FDA has worked with other PHS components and outside experts to develop the most effective measures for carrying out the recommendation.

Folic acid is available from several sources, including foods in which folate occurs naturally (such as citrus fruits and dark-green leafy vegetables), foods fortified with folic acid, and dietary supplements containing folic acid. Overconsumption of folic acid, however, can mask

symptoms of a vitamin B₁₂ deficiency, such as pernicious anemia, that can lead to nerve damage if left untreated.

To establish a safe level of intake even for heavy consumers of enriched grain products, FDA proposes adding folic acid only to a limited range of products and establishing new standards of identity that would stipulate the amount of folic acid the products must contain. The proposal would require manufacturers to add folic acid to enriched flours, breads, rolls, buns, corn grits, corn meal, farina, rice, macaroni, and noodle products.

FDA's sample health claim would read: "Daily consumption of 0.4 milligrams (mg) of folate by women of childbearing age may be a factor in helping to reduce the risk of neural tube defects in their offspring. Sources of folate include leafy dark-green vegetables, citrus fruits and juices, yeast, fortified breads and breakfast cereals, beans, and dietary supplements containing folic acid. Regular daily consumption of folate should not exceed 1.0 milligram from all sources."

About 2,500 live-birth cases of spina bifida and anencephaly neural tube birth defects occur each year in the United States. In spina bifida, the spinal cord is exposed and may be damaged, sometimes resulting in paralysis. Such youngsters may require a series of operations and other treatments, and most grow to adulthood with some disability. Babies with anencephaly have severe brain malformation and cannot survive.

People have until Dec. 8 to send comments on the proposed rules to Dockets Management Branch, HFA-305, FDA, Room 1-23, 12420 Parklawn Drive, Rockville, MD 20857.

Pesticide Report Available

Almost 99 percent of food produced in the United States, and over 96 percent of imports from 94 countries, have either no pesticide residues, or the levels detected are well within permitted limits set by the Environmental Protection Agency, according to the 1992 report of FDA's pesticide monitoring program now available to consumers. The findings are based on FDA's analyses of 16,428 food samples.

FDA collected 15,370 samples from shipments with no prior evidence of illegal residues. The foods included fruits and vegetables, grains and grain products, dairy foods (including eggs), and fin fish and shellfish. Produce, including bananas, were analyzed as the unwashed, whole, raw commodity—that is, with the peel or skin intact. From these shipments:

- Of the 7,548 domestic samples, 65 percent had no detectable residues, less than 1 percent had residues over EPA permitted levels, and less than 1 percent had residues for which there were no permitted limits for particular pesticides in specific foods.
- Of the 7,822 imported samples, 66 percent had no detectable residues, less than 1 percent had residues over EPA permitted limits, and 3 percent had residues for which there were no permitted limits for particular pesticides in specific foods.

FDA collected 1,058 samples from shipments with a known or suspected pesticide residue problem. From these shipments:

- Of the 229 domestic samples, 19 percent were violative.
- Of the 829 import samples, 14 percent were violative.

In addition, FDA surveyed certain aquaculture products and milk to learn more about particular pesticide and com-

modity combinations. In the aquaculture survey, 75 of 206 samples had no detectable residues. In the milk survey, 48 percent of 558 samples had residues of chlorinated pesticides. These pesticides have not been registered for food use in over a decade, but they are still present at low levels in some foods because of their persistence in the environment.

Free copies of the report, "Food and Drug Administration Pesticide Program, Residue Monitoring 1992," are available from Norma Yess, FDA, HFS-308, 200 C St., S.W., Washington, DC 20204. (Also see "FDA Reports on Pesticides in Foods," *FDA Consumer*, June 1993.)

FTC Accuses Five Diet Programs Of Deceptive Advertising

The Federal Trade Commission has charged that five of the nation's largest commercial diet-program companies have misled consumers by making unsubstantiated weight-loss claims and by using deceptive testimonials.

In a Sept. 30 statement, FTC alleged that some of the cases involved deceptive pricing, comparative superiority, weight-loss rate, or safety-related claims.

According to the statement, Diet Center, Inc., Physicians Weight Loss Centers of America, Inc., and Nutri/System, Inc., have agreed to settle the federal charges through consent agreements, and Jenny Craig, Inc./Jenny Craig International, Inc., and Weight Watchers International, Inc., plan to challenge the charges.

At the heart of the five cases are advertising testimonials claiming achievement of certain weight-loss goals. FTC alleges that none of the five firms can substantiate that their customers are typically successful in reaching their weight-loss goals or

in maintaining them over the long term. FTC also alleges that four of the companies made unsubstantiated claims that their customers maintained weight loss permanently.

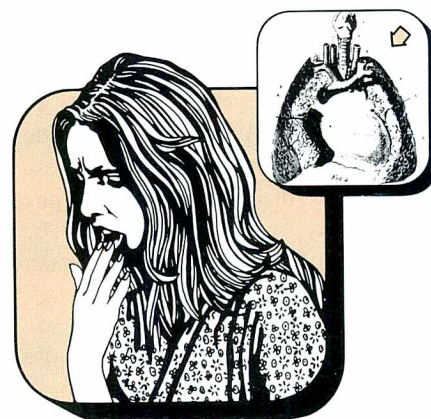
'Pot,' 'Crack,' Increases Pneumonia in AIDS Patients

Smoking marijuana or crack cocaine is significantly associated with an increase in the risk of bacterial pneumonia in people infected with HIV, according to a new study. Pneumonia is a major cause of death in people with AIDS.

In research supported by the National Institutes of Health, researcher Waleska Teixeira Caiiffa, M.D., and colleagues at the Johns Hopkins School of Public Health in Baltimore, said doctors counseling HIV-infected persons should advise them of the link.

The U.S. Public Health Service has previously warned that irritants and contaminants of smoked marijuana may be harmful to people with HIV.

Marinol (dronabinol), a prescription



drug containing a synthetic form of one of marijuana's active ingredients (delta-9-tetrahydrocannabinol), was approved in 1992 to prevent weight loss in AIDS patients. (See "Marinol for AIDS Patients" in the AIDS Page section of the April 1993 *FDA Consumer*.) It was first approved in 1985 to treat nausea and vomiting associated with cancer chemotherapy.

CDC Reports on Exercise And Coronary Heart Disease

Mild to moderate physical activity—such as walking, gardening, yardwork, and dancing—can help prevent coronary heart disease, according to a Sept. 10 report in the *Morbidity and Mortality Weekly Report* by the national Centers for Disease Control and Prevention.

Coronary heart disease (CHD) is the leading cause of death in the United States. Each year, approximately 1.5 million Americans are newly diagnosed with CHD, which accounts for an estimated \$47 billion in health-care costs. The costs associated with physical inactivity are estimated at \$5.7 billion.

Risk factors associated with CHD include family history of the disease, high levels of low-density lipoprotein (LDL) cholesterol, low levels of high-density lipoprotein (HDL) cholesterol, cigarette smoking, uncontrolled high blood pressure, obesity, diabetes mellitus, and physical inactivity.

The risk of CHD from physical inactivity is just as great as with other risk factors. CDC found that in 1986, 205,254 CHD deaths were attributed to lack of sufficient physical activity. That is higher than estimates of CHD deaths from smok-

ing (148,879), obesity (190,456), and high blood pressure (171,121) and similar to the estimate for high cholesterol (253,194).

Estimates suggest that 20,000 fewer Americans would die each year if half of those who report doing no leisure-time physical activity began to participate in moderate physical activity at least two or three times a week, CDC said.

Free Spanish Pub About Food Label

A brochure written in Spanish on how to read the new food label is now available free. (A free English version was made available previously.)

The brochure, "Cómo leer la Nueva Etiqueta De Los Alimentos" (FDA 93-2260S), was produced jointly by FDA and the American Heart Association.

To order single copies, write to FDA, HFE-88, 5600 Fishers Lane, Rockville, MD 20857. To order two to 100 copies, write to FDA, HFI-40, at the same ad-



dress, or fax your order to (301) 443-9057. Please be sure to give the brochure's publication number.

Mental Health Information

Single copies of the following publications are available free from the National Institute of Mental Health:

- Alzheimer's Disease (ADM 92-1696)
- If You're Over 65 and Feeling Depressed . . . Treatment Brings New Hope (ADM 90-1653)
- Let's Talk About Depression (prepared especially for African-American youth) (ADM 91-1695)
- Bipolar Disorder: Manic-Depressive Illness (ADM 90-1609)

Available in Spanish are:

- Plática Franca Sobre La Tensión (SP 91-0502)
- Cuando Un Amigo Tiene el S.I.D.A. (SP 90-1515)
- Datos Utiles Sobre Enfermedades Depresivas (SP 90-1702)
- Esquizofrenia Preguntas y Respuestas (SP 91-1457)
- No Estás Solo: Datos Acerca de Salud Mental y Enfermedades (SP 90-1178)
- Trastorno De Pánico (SP 92-1869)

Request copies from the Information Resources and Inquiries Branch, Room 15C-05, Office of Scientific Information, National Institute of Mental Health, 5600 Fishers Lane, Rockville, MD 20857. Include the publication title and number.

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

Honey Bears, Snowmen and Other Exceptions to Food Label Rules

by Paula Kurtzweil

Companies that sell honey in the bear-shaped squeeze container are finding themselves in a stickier situation than usual these days: how to comply with FDA's new guidelines for mandatory nutrition labeling.

It's not that they can't come up with the necessary nutrition information or that they don't have the means to produce a readable label. The problem is that the little bear's body doesn't have ample space for a nutrition label.



Manufacturers will continue to be responsible for ensuring the accuracy of the nutrient content information on the label.

It's a problem that hasn't caught FDA unawares. The 898-page *Federal Register* document that spells out how FDA requires foods to be labeled according to the Nutrition Labeling and Education Act of 1990 contains a provision for just such problems. It's found in Paragraph 101.9(g)(9) of the regulations.

There, the document specifically addresses foods for which a complete nutrition label on the package may not be "technologically feasible or some other circumstance makes it impracticable." For these foods, FDA will consider alternative means of compliance.

That is one of several provisions that, until recently, have received little attention. Now, as manufacturers begin to relabel their products to meet the May 1994 deadline, those provisions are getting a closer look.

The regulations, published in January 1993, are known more for:

- establishing mandatory nutrition labeling
- redesigning the format for presenting nutrition information
- defining nutrient claims, such as "low fat" and "high fiber"
- approving the use of seven nutrient-health and nutrient/food-health claims
- establishing more uniform serving sizes.

They are less noted for addressing the specifics of how to label uniquely packaged foods or foods with few nutrients, or for explaining the technicalities of determining a food's nutrient content. But these provisions are there, and, like their more prominent counterparts, they, too, will affect what consumers see on food labels of the future.

Looking in All the Right Places

Some of the specifics deal with placement of the nutrition label, now called "Nutrition Facts."

For most foods, nutrition information will continue to appear to the immediate

right of the principal display panel, which is usually the front of the package. But, for the first time, some exceptions are allowed. Among them:

- Packages with less than 40 square inches available for nutrition labeling—for example, the standard-size gelatin dessert box—may carry nutrition information on any panel. This is one of four options that manufacturers have to help them fit the nutrition information onto smaller packages.

- Nutrition information for variety-pack food items, such as ready-to-eat cereals or snacks, may appear on the individual product where a consumer can readily see it at the point of purchase—or be listed for each food on the outside wrapper.

- Cartons of eggs in shells may carry nutrition information on a package insert.

This exception targets egg cartons in which the top and bottom conform to the shape of the eggs and thus leave insufficient surface area for nutrition information.

- Assorted gift packages, such as a holiday gift box of cheeses, crackers and jellies, may provide nutrition information on a package insert. In allowing this option, FDA determined it is more important that the recipient of the gift see the information than the gift giver because the recipient will benefit more from the information. This provision also allows the gift box maker to use the same information for multiple gift boxes that may vary only slightly in size. (The regulations allow nutrition information for similar assorted foods to be listed for each item or as a composite of the entire contents.)

- Nutrition information for foods that are not individually packaged, such as condiments or cookies sold from bulk containers, may be presented on counter cards, posters, take-home brochures, or other written materials at the point of purchase. These materials also can be used for nutrition information for game meats. (Under

FDA's voluntary nutrition information program for raw fruit, vegetables and fish, point-of-purchase materials are the major means of presenting nutrition information.)

Firms Help Develop Options

Under the (g)(9) provision, FDA will consider other labeling options for other foods that do not lend themselves to the mandatory nutrition label. The options can range from a smaller nutrition label to posters and brochures at the point of purchase.

"The alternative can include a lot of things," said Virginia Wilkening, a registered dietitian and consumer safety officer in FDA's Office of Food Labeling. "But, it's up to the company to propose an option for presenting the nutrition information."

The provision requires manufacturers to write to FDA, explain their labeling problem, and offer a solution. FDA, in turn, will review the request and decide whether it's justified and reasonable before giving it an OK.

According to Wilkening, the agency already has received a number of (g)(9) requests, one of which is from the Sioux Honey Association, headquartered in Sioux City, Iowa. The association is asking permission to use a smaller Nutrition Facts panel than that required in the regulations on the honey bear container. The label would be attached to a redesigned honey bear, now shown carrying front and back "billboards." One of the flat billboards, about 2 square inches, would be used for nutrition information.

FDA received similar requests from several other groups that sell food in packages with limited label space, Wilkening said. As a result, in technical amendments published in August 1993, the agency added a new rule: Packages with less than 12 square inches available for nutrition labeling may use smaller type to present nutrition information. The Sioux Honey Association's redesigned honey bear

would fall under that category, she said.

"There really is no place to put the nutrition label on the traditional honey bear," Wilkening acknowledged. "But there are several possibilities: The billboard approach with smaller type is one. A tag around the neck might be another. We'll just have to decide each on a case-by-case basis."

Another (g)(9) request under FDA consideration involves 1-liter (1 quart) glass jars of strawberry jam in the shapes of Santa Claus and a snowman. Because of the containers' roundness and indentations, Wilkening said, FDA may exempt both products from nutrition labeling as long as their labels carry a telephone number or address for consumers to call or write to get the required nutrition information.

"What they've asked is for their product to be considered a small package," Wilkening said, citing a provision that allows packages with less than 12 square inches available for nutrition labeling to provide an address or telephone number for consumers to get the required information.

Wilkening said the agency probably will OK the request because the product is available only for short periods—around Christmas—and because it is sold next to other jams that will have the nutrition information. "Even though it may be on another container, consumers would have access to the same type of nutrition information," she said.

Determining Exemptions

Not all foods will have to carry nutrition information. The Nutrition Labeling and Education Act exempts food sold for immediate



Surprising Candidates for Nutrition Labeling

“We don’t need seizures and prosecutions if we get a complying label.”
—Elizabeth Campbell,
FDA’s Office of Food Labeling.

- **Baking powder.** A quarter teaspoon has 110 milligrams (mg) sodium and 60 mg calcium.
- **Blackstrap molasses.** A 1-tablespoon serving gives 55 calories, 14 grams (g) carbohydrate, and 140 mg calcium.
- **Chili powder.** A quarter teaspoon provides about 4 percent of the Daily Value for vitamin A and 5 mg of sodium.
- **Paprika.** A quarter teaspoon provides about 6 percent of the Daily Value for vitamin A.
- **Salt.** It provides 575 mg sodium per quarter teaspoon.
- **Bottled water,** if it naturally contains 5 mg or more sodium per 8 fluid ounces (240 milliliter [mL]), or if it is labeled “sodium-free,” “minerals added,” or carries some other nutrient claim.
- **Wine coolers.** An 8-ounce (240 mL) serving provides more than the cutoff level for total carbohydrate and calories. (FDA regulates wine with less than 7 percent alcohol, such as wine coolers; so, these products are bound by the food labeling regulations. The Bureau of Alcohol, Tobacco, and Firearms oversees all other alcoholic products, and FDA regulations do not apply.)
- **Prepackaged deli foods,** if they were primarily prepared and processed at a site other than the store in which they are sold. ■

—P.K.

consumption and food produced by small businesses if the food packages don’t carry a nutrition claim.

Also exempt are foods that contain insignificant amounts of all the nutrients that are required in nutrition labeling—as long as the product’s label doesn’t carry nutrition claims. A food contains insignificant amounts of the dietary components required in nutrition labeling if a serving of the food contains:

- less than 2 percent of the Daily Value for vitamins and minerals
- less than 1 gram (g) of carbohydrate, dietary fiber, and protein
- less than 2 milligrams (mg) of cholesterol
- less than 5 mg of sodium
- less than 0.5 g of fat, saturated fat, and sugars
- fewer than 5 calories.

The food labeling regulations specifically exempt plain coffee and tea, flavor

extracts, food colors, and other foods that are not significant sources of nutrients.

Most spices are not significant sources of nutrients, either—except for a few. For example, paprika and chili powder contain vitamin A and therefore will have to have nutrition labeling. (See accompanying list.)

In many cases, foods with few nutrients will qualify for the simplified nutrition label format, in which information about some nutrients otherwise required in nutrition labeling may be omitted. The simplified format is allowed when the food contains insignificant amounts of seven or more of the dietary components required in nutrition labeling. However, information about calories, total fat, sodium, carbohydrate, and protein is still required.

Nutrient Analysis

And how are these nutrient levels determined? That, too, is addressed in the regulations.

As before, manufacturers will continue to be responsible for ensuring the accuracy of the nutrient content information on the label.

They can use any means they desire to determine a food’s nutritional makeup. Typically, nutrients are analyzed in the laboratory using one or more chemical tests. In checking the validity of nutrient information on the label, FDA uses only tests approved by AOAC International, an association of official analytical chemists, and other procedures FDA accepts as valid. Manufacturers are encouraged to use these procedures, too.

FDA does not endorse any set of nutrient data for use in nutrition labeling. However, in the January 1993 *Federal Register* document, FDA expressed interest in working with the food industry to develop databases for nutrition labeling purposes. It also announced the availability of the *FDA Nutrition Labeling Manual: A Guide*

For More About Food Labeling...

For more information about FDA's food labeling regulations, see:

- "Nutrition Info Available for Raw Fruits, Vegetables, Fish" (January-February 1993 *FDA Consumer*)
- "Ingredient Labeling: What's in a Food?" (April 1993 *FDA Consumer*)
- "Good Reading for Good Eating," "Starting This Month: Look for 'Legit' Health Claims on Foods," "'Nutrition Facts' to Help Consumers Eat Smart," and "'Daily Values' Encourage Healthy Diet" (May 1993 *FDA Consumer*)
- "A Little 'Lite' Reading" and "The Food Pyramid-Food Label Connection" (June 1993 *FDA Consumer*).

These articles are reprinted together in the *FDA Consumer* special report *Focus on Food Labeling*. To order one free copy, write to FDA, HFE-88, 5600 Fishers Lane, Rockville, MD 20857. Ask for order number FDA 93-2262. ■

for *Developing and Using Databases* to help companies and trade organizations develop and use a database for nutrition labeling.

Checking Compliance

FDA checks the accuracy of nutrition labeling information by conducting its own nutritional analyses and applying several guidelines for determining the accuracy of the nutrition information.

For nutrients that are considered desirable—that is, vitamins, minerals, protein, total carbohydrate, dietary fiber, other carbohydrate, polyunsaturated fat, monounsaturated fat, and potassium—and that are present naturally in the food, the FDA-determined analytical value must be at least 80 percent of the value declared on the label.

For naturally occurring dietary components for which lower intakes are sometimes advised—that is, calories, sugars,

total fat, saturated fat, cholesterol, and sodium—FDA's analytical values must be no more than 20 percent higher than the label values.

For nutrients added to a food, FDA's determined values must be at least equal to the values stated on the label.

Enforcement

Before initiating enforcement action, the agency will consider factors such as the seriousness of the violation, information obtained during an establishment inspection, consumer complaints, and the firm's compliance history.

According to Elizabeth Campbell, director of the division of programs and enforcement policy in FDA's Office of Food Labeling, a warning letter to the company often puts an end to many violative practices. "Usually that's enough," she said. "We don't need seizures and prosecutions if we get a complying label."

*P*aprika and chili powder contain vitamin A and therefore will have to have nutrition labeling.

FDA won't be the only agency checking food labeling compliance. Under the Nutrition Labeling and Education Act, state governments may now enforce federal food labeling laws. The act for the first time prohibits states from enforcing their own labeling requirements on food in interstate commerce, unless those requirements are the same as FDA's. Thus, a state can adopt provisions identical to FDA's and enforce those regulations either at the state or federal level.

However, state involvement means that FDA will have to inform each state of any additional changes, exemptions and exceptions it makes to the nutrition labeling regulations and policies. Such changes would include decisions about the honey bear, snowman and Santa. ■

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

CONTROLLING 'YEAST' INFECTIONS

by Amy Roffmann New



Intense itching is usually the hallmark of a vaginal yeast infection. Once a woman has experienced it, she's not likely to forget it.

Nearly 75 percent of all women will have at least one such infection in their lifetime. Many are plagued by recurring yeast infections, which are most frequent between the ages of 16 and 35.

Yeast is a term for single-celled fungi. The technical name for the variety of fungus often present in the human body is candida, and the technical name for infections caused by these fungi is candidiasis. Such infections occur not only in the vagina, but also in other parts of the body in both sexes (see accompanying article).

In December 1990, the Food and Drug Administration approved the over-the-counter (nonprescription) sale of the first of several products for treating vaginal yeast infections in women previously diagnosed by their doctors as having them.

A woman who has had one vaginal yeast infection can usually recognize its symptoms if it recurs. And a woman who has had several infections has no doubt about what's wrong when the next yeast infection starts.

There are several symptoms, but, according to Michael Spence, M.D., director of the Public Health and Preventive Medicine Program at Hahnemann University in Philadelphia, "If a woman does not itch, it's unlikely that she has a yeast infection."

Another symptom is a thick, mostly odorless discharge. But this can be misleading because, according to Spence,

"Discharge in and of itself is not diagnostic. If you have a white discharge with an intense irritating itch, you may have an infection. Unfortunately, many women will, in response to increased estrogen at mid-cycle and the increased production of cervical mucus, develop a white, curdy discharge. That is not a yeast infection."

While not all women experience the following symptoms of a vaginal yeast infection, it's possible to have: vaginal soreness or irritation, a rash on the vulva around the vagina, pain or discomfort during intercourse, abdominal pain, soreness of the vulva or vagina, burning during urination, and even vaginal bleeding in some cases in addition to itching and discharge.

Causes of Yeast Infection

Candidiasis is caused by one of four varieties of candida: *Candida albicans*, *Candida glabrata*, *Candida tropicalis*, and *Candida krusei*. By far the most common—causing nearly 80 percent of vaginal yeast infections—is *Candida albicans*.

Most people have these organisms in the genital or intestinal tract to some degree at various times. It's the overgrowth of the fungus that causes problems.

According to Spence, there are a number of causes of the uncontrolled growth, usually related to some type of immune suppression. Sometimes there's been a significant change in diet. Other times it's due to use of antibiotics to treat another infection, such as strep throat or acne.

Broad-spectrum antibiotics such as penicillin or tetracycline can kill or suppress helpful bacteria in the genital tract, allowing yeast to grow unchecked, according to Philip Mead, M.D., Professor of Obstetrics and Gynecology at the University of Vermont College of Medicine.

It's even possible that an underlying disorder, like diabetes, is the root cause of the infection. "Whenever you see a fungal infection in a woman, these are the things

that come immediately to mind," says Spence.

When physicians see recurrent yeast infections without another cause, they have to wonder about HIV disease. Because HIV (the virus that leads to AIDS) involves a lowering of the immune system, it could significantly impair a woman's ability to combat yeast, says Spence.

"Yeast infections can be passed back and forth between partners in unprotected intercourse, but because yeast is frequently present anyway, a sexual partner is more likely to pick up the infection if his or her immune system is also depressed," says Mead.

Immunity can become depressed by a number of factors besides HIV infection. Illness or infection of any kind weakens the immune system. Physical or mental stress can also wreak havoc, leaving the immune system less able to combat yeast infections. Lack of sleep, poor nutrition, and taking any medication, including birth control pills, can upset the body's balance, allowing yeast to thrive. Pregnant women also have a tendency to have more yeast infections, as the immune system becomes temporarily altered by hormonal surges.

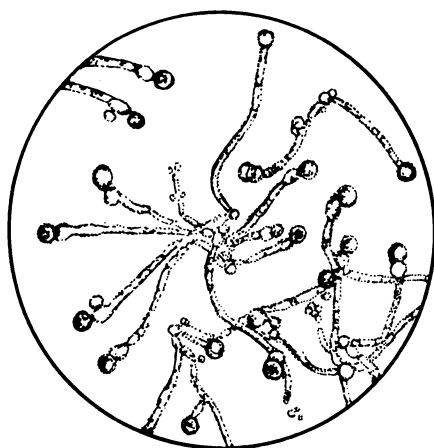
Diagnosis

Diagnosing vaginal yeast infections can be tricky, especially at first. Several other disorders, including inflammation of the cervix or sexually transmitted diseases such as trichomoniasis (a parasitic infection) or herpes, can have similar symptoms.

According to Mead, clinical diagnosis of yeast infections starts with a slide of vaginal secretions examined under the microscope. "Those slides [can be] very specific. If you see the yeast organisms, you

Women who get vaginal yeast infections may want to limit their use of pantyhose and other tight garb, and instead wear loose, natural-fiber clothing.

A WOMAN WHO HAS HAD ONE VAGINAL YEAST INFECTION CAN USUALLY RECOGNIZE ITS SYMPTOMS IF IT RECURS.



Candida albicans

can assume that's the diagnosis."

(Slides are actually examined for a particular stage of the fungus form called mycelia. While yeast is a commonly present form of fungus, mycelia is the variation of the fungus type that can grow out of control and cause infection problems.)

It's possible to have a yeast infection that doesn't show up in the limited examination of a single slide smear. Mead says that if a woman has a negative slide smear, but still has significant symptoms, her physician is likely to order a culture.

For example, there is one variety of candida—*Candida glabrata*—that causes symptoms but does not characteristically show up under the microscope. For that, a culture may be necessary. "A culture is more sensitive," says Mead. "It should pick up virtually anything."

While studies have shown that women

are able to correctly identify recurring vaginal yeast infections most of the time, there is still some concern about misdiagnosing and mistreating other problems that may mimic symptoms. Through package and product labeling of products sold without prescription, FDA and pharmaceutical companies are working to make sure that women with an infection that differs even slightly from the symptoms of a previous yeast infection return to their doctors.

OTC Availability—With Warnings

Until 1990, drugs to treat vaginal yeast infections were available only by prescription. In December 1990, after receiving the advice of a number of experts, FDA gave Schering-Plough HealthCare the go-ahead to market and sell over-the-counter its antifungal medication Gyne-Lotrimin, a brand name for clotrimazole. It has been joined by several other products that are either clotrimazole or another antifungal, miconazole nitrate. (The first miconazole nitrate drug to be allowed to be sold OTC for vaginal yeast infections was Advanced Care Products' Monistat 7.)

Both clotrimazole and miconazole nitrate are from the same anti-fungal drug family and work very similarly by breaking down the cell wall of the yeast organism, causing it to dissolve completely.

The products are supplied in one of two ways: as vaginal inserts or suppositories or as a cream with a special applicator. Both formulations are for use at bedtime every night for seven nights.

While most women note improvement within just a few days, it's important to finish the seven-day treatment to make sure all of the troublemaking fungus has been disabled. Women who don't see rapid improvement of their symptoms are likely to have a problem other than a vaginal yeast infection.

"The benefit [of OTC sale of these products] is that they are readily available for women to purchase without having to go to a physician," says Joseph Winfield, M.D., a medical officer in FDA's anti-infective drugs division. Ready availability of OTC treatments means that women no longer have to suffer while waiting for an appointment, or rearrange work and family life to find time to go to the doctor's office for a recurrent infection.

"Vaginal candidiasis is a rather common occurrence," says Winfield. "It doesn't present any life-threatening condition to the individual [with an infection] and it's okay to treat over the counter—but only for women [who] have had an infection diagnosed by a physician previously. As those same symptoms recur, they should be able to treat themselves."

In October 1992, FDA required additions to printed information accompanying OTC products for vaginal yeast infections. One significant addition to the patient package insert was a notice that recurrent vaginal yeast infections, especially those that do not clear up easily with proper treatment, may also be the result of serious medical conditions, including HIV infection. The labeling also says: *If you experience vaginal yeast infections frequently (they recur within a two-month period) or if you have vaginal yeast infections that do not clear up easily with proper treatment, you should see your doctor promptly to determine the cause and to receive proper medical care.*

"While it is true that women who are HIV-infected are much more likely to

OTHER YEAST INFECTIONS

Even though vaginal yeast infections are the most common type of candida infections, there are other ways in which yeast can cause problems.

Thrush is the name given to an oral yeast infection. It is most often seen in infants or in people with severely suppressed immune systems—as in AIDS. Its symptoms are painful sores in the mouth and throat that appear as creamy white patches and reveal red sores when scraped. Left untreated, thrush may spread to the throat and esophagus. (Other infections can cause similar symptoms, so anyone with these symptoms should have their condition accurately diagnosed by a health professional.)

Other candida infections can occur nearly anywhere on the body where there is a skin fold: under the arms, under the breasts, between the toes. The skin around the fingernails can be affected.

Candida infections have been reported in women who wear artificial fingernails. Fungal infections can start in the space between the artificial and natural nail if they become separated. The nails may become discolored by infection and may require drug treatment.

The drugs used to treat these other candida infections are similar, but not always identical to those used for vaginal yeast infections. Most of the treatments are from the “azole” drug family (clotrimazole, fluconazole). Some drugs are oral medica-

tions, although those are most often used only for stubborn or persistent infections. A fairly new drug (approved by FDA in January 1990), fluconazole is effective in a single dose by tablet or intravenous injection, but is most often used only in serious fungal infections, such as those in persons with HIV disease.

It's important to note that over-the-counter products for vaginal yeast infections are not appropriate for other types of fungal infections. Those products are only for the uses stated on the package. For any other yeast infection, see your doctor. ■

—A.R.N.

have chronic vaginal yeast infections,” says Mead, “most women with recurrent vaginal yeast infections aren't HIV-positive [HIV-infected].”

In addition to the HIV notice, the following warnings also appear on information accompanying the products:

- Do not use if you have abdominal pain, fever, or foul-smelling vaginal discharge. You may have a condition that is more serious than a yeast infection. Contact your doctor immediately.
- Do not use if this is your first experience with vaginal itch and discomfort. See your doctor.
- If there is no improvement within three days, you may have a condition other than a yeast infection. Stop using this product and see your doctor.

- If symptoms recur within a two-month period, contact your doctor.
- Do not use during pregnancy except under the advice and supervision of a doctor.
- This medication is for vaginal yeast infections only. It is not for use in the mouth or the eyes. If accidentally swallowed, seek professional assistance or contact a Poison Control Center immediately.
- Keep this and all other drugs out of the reach of children. This product is not to be used in children less than 12 years of age.

Prevention

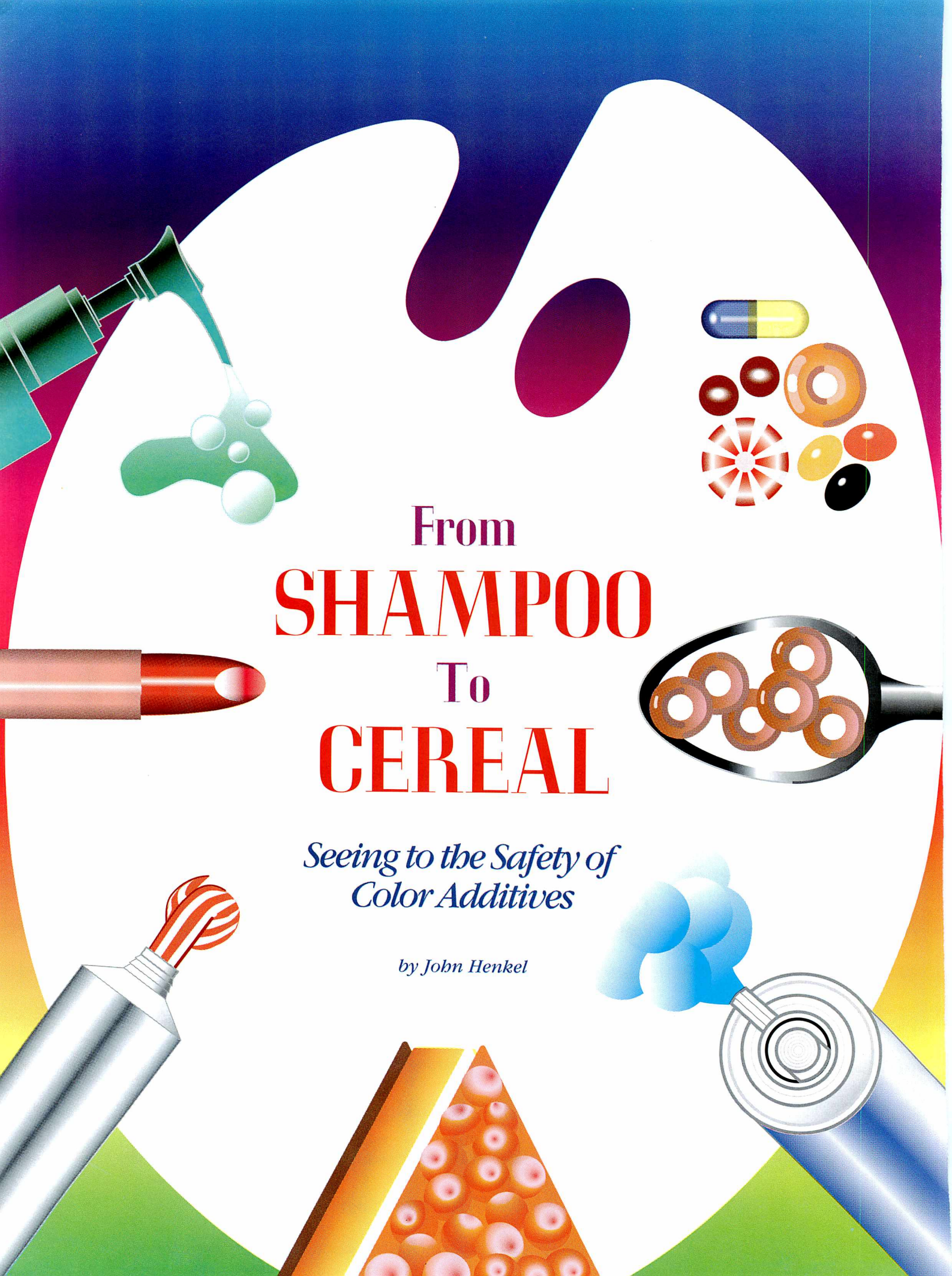
In general, candida likes warm, moist places. It's not possible to prevent every yeast infection, but a few simple steps can help reduce the number of infections women get.

Wear loose, natural-fiber clothing and underwear with a cotton crotch. As much as possible, avoid pantyhose, tights or leg-

gings, nylon underwear, and tight jeans. Limit the use of deodorant tampons and feminine hygiene products if you feel an infection beginning, as they can interfere with the helpful bacteria in the vagina. Keep genitals dry after bathing or swimming (don't stay in a wet swimsuit for hours).

Seasonal changes can affect the likelihood of getting an infection, too. During high-heat, high-humidity periods, it's easier to get a yeast infection. Heavy winter clothing, which prevents easy release of perspiration and moisture, can also spell trouble. ■

Amy Roffmann New is a writer in Chandler, Ariz.



From SHAMPOO To CEREAL

*Seeing to the Safety of
Color Additives*

by John Henkel

It starts when you get up in the morning. You snatch a bar of soap and scrub your face. That's likely your first dab into the palette of added tints and hues that will color much of your day. Most of us hardly notice them, but color additives surround us. They're in shampoos. In shaving cream. Toothpaste. Deodorant. Contact lenses. Lipstick, eyeliner, and mascara. At breakfast, the colors keep coming. Juice, cereal, pastry, coffee creamer, vitamins—all are likely to have added colors.

Color additives make things attractive, appealing, appetizing. They also serve as a code of sorts, allowing us to identify products on sight, like medicine dosages and candy flavors. We might reason, for example, that a pale green candy is mint flavored, while a darker green one is lime. Based on our color analysis alone, there will probably be no surprises when we pop the candy into our mouths.

With this rainbow hodgepodge bombarding us daily, it's only natural that consumers might wonder: Just how safe are all these colors? "Very," says John E. Bailey, Ph.D., acting director of FDA's Office of Cosmetics and Colors.

He explains that FDA has, over nearly a century, refined its process of monitoring and controlling color additive use. By law, industry must prove the safety of colors it sells. FDA ensures that colors on the market are safe for their intended purposes and do not cover up product inferiority or otherwise deceive consumers. FDA watches domestic color use closely, seizing products found unsafe.

Still, Bailey says, some consumers believe color additives can cause health prob-

lems or even be hazardous. This notion stems, he says, from persistent public attitudes about colors banned in the past. He says consumer confidence in the safety of all colors can be shaken when FDA removes a color from the market. But he emphasizes: "I think we can say with assurance that today's colors are safe if used properly and that consumers need not be worried."

Yellow Means Caution

Two categories make up FDA's list of permitted colors: those the agency certifies by batch (derived primarily from petroleum and coal sources) and ones exempt from batch certification (obtained largely from plant, animal, or other mineral sources—fruit juice, carmine, and titanium dioxide, for example). Colors found to be potentially hazardous have been purged from the list of permissible additives. What remains is a wide color spectrum approved for use in foods, over-the-counter and prescription drugs, cosmetics, or in medical devices such as surgical sutures and contact lenses.

Though these colors have a good safety record, one commonly used additive reportedly has prompted minor adverse reactions in some people. It is FD&C Yellow No. 5, listed as tartrazine on medicine labels, a color found widely in beverages, desserts, processed vegetables, drugs, makeup, and many other products. FDA certifies more than 2 million pounds of it yearly.

In 1986, an FDA advisory committee concluded that Yellow No. 5 may cause itching or hives in a small population subgroup. This kind of skin reaction usually is not a serious one, says Linda Tollefson, D.V.M., an FDA epidemiologist. "Reac-

Color additives

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appealing, appetizing,

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dosages and candy

flavors.



An FDA scientist prepares color additive samples for analysis. Manufacturers supply FDA with these samples, each of which represents a batch bound for marketing. Every color will undergo a battery of tests for purity. Certifiable colors not meeting certain tolerances are rejected and not allowed to be sold.

tions are classified as hypersensitive and are not true allergic reactions, which would be more severe."

Nonetheless, since 1980 (for drugs) and 1981 (for foods), FDA has required all products containing Yellow No. 5 to list the color on their labels so consumers sensitive to the dye can avoid it. (As of May 8, 1993, labels must list *all* certified colors as part of the requirements of the Nutrition Labeling and Education Act of 1990.)

A Certified Success

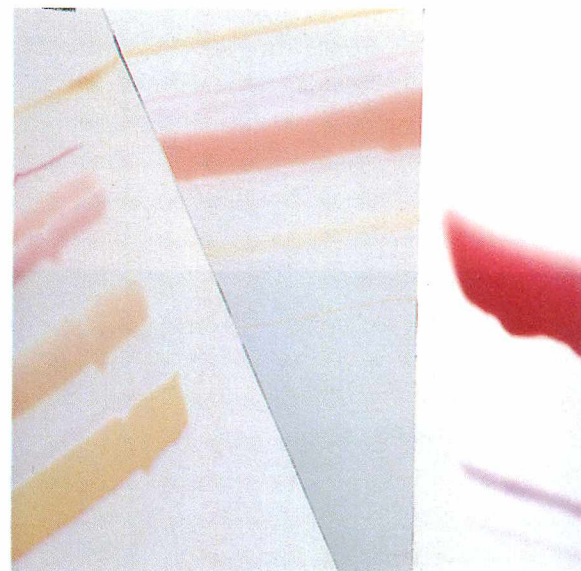
FDA requires domestic and foreign certifiable color manufacturers to submit samples taken from every batch of color produced. The agency has listed each certifiable color based on a specific chemical formula shown to produce no



harmful effects in laboratory animals.

Each color has chemical "specifications" that place restrictions on the levels of impurities allowed in the additive. In some cases, these limitations are designed to ensure that the color contains no cancer-causing substances. Using chromatography and other sophisticated analytical techniques, FDA scientists probe sample compositions to confirm that each batch is within these limitations.

"We analyze every batch because every batch is a little different from the one before it," says Bailey. He explains that complex organic chemical reactions occurring during manufacturing can throw off a sample's composition. It's like baking a cake: Even though you follow a recipe closely, the cake turns out just a little different each time.



Though they look attractive, the seized candy samples at left contain unauthorized color additives. FDA will not permit them to be marketed. Above, the colorful stripes are created by thin-layer chromatography, a chemical technique that splits a color sample into its component colors, revealing "subsidiary" colors. FDA allows only a small percentage of these impurities.

With certifiable colors, a shift in composition can mean rejection of an entire batch. In fiscal year 1992, of 3,943 batches tested, the agency rejected 40. FDA also regularly inspects color manufacturers and end users such as candy makers.

FDA is especially vigilant in monitoring products from foreign countries, which may contain color additives that are illegal domestically. The agency regularly seizes entire product shipments that contain prohibited colors. Often, this detective work comes easily. FDA, through its "import alerts," flags certain products. "You look for a pattern," says Bailey.

The batch certification program supports itself because the law requires manufacturers to pay FDA a user fee for every pound of color the agency certifies. "We

like to think of [batch certification] as a government success story," Bailey says.

The Red Scare

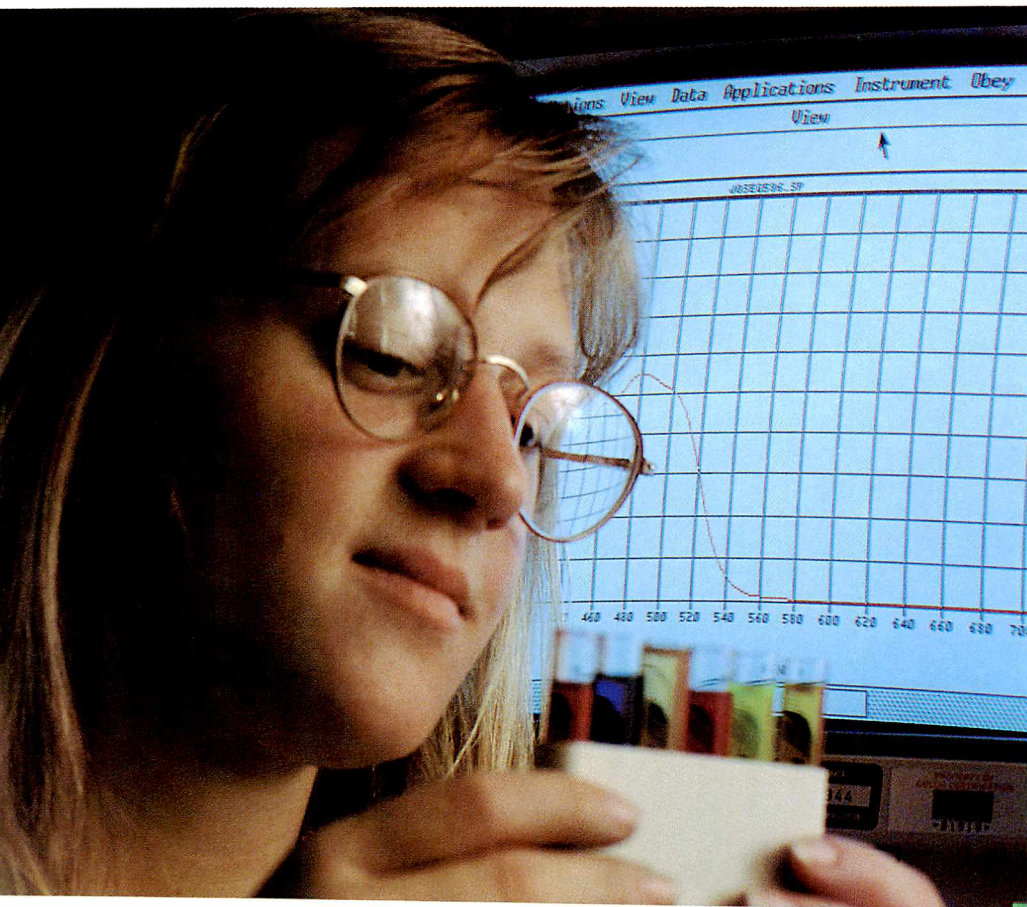
In 1960, amendments to the Food, Drug, and Cosmetic Act of 1938 added the so-called Delaney anti-cancer clause to FDA's legal mandate. Among other things, the clause prohibits marketing any color additive the agency has found to cause cancer in animals or humans, regardless of amount.

In recent years, regulators have faced a dilemma in light of technological advances that enable scientists to identify smaller and smaller concentrations of a substance and conduct more sensitive toxicological tests. Are such tiny amounts a health threat? Scientists have yet to answer this question. Congress has held

hearings to examine the pros and cons of liberalizing the Delaney clause. At press time, debates on the issue were in progress.

FDA applied the Delaney clause in 1990 when it outlawed several uses of the strawberry-toned FD&C Red No. 3. The banned uses include cosmetics and externally applied drugs, as well as all uses of the color's non-water-soluble "lakes." FDA previously had allowed these "provisional" uses while studies were in progress to evaluate the color's safety. Research later showed large amounts of the color causes thyroid tumors in male rats.

Though FDA viewed Red No. 3 cancer risks as small—about 1 in 100,000 over a 70-year lifetime—the agency banned provisional listings because of Delaney directives. At the same time, Red No. 3 has



FDA scientist Wendy Bachman examines several color additive solutions before analysis. On the screen behind her, an analytical “map” shows the composition of an FD&C Yellow No. 5 sample.

“permanent” listings for food and drug uses that are still allowed, although the agency has announced plans to propose revoking these uses as well. For now, Red No. 3 can be used in foods and oral medications. Products such as maraschino cherries, bubble gum, baked goods, and all sorts of snack foods and candy may contain Red No. 3.

According to the International Association of Color Manufacturers, Red No. 3 is widely used in industry and hard to replace. It makes a very close match for primary red, which is important in creating color blends. It doesn’t bleed, so drug companies use it to color pills with discernible shades for identification.

If Red No. 3 joins the ranks of colors forbidden for all uses, it won’t be the first

FD&C red in recent years to be pulled from the market. FDA banned FD&C Red No. 2, a tint that continues to be an enigma, in 1976.

In the early 1970s, data from Russian studies raised questions about Red No. 2’s safety. Several subsequent studies showed no hazards. FDA conducted its own tests, which were inclusive. The consumer-oriented Health Research Group petitioned FDA to ban the color, while congressional and public interest mounted.

FDA turned the matter over to its Toxicology Advisory Committee, which evaluated numerous reports and decided there was no evidence of a hazard. The committee then asked FDA to conduct follow-up analyses. Agency scientists evaluated biological data and concluded that “it appears

*Colors found to be
hazardous have been
purged from the list of
permissible additives.*

A Colorful History

Color additives have long been a part of human culture. Archaeologists date cosmetic colors as far back as 5000 B.C. Ancient Egyptian writings tell of drug colorants, and historians say food colors likely emerged around 1500 B.C.

Through the years, color additives typically came from substances found in nature, such as turmeric, paprika and saffron. But as the 20th century approached, new kinds of colors appeared that offered marketers wider coloring possibilities. These colors, many whipped up in the chemist's lab, also created a range of safety problems.

In the late 1800s, some manufacturers colored products with potentially poisonous mineral- and metal-based compounds. Toxic chemicals tinted certain candies and pickles, while other color additives contained arsenic or similar poisons. Historical records show that injuries, even deaths, resulted from tainted colorants. Food producers also deceived customers by employing color additives to mask poor product quality or spoiled stock.

By the turn of the century, unmonitored color additives had spread through the marketplace in all sorts of popular foods, including ketchup, mustard, jellies, and wine. Sellers at the time offered more than 80 artificial coloring agents, some intended for dyeing textiles, not foods. Many color additives had never been tested for toxicity or other adverse effects.

As the 1900s began, the bulk of chemically synthesized colors were derived from aniline, a petroleum product that in pure form is toxic. Originally, these were dubbed "coal-tar" colors because the starting materials were obtained from bituminous coal. (These formulations still are used today—albeit safely—for most certifiable color additives.)

Though colors from plant, animal and mineral sources—at one time the only coloring agents available—remained in use early in this century, manufacturers had strong economic incentives to phase them out. Chemically synthesized colors simply were easier to produce, less expensive, and superior in coloring properties. Only tiny amounts were needed. They blended nicely and didn't impart unwanted flavors to foods. But as their use grew, so did safety concerns.

In 1906, Congress passed the Pure Food and Drugs Act. This marked the first of several laws allowing the federal government to scrutinize and control color additive use. The act covered only food coloring. It was not until passage of the Federal Food, Drug, and Cosmetic Act of 1938 that FDA's mandate included the full range of color additives. That statute created the color designations consumers still can read on product packages: "FD&C" (permitted in food, drugs and cosmetics); "D&C" (for use only in drugs and cosmetics); and "Ext. D&C" (colors for external-use drugs and cosmetics).

Public hearings and regulations following the 1938 law gave colors the numbers that separate their hues. These letter and number combinations—FD&C Blue No. 1 or D&C Red No. 17, for example—make it easy to distinguish colors used in food, drugs or cosmetics from dyes made for textiles and other uses. Only FDA-certified color additives can carry these special designations.

The law also created a listing of color "lakes." These are water-insoluble forms of certain approved colors used in coated tablets, cookie fillings, candies, and other products in which color bleeding could make a mess or otherwise cause problems.

Though the 1938 law did much to bring color use under strict control, nagging questions lingered about tolerance levels for color additives. One incident in the 1950s, in which scores of children contracted diarrhea from Halloween candy and popcorn colored with large amounts

of FD&C Orange No. 1, led FDA to retest food colors. As a result, in 1960, the 1938 law was amended to broaden FDA's scope and allow the agency to set limits on how much color could be safely added to products.

FDA also instituted a pre-marketing approval process, which requires color producers to ensure, before marketing, that products are safe and properly labeled. Should safety questions arise later, colors can be reexamined. The 1960 measures put color additives already on the market into a "provisional" listing. This allowed continued use of the colors pending FDA's conclusions on safety.

From the original 1960 catalog of about 200 provisionally listed colors, which included straight colors and lakes, only lakes of some colors remain on the provisional list. Industry withdrew or FDA banned many, while the rest became permanently listed and are still used. Some of these colors, derived from coal or petroleum sources, are subject to certification and carry the F, D, or C prefix. Others, exempt from certification, are pigments and colors derived from plant, animal and mineral sources. They are found in a myriad of products—from the caramel that tints cola drinks to the orange annatto that gives color to cheese.

FDA certified over 11.5 million pounds of color additives last fiscal year. Of all those colors, straight dye FD&C Red No. 40 is by far the most popular. Manufacturers use this orange-red color in all sorts of gelatins, beverages, dairy products, and condiments. FDA certified more than 3 million pounds of the dye in fiscal year 1992, almost a million pounds more than the runner-up, FD&C Yellow No. 5. ■

—J.H.

Color Additive Terms

allura Red AC—the common name for uncertified FD&C Red No. 40

certifiable color additives—colors manufactured from petroleum and coal sources listed in the *Code of Federal Regulations* for use in foods, drugs, cosmetics, and medical devices

coal-tar dyes—coloring agents originally derived from coal sources

D&C—a prefix designating that a certifiable color has been approved for use in drugs and cosmetics

erythrosine—the common name of uncertified FD&C Red No. 3

exempt color additives—colors derived primarily from plant, animal and mineral (other than coal and petroleum) sources that are exempt from FDA certification

Ext. D&C—a prefix designating that a certifiable color may be used only in externally applied drugs and cosmetics

FD&C—a prefix designating that a certified color can be used in foods, drugs or cosmetics

indigotine—the common name for uncertified FD&C Blue No. 2

lakes—water-insoluble forms of certifiable colors that are more stable than straight dyes and ideal for products in which leaching of the color is undesirable (coated tablets and hard candies, for example)

permanent listing—a list of allowable colors determined by tests to be safe for human consumption under regulatory provisions

provisional listing—a list of colors, originally numbering about 200, that FDA allows to continue to be used pending acceptable safety data.

straight dye—certifiable colors that dissolve in water and are manufactured as powders, granules, liquids, or other special forms (used in beverages, baked goods, and confections, for example)

tartrazine—a common name for uncertified FD&C Yellow No. 5.

For a complete list of all colors approved for use in foods, drugs, cosmetics, and medical devices, contact:

Office of Cosmetics and Colors
(HFS-125)

Food and Drug Administration
200 C St., S.W.

Washington, DC 20204
(202) 205-4143 ■

—J.H.

Consumers can rest assured that color additives are among the most scrutinized of all food additives.

Adverse Reactions?

Though reactions to color additives are rare, FDA wants to know about them. The agency operates the Adverse Reaction Monitoring System (ARMS) to collect and act on complaints concerning all food ingredients, including color additives. Consumers can register complaints two ways—by contacting their FDA district office (see local phone directory) or by sending written reports of adverse reactions to:

ARMS
HFS-636
Food and Drug Administration
200 C St., N.W.
Washington, DC 20204

that feeding FD&C Red No. 2 at a high dosage results in a statistically significant increase” in malignant tumors in female rats.

There still was no positive proof of either potential danger or safety. FDA ultimately decided to ban the color because it had not been shown to be safe. The agency based its decision in part on the presumption that the color *might* cause cancer.

The judgment had a profound effect on consumer attitudes toward certifiable colors, says FDA’s John E. Bailey. “The Red No. 2 decision will always be with us,” he says. For example, some candy manufacturers reacted by removing red-colored pieces from their products, even if there was no Red No. 2 present. They were afraid sales would plummet because of public perception that red candies were dangerous.

Though long gone from U.S. shelves, products tinted with Red No. 2 still can be found in Canada and Europe. Whether the color is gone forever in the United States remains to be seen. FDA and industry officials say it could stage a comeback. Industry could petition FDA to list Red No. 2 as a certifiable color if animal study data adequately show safety. If FDA then agrees,

consumers could once again be munching on candies and using other products tinted with the deep-red dye.

Animal-less Studies?

Because of the cost, it is unlikely that industry will commission new animal studies to measure Red No. 2’s safety. But advances in toxicological trial methods could enable scientists to assess potential hazards without using animals. Technology is moving toward a time when chemical substances could be evaluated accurately with a battery of short-term tests conducted in the test tube. Such analyses would greatly shorten the time and expense of evaluating not only colors but other food additives and environmental chemicals.

These test tube trials are not here yet. But if and when they arrive, they may have government and industry taking another look at certain color additives, including Red No. 2.

As for the colors that remain in use, consumers can rest assured that color additives are among the most scrutinized of all food ingredients. Next time you quaff a glass of red fruit punch or pop a blue pill, consider that those colors have been studied, studied, and restudied, sometimes

dozens of times. And remember that FDA inspects every batch of certifiable colors used in consumer products.

You may, however, want to avoid consuming huge quantities of any one color additive. As Bailey says: “Good sense is the best policy. As with many other food ingredients, don’t overuse any one product. Practice everything in moderation.” ■

John Henkel is a staff writer for FDA Consumer.

Dental Amalgam

Filling a Need or Foiling Health?

by Laura Bradbard

Amalgam restorations—better known as “silver fillings”—are probably more familiar to millions of Americans than they would like.

Dental amalgam is the most widely used material to fill cavities in decayed teeth, technically known as caries. It has been used for 150 years; only gold has been used longer.

Amalgam is composed of approximately equal parts of liquid mercury and alloy powder containing silver, tin, copper, and sometimes lesser amounts of zinc, palladium or indium.

Despite amalgam's long history of use, some scientists and consumers are concerned that the mercury from

amalgam restorations might be harmful. Nearly half of 1,000 adult Americans surveyed by the American Dental Association in 1991 said they believed amalgam could cause health problems.

Besides having the broadest range of use in dental procedures, “amalgam is the most forgiving to place,” says William Kohn, D.D.S., National Institute of Dental Research, part of the National Institutes of Health. “It is not as sensitive to moisture [saliva], which can be a problem. With other restorations, the dentist has to be

more meticulous or the restoration fails when the filling is placed.”

Dental amalgam, which the Food and Drug Administration regulates as a medical device, is used in children and adults alike for:

- stress-bearing areas and small-to-moderate-sized cavities in back teeth, such as molars
- severe tooth damage
- when finances prohibit use of more expensive alternative filling materials
- as a foundation for cast-metal, metal-ceramic, and ceramic restorations
- when patient cooperation during the procedure or commitment to personal oral hygiene is poor. (Silver is cheaper and easier to place, more resistant to decay than other materials, such as composite [plastic, tooth-colored fillings], and less costly to replace.)

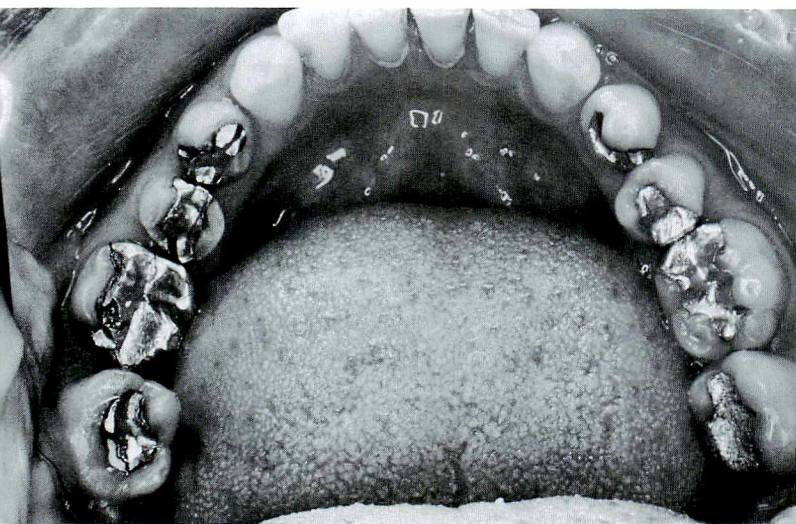
“Dental amalgam is the only material I’m aware of that, when it initially degrades, the restoration improves,” says Corbin. “A byproduct builds up and seals the interface between the tooth and the restoration. There may be drawbacks, but amalgam has allowed people to keep teeth in their mouths.”

Amalgam is not used when appearance is important (as in front teeth), in patients allergic to mercury, or for large restorations when use of costlier materials is not prohibitive.

In 1990, nearly half of the more than 200 million tooth fillings performed in the United States involved dental amalgam. This is down 38 percent from 1979.

Dental amalgam use began to decrease in the 1970s, primarily because dental caries among school children and young adults declined and new alternative materials were developed and improved.

Not only has the incidence been re-



Many a mouth can display back teeth with silvery amalgam fillings.

Some Restoration Characteristics

| | Amalgam | Composite | Glass Ionomer | Gold Foil | Gold Alloy (cast) | Metal-Ceramic Crowns |
|--|-----------------------------------|---|---|---|-------------------------|---|
| Median longevity estimate | 8–12 years | 6–8 years when used in conservative non-stress-bearing situations | no data; 5 years predicted | no data; 10–15 years estimated | 12–18 years | 12–18 years |
| Relative surface wear | wears slightly faster than enamel | excessive wear in stress-bearing situations | excessive wear in stress-bearing situations | excessive wear in stress-bearing situations | wears similar to enamel | porcelain surface may wear opposing tooth |
| Resistance to fracture | fair to excellent | poor to excellent | poor | fair to good | excellent | excellent |
| Conservation of tooth structure | good | excellent | excellent if initial restoration | good | poor | poor |
| Appearance | poor | excellent | good | poor | poor | excellent |
| Use | all ages | all ages | all ages | adult | adult | adult |
| Cost to patient | 1X | 1.5X | 1.4X | 4X | 8X + gold | 8X |

The longevity estimates reflect medians from published studies; however, under different clinical situations, many restorations will last longer. For materials that have emerged in the last decade and gold foil, estimates are speculative. In the figures for cost to patient, X = amalgam.

(Source: *Dental Amalgam: A Scientific Review and Recommended Public Health Service Strategy for Research, Education, and Regulation*, Department of Health and Human Services, 1993)

duced, but also the type of dental caries has changed, possibly as a result of fluoride used in toothpaste and topical gels and in water, sealant use, improved oral hygiene practices, and dietary changes.

Stephen Corbin, D.D.S., from the national Centers for Disease Control and Prevention, says that dentists see fewer caries, which are generally less aggressive once they start, and that today early caries can actually be reversed clinically.

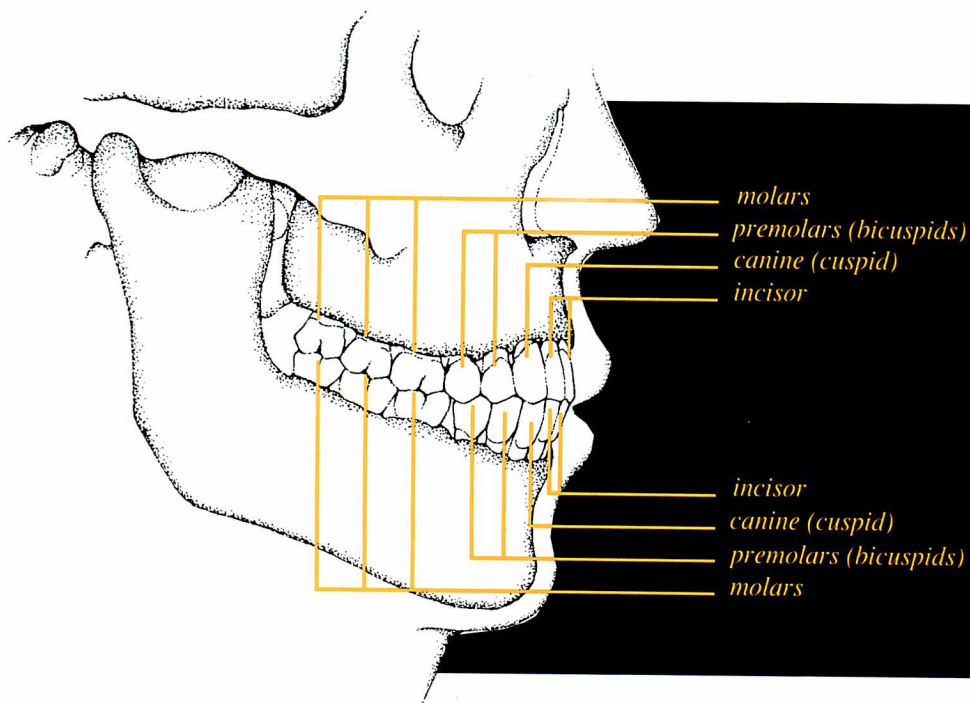
The decision to fill a tooth is complex, whether you are replacing a filling, repairing a damaged tooth, or filling a tooth for the first time. "The decision was simpler in the past. Today there are more choices to make because we see different disease patterns," says Kohn.

Alternative dental restorative materials (composites, glass ionomers, ceramics, and others) are being used more often because cavities are usually smaller and amalgam is therefore not the only choice. Since the alternatives are not as durable as amalgam, the most commonly used alter-

natives are not used for large fillings or stress-bearing areas. According to Kohn, this is often an inappropriate choice.

Approximately 70 percent of the fillings performed each year are replacements. Most replacements require amalgam or other metallic materials because, as more tooth is drilled away, the new area is larger with each replacement. Some patients do not want the silver showing in their teeth and choose other filling materials that match the natural tooth color.

Name That Tooth



ing them is beneficial. Removal itself may, in fact, expose patients to additional mercury absorption since drilling into the amalgam filling releases mercury into the air. Many questions remain unanswered, but for now the PHS report does not recommend either removing or not using amalgam. The report does, however, recommend more research into what the specific health effects of low-level mercury exposure might be, whether these effects can be produced by amalgam, and whether certain population groups, such as women and children, might be particularly sensitive. The report also recommends research on the safety of amalgam alternatives.

Alternatives

No single material can completely replace dental amalgam. Gold and ceramic inlays and crowns can replace amalgam in larger back cavities or in medium-sized cavities on other stress-bearing tooth surfaces. Smaller cavities in premolars and molars can now be restored with resin-based composite materials, glass ionomers, or compacted gold.

Alternatives to dental amalgam are not as durable, however, especially in larger cavities, and can cost significantly more.

"A wholesale conversion to non-amalgam materials would drive up national dental health-care costs by about \$12 billion in the first year, a tremendous cost impact," says Robert C. Eccleston, assistant to the director at FDA's Center for Devices and Radiological Health. "The cost would also increase in the years following any across-the-board conversion."

Also, according to the PHS report, it is possible that alternative dental restorative materials could have long-term toxicity problems of their own that have not yet been discovered. Since no definitive data exist to show that mercury in dental amalgam is directly linked to illness, and since amalgam is less expensive, easier to place, and more durable than alternatives, dental amalgam should continue to be used.

Amalgam Risks and Benefits

According to *Dental Amalgam: A Scientific Review and Recommended Public Health Service Strategy for Research, Education and Regulation*, published January 1993 by the Department of Health and Human Services, scientists have shown that dental amalgam emits minute amounts of mercury vapor.

"The toxicity of high-dose mercury levels in industrial settings has been established. Although mercury vapor can be absorbed through breathing and eating, research has not shown that low levels of mercury-containing amalgam are harmful except in rare cases of mercury allergies.

A literature review of amalgam research by the U.S. Public Health Service found no sound scientific evidence linking amalgam to multiple sclerosis, arthritis, mental disorders, or other diseases, as has been suggested by some critics of amalgam.

The PHS subcommittee, which prepared the amalgam report, reviewed the research of low-dose mercury toxicity. According to the findings, a fraction of the mercury in amalgam is absorbed by the body. People with amalgam fillings have higher concentrations of mercury in their blood, urine, kidneys, and brain than those without amalgam. A small proportion of patients may manifest allergic reactions to these restorations, but, Corbin says, there are only 50 cases of amalgam allergies, reported in the scientific literature.

According to the PHS report, the few human studies done to determine a possible public health risk from amalgam have been flawed or contained too few subjects. If there are long-term effects from the mercury in amalgam, they likely are subtle—slight neurological or behavioral changes—and difficult to detect.

The subcommittee could not conclude with certainty that mercury in amalgam fillings poses a health threat or that remov-

Composites

Composites, made from synthetic resins, are used to make attractive restorations in the front teeth. Dentists use a combination of composites and sealants, technically known as preventive resin restorations, to treat small cavities and conserve tooth structure. But the use of composites as substitutes for restorations in stress-bearing areas may be inappropriate because composites can leave a tooth susceptible to recurrent decay.

Pit and Fissure Sealants

In its report, PHS recommends dental sealants to prevent caries. Sealants prevent cavities by sealing with thin plastic coating the natural pits (round holes) and fissures (grooves) in their molars. Pits and fissures in permanent first molars account for 91 percent of the surface cavities in children up to 11 years of age.

"The best restoration that is ever placed cannot be as good as the sound tooth structure that was there in the beginning," Corbin says. "But some of the preventive materials [sealants] actually improve tooth structure."

Glass Ionomers

Glass ionomers, introduced to dentistry in the 1970s, chemically bond to the tooth structure and have the beneficial side effect of releasing fluoride.

Ionomer placement technique requires limited drilling, so the procedure is quick and the result fairly attractive. Because glass ionomers are generally not used in occlusal surfaces (biting surfaces), their use is limited to baby teeth and primarily root surfaces.

Gold Foil

Although not widely used today, gold foil restorations (compacted gold) date back many centuries. These fillings may last 20 years or longer, but are not used for large or very visible areas. Gold foil restorations require more skill and careful at-

tention to detail during placement to prevent harm to the tooth pulp (nerve) and gums. Its high cost also makes gold foil a less popular choice.

Cast Metal and Metal-Ceramic

Cast metal and metal-ceramic restorations generally require two or more dental appointments and are typically used for inlays, onlays, crowns, and bridges. Use of metal and metal-ceramic materials depends on the degree of tooth destruction from decay, breakage, or amount of tooth removed by drilling. It is also determined by the number of missing teeth, how important looks are to the patient, and the patient's oral hygiene and financial situation.

These restorations cost approximately eight times more than amalgam and are most often used:

- in teeth involved in the stress from chewing and biting
 - when moderate to severe breakdown of the tooth requires replacement
 - if the patient demands a more pleasing appearance than that produced by amalgam.
- Cast metal or metal-ceramic restorations are generally *not* used if:
- there is a danger of exposing the tooth pulp while preparing the tooth for restoration—for example, in patients under 18 whose pulp is higher in the tooth
 - the patient shows evidence of extensive teeth grinding or clenching
 - the patient is known to be allergic to the metals used in casting alloys (gold and certain non-precious casting metals).

Regulation

The PHS report recommends that FDA require restorative material manufacturers to identify the ingredients used in their products, and FDA is considering such an action. Industry disclosure of product ingredients would provide dentists with information necessary to prevent sensitivity reactions in allergic patients.

The PHS findings indicate that it is inappropriate to recommend restrictions on the use of dental amalgam unless more

PHS Report Available

For a copy of *Dental Amalgam: A Scientific Review and Recommended Public Health Service Strategy for Research, Education and Regulation* from the Department of Health and Human Services, January 1993, write to:

Les Grams

HFZ-220

Subcommittee on Risk Management/
CCEHRP

5600 Fishers Lane
Rockville, MD 20857

studies show a definite link between amalgam and illness.

"The science simply doesn't justify such an action," FDA's Eccleston points out. "There are several reasons for not restricting amalgam. First, current evidence does not show that exposure to mercury from amalgam restorations poses a serious health risk in humans, except for a very small number of allergic reactions. Second, there is insufficient evidence that alternative materials have fewer potential health effects than amalgam. And, as stated previously, amalgam use is declining." ■

Laura Bradbard is a member of FDA's public affairs staff.



Food Allergies

When Eating Is Risky

by Audrey T. Hingley

Do you start itching whenever you eat peanuts? Does seafood cause your stomach to churn? Symptoms like these cause millions of Americans to suspect they have a food allergy.

But true food allergies affect a relatively small percentage of people: Experts estimate that only 2 percent of adults, and from 2 to 8 percent of children, are truly allergic to certain foods. Food allergy is different from food intolerance, and the term is sometimes used in a vague, all-encompassing way, muddying the waters for people who want to understand what a real food allergy is.

"Many people who have a complaint, an illness, or some discomfort attribute it to something they have eaten. Because in this country we eat almost all the time, people tend to draw false associations [between food and illness]," says Dean Metcalfe, M.D., head of the Mast Cell and Physiology Section at the National Institute of Allergy and Infectious Diseases.

For example, food intolerance may produce symptoms similar to food allergies, such as abdominal cramping. But while people with true food allergies must avoid offending foods altogether, people with food intolerance can often eat small amounts of the offending food without experiencing symptoms.

Lactose intolerance, for instance, is sometimes mistaken for milk allergy. Lactose intolerance

is a problem of digestion due to an enzyme deficiency, with cramps and diarrhea the common hallmarks. Estimates are that about 80 percent of African-Americans have lactose intolerance, as do many people of Mediterranean or Hispanic origin. It is quite different from the true allergic reaction some have to the proteins in milk. Unlike allergies, intolerances generally intensify with age.

Dangerous Dishes

For people with true food allergies, the simple pleasure of eating can turn into an uncomfortable—and sometimes even dangerous—situation. For some, food allergies cause only hives or an upset stomach; for others, one bite of the wrong food can lead to serious illness or even death.

FDA regulates drugs used to treat severe allergic reactions and has recently issued regulations under the Nutrition Labeling and Education Act of 1990 to make such reactions less likely.

The early Greek philosopher and physician Hippocrates was one of the first to note that cow's milk caused health problems for some people, but it was not until the early 1900s in Europe that the first scientifically documented food allergy reports began to appear. The word "allergy" is derived from a Greek word meaning "altered reaction," and initially conveyed

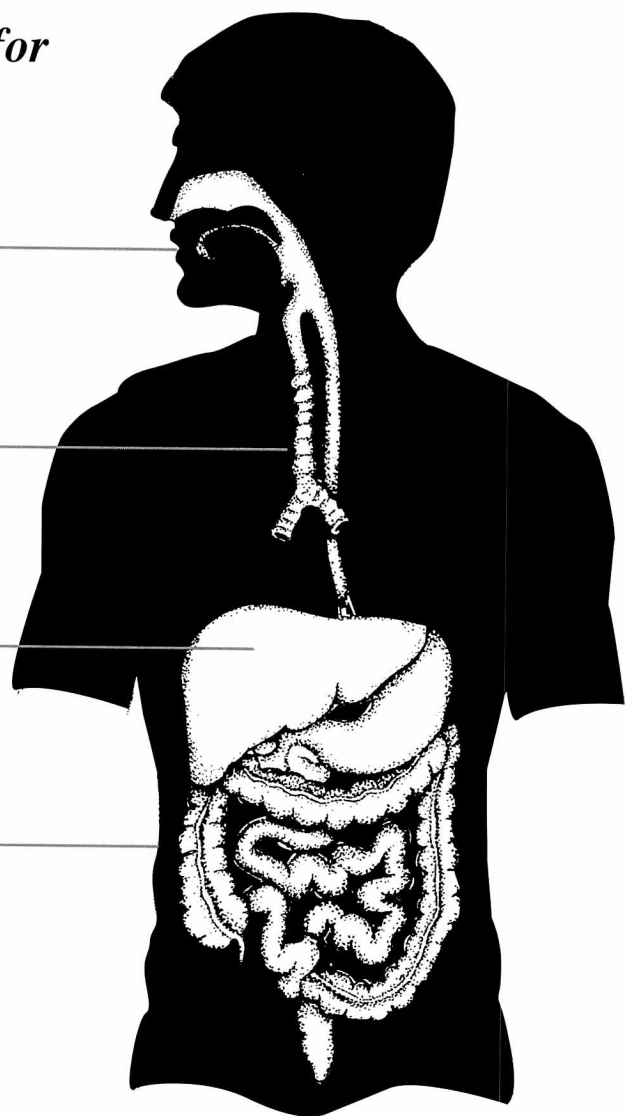
Common Sites for Allergic Reactions

mouth
(swelling of the lips or
tongue, itching lips)

airways
(wheezing or
breathing problems)

digestive tract
(stomach cramps,
vomiting, diarrhea)

skin
(hives, rashes or
eczema)



the idea that certain substances could cause adverse reactions in some people while having no effect on the public at large.

By the mid-1920s, allergists had defined food allergy as an abnormal response of the immune system to an otherwise harmless food. Food allergens, those parts of food causing allergic reactions, are usually proteins. When the allergen passes from the mouth into the stomach, the body recognizes it as a foreign substance, producing antibodies to halt the invasion. In allergic individuals, as the body fights off the invasion, symptoms begin to appear throughout the body. The most common sites are the mouth (swelling of the lips or tongue, itching lips), digestive tract (stomach cramps, vomiting, diarrhea), the skin (hives, rashes or eczema), and the airways (wheezing or breathing problems).

Food allergies are much more common in infants and young children, who often later outgrow them. Increased susceptibility of young infants to food allergic reactions is believed to be the result of immunologic immaturity and, to some extent, intestinal immaturity. Older children and adults may lose their sensitivity to certain foods if the responsible food allergen can be identified and completely eliminated from the diet, although some food allergies can last a lifetime.

Heredity may cause a predisposition to have allergies of any type. Some experts believe that, rarely, a specific allergy can be passed on from parent to child. Several studies have indicated that exclusive breast-feeding, especially with maternal avoidance of major food allergens, may deter some food allergies in infants and young children. (Smoking during pregnancy can also result in the increased possibility that the baby will have allergies.) Most patients who have true food allergies

have other types of allergies, such as dust or pollen, and children with both food allergies and asthma are at increased risk for more severe reactions.

Repeated exposure to allergens starts sensitizing those who are susceptible. Cow's milk, eggs, wheat, and soy are the most common food allergies in children. An early peanut allergy may be lifelong. Adults are usually most affected by nuts, fish, shellfish, and peanuts.

Life-Threatening Reactions

The greatest danger in food allergy comes from anaphylaxis, a violent allergic reaction involving a number of parts of the body simultaneously. Like less serious allergic reactions, anaphylaxis usually occurs after a person is exposed to an allergen to which he or she was sensitized by

previous exposure (that is, it does not usually occur the first time a person eats a particular food). Although any food can trigger anaphylaxis (also known as anaphylactic shock), peanuts, tree nuts, shellfish, milk, eggs, and fish are the most common culprits. As little as one-fifth to one-five-thousandth of a teaspoon of the offending food has caused death.

Anaphylaxis can produce severe symptoms in as little as 5 to 15 minutes, although life-threatening reactions may progress over hours. Signs of such a reaction include: difficulty breathing, feeling of impending doom, swelling of the mouth and throat, drop in blood pressure, and loss of consciousness. The sooner anaphylaxis is treated, the greater the person's chance of surviving. The person should be taken to a hospital emergency room, even

How to Cope

What do you do if you suspect you have a food allergy?

The Food Allergy Network's Anne Munoz-Furlong suggests keeping a food diary as a first step, writing down everything you eat or drink for a one- or two-week period. Note any symptoms and how long it took for such symptoms to develop.

But Furlong and other experts agree that those who suspect food allergies also need to be evaluated by a physician with intensive specialty training in allergy and immunology. Be sure to discuss what diagnostic and treatment plan is anticipated, and the costs.

Ask if the tests have been proven effective by accepted standards of scientific evaluation.

"Go to a board-certified physician who is an allergy expert," advises Paul C. Turkeltaub, M.D., associate director of the division of allergenic products and parasitology at FDA's Center for Biologics Evaluation and Research. "Be very wary of claims of food allergy to explain chronic, common complaints."

The diagnosis of food allergy requires a careful history, physical exam, appropriate exclusion diet, and diagnostic tests to rule out other conditions. Tests can include direct allergy skin tests, blood tests, or "elimination and challenge" tests for suspected foods.

The most accurate kind of test is a controlled challenge test, often done in "blind" or "double-blind" fashion to

eliminate psychological factors. In a blind challenge, the patient is given either a sample of the food, without being told what it is, or a placebo, an inert substance used as a control in the test. The observer (a doctor or assistant), however, knows what the substance is. Both patient and observer record any symptoms of allergic reaction. In a double-blind challenge, neither the patient nor the observer knows if the patient is given the food (allergen) or the placebo.

In recent years, unproven tests such as "food cytotoxic blood tests" and "sublingual provocation food testing" have been promoted as supposed "diagnostic" tools to detect food allergies. FDA believes that food cytotoxic blood tests are not supported by well-controlled studies and clinical trials.

In food cytotoxic testing, a test tube of blood is taken from the patient. The white cells (leukocytes) are mixed with plasma and sterile water and placed on microscope slides coated with dried extracts of a particular food. The reaction of the cells is then examined under a microscope; if they change shape, disintegrate, or collapse—or the person examining them says they do—the patient is supposedly allergic to that particular food. Test results may be interpreted by a "nutritional counselor" working on commission, who recommends vitamins and minerals (often available on site) that the patient needs to correct his or her "allergic condition." But FDA and other experts emphasize there is no evidence that such tests are valid in diagnosing food allergies.

Sublingual provocation food testing dates back to 1944. The test consists of

placing three drops of an allergenic extract under a patient's tongue and waiting 10 minutes for any symptoms to appear.

When the doctor is satisfied he has determined the cause of the symptoms, he administers a "neutralizing" dose, which is usually three drops of a diluted solution of the same allergenic extract. The symptoms are then expected to disappear in the same sequence in which they appeared. Advocates claim that if the neutralizing dose is given before a challenge test (for instance, eating a meal containing the offending food), the person will not have symptoms.

But after careful study of existing data, The American Academy of Allergy and Immunology says no controlled clinical studies demonstrate either diagnostic or therapeutic effects of sublingual provocation food testing. The academy concludes that use of the tests should be reserved for experiments in well-designed trials.

If you are diagnosed with a food allergy, scrutinize food labels to detect potential sources of food allergens. When eating out, ask about ingredients if you are unsure about a particular food; ask to talk to the manager of the restaurant about ingredients in specific dishes.

Keep epinephrine with you and know how to administer it. If you do experience a reaction, seek medical attention immediately, even if the symptoms are mild or seem to subside. Mild symptoms may be followed 10 to 60 minutes later by the onset of severe problems. ■

—A.H.

More Information

For more information about food allergies, contact the following groups:

The Food Allergy Network
4744 Holly Ave.
Fairfax, VA 22030-5647
(703) 691-3179

American Academy of Allergy and
Immunology
611 East Wells St.
Milwaukee, WI 53202
(414) 272-6071

Physician Referral Hotline
(1-800) 822-ASMA

The American Dietetic Association
216 W. Jackson Blvd.
Chicago, IL 60606-6995
(1-800) 877-1600

For a free copy of *An FDA Consumer Special Report: Focus on Food Labeling*, which includes the article on ingredient labeling, write to FDA, HFE-88, 5600 Fishers Lane, Rockville, MD 20857. ■

if symptoms seem to subside on their own.

There is no specific test to predict the likelihood of anaphylaxis, although allergy testing may help determine what a person may be allergic to and provide some guidance as to the severity of the allergy. Experts advise people who are susceptible to anaphylaxis to carry medication, such as injectable epinephrine, with them at all times, and to check the medicine's expiration date regularly. Doctors can instruct patients with allergies on how to self-administer epinephrine. Such prompt treatment can be crucial to survival.

Injectable epinephrine is a synthetic version of a naturally occurring hormone also known as adrenaline. For treatment of an anaphylactic reaction, it is injected directly into a thigh muscle or vein. It works directly on the cardiovascular and respiratory systems, causing rapid constriction of blood vessels, reversing throat swelling, relaxing lung muscles to improve breathing, and stimulating the heartbeat.

Epinephrine designed for emergency home use comes in two forms: a traditional needle and syringe kit known as Ana-Kit, or an automatic injector system known as Epi-Pen. Epi-Pen's automatic injector design, originally developed for use by military personnel to deliver antidotes for nerve gas, is described by some as "a fat pen." The patient removes the safety cap and pushes the automatic injector tip against the outer thigh until the unit activates. The patient holds the "pen" in place for several seconds, then throws it away.

While Epi-Pen delivers one pre-measured dosage, the Ana-Kit provides two doses. Which system a patient uses is a decision to be made by the doctor and patient, taking into account the doctor's assessment of the patient's individual needs.

Advice from Study

Hugh A. Sampson, M.D., and colleagues at Johns Hopkins University School of Medicine in Baltimore, Md., published a study of anaphylactic reactions in children in the Aug. 6, 1992, issue of *The New England Journal of Medicine*. The study involved 13 children who had severe allergic reactions to food: Six died, and seven nearly died. Among the study's conclusions:

- Asthma, a disease with allergic underpinnings, was common to all children in the study.
- Epinephrine should be prescribed and kept available for those with severe food allergies.
- Children who have an allergic reaction should be observed for three to four hours after a reaction in a medical center capable of dealing with anaphylaxis.

Anne Munoz-Furlong, who founded The Food Allergy Network for people with food allergies in 1991 after struggling to deal with her own child's allergies, comments: "My youngest daughter was diagnosed with milk and egg allergies when she was 9 months old, nine years ago. We tried to lead a life around her restricted diet. For example, we had Jell-O mold for her first birthday because I didn't know it was possible to create a cake without milk or eggs. I knew there must be other families struggling with the same issues."

Finding the Forbidden

Because there is no "cure" for food allergies other than strict avoidance of an offending food, one of the biggest problems those with food allergies face is verifying whether a forbidden product is contained in a particular food. For example, in Sampson's study, all six deaths occurred because either the child or the parent was

Experts estimate that only 2 percent of adults, and from 2 to 8 percent of children, are truly allergic to certain foods.

unaware the food contained a substance to which the child was allergic. Munoz-Furlong says the Nutrition Labeling and Education Act, which requires more complete food labeling, should greatly help people with food allergies to avoid dangerous foods.

"The new labeling changes will make it easier for the consumer to readily identify things they could be allergic to," says Linda Tollefson, D.V.M., chief of the epidemiology branch at FDA's Center for Food Safety and Applied Nutrition. "Before this law was passed, true allergens were required to be on the label, but the exceptions were standardized foods, which will now have to list all ingredients."

According to Elizabeth J. Campbell, director of the center's division of programs and enforcement policy, the principle underlying standardized foods originally was that people basically knew what was in various foods.

"Originally food standards were adopted to ensure uniformity. If you saw a product labeled mayonnaise, food standardization meant it had to be mayonnaise. People used to know what was in mayonnaise; nowadays they have to be told that mayonnaise contains both eggs and oil," Campbell says. "Years ago when the law was first written to provide for standards of identity for certain foods, it only required that optional ingredients be declared. The new law stipulates that all ingredients in standardized foods must be declared." (See "Ingredient Labeling: What's in a Food?" in the April 1993 *FDA Consumer*.)

Campbell believes that once the labeling is in place, consumers will have the information they need to make correct food choices. "In most cases, ingredients have to be labeled simply because they are in-

gredients, not because they are unsafe," she stresses. "For those with food allergies, I think it is more of a patient education problem."

Food additives, such as sulfites and certain colors, can also cause problems for people sensitive to them. (See "A Fresh Look at Food Preservatives" in the October 1993 *FDA Consumer* and "From Shampoo to Cereal: Seeing to the Safety of Color Additives" on page 14 of this issue.)

"If you have a food allergy, you really have to alter your life," Tollefson says. "You have to really read labels, and really be careful about what you eat."

Steve Taylor, Ph.D., a professor and head of the Department of Food Science and Technology at the University of Nebraska in Lincoln, says the biggest problem for people with food allergies is restaurant food. Historically, restaurants have been regulated by local health departments and have not had to label foods.

"For many restaurants, labeling of food products they serve would cause horrendous problems . . . what about chalkboard menus? How would you include all the ingredients? Enforcement would be a nightmare," he admits.

But steps are being taken to better educate restaurant employees. The Food Allergy Network and The American Academy of Allergy and Immunology, along with The National Restaurant Association, recently produced a pamphlet on food allergies, which has been distributed to 30,000 members of the association. The brochure explains what restaurants can do to help customers who need to avoid certain foods, defines anaphylaxis, and advises employees on what to do if food allergy incidents occur.

John A. Anderson, M.D., director of the Allergy and Immunology Training Pro-

gram at Henry Ford Hospital in Detroit, says changes in food habits may be responsible for the feeling some physicians have that food allergies may be on the rise.

"You could make a case for the fact that we are introducing peanuts, in the form of peanut butter, to people at a very young age, which would affect the prevalence rate for people who are sensitive to that allergen," he notes. "In Japan, where they use more soy, there is a higher prevalence of soy allergy. My feeling is that as soy, a cheap protein supplement, is put in a lot of commercial foods you will see an increase in the rate of sensitivity worldwide."

Metcalf says that if food allergies are rising, it is due to more common use of foods that tend to be allergenic. He cites milk as a source of protein supplement in many prepared foods, and points out that people are eating more exotic seafood and more fish.

"But it's important to remember that the majority of people with true food allergies are allergic to three or fewer foods," Metcalfe says.

Other than advising anyone with a known or suspected severe food allergy to carry and know how to self-administer epinephrine, there is no treatment for food allergy other than to eliminate the offending food. But Metcalfe is optimistic about the future.

"I don't think it is likely a drug will be found to prevent food allergies. But I do think within 10 years we will see allergy shots available for some of the more common food allergies, because we are learning to identify and purify food allergens. I think we will see some development of immunotherapy for food allergies," he says. ■

Audrey T. Hingley is a writer in Mechanicsville, Va.

A Balanced Look at the Menstrual Cycle

by Marian Segal

This article is part of a series with important health information for teenagers.

Some young women feel it coming days before they get it. Others are hardly aware they have it. Friends who compare notes about their periods will probably find that menstruation—the monthly shedding of the lining of the uterus, or womb—affects each of them a little differently, both physically and emotionally.

“The menstrual cycle has its ups and downs of hormones, and different people react differently to hormonal swings,” says Lisa Rarick, M.D., a gynecologist in FDA’s Center for Drug Evaluation and Research. She explains that just before and during menstruation, levels of the female hormones estrogen and progesterone are low. That’s when some women feel bloated, irritable or blue, or “just crummy,” she says.

“Just crummy” might mean cramps, sore breasts, backache, headache, nausea, and feeling tired.

“A day or two after your period starts you begin to feel better. Hormone levels go back on the upswing and you get back to what you’re accustomed to during the rest of your cycle,” Rarick explains. (See “Monthly Changes” on page 35.)

Cramps—A Common Complaint

More than half of menstruating women have cramp-like pain during their periods. The medical term for menstrual pain is dysmenorrhea. Cramps are usually felt in the pelvic area and lower abdomen, but

can radiate to the lower back or down the legs.

“Many girls have cramps severe enough to keep them home from school,” Rarick says. In fact, according to Danforth’s *Obstetrics and Gynecology*, dysmenorrhea is the most frequent cause of absenteeism from school among younger women. Rarick says women seem to go through phases when cramps are severe, then get better for several years, and then maybe worsen again. She adds that most women find they have less menstrual pain after having children.

Mechanically, cramps are like labor pains. Just as the uterus contracts to open up the cervix (neck of the uterus) and push out a baby, it contracts to expel menstrual blood. Often, after several years of menstruating or after childbirth, the cervical opening enlarges. The uterus doesn’t have to contract as much to discharge the menstrual flow, so there is less cramping.

Menstrual pain may also come from the bleeding process itself. When the uterine lining separates from the wall, it releases chemicals called prostaglandins. Prostaglandins cause blood vessels to narrow, impeding the supply of oxygen to the uterus. Just as the pain of a heart attack comes from insufficient blood to the muscles of the heart, too little blood to the uterine muscle might cause the pain of menstrual cramps.

Menstrual pain can have other causes, although these are rare among teenagers. They include tumors, fallopian tube infection, and endometriosis, a condition





in which fragments of the lining of the uterus become embedded elsewhere in the body (see “On the Teen Scene: Endometriosis—Painful but Treatable” in the January-February 1993 *FDA Consumer*).

Pain, Pain Go Away

Sometimes, simple measures are all that's needed to feel better. Cutting down on salt might help reduce fluid buildup, and support hose may alleviate swelling in the legs or ankles. Crawling into bed for some extra rest or sleep is one way to deal with fatigue, and taking along a heating pad or hot water bottle eases cramps for some. Exercising also helps reduce pain in many young women, and may lift a blue mood as well.

Charles Debrovner, M.D., associate clinical professor of obstetrics and gynecology at New York University School of Medicine, explains that exercising during menstruation lessens pain because it causes release of brain chemicals called endorphins, which are natural painkillers. He says exercise may also decrease pain by affecting prostaglandin metabolism.

Rarick adds that exercise may also help because it increases blood flow, and because it “just makes a lot of people feel better in general.”

If symptoms interfere with work, school or sleep, the American College of Obstetricians and Gynecologists recommends seeing a doctor, who may suggest taking one or more medicines. Certain anti-inflammatory drugs called NSAIDs (an

Technical Talk

amenorrhea: the absence of menstrual periods

dysmenorrhea: pain or discomfort during menstruation

fallopian tubes: two slender tubes—one on either side of the uterus—that carry the egg (ovum) from the ovary to the uterus

menarche: a young woman's first period

mittelschmerz: pain or discomfort during ovulation

ovaries: two female reproductive organs—one on either side of the uterus—that contain the eggs, or ova, and make hormones

ovulation: release of an egg from the ovary

prostaglandin: a chemical made by the body that causes the muscle of the uterus to contract, often causing cramps

uterus (womb): the female organ in which a fertilized egg grows and develops into a baby ■

Certain anti-inflammatory drugs called NSAIDs inhibit prostaglandin production, thus easing cramps.

continue for one or two days, as needed.

Some 20 to 40 percent of menstruating women have PMS, or premenstrual syndrome. Starting anywhere from mid-cycle to a few days before menstruation begins, women with PMS may have one or all of a virtual laundry list of physical and emotional symptoms. They include breast swelling and tenderness, fluid retention, increased thirst or appetite, craving for sweets and salty foods, headaches, anxiety, restlessness, irritability, depression, hostility, and loss of self confidence. Experts say PMS doesn't usually affect teenagers, though. It increases with age and is more prevalent in the 30s and 40s.

From Menarche to Menopause

In the United States, the average age of menarche—a girl's first period—is 12 years, although it's normal to start as early as 10 or as late as 16. Menopause—when periods stop—usually occurs around age 50, although that, too, can vary by several years. Except perhaps for the first two years of menstruation—and barring pregnancy, nursing, and certain illnesses or other problems—the reproductive cycle repeats with predictable regularity every month.

Exercise, diet and stress can delay the onset of menstruation, Rarick says, or alter cycles once they've been established.

"Gymnasts, ballerinas and others who exercise strenuously can sometimes delay the onset of their periods, so you might not be surprised to find a 16- or 17-year-old in that group who hasn't started menstruating," she says. "Some experts believe the connection between exercise and amenorrhea [the absence of menstrual periods] is

abbreviation for nonsteroidal anti-inflammatory drugs) inhibit prostaglandin production, thus easing cramps. Prescription NSAIDs include naproxen (Naprosyn, Anaprox), ibuprofen (Motrin, IBU), indomethacin (Indocin), and mefenamic acid (Ponstel).

If needed, your doctor may prescribe stronger painkillers or diuretics, or even oral contraceptives. One side effect of birth control pills is relief of menstrual cramps.

"Birth control pills work two ways to lessen cramps," says Rarick. "They prevent the lining of the uterus from building up so much, so there's less bleeding. This means less prostaglandin production and blood vessel narrowing because there's less lining to separate, and fewer contractions because there's less tissue to push out."

Over-the-Counter Relief

In 1984, FDA approved ibuprofen in over-the-counter (OTC) strengths to be sold without a prescription. It's the active ingredient in medicines such as Advil, Nuprin and Motrin IB. Like NSAIDs, aspirin also suppresses prostaglandins, but it's often not as effective as other NSAIDs for menstrual pain. *Aspirin should never*

be used by children or teenagers who have chickenpox or flu symptoms before checking with a doctor. This is because Reye syndrome, a rare but sometimes deadly illness, may develop in children and teenagers who have taken aspirin or products that contain it while they were sick with chickenpox or flu.

Several OTC products, such as Midol and Pamprin, are specifically formulated for menstrual symptoms. Read the labels of these medicines before you buy them, because different formulations often contain different ingredients or strengths of ingredients. For example, Teen Formula Midol contains acetaminophen for pain and pamabrom (a mild diuretic) for fluid retention. Pamprin contains acetaminophen, pamabrom and pyrilamine maleate (an antihistamine) for tension and irritability. Cramp Relief Formula Midol IB contains as its sole ingredient ibuprofen. Manufacturers may change their products' ingredients from time to time, so it's a good idea to check the label each time you buy the product.

Plain acetaminophen products like Tylenol, Datril, and Aspirin-Free Anacin also may help menstrual pain. It takes time for pain relievers to work, so it's best to take them before the pain gets bad and

Monthly Changes

Menstruation is just one part of the menstrual cycle, in which a woman's body prepares for pregnancy each month. A cycle is counted from the first day of one period to the first day of the next. An average cycle is 28 days, but anywhere from 23 to 35 days is normal.

Estrogen and progesterone levels are very low at the beginning of the cycle. During menstruation, levels of estrogen, made by the ovaries, start to rise and make the lining of the uterus grow and thicken. In the meantime, an egg (ovum) in one of the ovaries starts to mature. It is encased in a sac called the Graafian follicle, which continues to produce estrogen as the egg grows.

At about day 14 of a typical 28-day cycle, the sac bursts and the egg leaves the ovary, traveling through one of the fallopian tubes to the uterus. The release of the egg from the ovary is called ovulation.

Some women know when they're ovulating, because at mid-cycle they have some pain—typically a dull ache on either side of the lower abdomen lasting a few hours. The medical word for this is *mittelschmerz*, from the German, meaning middle pain. Some women also have very light bleeding, or spotting, during ovulation.

After the egg is expelled, the sac—now called a corpus luteum—remains in the ovary, where it starts producing mainly progesterone. The rising levels of both estrogen and progesterone help build up the uterine lining to prepare for pregnancy.

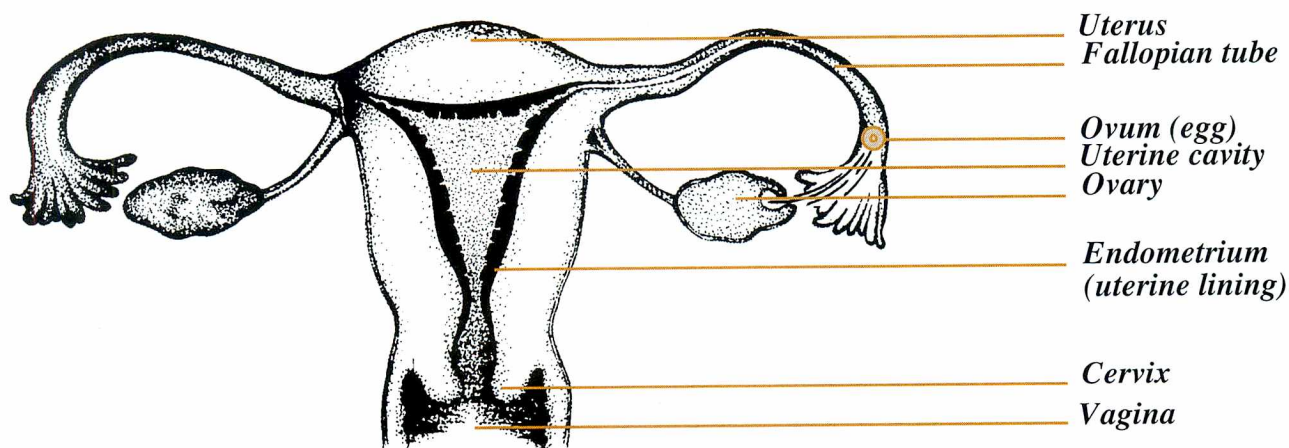
The few days before, during and after ovulation are a woman's "fertile period"—the time when she can become pregnant. Because the length of menstrual cycles vary, many women ovulate earlier or later than day 14. It's even possible for a woman to ovulate while she still has her period if that month's cycle is very short.

(Stress and other things can sometimes cause a cycle to be shorter or longer.) If a woman has sex with a man during this time and conception occurs (his sperm fertilizes the egg), she becomes pregnant.

The fertilized egg attaches to the uterus, and the corpus luteum makes all the progesterone needed to keep it implanted and growing until a placenta (an organ connecting the fetus to the mother) develops. The placenta then makes hormones and provides nourishment from the mother to the baby.

If an egg is not fertilized that month and the woman doesn't get pregnant, the corpus luteum stops making hormones and gets reabsorbed in the ovary. Hormone levels drop again, the lining of the uterus breaks down, menstruation begins, and the cycle repeats. ■

—M.S.



Here, an egg has left an ovary after ovulation and is on its way through a fallopian tube to the uterus.

Young women with severe eating disorders such as anorexia or bulimia often do not menstruate.

Menstrual Bleeding

What's Normal, What's Not

Most menstrual periods last from three to five days, but anywhere from two to seven days is normal. The amount of blood flow varies, too, but for most women, bleeding starts out light at first, followed by heavier flow for a day or two and then another light day or two. Sanitary pads or tampons, which are made of cotton or another absorbent material, are worn to absorb the blood flow. Sanitary pads are placed inside the panties; tampons are inserted into the vagina.

"The amount of bleeding varies from woman to woman because everybody's body has a different way of building up the lining of the uterus," says Lisa Rarick, M.D. "A lighter flow or heavier flow doesn't mean you can't get pregnant as easily or you're never going to get pregnant, or that your periods will always stay the same way. But if you're bleeding excessively—soaking one or more tampons or pads an hour—you should see a doctor to see if there's a problem."

Rarick, a gynecologist with FDA's Center for Drug Evaluation and Research, says teenagers often are concerned if they expel blood clots during their periods. She says this is not dangerous; they are clumps

of pooled blood in the vagina. Sometimes, instead of flowing freely, blood drains from the uterus and stays in the vagina until there's a change in position—say, from sitting to standing.

Women who use tampons should be aware of toxic shock syndrome, or TSS, a rare but serious—and sometimes fatal—disease that's been associated with tampon use. Tampon packages carry information about TSS on the box or inside. Because TSS mostly affects 15- to 19-year-olds, it's especially important for teenagers to know what signs to look for. If you develop the following symptoms while menstruating, remove the tampon and get medical help right away:

- sudden fever over 102 degrees Fahrenheit
- vomiting
- diarrhea
- dizziness, fainting, or near fainting when standing up
- a rash that looks like a sunburn.

For more on toxic shock syndrome, see "On the Teen Scene: TSS—Reducing the Risk" in the October 1991 *FDA Consumer*. ■

—M.S.

related to body fat content, because fat affects estrogen. Young women who are very thin from malnourishment may not start menstruating until they gain weight, with a certain portion of that weight being fat. So, girls who exercise a lot—who are all bone and muscle with no fat—may delay their periods."

Similarly, young women with severe eating disorders such as anorexia or bulimia often do not menstruate. (See "On the Teen Scene: Eating Disorders Require Medical Attention" in the March 1992 *FDA Consumer*.)

The American College of Obstetricians and Gynecologists recommends that a girl see her doctor if she hasn't started menstruating by age 16, or if by age 13 or 14 she hasn't begun to develop breasts or pubic and underarm hair.

Just Like Clockwork?

Many young women have very irregular periods the first couple years of menstruating—even skipping some months, until, as Rarick says, "the system is well-tuned."

In addition, she says, young women don't always ovulate every month when they first get their periods. She adds that there's no sure way for a young woman to know which month she is ovulating and which she is not. So, from the time her periods begin, a young woman should assume she can get pregnant each and every month, even if her periods are irregular.

Eventually, periods become regular, but even when they do, a missed or late period once a year—especially at a stressful time—is considered normal, according to Rarick.

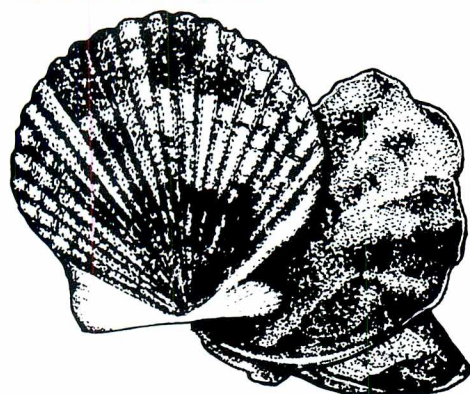
Also, just as strenuous exercise and eating disorders can delay the onset of menstruation, they can also cause previously regular menstrual cycles to become irregular or stop completely. ■

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



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

■ **"Guidance Document for Lead in Shellfish"** is now available from FDA. The document, developed in response to requests from various state health and environmental agencies, can help officials decide when to issue consumption advisories or to close particular harvesting waters. For a free copy, request docket number 93D-0287 and send two self-addressed labels to FDA, Policy Guidance Branch (HFS-416), 200 C St., S.W., Washington, DC 20204. (FR Sept. 15)



■ **Identification code** imprinting is now required on drug tablets and capsules, according to an FDA final rule that became effective last Sept. 13. The new requirements allow poison control centers to quickly identify drug products, allow consumers and health professionals to make sure the correct prescription has been dispensed, and assist public officials in preventing tampering and tracing counterfeit and defective drugs. (FR Sept. 13)

■ **Calorie counts** on labels of regionally and locally distributed foods are more often wrong than those on nationally distributed products, according to a study by David B. Allison, Ph.D., and colleagues at the Obesity Research Center, New York City. The researchers studied the accuracy of caloric labeling on "diet" and "health" foods among locally, regionally and nationally distributed brands. Locally prepared foods contained, on average, 85.4 percent more calories than the labels listed; regionally distributed foods contained 25.2 percent more calories; while nationally distributed foods did not differ significantly between listed and actual calories. (*Journal of the American Medical Association*, Sept. 21)

■ **Toxic substance contamination** at 2,302 nationwide sites that are closed to the public is discussed in a publication available from the National Governors' Association (NGA). "Restrictions Imposed on Contaminated Sites: A Status of State Actions" describes a survey of the affected environment, types of contamination, and public restrictions. Survey information and report copies are available from Barbara Wells, NGA, 444 North Capitol St., Washington, DC 20001; telephone (202) 624-5822; facsimile (202) 624-5313. (*Morbidity and Mortality Weekly Report*, Sept. 24)

■ **Most heart attack victims** who don't respond to advanced cardiac life support (ACLS) in the field don't improve by being rushed to an emergency room, according to two studies in the Sept. 21 *Journal of the American Medical Association*. Researchers found that victims whose hearts don't begin beating normally after pre-hospital ACLS have little chance of survival. Knowing when to stop rescue ef-

forts could save the U.S. health-care system as much as \$500 million yearly, the researchers estimate. (*JAMA* Sept. 21)

■ **Burns** are a leading cause of work-related injury in the United States, according to a study in the *Morbidity and Mortality Weekly Report* by the national Centers for Disease Control and Prevention. The study found that approximately 1.4 million Americans suffer burns each year, 20 to 25 percent of which occur at work. Restaurant deep fryers are a major source of injury, particularly among adolescents. In 1986, 6 percent of all work-related burns occurred among 16- to 19-year olds. (*MMWR* Sept. 24)

■ **Vehicle air bags** on the driver's and front passenger's sides will be required on all passenger cars manufactured after Sept. 1, 1997, and on all light trucks manufactured after Sept. 1, 1998, according to a National Highway Traffic Safety Administration final rule that takes effect March 1, 1994. The rule also requires manufacturers to include specific safety information about air bags in the owner's manual and in labels attached to the vehicles' sun visors. (FR Sept. 2)

■ **Health-care organization meetings** this February include:

- National Coalition of Hispanic Health and Human Services Organizations, Feb. 3-6 in Washington, D.C.; contact Mary Wallace at (301) 443-5006
- Association of Operating Room Nurses, Feb. 13-18 in New Orleans; call (303) 755-6300
- American Academy of Orthopaedic Surgeons, Feb. 24-March 1 in New Orleans; call (708) 823-7186.



Selling Used Pacemakers Lands Businessman in Jail

by Kevin L. Ropp

A Hammond, Ind., businessman was sentenced last Aug. 5 to six years in jail for relabeling, re-packaging, and selling as new outdated and previously used pacemakers and pacemaker leads. He also received two years supervised probation.

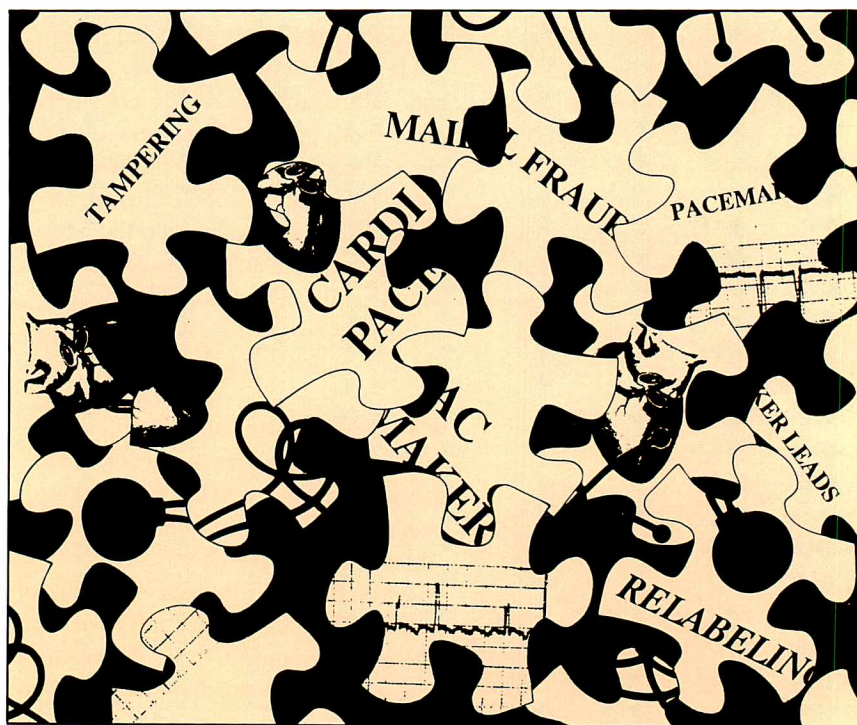
Michael M. Walton, 43, sentenced in the U.S. District Court for the Northern District of Indiana, was also barred for 20 years from receiving reimbursement from the Medicare program and from serving as an officer, director, shareholder, or in any significant managerial position in a medical device company.

Walton pleaded guilty June 10, 1993, to felony charges of tampering with a consumer product, mail fraud, and fraud in connection with identification documents.

Eight of Walton's employees were also charged with altering labels of pacemakers and leads, selling misbranded pacemakers, offering gratuities to physicians, and Medicare fraud. Timothy Hyzy, Robert Cetrone, and Vicky Finney pleaded guilty before trial and received one year probation after cooperating with federal investigators. Jan Stankowicz, Gerald Seymour, Maria Paradise, and Michelle Tynes Rauscher pleaded guilty after their trials began and received one year probation. All reside in Hammond.

Luisito Sison, also of Hammond, pleaded guilty to one count of mail fraud on Sept. 10, 1993, and faces up to five years in jail and a \$250,000 fine.

Robert Thomson Jr., M.D., a cardiologist at J.F. Kennedy Hospital in Chicago,



was sentenced to one year probation and fined \$5,000. He pleaded guilty to a misdemeanor charge of knowingly implanting a non-programmable pacemaker labeled as a programmable one.

"This was a tremendously complex case. It was like a two-sided, 100,000-piece jigsaw puzzle with no picture on the cover of the box," says William Nelson, resident in charge of FDA's South Bend, Ind., resident post.

The FBI received information in December 1989 suggesting that Walton might be involved in illegal activities. They investigated and found "that something was going on with cardiac pacemakers," Nelson says.

On Feb. 2, 1990, FBI agent Sharon Ormsby and agent Greg Zarnick of the Department of Health and Human Services Inspector General's Office (OIG) asked Nelson to join the investigation.

"They had unconfirmed information that pacemakers and pacemaker leads were being labeled to extend expiration dates, that labels were being mutilated and obliterated, and that pacemakers and leads were being reused," Nelson says.

Armed with a warrant, Nelson, five OIG agents, nine FBI agents, a postal inspector,

and a Hammond police detective searched Walton's business on Feb. 20. They found:

- leads being repackaged from the manufacturers' boxes to unmarked white boxes with generic labels listing no manufacturer
- pacemakers whose corporate logos and brand names had been forcibly removed or blacked out
- pacemakers with identical sterilization and expiration dates (typically, these dates are 18 months to two years apart)
- pacemakers whose expiration dates had been altered
- pacemakers that were five to six years out of date
- pacemakers with dried blood on them.

"When we found the bloody pacemakers," Nelson says, "we thought there might have been something to allegations we'd received that pacemakers were being re-used."

The team seized over 100 pacemakers and leads and 100,000 to 200,000 pages of documents.

Nelson and the investigators compiled a computer database file from approximately 1,000 seized sales invoices. "It took us about two months to enter all this data into the computer," Nelson says. "[He] never threw anything away—we had 98 percent of his invoices going back to 1983. Each invoice listed the model number and serial number of the implanted device, the patient, the hospital, the salesperson, the date of the implant, the date of sale, the hospital location, and the doctor involved."

An FBI search of Walton's apartment in August 1990 also revealed that he used about 33 aliases. Agents found social security cards, drivers licenses, methadone treatment cards, and draft cards. They also

seized two one-inch-high stacks of blank Illinois and Indiana birth certificates and the embossing stamps to complete them.

Working with the database, investigators determined which pacemakers and leads had been implanted more than once.

"Then we started pulling hospital records to find out what was going on. In some cases, it was a false billing. . . . Walton's records would say the pacemaker was 'opened by the doctor accidentally in surgery' or 'accidentally dropped on floor.' Walton was retrieving these and reusing them," Nelson says. (The pacemaker sales representative is usually present during implantation.)

In other cases, records showed the same pacemaker or lead was implanted in two separate individuals at two different times.

A patient would have a pacemaker or lead implanted, Nelson explains, and "several days later, the doctor would say it didn't seem to be functioning correctly, so he surgically removes it and another pacemaker is implanted."

Walton would send the removed pacemakers and leads to various pacemaker and lead manufacturers to be resterilized. For example, on June 12, 1987, Walton sent Coratomic (now Biocontrol Technology), Indiana, Pa., a pacemaker. On June 17, Walton wrote Coratomic that the pacemaker had never been implanted in a patient.

As a matter of course, Coratomic resterilized and returned the pacemaker to Walton, assuming it had not been used, and on Aug. 20, Cardiotronics (a Walton firm) received the resterilized pacemaker. The pacemaker had, in fact, been implanted in a patient on June 4 and removed June 6 because of a malfunction. On Oct. 27, Walton sold the used device as new to J.F. Kennedy Hospital, where it was implanted into another patient.

"We also found one instance where Walton told the resterilizer he wanted the

used pacemaker resterilized for a dog lab. Walton received the resterilized pacemaker, which was labeled on the invoice 'Not For Human Implant.' Walton resold the pacemaker to a hospital and it was implanted into a patient," Nelson says.

Walton also had pacemaker leads resterilized and resold them.

Walton destroyed the pacemaker and pacemaker lead registration forms and replaced them with his own forms, making it impossible for the manufacturers to comply with medical device reporting requirements. (Pacemakers and leads must be registered with the manufacturer and FDA so that, if for any reason the device needs to be recalled or patients must be notified, the devices can be traced.)

As a pacemaker repackager and relabeler, Walton was considered a manufacturer and therefore was required to register his firm and list his devices with FDA. But he never registered with the agency.

Walton operated under 18 different company names, including Cardiotronics, Inc.; Cardiac System, Inc.; Central Hospital Purchasing; Consolidated Hospital Purchasing; Corapace, Inc.; Coratronics; Independent Pacers; Pacetech, Inc.; Pulstar, Inc.; All Best Tickets; Arco Medical; Cardiac Systems, Inc.; Cardiomed, Inc.; and Medical Technologies, Inc.

"He didn't register—we didn't know he was out there," Nelson says. "He totally circumvented the FDA system of consumer protection—that's the bottom line."

Walton's scheme would not have worked, however, without offering gratuities to the doctors. The investigators learned through hundreds of interviews that Walton illegally provided doctors with tickets to sports and entertainment events, educational tapes and materials,

televisions and video cassette recorders, travel and entertainment expenses, registration fees for medical seminars, medical equipment, cash, and female escorts and prostitutes.

In addition, Walton charged hospitals for devices and accessories that were either misrepresented or not supplied:

- He bought non-programmable pacemakers for about \$900 and sold them as

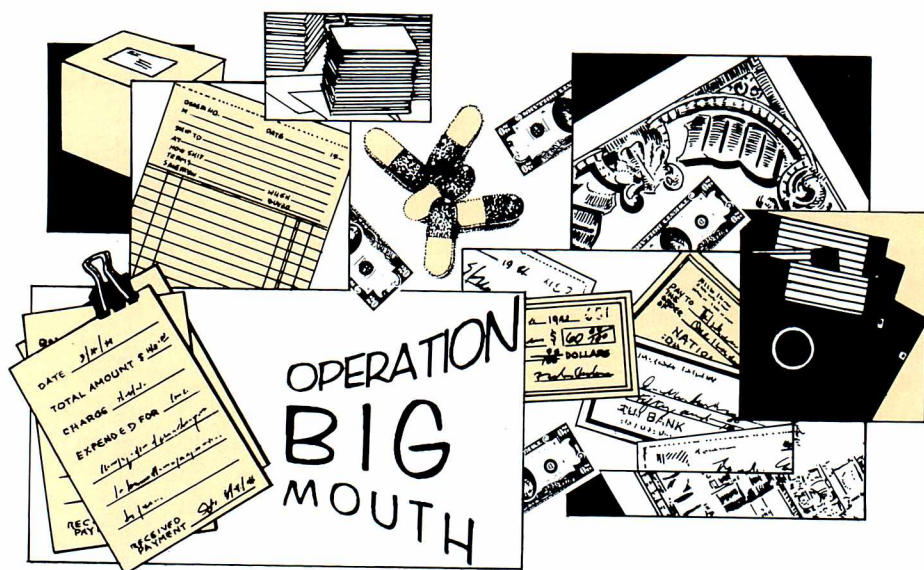
programmable pacemakers for \$5,000 to \$6,000.

- He labeled standard leads as “custom F-set leads,” and charged double the cost of the standard leads. Custom F-set leads do not exist.
- He sold \$895 accessory kits he never delivered.
- He sold regular pacemakers as “high output” pacemakers.

Based on this evidence, a grand jury issued a 13-count indictment June 11, 1992, against Walton and his employees.

Walton was arrested June 22 in Las Vegas and returned to South Bend, Ind., for trial. He pleaded guilty several weeks after trial began.

Kevin L. Ropp is a staff writer for FDA Consumer.



'Operation Big Mouth' Nets Drug Conspirator

A New Orleans dealer of smuggled, unapproved drugs is serving 10 months in a Louisiana halfway house after being nabbed earlier this year by federal agents.

Marlene Chauvin, 48, was sentenced July 2 in the U.S. District Court for the Eastern District of Louisiana after pleading guilty to one count of conspiracy. The judge also sentenced her to two years of supervised probation.

Chauvin was one of several illicit drug traffickers netted in “Operation Big Mouth,” a massive effort involving FDA, the U.S. Customs Service, the U.S. Attorney’s Office, and other government agencies.

Officials so named the operation because defendants—including Chauvin—cooperated with authorities by admitting guilt and identifying sources. Others apprehended in the operation received prison terms of up to one year and fines up to \$10,000. Though most Operation Big Mouth cases are now closed, a few still are pending.

Chauvin was a major link in a large distribution ring that operated in Louisiana.

Nevada and California. She and others sold unapproved drugs touted to treat serious diseases such as AIDS and cancer, as well as ones promoted to boost bodybuilding and enhance sexual performance. Many of the drugs came into the United States illegally from Germany, Romania, and other countries.

“This operation was of such a large scale that we formed a task force with other agencies to deal with it,” says Thomas Sawyer, compliance director for FDA’s Los Angeles district, which spearheaded the investigation. “In one action, agents seized guns, gold bullion, money, even a loaded submachine gun,” Sawyer says, adding, “These people are not amateurs.”

Chauvin ran two companies, Youth and Health Today and Preventative Medicine Pharmaceutical, from a building in New Orleans. The companies offered wholesale-quantity drugs such as the unapproved and unproven cancer treatment Laetrile, which they sold in either pill or injectable form. Promotional materials listed drugs such as the prescription-only skin cream Retin A, which was available through the companies to anyone professing to be a physician, health professional, retailer, or distributor.

Some drugs in the companies' inventory carried claims of bolstering rejuvenation and prowess. A Youth and Health Today catalog listed Aslavital, an alleged anti-aging drug claimed to help "activate the body defense against infections" and help "prevent the pains caused by the aging digestive tract." Aslavital is one of several formulations the companies offered of GH3, an unapproved drug made outside the United States. GH3 typically contains procaine hydrochloride, a prescription drug approved for use only as a local anesthetic. A seized promotional flyer for GH3 suggests Chauvin and her associates were aware their activities were illegal and that FDA had not approved the drug for anti-aging.

The companies' literature described another illegal drug, Zumba, as containing a formula "known to stimulate desire and improve sexual performance, vigor and physical stamina." Banned in this country, Zumba is made in Munich, Germany, and contains the anabolic steroid methyltestosterone.

But FDA chemists who analyzed the evidence discovered the seized pills were not what their label said. "Not only was she claiming to sell Zumba, which is illegal," says Dannie Rowland, FDA compliance officer, "but the Zumba she was selling was fake Zumba, which also is illegal."

Chauvin's case began Sept. 26, 1991, when FDA and other federal agents arrested a California man in Los Angeles for selling counterfeit Retin A and other unapproved drugs. After pleading guilty to federal charges of illegal drug trafficking, he decided to aid the government in its investigation by becoming a cooperating defendant. A search of his home turned up price

lists, canceled checks, invoices, and other evidence showing that he was obtaining drugs from Chauvin's two businesses. Utility company records confirmed Chauvin's connection with the businesses through bills she had paid for services to the building that housed her enterprises.

The task force then began long-term surveillance of Chauvin's enterprises and undercover "buys" of her companies' products. On Oct. 11, an agent called the number listed in seized price lists and ordered Zumba, Aslavital, and other drugs, paid for by postal money order to one of several Louisiana mail drops Chauvin used. On Oct. 30, the drugs arrived at a federal mail drop in California and were confiscated by FDA agents. Analysis showed that only the Aslavital contained its labeled ingredients.

From Oct. 29, 1991, to April 14, 1992, agents bought drugs five more times by phone. During the same period, investigators staked out Chauvin's business, as well as a New Orleans commercial storage facility and parcel service. They observed Chauvin or her associates sending or readying packages for shipment to various locations. In one instance, the parcel service revealed that Chauvin's business paid for shipping with a check written to the same account number found on canceled checks seized from the California cooperating defendant.

Investigators periodically went through Chauvin's garbage, looking for other evidence. Among items retrieved were an Aslavital label listing Romania as the country of origin and phone message forms referencing GH3, Retin A, and other drugs. Agents secured several search warrants, and on April 24, 1992, seized drugs, documents, bank accounts, phone records, and computer data from Chauvin's businesses.

When confronted with this evidence, Chauvin agreed to cooperate with investi-

gators. For several months after the search, she worked undercover, monitoring phone calls and arranging for drug purchases from others in the distribution ring.

On Feb. 12, 1993, a grand jury indicted Chauvin on one conspiracy count. The indictment charged that she conspired to "receive and store unapproved drugs . . . brought into the United States contrary to law, . . . dispense such drugs without a licensed practitioner's prescription," and misled buyers by claiming "uses for which there had been no evidence of safety and efficacy."

She began serving her sentence last July 2. Officials say prosecutors considered Chauvin's cooperation in the case when they sought to indict her on only one conspiracy count.

—John Henkel

Red Cell 'Refresher' Taken off Market

An unincorporated enterprise went out of business last June after having failed to meet FDA standards for making a blood processing solution. The drug product was intended to refresh red blood cells nearing their expiration dates. FDA knows of no illnesses caused by the adulterated PIPA Red Blood Cell Processing Solution.

At FDA's request, the Department of Justice filed a complaint for injunction on Jan. 22, 1993, in the U.S. District Court for the District of Massachusetts, against Charles Ellis, M.D., doing business as PIPA Laboratories, Inc., in Roslindale, Mass. Ellis signed a consent decree of permanent injunction on Feb. 10, agreeing

not to sell in interstate commerce any drug product unless that product is manufactured in conformance with good manufacturing practice (GMP) requirements.

PIPA Laboratories was first inspected by FDA's Boston district office in April 1983. During that inspection, FDA noted numerous GMP deficiencies. For example, the firm had no written procedures for cleaning, maintaining, calibrating, or inspecting equipment. It did not calibrate the temperature and pressure indicators on the sterilizer or test components for conformity to written specifications. It had no written procedures for preventing microbial contamination, although the solution was labeled as sterile. Following the inspection, the FDA investigator informed Ellis of the problems.

FDA also sent Ellis a regulatory letter, dated Aug. 10, 1983, admonishing him for the deficiencies, requesting additional information on product testing, and asking for a response in 10 days specifying his corrective steps.

Ellis wrote back on Aug. 29, detailing the measures he had taken or intended to take.

In a follow-up inspection in December, investigators found that many serious problems continued. The agency sent Ellis a notice of adverse findings on May 31, 1984, and asked for a response within 30 days.

Corresponding with FDA during the following summer, Ellis promised to improve the monitoring of the room temperature where he tested for microbial contamination, purchase a 10-channel

electronic thermometer and other temperature-sensing equipment, institute studies every three to four months to verify the solution's sterility, and negotiate with Tufts University School of Medicine for stability testing of the solution.

FDA inspected PIPA Laboratories several times over the next few years and warned Ellis about continuing GMP deficiencies. The agency sent warning letters in October 1991 and February 1992. Ellis repeatedly promised corrections. However, FDA's inspection in September 1992 showed Ellis had still not corrected many problems.

On Nov. 18, 1992, FDA asked the Department of Justice to file a complaint to permanently enjoin Ellis from manufacturing, processing, packaging, and distributing PIPA Solution.

John Levchuk, Ph.D., a consumer safety officer with FDA's Center for Drug Evaluation and Research, reviewed the documents about recent inspections of PIPA Laboratories. As an FDA expert on the manufacture of sterile drugs, Levchuk stated that Ellis' violations reflect a "serious lack of appreciation for the importance of good manufacturing practice to ensure consumers receive safe and effective drugs. Without adequate controls, there is no assurance that PIPA Solution will perform as labeled or be safe and effective for its intended use."

For example, Levchuk had serious concerns about PIPA's ability to ensure sterility, because the firm didn't maintain adequate cleanliness controls in the filling room, adequately test for sterility, or verify its sterilization process.

FDA's complaint cited Ellis for numerous violations, including his failure to:

- properly control microbial contamination
- validate the manufacturing process
- follow a written testing program for stability

- visually examine samples or record the results of such examination
- follow written standards or specifications for drug product stoppers and seals or methods for removing "pyrogenic" (fever-forming) substances from them
- follow a written program for calibrating equipment or maintain records of such calibration checks
- maintain proper records.

—Dixie Farley

Manufacturer Ordered to Stop Selling Illegal Drugs

A vitamin and food supplement manufacturer was sentenced last July 29 to six months home detention, five years probation, and a \$5,000 fine on two felony counts of concealing drugs and promotional material from government inspectors. The corporation, Highland Laboratories, Inc., was sentenced to three years probation on two misdemeanor counts of distributing unapproved new drugs.

Highland manufactures dietary supple-



ments for distribution under its own brand names and custom formulates similar products for other distributors.

Kenneth D. Scott, president of the Mount Angel, Ore., corporation, entered into a plea agreement Jan. 19, 1993, in the U.S. District Court for the District of Oregon. Scott signed a consent decree ordering the corporation to stop manufacturing and promoting its products without FDA approval for new drugs. In addition, the company agreed to submit to FDA for three years all new promotional materials, labels and literature of renamed products for agency approval at least 60 working days before distribution.

FDA's first encounter with the firm's illegal operation was during a June 1982 inspection. FDA investigators found 1.5 million tablets of procaine hydrochloride, manufactured at Highland, labeled for rejuvenating the skin and minimizing wrinkles and lines. Scott claimed they were for export only. On a second inspection three months later, investigators found Highland manufacturing procaine hydrochloride cream, also for export. The investigators told Scott the tablets and cream were unapproved new drugs and therefore illegal for export. Scott said he would fight the new drug classification and continue to manufacture the products "if the money's there." At FDA's request, the tablets and cream were seized in November 1982.

On an April 1984 inspection, investigators found in the firm's storage area approximately 89,000 "starch blocker" tablets, an unapproved new drug promoted for weight loss. Scott said he knew FDA had taken action against starch blockers in the past, and voluntarily destroyed the lot during the inspection.

Around that same time, FDA investigators saw advertisements for various vitamin and mineral supplements containing dimethyl sulfone (MSM)—an unsafe food additive—distributed by Dunsmuir Corporation. FDA traced the manufacture to Highland and sent the firm a regulatory letter. Scott replied that he had stopped manufacturing the product. Following a December 1984 inspection, federal agents seized 34 drums of MSM and various vitamin and mineral supplements containing the additive. In April 1985, investigators found another thirty-four 70-pound drums of MSM. Scott said he had obtained the MSM from Dunsmuir, a bankrupt corporation, as payment for past services, and signed an agreement with FDA that he would use MSM only in cosmetics or sell the raw material to a cosmetic manufacturer.

In June 1987, FDA detained at port a product being shipped to Scott. The Canadian-manufactured product, Immun-Aid, was an unapproved new drug because it suggested unsubstantiated health claims. In addition, its labeling did not include adequate directions for use and it contained linseed oil, an unsafe food additive, among its ingredients.

During an FDA inspection at Highland from April 10 through May 31, 1989, FDA found the firm manufacturing 13 types of vitamin and mineral supplements, some containing illegal food additives, with accompanying literature that made unsubstantiated therapeutic claims. During the inspection, investigators found very little of two Highland products—Co-Q10 capsules and Ge Oxy 132. Co-Q10 was promoted for use in treating and preventing congestive heart failure, cardiac arrhythmias, heart attacks, high blood pressure, and diseases associated with aging. Ge Oxy 132 capsules were promoted for treating and preventing cancer, leukemia, hepatitis, cardiovascular disease,

asthma, cataracts, and chronic allergies, and for boosting the immune system.

Scott told the investigators he kept his stock low to minimize the effect of a seizure, but investigators found in a storage area twenty-five 33-gallon plastic bags of pills. Scott said he was planning to destroy the pills, and he poured paint and kerosene into the open bags as the investigators looked on.

In December 1989, FDA made undercover purchases of Highland's illegal products, and on March 20, 1990, the agency sent Scott a regulatory letter warning that his products were unapproved new drugs and contained illegal food additives.

During a Sept. 26, 1990, inspection, Scott refused to allow FDA investigators to review batch production and distribution records. He claimed he had stopped distributing the promotional literature for products referenced in the agency's March regulatory letter. FDA discovered that Scott had shipped the literature to his daughter's home, 200 miles away, and she was mailing it out under the name and address H.A. Lyons, Talent, Ore.

On Oct. 16, FDA and federal agents, with search warrants for Highland and H.A. Lyons, simultaneously seized from both places relevant records, literature and products as evidence of criminal violations of the Food, Drug, and Cosmetic Act. The evidence was turned over to the Department of Justice for prosecution.

—Judith E. Foulke

SUMMARIES OF COURT ACTIONS



SEIZURE ACTIONS

Food/Contamination, Spoilage, Insanitary Handling

PRODUCT: Chili powder, black pepper, paprika, onion, granulated garlic, ginger, oregano, and other spices, at Brooklyn, E. Dist. N.Y.; Civil No. 90-0735 (JBW).

CHARGED 3-2-90: While held by Schiff Food Products Co., Inc., Brooklyn, N.Y., nine cases of chili powder and six cases of black pepper contained insect filth—402(a)(3); and the other articles had been held under insanitary conditions—402(a)(4).

DISPOSITION: Consent—authorized release to the dealer for salvaging. (F.D.C. No. 65834; S. No. 90-600-019 et al.; S.J. No. 1)

PRODUCT: Crab meat, at Phoenix, Dist. Ariz.; Civil No. 91-828 PHX PGR.

CHARGED 5-23-91: When shipped by Longline Fresh Expeditors, Covington, La., the article labeled "Pasteurized crab meat . . . Longline Fresh Expeditors . . . Covington, Louisiana" contained decomposed crab meat—402(a)(3).

DISPOSITION: The article was claimed by L.M. Sandler & Sons, Inc., t/a Ocean Seafood Sales, Virginia Beach, Va., who denied the charge. After lengthy discussion, a consent decree of condemnation was entered authorizing release to the claimant to attempt to bring the article into compliance. Ultimately, the article was destroyed. (F.D.C. No. 66155; S. No. 91-640-041 et al.; S.J. No. 2)

PRODUCT: Crab meat, two lots, at Norfolk, E. Dist. Va.; Civil No. 91-333-N.

CHARGED 5-30-91: When the lot labeled "Backfin . . . Crabmeat . . . Currituck Crab Co., Inc. Barco NC" was shipped from Barco, N.C., and when the commingled lot labeled "Crabmeat . . . Long Line Fresh Expeditors, Covington, La. . . Product of Mexico," or "Crabmeat . . . Bayside Shellfish Inc., Apalach, FL," or "Crabmeat . . . Marsiscos Rey Del Sur, S.A. DE C.V. Los Mochis, SIN" was shipped from Phoenix, Ariz., both lots contained decomposed crab meat and were unfit for food due to swollen and abnormal cans—402(a)(3); and the labeling of the commingled lot was misleading because the labeling (can lid and label) bore more than one common or usual name or descriptive term to identify the article—403(a)(1). **DISPOSITION:** The article was claimed by L.M. Sandler & Sons, Inc., t/a Ocean to Ocean Seafood Sales, Virginia Beach, Va., who denied the charges. The government served written interrogatories, requests for admissions, and requests for the production of documents upon the claimant. The claimant served written interrogatories and requests for the production of documents on the government. After lengthy discussions concerning proposals for reconditioning, a consent decree of condemnation of the article was entered authorizing release of the article to the claimant for the purpose of attempting to bring the article into compliance. Subsequently, the claimant determined that it was economically infeasible to recondition the article, and the article was destroyed. (F.D.C. No. 66078; S. No. 91-585-309 et al.; S.J. No. 3)

PRODUCT: Flour, and cookies, at Hammonton, Dist. N.J.; Civil No. 91-2077.

CHARGED 5-17-91: While held by Deer Park Baking Co., Hammonton, N.J., who prepared the cookies using interstate flour, the seized flour contained rodent filth—402(a)(3); and the seized articles had been prepared, packed and held under insanitary conditions—402(a)(4).

DISPOSITION: Default—ordered destroyed. (F.D.C. No. 66158; S. No. 91-523-925 et al.; S.J. No. 4)

Food Additives

PRODUCTS: Coenzyme Q10 capsules, coenzyme Q10 and germanium sesquioxide combination product, and other products containing germanium, at Farmingdale, E. Dist. N.Y.; Civil Nos. 89-1626(LDW) and (on appeal) 92-6051.

CHARGED 5-17-89: While held for sale by Natural Organics, Inc., Farmingdale, N.Y., the articles, which had labeling such as "Nature's Plus Coenzyme Q10 Complex . . . [or "Immunectar . . . Coenzyme Q10 . . . GeOxy-132 (organic germanium sesquioxide)]" . . . Nature's Plus . . . Farmingdale, N.Y., Div. of Natural Organics, Inc.," contained the nonconforming food additives coenzyme Q10 and/or germanium sesquioxide—402(a)(2)(C).

DISPOSITION: The articles were claimed by Natural Organics, Inc., Farmingdale, N.Y., and National Nutritional Laboratories, Inc., Huntington Station, N.Y., who denied the charge and, as affirmative defenses, asserted that the articles were not food additives, that they were not subject to food additive regulatory strictures, and that they were generally recognized as safe for use as dietary supplements and were thus legally marketed in the United States. The government served written interrogatories and requests for the production of documents on the claimants. The claimants served several sets of written interrogatories on the government. Pursuant to stipulation, post-seizure sampling of the seized articles was authorized. The claimant served a set of document requests on the government.

After additional discovery proceedings and the entry of a stipulation in which the parties agreed that the issue of "generally recognized as safe" would not be litigated in this action, the claimants moved for summary judgment, and the government cross-moved for summary judgment. The court found for the government, finding that CoQ10 and germanium satisfied the plain meaning of the "component" requirement of the food additive definition, that there was a legislative intent to treat nutrients as food additives, that the court should defer to FDA's construction of the statute if it was "permissible," and that FDA's interpretation of CoQ10 and germanium as food additives was, at the very least, permissible and took precedence over the claimants' interpretation. Accordingly, the court condemned the articles.

The claimant appealed the decision of the district court. However, several months later, pursuant to stipulation of the parties, the appeal was dismissed with prejudice. Thereafter, the government moved the district court for an order of destruction and requested the

assessment of court costs and fees, storage costs, and other proper expenses. Natural Organics, Inc., opposed the government's motion, asserting that there had been an erroneous legal determination, that the court had neglected to differentiate between single-ingredient and multiple-ingredient products, that the assessment of costs was within the discretion of the court, and that the court should not assess the requested costs. Nevertheless, the court granted the government's motion, ordered the articles destroyed, and ordered the recovery of costs. (F.D.C. No. 65635; S. No. 89-521-113 et al.; S.J. No. 5)

PRODUCT: Evening primrose oil capsules, two seizure actions, at St. Louis, E. Dist. Mo.; Civil Nos. 87-2063-C-4 and 87-2103-C-4.

CHARGED 11-6-87 and 11-13-87: While held for sale, the article was a nonconforming food additive—402(a)(2)(C).

DISPOSITION: A default decree in the earlier action condemned the article, authorized delivery to FDA of 50 bottles of the article for use in consumer education programs, and ordered the destruction of the remainder of the article. In the other action, a default decree ordered destruction. (F.D.C. Nos. 65282/3; S. Nos. 87-526-405/6; S.J. No. 6)

Drugs/Human Use

PRODUCT: Oxygen in pocket-size containers, and personal oxygen systems, at Rochester, W. Dist. N.Y.; Civil No. 90-0274T.

CHARGED 7-14-90: When shipped by Ultramotive Corp., Bethel, Vt., the articles labeled [4-oz. container] "Personal Size PR-O2 Oxygen . . . Proline Intl., Inc., Rochester, N.Y." and [face mask with 4-oz. container] "New PR-O2 Personal Oxygen System . . . portable compact design fits in gym bag . . . Pro-Line International, Inc., Rochester, N.Y." were new drugs without effective approved New Drug Applications—505(a); the articles' labels lacked adequate directions for their intended use—502(f)(1); the articles had been manufactured, prepared and processed in an unregistered establishment—502(o); and the articles were prescription drugs lacking the prescription legend—503(b)(4).

DISPOSITION: The articles were claimed by Pro-Line International, Inc., Rochester, N.Y. The government served written interrogatories on the claimant. Subsequently, the government moved for summary judgment. The court found for the government, stating that the products' advertising and packaging clearly indicated that they were intended to affect the function of the human body, which brought them within the definition of a drug, and that since they were offered for recreational use, not emergency use, they were new drugs that lacked testing and FDA approval. Accordingly, the products were condemned and ordered destroyed. (F.D.C. No. 65684; S. No. 89-543-625; S.J. No. 7)

PRODUCTS: Various herbal capsules, at Lynwood, W. Dist. Wash.; Civil No. C92-754.

CHARGED 5-5-92: While held by Albi Imports, Ltd., Lynwood,

Wash., who manufactured the articles using interstate components, the articles labeled "Formula 1 Herbal Laxatives I [or "Formula 3 Super Compound" or "Formula 6 Sum Yuen Li" or "Formula 8 . . . K&B Capsules"] . . . Li Chung Yun Ltd., Lynwood, Washington" were new drugs without effective approved New Drug Applications—505(a); and the articles' labeling lacked adequate directions for use—502(f)(1).

DISPOSITION: Default—ordered destroyed. (F.D.C. No. 66404; S. No. 92-669-329 et al.; S.J. No. 8)

Drugs/Veterinary

PRODUCT: Neomycin sulfate for oral or topical veterinary use, at Kansas City, W. Dist. Mo.; Civil No. 92-0891-CV-W-6.

CHARGED 10-5-92: While held for sale after manufacture by Sparhawk Laboratories, Inc., Kansas City, Kan., the circumstances used for the article's manufacture, processing, packing, and holding failed to conform with current good manufacturing practice—501(a)(2)(B).

DISPOSITION: Default—ordered destroyed. (F.D.C. No. 66604; S. No. 92-598-271 et al.; S.J. No. 9)

Medical Devices

PRODUCT: Catheter set, and medical procedure tray, at Cranford, Dist. N.J.; Civil NO. 92-2349 (HAA).

CHARGED 6-4-92: The articles, which were processed by Ackrad Laboratories, Inc., Cranford, N.J., and were labeled "H/S Catheter Set [or "Procedure Tray"] for Hysterosalpingography . . . Sterile . . . Ackrad Laboratories, Inc., Cranford, NJ," had been processed, packed and held under circumstances that failed to conform with current good manufacturing practice—501(h).

DISPOSITION: Consent—ordered destroyed. (F.D.C. No. 66408; S. No. 92-588-758; S.J. No. 10)

PRODUCTS: Catheter trays, and sterile gauze sponges, at Chicago, N. Dist. Ill.; Civil No. 92 C1651.

CHARGED 3-6-92: While in transit, the articles were held under insanitary conditions whereby they might have been rendered injurious to health due to orthodichlorobenzene, a potent chemical irritant from a drum that ruptured during transit in a truck—501(a)(2)(A).

DISPOSITION: Default—ordered destroyed. (F.D.C. No. 66367; S. Nos. 91-610-936/7; S.J. No. 11)

PRODUCT: Laser stimulator device, at Dallas, N. Dist. Texas; Civil No. 3-91-0910-D.

CHARGED 5-13-91: A device bearing serial number 8187007 (which was labeled "Fujinon YAG Laser Stimulator . . . Made in Japan by Fuji Photo Optical Co., Ltd." and which was previously the subject of an Investigational Device Exemption but which was held at a local hospital for non-payment of rent) was a class III device which might not be distributed without the approval of an applica-

tion for pre-market approval and which was not exempt from such approval—501(f)(1)(B); and, although an exemption had been granted, the possessor of the device was not the person named in the exemption—501(i).

DISPOSITION: The article was claimed by Stratford Leasing Co., Northbrook, Ill. The claimant asserted that the device had been imported by a local physician under an exemption and that the claimant acquired the devices and thereafter leased them to that physician, who subsequently became involved in a bankruptcy proceeding. Subsequently, a consent decree of condemnation was entered, and the device was destroyed. (F.D.C. No. 66098; S. No. 91-617-489; S.J. No. 12)

Cosmetics

PRODUCT: **Eye shadow pencils**, at Miami, S. Dist. Fla.; Civil No. 91-2744-Civ-Nesbitt.

CHARGED 11-29-91: When shipped by Iota Cosmetics, S.A., Barcelona, Spain, the article labeled “Iota Cosmetics Eye Shadow Made in Italy” lacked a quantity of contents statement—602(b)(2); and the article was in violation of the Fair Packaging and Labeling Act since the label lacked the common or usual name of each ingredient in order of decreasing predominance—15 U.S.C. 1454(c)(3)(B).

DISPOSITION: Consent—authorized release to Perfumania, Inc. (an interest successor to LeMott, Inc.), Miami, Fla., for relabeling. (F.D.C. No. 66294; S. No. 91-594-101 et al.; S.J. No. 13)

CRIMINAL ACTIONS

DEFENDANT: **Imre Pinter**, president of a diagnostic device firm, Hauppauge, E. Dist. N.Y.; Criminal No. 91-CR-1330-01.

CHARGED 12-9-91 by grand jury: When testing kits (containing human blood components and intended for use by medical laboratories to calibrate and insure the accuracy of blood testing equipment) were shipped (five felony counts) with the intent to defraud and mislead to Cleveland, Ohio, New Orleans, La., and Milwaukee, Wis., and (two shipments) to Pittsburgh, Pa., such kits contained blood infected with HIV and hepatitis—501(c); and the labeling of the kits was false and misleading in that the labeling indicated that such medical devices had been tested to be free from HIV and hepatitis infection when in fact they had tested positive for HIV and hepatitis infection—502(a). When similar testing kits were shipped (four misdemeanor counts) to Great Falls, Mich., San Diego, Calif., Santa Monica, Calif., and Bakersfield, Calif., such kits contained similarly infected blood—501(c); and the labeling of the kits was similarly false and misleading—502(a). In addition, the defendant, together with others, knowingly obstructed the administration of the law by falsely informing FDA inspectors that they had no knowledge of who altered the records of the diagnostic device firm or why such records had been altered—18 U.S.C. 1505.

DISPOSITION: The defendant pleaded not guilty. After a trial by a jury, the defendant was found guilty of five felonious Food, Drug,

and Cosmetic Act counts, four misdemeanor Food, Drug, and Cosmetic Act counts, and one obstruction-of-justice count. The defendant was fined \$25,000. (F.D.C. No. 65320; S. No. 2-89-921-3; S.J. No. 14)

INJUNCTION ACTIONS

DEFENDANT: **Arnold F. Anklaam, t/a Cash**, Minneapolis, Dist. Minn.; Civil Nos. 4-90-293 and (upon appeal) 91-1249 MNMT.

CHARGED 4-18-90 in a complaint for injunction: The defendant repacked, labeled, stored, promoted, and distributed in interstate commerce “35% Food Grade Hydrogen Peroxide Solution” (HPS) accompanied by promotional literature establishing the drug’s intended use for various human diseases (e.g., AIDS, cancer, arthritis, diabetes, tuberculosis, lupus, emphysema, and Parkinson’s disease). HPS was a new drug without an effective approved New Drug Application, because it was not generally recognized as safe and effective for use as suggested in such accompanying promotional labeling—505(a); and the labeling of HPS failed to bear adequate directions for HPS’s intended uses—502(f)(1). Similarly, the defendant was trading and promoting a “brain tuner” (BT-5) device and pinhole glasses, which were intended for uses such as the following: “*brain tuner*”—to restore and enhance memory and to treat drug, alcohol and tobacco addiction, depression, insomnia, anxiety, stress, hypertension, dyslexia, and headaches; *pinhole glasses*—to exercise and relax eye muscles, “see things you never saw before,” improve sight, and provide help for presbyopia, nearsightedness, farsightedness, and astigmatism. Because of such intended uses, the BT-5 and the pinhole glasses were medical devices. Such devices had not been manufactured in a registered establishment and were not listed as required—502(o). Despite having been repeatedly informed that his distribution of HPS violated the law, the defendant continued such violative conduct; and the government was informed and believed that, unless restrained by the court, the defendant would continue to promote and distribute HPS, the brain tuner, and the pinhole glasses.

DISPOSITION: The government moved for a preliminary injunction. After a hearing, the court granted the motion and issued a preliminary injunction against the defendant. The defendant filed a request for admissions relating to an asserted Ninth Amendment right to “Freedom of Choice in Medicine and Health Care.” Subsequently, the defendant moved to enter admissions, to rescind the injunction, and to dismiss the case. The government filed an answer to the motion to enter admissions and a motion for summary judgment. After a hearing, the court denied the defendant’s motion to enter the admissions, granted summary judgment to the government, and issued a permanent injunction against the defendant. The defendant appealed.

Upon appeal, the defendant argued that the district court had abused its discretion by failing to enter the requested admissions when the government failed to answer within the prescribed 30 days and that his Ninth Amendment rights encompassed the right “to make truthful claims about any health product or device” and to

make known the intended use of a product or device. The Court of Appeals found that the defendant's arguments on appeal were without merit. Accordingly, the decree of permanent injunction of the district court was affirmed. (Inj. No. 1211; S. No. 89-572-529 et al.; S.J. No. 15)

DEFENDANTS: Vitality Systems, Inc., and William L. Bartels, president and owner, Portland, Dist. Ore.; Civil No. 89-1009-DA. CHARGED 9-25-89 in a complaint for injunction: That the defendants, at their Portland, Ore., plant, promoted and distributed in interstate commerce various products containing methylsulfonylmethane (MSM) (e.g., multi-ingredient articles such as tablets labeled "Super Sulf MSM plus C" and feed supplements labeled "E-Quest type A" and "E-Quest type G"), as well as other MSM products (e.g., powders labeled as "MSM Ultra Pure Methylsulfonylmethane" and "Equi-Sulf Crystals" and tablets labeled "Ultra Pure Super Sulf MSM"); that such articles contained the nonconforming food additive MSM—402(a)(2)(C); and that the labeling of the articles contained false and misleading claims that horses, dogs and cats needed a supplemental source of sulfur, that the above products provided a substantial quantity of sulfur and that MSM had nutritional value beyond that provided by its sulfur—403(a)(1). Despite FDA notice to the defendants that their activities were in violation of the law, the defendants continued the promotion and distribution of such products. The government was informed and believed that, unless enjoined, the defendants would continue such violations of the law.

DISPOSITION: The defendants denied the charges, asserting that MSM was not a food additive. The government served requests for admissions on the defendants.

The government moved for summary judgment, and the defendants filed a cross-motion for partial summary judgment. The case was heard by a U.S. magistrate. The U.S. magistrate recommended that both the government's and the plaintiff's motions be granted in part and denied in part, accepting the defendants' contention that MSM in its pure form was not a food additive and accepting the government's contention that multi-ingredient formulations of MSM were food additives. The district court adopted those findings. The government filed a motion for reconsideration, which the court denied. Subsequently, all remaining issues were dismissed by stipulation of the parties. The parties agreed to an entry of a final order implementing such findings. Although denying the government's request that further distribution of pure MSM be enjoined, the court issued an order perpetually restraining and enjoining the defendants from shipping any multi-ingredient product containing MSM unless and until FDA issued a regulation or exemption. (Inj. No. 1215; S. No. 89-502-981 et al.; S.J. No. 16)

MISCELLANEOUS ACTIONS

SUBJECT: Importation of garlic bulbs, and FDA's detention criterion, San Juan, Dist. Puerto Rico; Civil Nos. 88-1562(PG) and (upon appeal) 89-1257.

CHARGED 9-1-88 and amended 2-7-90 by Caribbean Produce Exchange, Inc., San Juan, Puerto Rico, against the Department of Health and Human Services, the Food and Drug Administration (FDA), the Secretary of the Treasury, and the U.S. Customs, in a complaint for injunction: That a ship from Alicante, Spain, arrived in San Juan, Puerto Rico, with 6,912 crates of purple garlic consigned to the plaintiff. The garlic bulbs were sampled by FDA, and the shipment was thereafter held intact by the plaintiff. Meanwhile, the plaintiff requested an inspection by the Agricultural Marketing Service of the U.S. Department of Agriculture (AMS/USDA) and requested an immediate hearing with the FDA district director. The AMS/USDA reported that the condition of the garlic bulbs was "Generally well cured and dry. Average 2% damage by Sunken Discolored Areas. Less than 1/2 of 1% decay." FDA issued a notice of detention because FDA's examination indicated that the garlic "appeared to consist wholly or in part of decomposed and moldy garlic." A formal FDA administrative hearing was held at which the plaintiff opposed the detention, asserting that FDA had not issued a regulation establishing a standard of identity or quality that covered imported garlic and also asserting that the detained garlic was not decomposed. Analysis by FDA found 6.7 percent moldy bulbs and 46.7 percent otherwise decomposed. The plaintiff asserted that FDA's detention and notice of refusal of admission was *ultra vires* because section 401 of the Federal Food, Drug, and Cosmetic Act provided that no standard of quality should be established for fresh or dried vegetables and that the AMS/USDA examination was irrefutable and *prima facie* evidence that the garlic fully complied with all U.S. quality standards. Accordingly, the plaintiff sought an injunction against FDA.

DISPOSITION: District Court—The plaintiff moved for a preliminary injunction and permanent injunction. The court considered that, as a result of FDA's notice of detention, the plaintiff might suffer irreparable injury and that the case might become moot upon any delay; and, accordingly, the court issued an order to show cause. The government moved to dismiss the action. At a limited hearing, the court considered the plaintiff's contention that FDA lacked jurisdiction over fresh vegetables such as garlic due to section 401. The court noted that section related to misbranding and that section 401 had no relation to, and no connection with, the adulteration provisions upon which FDA had made its finding that the article appeared to be in violation. As to the AMS/USDA inspection of the garlic, the court noted that FDA standards were designed to protect the consumers and the standards of USDA were considered a service to producers. The court reviewed the results of FDA's original and subsequent analyses, found that FDA's action had not been shown to be arbitrary or capricious, and ordered the action dismissed.

The plaintiff moved for a rehearing and/or reconsideration, citing a case involving the establishment of action levels for aflatoxin in corn (*Community Nutrition Institute v. Young*, 818 F. 2d 943).

The district court granted another hearing. Although the district court stated that "the facts and law applicable in the *Community Nutrition Institute* case are clearly distinguishable from the facts of the present case," the district court reconsidered its dismissal of the

action and granted the plaintiff all of its requested relief. The court noted that the case involved 152,064 pounds of garlic (i.e., more than a million bulbs) and that FDA's sample of 50 bulbs did not appear to be a reasonable sample to apply the 10 percent rule of thumb. The court found that FDA's 10 percent rule of thumb for adulterated garlic and FDA's *Microanalytical Procedures Manual* were apparently unreasonable and arbitrary and had a great financial impact on the garlic industry, and that an adequate statement of the basis and purpose of the rule must be provided. The court concluded that "the procedure for the inspection of garlic established by FDA is arbitrary and unreasonable and [the court] further finds that the [10%] rule of thumb [for adulterated garlic] and the [*Microanalytical Procedures Manual*] are invalid in that they have a substantial impact on the garlic industry and were issued without the notice and comment requirements of APA [Administrative Procedure Act]." The government appealed. Meanwhile, although the government moved for and subsequently was granted a stay of the district court's order, all of the garlic had been sold by the plaintiff.

Court of Appeals—the Court of Appeals set the district court's judgment aside and remanded the case. The Court of Appeals stated that the district court was obviously pursuing the generally admirable objective of saving time and duplication of effort by consolidating the proceedings seeking preliminary injunctive relief with those seeking permanent relief. However, in this case there had been no notice of consolidation and no affidavits or documentary evidence addressed to the notice-and-comment APA issue on which the permanent injunction was principally based. Because the circumstances of the case demonstrated that the decision on the merits was premature, the Court of Appeals remanded the case to the district court, noting a number of issues and questions that might be considered by the district court on remand. Such issues and questions included the following: whether the 10 percent rule of thumb should be considered a binding norm having the force of law and, therefore, subject to the notice-and-comment procedures; whether 21 C.F.R. 10.40 would limit FDA's ability to invoke the exemption for interpretive rules or rules of agency practice; and whether FDA could take advantage of the "good cause" provision of 21 C.F.R. 10.40(e)(1). In the Court of Appeals' final comment, it noted that "the purpose of the sampling procedure is to arrive at a reasonably accurate estimate of the number of effective bulbs in a large shipment by extrapolating the results obtained from a representative sample. If the sample can be deemed to be representative, then the percentage of defective bulbs emerging from a study of the sample can be projected to the shipment at large."

District Court upon Remand—The government moved for dismissal or, in the alternative, for summary judgment, asserting that the case was moot (because the garlic had been released and distributed), because it was not ripe for judicial review, and because the plaintiff lacked standing to bring the action. The court granted the government's motion to dismiss. Because the garlic had been distributed and none of the plaintiff's garlic was currently the subject of any import detention or refusal imposed by FDA, the case no longer presented a "live" issue and the case was moot. Because the

plaintiff could not at the present time show any "injury in fact" and there was no present harm alleged, the plaintiff lacked standing. In addition, the case was not ripe for review because there was, at present, no agency action that affected the plaintiff. Accordingly, the complaint was dismissed. (Misc. No. 881; S.J. No. 17)

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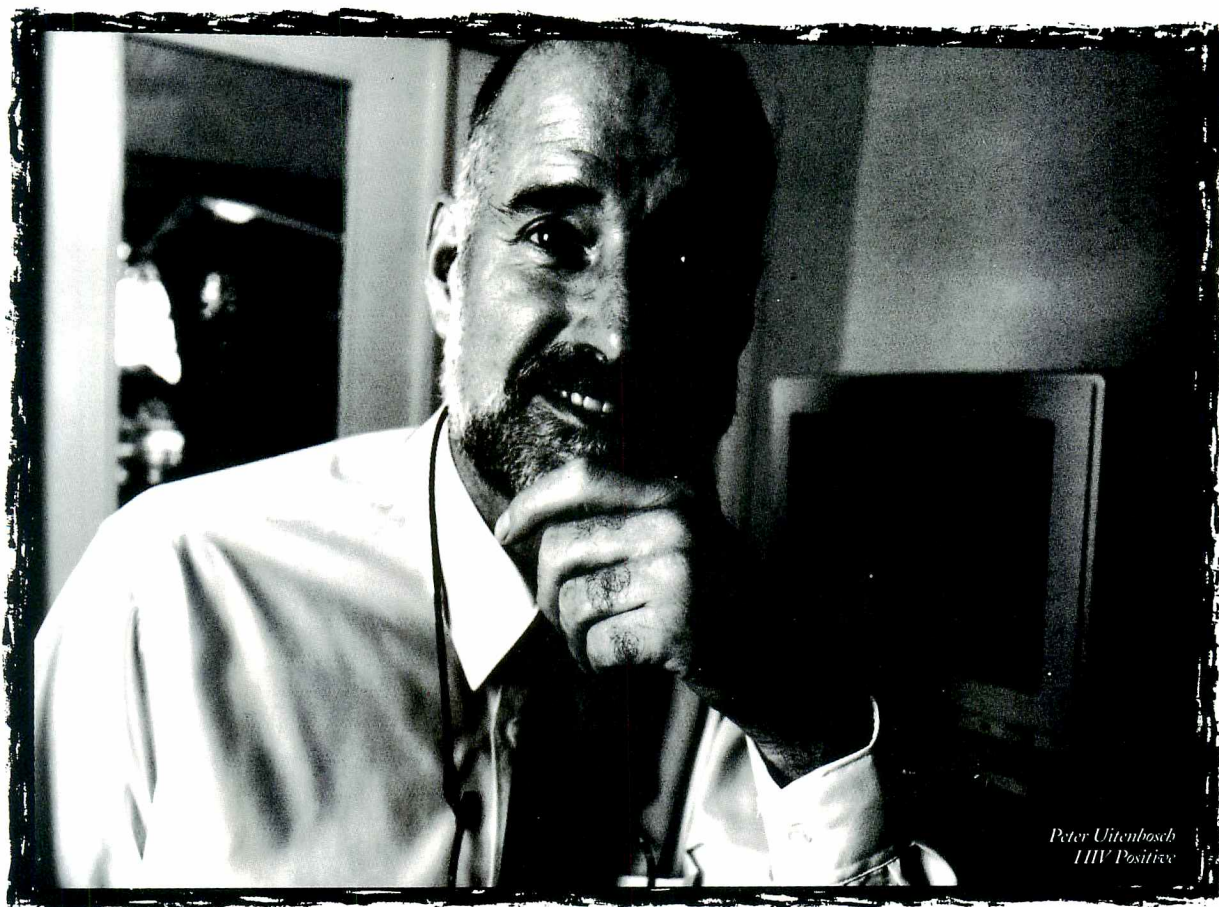
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I certify that the statements made by me above are correct and complete.

Judith Levine Willis, editor



"I'm a chairman, a treasurer, and a board member.

I go to meetings around the world.

I make speeches in three languages.

I jog to stay healthy.

I work in my garden to stay happy.

I spend as much time as possible with family, friends, and loved ones.

Sometimes I have so much going on I forget I have HIV.

I wish you would, too."

For more information on HIV and AIDS, call the CDC National AIDS Hotline at 1-800-342-AIDS.

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