Drugs That Do Double Duty
Pets And People Get Similar Medications
FDA Consumer
The Magazine of the U.S. Food and Drug Administration
November–December 2000 • Vol. 34 No.6

Cover Story

24
Prescriptions for Healthier Animals
Increasingly, veterinarians treat animals with the same active ingredients found in drugs for people.

7
FDA Approves Mifepristone for Termination of Early Pregnancy
FDA approves marketing of oral medication after finding it safe and effective.

8
Home for the Holidays: Preventing Foodborne Illnesses at Family Gatherings
Holiday meals provide a perfect venue for transmitting microorganisms, but simple steps can keep the family safe.

11
Health Claim For Foods That Could Lower Heart Disease Risk
FDA approves health claim for foods that contain plant sterol and stanol esters, shown to reduce cholesterol levels in the blood.

12
Robots Help Surgeons Perform More Precise Surgery
Doctors use computer-controlled instruments to operate with minimum intrusion into the body.

14
Preventing Colon Cancer: Screening and Early Detection Save Lives
Colorectal cancer can be beat if it’s caught before it spreads. New, high-tech methods make screening easier; new treatments improve survival.

19
Cell Phones and Brain Cancer: No Clear Connection
FDA is involved in new studies to determine the real risks from cell phone use.

31
Planning to Look Flab-u-less? Know the Facts About Liposuction
Surgery offers a quick fix for fat, but carries certain risks. Patients can protect themselves by asking questions and having realistic expectations.

Departments

2
Observations

2
Letters to the Editor

4
Updates

36
fda.gov

37
Summaries of Court Actions

39
Investigators’ Reports

40
The Last Word

The rise in the popularity of liposuction and changes in techniques have raised concerns within FDA that there may be an increased risk of post-surgical complications and even death. Here, a circulating nurse organizes the surgical tools used to remove unwanted fat. Story on page 31.
The Food and Drug Administration is a rare organization within the federal government; it functions at a place where science and the law intersect. The agency’s scientists and lawyers, working together with other agency regulators, make decisions that affect all Americans every day of their lives.

The FDA Consumer, too, occupies a strange and unique position within the portfolio of government publications. For one thing, it is generally readable, the Summaries of Court Actions notwithstanding.

Moreover, it’s directly aimed at the consumer, who I define as my mother.

My Mom grew up in a time when women were not generally trained in a profession. She didn’t go to college, but she was a straight A student in high school. She has lots of common sense, much of it hard-won by the trials of life, and she has a good heart. What’s more, my Mom is generally curious about the world and likes to know what her oldest son is up to, so she reads my stuff. I like that, so I try to write—or edit—stories so she can understand them.

These two facts—that FDA is a regulatory agency and FDA Consumer speaks to a general audience—occasionally come into conflict. Sometimes, our efforts to translate the agency’s dense regulatory language make my colleagues in other parts of FDA nervous. They seem to worry that if we simplify the articles too much, readers—the public, industry, even Congress—will misinterpret the FDA’s policies, decisions and actions. And misunderstandings can lead to lawsuits.

So, I thought I might make a few statements about what FDA Consumer magazine is and is not. First, as it says on the front cover, FDA Consumer is the magazine of the U.S. Food and Drug Administration. As such, the editors and writers work very hard to ensure that the articles reflect the policies and viewpoints of the agency. To help make the articles accurate and authoritative, the writers work with FDA scientists during the research and writing process, and then we ask FDA experts to review the final manuscript. This process provides the reader with the most current and accurate information possible.

But a magazine article neither makes nor embodies FDA policy. It’s a journalistic enterprise. The articles merely reflect and explain the policy decisions made by the agency’s experts. An article can’t describe the agency’s regulations and guidelines in all their glory—or detail. When FDA puts forth a regulation, it fills tens to hundreds of pages in the Federal Register, the official publication of the executive branch. The FR is good reading if you have insomnia.

We try to keep it more interesting. We take a complex story and tell it simply. We struggle for the balance between accuracy and accessibility. To do that, we leave things out, including many of the nuances behind an FDA decision.

Telling the government’s story—the story of how democratic people govern themselves—is an essential task. Associate Commissioner for Public Affairs Lawrence Bachorik, Ph.D., describes this responsibility and how the agency responds in this issue’s The Last Word (page 40). That’s a job FDA Consumer takes on joyously.

The need for teachers, for translators of arcane language, has been known for a long time. In May 1959, C. P. Snow gave a now-famous lecture at Cambridge University called “The Two Cultures.” Lord Snow observed that the gap between those trained in science and those trained in literature had become so large that these two cultures no longer communicated with each other—to the detriment of all. Since Lord Snow’s lecture, a class of writers has emerged—medical and science writers—who see it very much as their mission to serve as a bridge between the two cultures. Add a third culture, the culture of law, and the mission becomes even more complex.

But that mission is FDA Consumer’s raison d’être. The magazine exists to bridge the gaps and it will continue to do that by writing accessible stories.

Besides, I want my mother to keep reading.

Jesse Gelsinger

In the article “Human Gene Therapy: Harsh Lessons, High Hopes” (September-October 2000 FDA Consumer), you describe the illness of my son, Jesse Gelsinger. I would like to correct your description of the status of my son’s illness during his lifetime. In your description of Jesse, you said, “During his youth, he had many episodes of hospitalization, including an incident just a year before the OTCD trial in which he nearly died from a coma induced by liver failure. But a strict diet that allowed only a few grams of protein per day and a pile of pills controlled his disease to the point where he appeared to be a normally active teenager.” That shows how little you know about him.

Jesse had only three hospitalizations in his lifetime for his disorder: When he was first diagnosed in March 1984; in October of 1991 following a protein load; and in December 1998, following decompensation as a result of medication non-compliance and a probable problem with one of his medications.
causing hypoglycemia. In the 1998 experience, Jesse’s metabolic geneticist changed Jesse’s medications entirely. Upon an impressive recovery following administration of the new drugs, Jesse was non-symptomatic of his illness from that time until he signed himself into the care of the Institute for Human Gene Therapy at the University of Pennsylvania. Jesse even had a serious case of influenza in February 1999 and suffered no ill effects from his metabolic disorder, delighting us to no end. He was healthier than he had ever been in his life. In addition, sixty grams of protein a day, Jesse’s allowance at the time of his death, was easily manageable. He did need to take a lot of pills all his life ... and we thanked God every day for them because they allowed him to live as normal a life as you and I most of the time. In fact, Jesse probably lived a better life than you and I. He had a greater awareness of death, something that we all tend to ignore until it is upon us.

Paul L. Gelsinger
Tucson, Ariz.

Prescription IDs

The article “Make No Mistake: Medical Errors Can Be Deadly Serious” (September-October 2000 FDA Consumer) indicates that name confusion and sloppy handwriting are the most common causes of drug-related errors.

The problems of drugs with similar names and sloppy handwriting clearly indicate another type of description is needed!

It appears most of these problems could be solved by giving each drug a numerical ID. If sloppy handwriting is a problem, the number assigned to the drug would be unique—not subject to error. The numbers would also allow the use of bar codes for easy scanning. This technique would allow the use of many devices that are now available and being used to solve similar problems.

Whitney A. Brown
Winter Haven, Fla.

Single-Use Device Reprocessing

In FDA Consumer’s September-October 2000 article, “Reusing Medical Devices: Ensuring Safety the Second Time Around,” the story’s sensationalistic tone served only to distract and alarm readers, without providing them with the real news about reprocessing. Unfortunately, the article neglected to report that medical device reprocessing enjoys overwhelming support from the clinical community, reprocessed devices have an outstanding 20-year record of safe use (as good as, if not better than, original equipment), and they cost half as much as new devices. These savings help contain the always increasing cost of health-care. Furthermore, only a very small number of the thousands of devices used by hospitals are reprocessed.

Particularly troubling was FDA Consumer’s misrepresentation of the safety record of reprocessing. The article noted that FDA’s Medical Device Reporting (MDR) system contains 245 reports of adverse events associated with reprocessed devices. However, what FDA Consumer failed to report is that FDA receives 100,000 MDR reports every year. Thus, when put in its proper context, the tiny number of reports associated with reprocessed devices confirms the outstanding safety record of medical reprocessing.

Another piece of the real story that FDA Consumer missed was the meaning of the single-use label itself. Indeed, the article failed to clarify that the “single-use” label is not an FDA requirement. Rather, it is a designation chosen at the discretion of device manufacturers—more often for marketing reasons than for patient safety concerns. This means hospitals throw away millions of dollars a year in otherwise functional medical devices. Clearly, manufacturers have no commercial incentive to recommend that a “single-use” device be reused.

The truth is that third-party reprocessing is a safe, FDA-regulated industry. We strongly support vigorous FDA oversight of reprocessing, and we look forward to complying with the agency’s new guidelines.

Pamela J. Furman
Executive Director,
Association of Medical Device Reprocessors

FDA Consumer accepts letters to the editor. Letters can be e-mailed to FDAC-letters@oc.fda.gov, or mailed to FDA Consumer, Food and Drug Administration (HF1-40), 5600 Fishers Lane, Rockville, MD 20857. Letters should be 300 words or less, signed, and include an address and telephone number for verification. The editor reserves the right to edit letters for space and appropriateness.
New Implant Device Sends Vibrations to the Brain to Help Hearing Impaired

A first-of-its-kind hearing device has been approved that sends vibrations to the brain rather than simply magnifying sound like traditional hearing aids. The surgically implanted device is for adults with moderate to severe nerve hearing loss, not for the profoundly deaf.

Implanted in the skull bone behind the ear, the Vibrant Soundbridge device converts sound into mechanical energy and transfers the energy to the wearer’s middle ear via a wire. The energy vibrates delicate structures in the middle ear in much the same way that sound normally would, allowing the brain to interpret the vibrations as sound.

In clinical studies, the Vibrant Soundbridge was shown to improve hearing about as much as conventional hearing aids. On the plus side, the new device was less visible than some standard hearing aids, and it wasn’t hampered by earwax and moisture, which can be problematic with conventional devices.

But the surgery to implant the Vibrant Soundbridge entails the usual risks from surgical procedures, including infections and anesthesia risks. Other complications reported by patients in clinical studies included worsened hearing (2 percent), permanently altered taste (2 percent), long-term pain in the ear (5 percent), and a permanent feeling of “fullness” in the ear (16 percent).

FDA approved the implant in August based on a U.S. study of 81 patients, supporting data from European studies, and the recommendation of an FDA advisory committee. The device’s manufacturer, Symphonix Devices Inc., San Jose, Calif., is doing an 18-month follow-up study to determine the implant’s long-term safety and effectiveness.

Inhalant Marketed for Use in Young Children with Asthma

The first inhaled corticosteroid for young children with asthma was approved by the Food and Drug Administration in August. Pulmicort Respules (budesonide inhalation suspension), a synthetic hormone, is for use in a nebulizer—a device that turns liquid into an aerosol so the drug can be inhaled through a mask or mouthpiece. FDA approved the drug for children one to eight years old; before this, no corticosteroid was available for children younger than four.

Inhaled corticosteroids are considered by many asthma experts to be standard care for asthma sufferers with persistent symptoms and are believed to be effective in reducing the inflammation in the airways that may lead to an asthma attack.

Pulmicort Respules is designed for use once or twice daily to prevent asthma attacks, but it should not be used to treat acute attacks of asthma. Acute asthma attacks should be treated with a fast-acting inhaled bronchodilator (a drug that quickly opens up the lung’s airways). Improvement in asthma control following treatment with Pulmicort Respules can start in a few days, but it may take four to six weeks for full effects to occur.

The drug is generally well tolerated. The most frequent side effects reported by patients using Pulmicort Respules were respiratory infection, coughing, and congestion. In addition, studies have shown that inhaled corticosteroids may reduce a child’s growth by an average of one centimeter per year. The effect of corticosteroids on eventual adult height is not known. The effect on growth appears to be related to both the dosage and duration of exposure to the drug. Physicians or other care providers should work with the children and their families so that the child is receiving the lowest dose that maintains adequate asthma control.

Children using the inhalant who have not been vaccinated and have not had chicken pox or measles, but who are exposed to these diseases, should see a doctor immediately.

Pulmicort Respules is manufactured by the AstraZeneca Group of Wayne, Penn.
New Once-a-Day Formulation of Methylphenidate Available for Attention Deficit-Hyperactivity Disorder

A controlled-release form of a widely used drug that treats attention deficit-hyperactivity disorder (ADHD) has been approved by the Food and Drug Administration. The drug methylphenidate, best known as Ritalin, must be taken two or three times a day when given in the immediate-release form; the new extended-release formulation requires only a single daily dose.

FDA approved Concerta, a controlled-release form of methylphenidate, in August to treat the symptoms of ADHD, which include inattention, hyperactivity and impulsiveness. Concerta is administered once in the morning, as opposed to current immediate-release forms of methylphenidate, which must be taken two or three times daily.

Methylphenidate has long been prescribed for the treatment of ADHD, but use of the immediate-release forms can be disruptive to a child’s daily schedule, requiring the child to visit the school nurse, who administers the drug. Concerta may eliminate the need for in-school and after-school dosing.

Typically, children and adults suffering with ADHD make careless mistakes, fidget, interrupt others, talk excessively, and have problems paying attention. The disorder first appears during childhood.

The side effects associated with Concerta include headache, stomach pain, insomnia, and decreased appetite. Concerta may not be appropriate for patients with certain types of gastrointestinal disorders. Concerta is manufactured and marketed by ALZA Corp. of Mountain View, Calif.

Testicular Cancer Treatment Increases Leukemia Risk

Men who receive either of two kinds of treatment for testicular cancer appear to be at increased risk for leukemia, according to a recent study. Researchers found leukemia in men who received radiation therapy and in some taking cisplatin, a chemotherapy drug commonly used to treat testicular cancer.

The risk for men taking radiation therapy was three times greater than in those not receiving radiation, and men who received higher doses were at even greater risk. Cisplatin, a standard part of most testicular cancer chemotherapy combinations, also increased the risk of leukemia to three times higher than normal, and men receiving especially high doses were at greater risk for leukemia.

Researchers point out, however, that the benefits of both treatments far outweigh the small risk of leukemia. (Journal of the National Cancer Institute, July 19, 2000)

Study Shows Heart Disease Risk Factors Can Start in Adolescents as Young as 15

The blockages in arteries that can lead to a heart attack or sudden death appear to start forming early in life, in young adults and adolescents as young as 15, according to a recent study. Some teenagers and young adults with risk factors for heart disease—high cholesterol, high blood pressure, and obesity, for example—have fatty plaques in their heart arteries indicating the earliest signs of atherosclerosis, while others are already in the more dangerous advanced stages, according to the study.

Researchers at the Southwest Foundation for Biomedical Research in San Antonio, Texas, looked at the left coronary arteries (large blood vessels that supply blood to the heart muscle) from the autopsies of 760 men and women aged 15 to 34 who had died from an accident, murder, or suicide. Autopsies of American soldiers killed in combat during the Korean War first alerted researchers that the biological changes leading to heart attacks and stroke begin early in life. Autopsies of American casualties during the Vietnam War found similar trends. Despite decades of awareness, the trend continues.

In the San Antonio study, young people who had high blood levels of “bad” cholesterol (called low-density lipoproteins, or LDL) were about 2½ times more likely to have advanced plaque blockages than those who did not have high LDL levels. And those who were obese were more than 2½ times more likely than the others to have advanced plaques, regardless of cholesterol levels or other risk factors.

In total, about 2 percent of the 15- to 19-year-old men and 20 percent of 30- to 34-year-old men in the study had advanced plaques. While no women aged 15 to 19 had advanced plaques, 8 percent of women aged 30 to 34 died.

According to the study’s lead author, Henry C. McGill, Jr., M.D., early risk factors “may be a significant predictor of a person’s chance of developing heart disease later in life.”

The study suggests the need to tailor messages about heart disease prevention to children, according to the study’s authors, and to recommend nutritional guidelines for heart disease prevention to children as well as adults. (Circulation, July 24, 2000)
Guide Developed for Lotronex Patients

Women taking Lotronex to treat irritable bowel syndrome will start getting a plain-language consumer Medication Guide along with their pills. The Lotronex guide cautions patients to be aware of rare, but serious, side effects that have been reported in some people taking the drug. It spells out important information about the prescription drug, its possible risks, and what consumers can do to avoid problems.

This is the first time the Food and Drug Administration has required an FDA-approved Medication Guide under regulations that went into effect in 1999.

Irritable bowel syndrome (IBS) is a condition affecting up to 15 percent of Americans that is marked by chronic abdominal pain, diarrhea, or constipation. Lotronex was approved earlier this year for treating the pain and discomfort of women who have the diarrhea-predominant form of IBS. It has not been shown to help men with the condition. Since its approval, FDA has received reports of several cases of serious complications from constipation in patients taking Lotronex, some of which resulted in hospitalization and surgery. Cases of ischemic colitis, an inflammatory condition caused by reduced blood flow to the intestines that also sometimes requires surgery, have been reported as well.

The Lotronex guide cautions women whose main IBS symptom is constipation not to take the drug. It warns further that patients taking Lotronex should contact their doctor immediately if they experience constipation, and should stop taking the drug if they develop severe constipation, new or worsening abdominal pain, or bloody stools. It counsels patients to discuss with their doctors how troublesome their IBS symptoms are and the benefits and risks of the drug, so that they can decide if Lotronex is the right medication choice.

Another Use for Viagra?

The popular impotence treatment drug Viagra may have another use, according to a study conducted at Johns Hopkins University School of Medicine. Researchers say that Viagra could be an effective remedy for a digestive condition common among people with diabetes that blocks or slows the passage of food from the stomach to the intestine, known as gastroparesis.

Gastroparesis, which commonly affects up to 75 percent of diabetic individuals, causes bloating, loss of appetite, vomiting and dehydration, and can complicate efforts to control blood sugar levels with medication because it disrupts the timing of the digestive process. Viagra appears to cause muscles in the digestive tract to relax in the same way it prompts muscles in the penis to ease and facilitate an erection. (Journal of Clinical Investigation, August 2000)

Free Publications

FDA Consumer Reprints

To order single copies of these FDA Consumer articles, use the contact information listed after each title. Include the publication number with your request. To order two to 50 copies, write to FDA (HFI-40), 5600 Fishers Lane, Rockville, MD 20857.

- Arthritis: Timely Treatments for an Ageless Disease (FDA) 00-1313
- Breast Cancer: Better Treatments Save More Lives (FDA) 00-1306
- Taking Charge of Menopause (FDA) 00-1310
  For these three reprints, write to: FDA (HFD-210), 5600 Fishers Lane, Rockville, MD 20857
- Bone Marrow Transplants Come of Age: New Hope for Deadly Diseases (FDA) 00-4273
  Write to: FDA (HFM-45), 11400 Rockville Pike, Rockville, MD 20852-1448
- Cosmetic Laser Surgery: A High-Tech Weapon in the Fight Against Aging Skin (FDA) 00-4272
  Write to: FDA (HFZ-210), 1350 Piccard Drive, Rockville, MD 20850
- How to Spot Health Fraud (FDA) 00-1309
  Write to: FDA (HFS-555), 200 C St., S.W., Washington, DC 20204

Easy-to-Read Brochures

FDA provides easy-to-read health brochures in both English and Spanish on its Web site. These publications have recently been updated and revised. Brochures can be viewed and downloaded in PDF (graphic) or HTML (text) formats. Check out the list at www.fda.gov/opacom/lowlit/lowlit.html.
THE FOOD AND DRUG ADMINISTRATION approved mifepristone (trade name Mifeprex, previously known as RU-486) on September 28 for the termination of early pregnancy. Mifepristone blocks the hormone progesterone, which prepares the lining of the uterus for a fertilized egg and helps maintain pregnancy. Early pregnancy is defined as 49 days or less, counting from the beginning of the last menstrual period.

Mifepristone is part of an approved treatment regimen that calls for at least three visits to a doctor’s office or clinic. On the first visit, the woman receives counseling and a medication guide. She then takes 600 milligrams of mifepristone (three 200-milligram pills) by mouth while in the doctor’s office. Two days later, she returns to the physician and, if she is still pregnant, takes 400 micrograms (two 200-microgram pills) of misoprostol—again while in the doctor’s office. Misoprostol, a prostaglandin previously approved by FDA for the treatment of ulcers, causes the uterine muscles to contract and end the pregnancy.

Approximately 14 days after the first visit, the woman returns to her doctor to determine whether the pregnancy has been terminated. The combination of mifepristone and misoprostol has been shown in studies to end pregnancy in about 92 to 95 percent of women. In the few cases where the pregnancy is not terminated by the drug treatment, the doctor then discusses options with the patient, including surgery to end the pregnancy. There is a chance that there may be birth defects if the pregnancy results in a live birth after treatment with mifepristone and misoprostol.

The medication guide given to each woman who is prescribed mifepristone fully explains how to take the drug, who should avoid taking it, and what side effects can occur. Both the doctor and patient must sign a Patient Agreement Form stating that the patient understands the benefits and risks of the treatment and has decided to end her pregnancy.

“The approval of mifepristone is the result of the FDA’s careful evaluation of the scientific evidence related to the safe and effective use of this drug,” said FDA Commissioner Jane E. Henney, M.D. “The FDA’s review and approval of this drug has adhered strictly to our legal mandate and mission as a science-based public health regulatory agency.”

FDA based its approval on data from clinical trials in the United States and France.

The drug’s label emphasizes that most women using mifepristone will experience some side effects, mostly cramping and vaginal bleeding. Bleeding and spotting will typically last between nine and 16 days. In about one out of 100 women, bleeding can be so heavy that surgery will be required to stop it. The drug’s labeling also warns that mifepristone should not be used in women with certain conditions, including ectopic (“tubal”) pregnancy. An ectopic pregnancy occurs when a fertilized egg begins to grow in one of the fallopian tubes that connect the ovaries to the uterus.

Mifepristone, not available in pharmacies, is distributed only to physicians who can accurately determine the duration of a patient’s pregnancy and detect an ectopic pregnancy. Physicians who prescribe the drug must also be able to perform surgery in cases of an incomplete abortion or severe bleeding—or they must have made plans in advance to provide this care through other qualified physicians.

Mifepristone was developed by a French pharmaceutical firm and was first approved for use in France in 1988. Since then, more than 620,000 European women have taken mifepristone in combination with a prostaglandin (such as misoprostol) to terminate pregnancy. Mifepristone has also been approved in the United Kingdom, Sweden, and other countries.

Mifepristone’s sponsor is a New York-based nonprofit group, the Population Council. The drug will be distributed in the United States by Danco Laboratories, LLC, New York.

More detailed information about mifepristone is available on FDA’s Web site at www.fda.gov/cder/drug/infopage/mifepristone/.
Home For The Holidays:
Preventing Foodborne Illness
At Family Gatherings

By Paula Kurtzweil Walter

Stephanie K. of Eau Claire, Wis., spent her 1997 Thanksgiving break at her grandparents’ home—in bed, sick with what her family assumed was a stomach virus. But when her grandparents both came down with the same symptoms 12 hours later, some family members started to question whether the real culprit was their Thanksgiving dinner.

It certainly wouldn’t be unheard of. Foodborne illness is a frequent uninvited guest during the holiday season, and it’s often a food handler who allows it to come in and set up housekeeping. For instance:

• In 1997 in Pike County, Ohio, 13 people came down sick at a Thanksgiving family get-together. Nine tested positive for the bacterium Salmonella enteritidis. The microbe also was found in turkey, gravy, stuffing, two pies, and several
FOODBORNE ILLNESS is a frequent uninvited guest during the holiday season, and it's often a food handler who allows it to come in and set up housekeeping.

Other foods served at the Thanksgiving dinner, suggesting that a food handler had somehow transferred bacteria from one food to the next. This is known as cross-contamination. Also, the turkey had not been cooked to the proper temperature.

- At Christmas time in 1997, all 56 guests at a catered event in Spokane, Wash., developed cryptosporidiosis, a parasitic disease whose symptoms can persist for weeks. The unlikely source was the garnish used on a number of dishes—green onions. They became contaminated through bare-hand contact by an infected food worker.

- At Thanksgiving time in 1998, a father and son in eastern Washington state who made themselves oyster shooters got an unexpected shot of something else—disease-causing Campylobacter bacterium. The oysters, apparently the source of the bacteria, were eaten raw. Proper cooking would have killed the microbes.

Though most foodborne disease outbreaks don’t occur during the holidays (they occur most often in the summer), the holidays warrant special attention because certain foods and food practices popular during the season can increase the risk for foodborne illness. But just as traditions prevail during the season, so, too, should they when it comes to keeping food safe at the holidays.

“It’s the key health messages we talk about again and again,” says Charles “Burt” Bartleson, technical expert for the Washington State Department of Health’s food safety and shellfish program. The Fight BAC! campaign of the Partnership for Food Safety Education, of which the Food and Drug Administration is a member, sums up the key health messages this way:

- **Clean:** Wash hands and food-contact surfaces often. Bacteria can spread throughout the kitchen and get onto cutting boards, knives, sponges, and countertops.

- **Separate:** Don’t cross-contaminate—don’t let bacteria spread from one food product to another. This is especially true for raw meat, poultry and seafood. Experts caution to keep these foods and their juices away from ready-to-eat foods.

- **Cook:** Cook to proper temperatures. Foods are properly cooked when they are heated for a long enough time and at a high enough temperature to kill the harmful bacteria that cause foodborne illness.

- **Chill:** Refrigerate promptly. Public health officials advise consumers to refrigerate foods quickly because cold temperatures keep most harmful bacteria from growing and multiplying. Refrigerators should be set at 40 F and the freezer unit at 0 F, and the accuracy of the settings should be checked occasionally with a thermometer.

**Cooking Up a Spread**

But the holidays don’t always make it easy for food handlers to follow this advice. One reason, says Marjorie Davidson, Ph.D., FDA’s director of food safety education, is that people get caught up in the hectic pace of the holiday season.

“People get sloppy,” she says. “They’re busy, and they lose the vigilance that they might follow at other times of the year.”

At the same time, she says, most consumers are dealing with foods they seldom prepare outside of the holiday season. “A lot of people just aren’t familiar with [fixing] the big pieces of meat and poultry often served at this time of year,” she says.

The amount of time to properly thaw and cook a whole turkey, for example, is much longer than the standard-size poultry pieces and cuts of meat served year-round. When thawed correctly in the refrigerator or at a temperature of no more than 40 F, a 20-pound turkey needs two to three days to thaw completely. Thawing the turkey completely before cooking is important. Otherwise, the outside of the turkey will be done before the inside, and the inside will not be hot enough to destroy disease-causing bacteria. A stuffed turkey needs 4¼ to 5¼ hours to cook completely. To check a turkey for doneness, insert a food thermometer into the inner thigh area near the breast of the turkey but not touching bone. The turkey is done when the temperature reaches 180 F. If the turkey is stuffed, the temperature of the stuffing should be 165 F.

Many people also may be unused to juggling at one time the large number of dishes that often go into a traditional holiday dinner. Though they should, few may consider whether they’ll have adequate refrigerator space to store their planned menu items both before and after the dinner is served.

The party spreads and buffet dinners that often are a part of the holiday scene also pose unique challenges. How many times as a guest have you seen party and buffet foods sit out for hours on end? For safety’s sake, perishable foods should not be left at room temperature for more than two hours.

The traditional advice applies: Keep hot foods hot and cold foods cold.

**Holiday Specials**

Add to these challenges typical holiday foods that carry their own set of risks. Traditional eggnog made with raw eggs is a common one. Fresh eggs may contain bacteria that can cause an intestinal infection called salmonellosis. Cooking can destroy the bacteria.

Bartleson recalls an outbreak three years ago in which four people at a holiday family gathering in Washington state got sick after drinking eggnog made with raw eggs. The risk associated with the raw eggs was compounded by the fact that the eggnog had been left at room temperature for several hours before being consumed, Bartleson says.

Safe alternatives are the pasteurized eggnog beverages sold in grocery dairy cases, although they, too, should be kept refrigerated.

The risk of illness from raw eggs is associated with another favorite holiday
activity—baking. Eating cookie dough or batters with raw eggs carries the same
risk as eggnog made with raw eggs. Unfortunately, the ones who often are the
most eager to sample cookie dough or lick the spoon or bowl are among those
most vulnerable to foodborne illness—kids. Commercial dough does not carry
the same risk because it is made with pasteurized eggs; that is, eggs that have
been heated sufficiently to kill bacteria. It also may contain an acidifying agent
that kills bacteria. However, it is best to not eat raw cookie dough—instead enjoy
your cookies after they have been properly cooked in the oven.

Handle with Care
Another popular food item at the holidays—mail-order food gifts—also car-
ries risks that many consumers may be unaware of. Because mail-order food
gifts can include meat, poultry, fish, and other perishables like cheesecake, these
gift packages need to be handled with care. Although the mail-order food in-
dustry enjoys a good safety record, according to the Food Safety and In-
spection Service of the U.S. Department of Agriculture, the gift giver and recipi-
ent need to take special precautions to ensure the safety of the food when it ar-
rives. The giver needs to alert the recipient to the pending arrival of the food
gift. And the recipient needs to open the package immediately to make sure that,
if it’s labeled “keep refrigerated,” the food arrives in a chilled state.
Many people also like to give gifts of homemade food at the holidays.
Generally, homemade foods do not pose a food-safety problem. But in
some cases they can. Bartleson recalls a case in which a woman gave her fa-
ther-in-law a gift of her home-pickled asparagus. She also gave him some-
thing else—a case of botulism. Fortunately, he recovered. But his experi-
ence points to the need for consumers to follow instructions carefully when
preserving foods. Guidelines for home canning procedures can be found on
the Internet at www.ext.usu.edu/publica/foodpubs.htm.

Advice for the Holidays
Even though the holidays present a
number of unique food-safety challenges,
consumers have plenty of places to go for
good information on how to do things
right. Among them:
• The Fight BAC! Web site,
   www.fightbac.org
• FDA’s Food Information Line, toll-free
   1-888-SAFEFOOD (1-888-723-3366)
• The USDA’s Meat and Poultry Hotline,
   1-800-535-4555 (202-720-3333 in the
   Washington, D.C., area). The TTY num-
   ber for the hearing impaired is 1-800-256-
   7072. The e-mail address is
   mphotline.fsis@usda.gov.
Most people would agree that the holi-
days are a special time for special activities,
many of them food-related. Who would
want to spoil the season by giving someone
a foodborne illness? Though it certainly has
been done in the past, it’s one holiday tradi-
tion not worth keeping.

—Paula Kurtzweil Walter is a writer in
Gaithersburg, Md.

What’s Up With Thermometers?
The Thermy Campaign

If you’re looking for that perfect gift for
the family, consider a food thermometer. Ev-
every household needs at least one, according
to the Food Safety and Inspection Service
(FSIS) of the U.S. Department of Agriculture.
In May, FSIS launched the Thermy Cam-
paign, a national consumer education initia-
tive, to promote the use of food thermometers
in the home. The agency says that consumers
should use a food thermometer every time
when cooking meat, poultry, and egg dishes:
It’s the only way to ensure that food reaches a
temperature high enough to destroy harmful
bacteria.

For more on how and when to use food
thermometers and the various types available,
check out the Thermy Campaign Web site at

—P.K.W.
Planning a healthier diet that helps reduce the risk of heart disease just got easier. And a little tastier. Foods containing certain plant extracts, which have been shown to reduce blood cholesterol levels, have received the go-ahead to tout their ability to lower the risk of heart disease.

In September, the Food and Drug Administration gave food manufacturers permission to put labels on foods containing plant sterol esters and plant stanol esters to indicate that they may reduce the risk of coronary heart disease (CHD). As in authorizing similar health claims for soy, oat bran, and other foods, FDA based this action on a review of the scientific evidence that shows the benefits of these plant extracts in a healthy diet. FDA-authorized health claims are intended to help otherwise healthy consumers make informed choices about products that may help promote health and prevent disease.

High blood cholesterol levels are a major risk factor for developing CHD or other heart problems. According to the American Heart Association, CHD accounts for more deaths in the United States than any other disease or group of diseases.

Although cholesterol seems to be widely condemned as the cause of heart disease, the body actually needs it to function properly. Produced in the liver and absorbed from the diet, cholesterol helps build structures like cell membranes and some hormones. It circulates in the body in several complex forms, including low-density lipoprotein (LDL) cholesterol—sometimes called “bad” cholesterol, and high-density lipoprotein (HDL) cholesterol—often referred to as “good” cholesterol.

Excess cholesterol contributes to fatty buildup in the arteries that forms plaque deposits, narrowing the arteries. If the plaques accumulate in the coronary arteries that supply blood to the heart muscle, then blood flow is impeded and the heart itself becomes starved for oxygen, causing pain. If a blood clot forms and completely obstructs the artery, a heart attack can occur.

Plant sterol and stanol esters work by blocking the absorption of cholesterol from the diet, and have been known for some time to reduce the blood cholesterol levels that are responsible for most heart attacks. Plant sterol esters can be found in soybean oil as well as in many fruits, vegetables, nuts, cereals and other plant sources. Plant stanols occur naturally in smaller quantities in some of the same sources.

Research on the cholesterol-lowering benefits of the plant sterol and stanol esters led food manufacturers to consider adding these compounds to products that could substitute for high-saturated fat, high-cholesterol products, such as butter.

Following a heart attack in 1996, with the recommendation of his physician to follow a heart-healthy diet, 51-year-old “health nut” Phillip Terry reluctantly decided to switch to one of the two cholesterol-busting spreads currently being marketed as butter alternatives to reduce LDL cholesterol. He hoped it would lower his risk of future heart disease.

“It tastes just like margarine,” says the Dallas, Tex., resident, although he admits he was initially skeptical about using a food product containing fat to aid in controlling his cholesterol levels. Skeptical or not, Terry’s cholesterol levels told the tale.

“He is the most impressive case,” says Terry’s physician, Nilo Cater, M.D., assistant professor of medicine at the University of Texas Southwestern Medical Center at Dallas. Cater says that Terry “has had a significant, consistent response that has reduced his LDL cholesterol from 102 milligrams per deciliter (mg/dL) of blood, to 66 mg/dL. While the ideal LDL-cholesterol level for most people is less than 130 mg/dL, the desirable level for prior heart attack patients, like Terry, is less than 100.”

For manufacturers to make a hearthealthy claim on any product containing these plant esters, the product must meet certain conditions. For example, the claim must specify that the daily dietary intake of plant sterol esters or plant stanol esters should be consumed in two servings eaten at different times of the day with other foods. FDA is also requiring that health claims about plant sterol and plant stanol esters state that they should be consumed as part of a diet low in saturated fat and cholesterol.

Under this interim final rule, manufacturers are able to use the claim immediately while FDA accepts public comments for 75 days. FDA will consider all comments it receives and will publish a final rule next summer. If the comments convince FDA to make changes in the rule, manufacturers may have to revise their labeling.

Doctors believe that, by reducing LDL cholesterol through exercise and diet, many Americans may be able to avoid drug therapy to reduce their risk of heart disease. And incorporating plant sterol and stanol esters into the diet is one option for Americans who are trying to lower their cholesterol levels to benefit their hearts.
Robots Help Surgeons Perform More Precise Surgery

By Linda Bren

While gripping hand controls, depressing foot pedals, and watching a 3-D video display, a surgeon removed the gall bladder of a 35-year-old woman at Henrico Doctor’s Hospital in Richmond, Va. The surgery occurred this summer, just one day after FDA cleared for marketing a robotic device to perform laparoscopic gall bladder and gastroesophageal reflux disease (severe heartburn) surgery.

In standard laparoscopic surgery, the surgeon, while standing over the patient, makes up to four small incisions in the abdomen through which tubes are inserted. A miniature camera at the end of one tube enables the surgeon to see into the body and guide instruments through the other tubes to perform minor surgery.

With the robotic device, called the da Vinci Surgical System, the surgeon performs the operation while sitting at a console nearby the operating table. The surgeon views a motionless image, magnified up to 20 times, of the patient and operative site on a video monitor.

From the console, the surgeon controls three robotic arms holding surgical tools above the operating table. The robotic technology translates the surgeon’s movements into precise, real-time movements of the surgical instruments inside the patient. A built-in “wrist” at the end of the tools helps the surgeon to perform more exact and intricate motions without the natural tremors that accompany a surgeon’s own hands.

In clinical studies, results of 113 surgeries for gall bladder or gastroesophageal reflux disease using the robotic device were found comparable in safety and effectiveness to the results in 132 patients who underwent standard laparoscopic surgery. However, the robotic surgery took 40 to 50 minutes longer than the standard surgery, which was attributed in part to the lack of
experience with the new technology. FDA is working with the manufacturer to develop a training program for surgeons on the device.

Up until now, surgical robots were approved for experimental surgery only. The da Vinci Surgical System, made by Intuitive Surgical, Inc., of Mountain View, Calif., is the first device to be approved for commercial marketing.

“This system is the first step in the development of new robotic technology that eventually could change the practice of surgery,” says FDA Commissioner Jane E. Henney, M.D.

Changes in heart surgery are already on the horizon. Robotic devices have been used experimentally to perform heart bypass surgery and heart valve repair and replacement. In April, surgeons at the New York University Medical Center performed the first minimally invasive robotic heart valve surgery in the United States. This successful mitral valve repair on a 50-year-old male was part of an FDA-approved clinical study.

Surgeons currently perform most heart surgery by making a large incision in the chest and cracking open the rib cage. According to Neil Ogden, chief of the General Surgery Devices Branch in FDA’s Center for Devices and Radiological Health, “robotics has the potential to allow minimally invasive heart surgery with the chest completely closed.”

Photos and diagram courtesy of Intuitive Surgical Inc., Mountain View, Calif.

Robotic instruments—highly magnified here—are modeled after the human wrist, hand, and fingers (above, top photo) to allow precise motions when performing surgery. The surgeon manipulates the interchangeable instruments [center] using hand grips (bottom) while sitting at a console a few feet from the operating table.
Imagine taking a fantastic voyage through the highways and byways of the human body. With a touch of a finger on the controls of your vehicle, you “fly” down strangely scenic routes and dark tunnels. Along the way, you note dangers and relay them back to technicians for future repair. Sound far-fetched? Not really.

By using new computer-assisted technology, doctors can visualize a person’s colon just as if they were there. Called “virtual colonoscopy,” this screening test projects a three-dimensional image of the colon onto a computer screen. The physician “flies” through its length, searching for lumps that might be cancerous. The test is non-invasive and often involves much less discomfort than conventional methods of examining the colon. Sedation is seldom required, and the patient can go home immediately after the procedure.

“Virtual colonoscopy has the potential to revolutionize how we screen for colon cancer,” says Brian E. Harvey, M.D., a senior medical officer in the Food and Drug Administration’s Center for Devices and Radiological Health. “It’s very exciting, and once all the data are in, we may find we can screen the entire population over the age of 50, which can lead to early detection of more colonic polyps and colorectal cancer.”

When this technique is perfected, it will be added to the arsenal of tools used for the prevention and early diagnosis of colorectal cancer. Although this cancer remains a very scary disease, such new detection technologies improve the chance of finding the tumor early in its growth when it’s most curable. In addition, therapeutic advances offer new hope that, even if the cancer has spread, the diagnosis of colon cancer will not be fatal.

A Killer Disease and Its Risk Factors
Colorectal cancer—cancer of the large intestine and rectum—is second only to lung cancer in the number of cancer deaths it causes. The American Cancer Society estimates that more than 130,000 Americans will be diagnosed with colorectal cancer in 2000, and more than 56,000 will die from the disease this year. On average, one in 20 people will develop the disease in the course of a lifetime. Ninety percent of cases occur in patients over age 50, and the majority of cases—75 percent—occur in people with no known medical risk factors for colorectal cancer. But certain factors can sharply increase risk. They include:

- **Family history.** Having a first-degree relative—mother or father, for example—with colorectal cancer increases the lifetime risk of developing the disease to as high as eight-fold greater than people without a family history.
- **History of bowel disease.** Risk increases 30-fold in patients with a history of inflammatory bowel disorders, such as Crohn’s disease or ulcerative colitis.
- **History of adenomatous polyps.** Most colorectal cancers begin as small precancerous growths, called polyps, inside the colon or rectum. Villous adenomatous polyps are the most likely to become cancerous (up to 25 percent). Tubular adenomatous polyps are estimated to become malignant 1 to 5 percent of the time.
- **Genetic traits.** A genetic syndrome known as Familial Cancer Syndrome or Hereditary Non-Polyposis Colon Cancer markedly increases the risk for developing colorectal cancer at an earlier age than those patients at average risk.

**Signs and Symptoms**
The colon and rectum make up the large intestine, the end of the long tube of the gastrointestinal tract through which food passes during digestion. (This interconnected gastrointestinal organ system also includes the esophagus, stomach and small intestine.) The colon is the upper five or six feet of the large intestine, and the rectum is the last six to eight inches. Cancer begins to develop when cells in the colon multiply uncontrollably. These cell mutations result in precancerous polyps, small protrusions from the intestine’s lining.

There are several types of polyps, and they become increasingly common with age. By age 50, 10 percent of the population has polyps, but by age 65 that number grows to 30 percent. If left untreated, 8 to 12 percent of polyps will become cancerous. If allowed to grow, the tumor can invade nearby organs. Once the disease enters the lymph nodes or bloodstream, it most often spreads to the liver.
Colon cancer survivor Kim Vallarelli with her daughters (clockwise) Katie, Sarah, and Brittnay. Vallarelli’s uterus and part of her liver had to be removed because her colon cancer had spread. Cancer-free four years later, she advises others not to put off screening.

As with many cancers, there are usually no symptoms in the early stages. Polyps do sometimes bleed, and there may be some noticeable rectal bleeding. However, most of the time, this blood is invisible to the naked eye and is only detectable microscopically.

Patient symptoms begin to appear once the tumor is large enough to cause obstruction of the bowel. They include:
- anemia
- rectal bleeding with bright red blood
- blood in the stool, characterized by black, “tarry” stools
- a change in bowel habits, such as recurrent diarrhea or worsening constipation
- persistent abdominal pain

• generalized weakness or fatigue
• unexplained weight loss

Early Detection Means Survival
If diagnosed and treated in its early stages, colorectal cancer is highly curable. Patients whose tumors are entirely localized to the bowel have an 80 to 90 percent chance of surviving for 10 years. With tumors that spread to the liver, however, the five-year survival rate is less than 5 percent.

The lack of symptoms in early stages may be one reason colorectal cancer has a high mortality rate. “By the time this disease becomes symptomatic, it’s often in the late stage,” says Robert Kurtz, M.D., chief of gastroenterology and nutrition at Memorial Sloan-Kettering Cancer Center in New York. “There’s no question that the earlier colon cancer is found, the more likely the patient will be cured with surgery.”

“In fact,” Kurtz says, “prevention is the best solution.” Because colorectal cancer begins as a slow-growing precancerous polyp, finding and removing these polyps can prevent cancerous changes from taking place. However, since there is no way to know if a polyp is precancerous without a biopsy, medical professionals generally agree that all polyps should be removed upon discovery.

FDA has cleared, or approved, several screening and diagnostic methods for colorectal cancer. When performed regularly, these tests allow the removal of polyps before they become cancerous, which can reduce the incidence of colon cancer by 40 percent. And, by preventing tumor formation, these tests can cut the death rate from colorectal cancer in half.

Screening for patients with no medical or family risk factors should begin at age 50 and be performed regularly. Available screenings include:

- **Fecal occult blood test.** Both colon cancer and polyps can cause bleeding, which will be passed into the stool. In this test, a small stool sample transferred to a collection card with a narrow stick is screened for the presence of blood. The sample can be collected at home by patients, who send it to their doctors, or by the doctor during a physical examination. Because other conditions, such as stomach ulcers and hemorrhoids, can cause blood in the stool, this test has a high rate of false positives and may result in unnecessary follow-up screenings. It may also fail to detect some tumors.

- **Flexible sigmoidoscopy.** A short, flexible fiber optic tube is inserted to inspect the rectum and part of the colon. Although this can be an effective diagnostic tool, it is limited in that it inspects only the lower third of the colon.

- **Barium x-ray.** In this test, a contrast material is infused through the rectum. This material expands the colon and allows a radiologist to see large polyps or cancers (greater than 10 millimeters) in the entire colon. The bowel must be cleansed by laxatives or enemas before
Lifestyle Changes Could Save Your Life

In June 1999, the Harvard Center for Cancer Prevention released a report summarizing the impact of diet and lifestyle factors on colon cancer. The report came to a startling conclusion: Half of all colon cancers can be prevented through lifestyle changes and widespread screening.

Behaviors recommended by the Harvard report for lowering colon cancer risk include:

- **Regular screening after age 50.** This can reduce the risk of dying from colon cancer by at least 33 percent.
- **Regular exercise.** Physically active adults are half as likely to develop colon cancer as sedentary adults. The report recommends a daily workout of 30 minutes of vigorous exercise or one hour of brisk walking.
- **Cut down on red meat.** Eating one serving per day of red meat is associated with a 50 percent increase in risk.
- **Regular screening after age 50.** This can reduce the risk of dying from colon cancer by at least 33 percent.

The report also recommended main functions and lifestyle factors on colon cancer. The report came to a startling conclusion: Half of all colon cancers can be prevented through lifestyle changes and widespread screening.

Behaviors recommended by the Harvard report for lowering colon cancer risk include:

- **Regular screening after age 50.** This can reduce the risk of dying from colon cancer by at least 33 percent.
- **Regular exercise.** Physically active adults are half as likely to develop colon cancer as sedentary adults. The report recommends a daily workout of 30 minutes of vigorous exercise or one hour of brisk walking.
- **Cut down on red meat.** Eating one serving per day of red meat is associated with a 50 percent increase in risk.
- **Regular screening after age 50.** This can reduce the risk of dying from colon cancer by at least 33 percent.

Despite the availability of screenings and their relative effectiveness, the mortality rate for colorectal cancer remains high. Experts say there are several reasons for this, including the fact that some screenings may fail to detect tumors. Another reason, according to David Ahlquist, M.D., professor of medicine and director of the Colorectal Neoplasia Clinic at the Mayo Clinic in Rochester, Minn., is a reluctance of patients to have the tests performed due to the discomfort and embarrassment involved. "We could have had a much larger impact on this disease if the screening tools we have were more widely used," Ahlquist says. "There's a challenge for science to come up with screenings that are more accurate and more comfortable so more people will have them performed."

Kim Vallarelli confirms that embarrassment was a factor in screening for her. "It's such a private thing," says the Harrison, N.Y., resident. "It just seemed too embarrassing to go through."

Vallarelli, however, was experiencing recurring symptoms, including bright red blood in the stool, bloating and persistent abdominal pain. Her doctor recommended a colonoscopy, which revealed a grapefruit-sized malignant tumor.

Vallarelli vividly recalls her terror at the news. "I was hosting my daughter's birthday party the next day. I remember children laughing all around me," she says, "but all I could feel was fear."

**Meeting the Challenge**

Virtual colonoscopy is one way science can provide more accurate and more comfortable screening. FDA first cleared this computer-assisted technology in 1995. As in the early devices, updated versions use digital information to produce a three-dimensional reconstruction of internal hollow structures of the human body, including the colon.

Before performing virtual colonoscopy, the bowel is first cleansed with oral laxatives. A small tube is inserted into the rectum and the colon is inflated with air. A computerized axial tomography (CAT or CT) scan or magnetic resonance imaging (MRI or MR) is then performed. The entire procedure takes less than five minutes, and since sedation is usually unnecessary, the patient can leave immediately after the scanning is completed.

In earlier versions of these devices, the technician loaded the CAT or MRI images into a computer, where special software reconstructed the digital data into 3-D images. Now, with later versions, the digital data transfer and reconstruction are automated in "real time." Medical professionals can now "fly" inside the images, identifying polyps, cancers or other structural abnormalities. Using a computer mouse or a joystick, the doctor controls the speed of the voyage, going forward and backward—even making a complete circle—at will. The technology is able to consistently identify polyps 10 millimeters in diameter—about the size of a blueberry—or larger. If an abnormality is found, the patient then undergoes a conventional colonoscopy so the polyp can be removed.

There are other potential benefits to this new technology. For example, it may reduce the number of conventional colonoscopies performed for diagnostic purposes, and increase the number performed therapeutically for the specific purpose of removing polyps. These procedures also can provide an electronic record that can be stored, transmitted to distant locations, and used for future analysis. As the technology becomes more sophisticated, a cleansing bowel preparation may no longer be necessary, making the test even more acceptable to patients.

FDA's Harvey says that although the agency has cleared this new technology as a general radiological tool, there is not yet a Medicare coverage policy for virtual colonoscopy. In addition, many insurance companies do not currently pay for the procedure because outcome data from large patient groups are not yet available. Currently, virtual colonoscopy is most often performed in clinical trials designed to establish whether this type of testing is an effective method for colorectal cancer screening.
Other technologies may be available within the next several years, such as more accurate stool testing. These tests could be conducted in a manner similar to the current fecal occult blood tests. However, instead of testing for microscopic blood, these tests could detect DNA mutations in the cells that have been sloughed off by polyps and cancers. This approach promises to be more sensitive and specific in detecting abnormalities, and could result in fewer false positive tests.

According to the Mayo Clinic's Ahlquist, the ability to detect polyps accurately through virtual colonoscopy and DNA testing can reduce the frequency of testing, and thereby reduce overall medical costs. "The transition from a flat [normal] colon lining to a polyp to a cancer takes seven to 10 years. That's a large window of opportunity. If a diagnostic tool has the potential to detect the polyps, it probably does not need to be applied more frequently than every five years."

**Treating the Disease**

The type and duration of colorectal cancer treatment depend upon the extent of the disease and when it is discovered. Treatments can include surgery, chemotherapy, radiation, or a combination of all three.

Surgery is the most commonly performed treatment for colorectal cancer. If the tumor is discovered before it has penetrated the bowel wall, removal of the cancer is usually all that is necessary for a complete cure. Specific surgical procedures may require the removal of a portion of the large bowel, which is reconstructed by sewing or stapling the two ends together. In part due to new surgical techniques and devices, a colostomy, where a portion of the colon is rerouted through the abdominal wall to the outside surface and a bag is worn to collect wastes, may not be necessary.

Small cancers localized to the rectum can be removed surgically, with radiation therapy follow-up. For large cancers that have grown through the rectal wall, a technique called "mesorectal excision" can be performed. The procedure allows removal of all cancerous tissue, but avoids severing of nerves involved in sexual and urinary function. Large rectal tumors are often treated with chemotherapy and radiation before surgery.

If surgery reveals that the cancer has spread to the lymph nodes or other organs such as the liver, chemotherapy is usually prescribed. This was the case for cancer patient Vallarelli. Two days after her daughter's birthday, she awoke from surgery to learn that the tumor had invaded her uterus, and the doctors had performed a hysterectomy. It was devastating news for the 30-year-old, but nothing compared to what came next. Her sister gently informed her that the cancer had spread to her liver. Her chances for survival were not good, but, she says, her sister would not let her give up.

Just 44 days following her first surgery, Vallarelli returned to the operating room to have the left half of her liver removed. She spent two weeks in the hospital, weakened by the two surgeries, but encouraged by tests showing there was no cancer in the remaining part of her liver. Then she underwent chemotherapy, in which she was given a regimen of intravenous drugs.

The main approved drug for colorectal cancer treatment is 5-fluorouracil (5-FU), which has been in use for more than 30 years. This drug works by inhib-
combination with 5-FU and leucovorin as a primary treatment for advanced colorectal cancer. Previously, Camptosar was used only in patients who failed to respond to the 5-FU and leucovorin combination. Recent studies have shown that the addition of Camptosar significantly delays tumor progression and improves the chances of survival. Camptosar’s main side effect is diarrhea, which may be severe.

Vallarelli, whose chemotherapy took place before the approval of Camptosar as a primary treatment, says she experienced some weakness and diarrhea but was grateful that her hair loss was minimal.

An alternative method for the delivery of chemotherapy drugs is to use a pump and catheter. A small pump is implanted beneath the skin of the abdomen, and a catheter, a small, flexible tube, connects the pump to an artery that carries the drug directly to the tumor. After several weeks, the pump must be reloaded with chemotherapy by injecting more of the drug into the pump’s reservoir. This method provides a continuous supply of the chemotherapy agent, though it may still cause side effects in the patient.

Many drugs are being studied that may improve colorectal cancer treatment, including oral drugs that are analogs of 5-FU or that increase 5-FU absorption from the gastrointestinal tract. This oral treatment results in prolonged exposure to 5-FU. “In advanced disease, it’s been shown that prolonged exposure to 5-FU gives better results,” says Martin Cohen, M.D., an FDA medical officer.

Cohen cites another class of drugs in the early stages of study: matrix metalloproteinase inhibitors. “The idea behind these drugs is that they would prevent cancer cells from spreading and thus would allow you to live with the cancer,” he says. “It’s too early for real data, but they’re drawing much interest.”

Living with cancer is something survivor Vallarelli knows plenty about. She has been cancer-free for four years, though she awaits the five-year mark when doctors will tell her she’s likely to have beaten the disease. Meanwhile, she keeps a vigilant watch for signs of recurrence with periodic blood tests, CAT scans and MRIs to screen for new growths.

“Going in for the testing ... is hard sometimes. It brings everything back to me. My strongest message to everyone is: Don’t put off screening because of embarrassment. A little embarrassment or discomfort is a small price to pay to save your life.”

Lynne L. Hall is a writer in Birmingham, Ala.
of the 100 million American cellular phone subscribers, some use their wireless phone only in a crisis—to call a friend or 911. They put their rap sessions on hold until arriving home, where phoning a friend costs no cents per minute.

For other wireless phone owners, it could be the fear of brain cancer, not an unwieldy wireless bill, that keeps them from using their cell phones for leisure chats.

Convinced that a nine-year cell phone habit led to his brain cancer, neurologist Chris Newman, M.D., has filed an $800 million lawsuit in Baltimore against his cell phone’s maker and several other telecommunications companies. His suit comes five years after the dismissal, for lack of evidence, of a lawsuit filed in Florida by David Reynard, who alleged that a cell phone was responsible for his wife’s fatal brain cancer.

In Newman’s case, his lawyer has said, “it’s really not a question at all” whether the cancer is cell phone-related. The evidence, she says: Newman’s own doctors made the connection between his long-time cell phone use and his tumor, which is positioned in “the exact anatomical location where the radiation from the cell phone emitted into his skull.”

Newman has been front and center in a renewed public focus over the last few months on whether the fear of brain cancer from wireless phones is well-founded or folly. For his part, epidemiologist Sam Milham, M.D., recently expressed a breakaway scientific viewpoint when he told the television audience of CNN’s Larry King Live show that there is “plenty of reason for concern” about cell phones causing brain cancer.

Radiation Without Risk?

Like televisions, alarm systems, computers, and all other electrical devices, mobile phones emit electromagnetic radiation. FDA can regulate these devices to ensure that the radiation doesn’t pose a health hazard to users, but only once the existence of a public health hazard has been established. (See “It’s Not a Food or Medical Product, So Why FDA?” on page 22.)

In the United States, mobile phones operate in a frequency ranging from about 850 to 1900 megahertz (MHz). In that range, the radiation produced is in the form of non-ionizing radiofrequency (RF) energy. This RF energy is different than the ionizing radiation like that from a medical x-ray, which can present a health risk at certain doses.

At high enough levels, RF energy, too, can be harmful, because of its ability to heat living tissue to the point of causing biological damage. In a microwave oven, it’s RF energy that cooks the food, but the heat generated by cell phones is small in comparison.

A mobile phone’s main source of RF energy is its antenna, so the closer the antenna is to a phone user’s head, the greater the person’s expected exposure to RF energy.

Because RF energy from a cell phone falls off quickly as distance increases between a person and the radiation source, the safety of mobile phones with an antenna mounted away from the
Radiation risk?
Step To Take: If You’re Still Concerned

Earlier this year, the British government recommended that children’s use of cell phones be limited to essential calls. The recommendation was not based on any scientific evidence that cell phones pose a special risk to children. Rather, it was a precautionary recommendation, the government explained, to protect a vulnerable population with still-developing nervous systems.

FDA has suggested some simple steps that American cell phone users can take if they remain concerned about potential health risks but don’t want to give up their mobile phones.

First, people can of course consider reserving the use of mobile phones for shorter conversations or when a conventional phone is not available. Also, they can switch to a type of mobile phone with a headset to place more distance between the antenna and their bodies. And for the car, people can switch to a mobile phone with the antenna mounted outside the vehicle.

With the recent media spotlight on cell phones, cancer researcher John Moulder, Ph.D., warns that some marketers are preying on people’s fear of radiation, selling fraudulent devices with claims that they are protective. Moulder has seen a variety of creative but useless items, mostly on the Internet, from pendants worn around the neck to so-called RF-proof lingerie. As to products sold as shields for the phone to cut your RF exposure while not interfering with the communication signal, Moulder says, “I have yet to see one that can do both of those things.”

—T.N.

Studies in Perspective

Some mobile phone users have been diagnosed with brain cancer, and many others who have not used mobile phones have gotten the disease, too. Each year in the United States, brain cancer occurs at a rate of about six new cases per 100,000 people. Among the 100 million Americans who own mobile phones, then, about 6,000 cases of brain cancer would be expected among them in a year, even if they had not used mobile phones.

Scientific studies have focused on the question of whether the statistical risk of getting brain cancer is increased in those who use mobile phones compared to non-users, leaving to the courts the judgment of whether Chris Newman or other individuals would have gotten the disease had they not used a cell phone.

Two types of studies are generally used to investigate suspected cancer causes: epidemiological studies, which look at the incidence of a disease in certain groups of people, and animal studies.

Epidemiological studies are sometimes difficult to carry out in a way that can determine whether a cause-and-effect relationship exists between a single variable in a person’s life (in this case, cell phone use) and the person’s disease (brain cancer). Some factors that complicate research into the asserted link between cell phones and brain cancer:

- Brain cancer can take years or even decades to develop, making possible long-term effects of mobile phone use difficult to study; mobile phone technology is ever-evolving; and so many lifestyle factors—even down to the precise position in which a person holds the phone, as well as his or her own anatomy—can affect the extent of radiation exposure.

- Studies in animals are easier to control, but entail complications of their own. For example, how should results obtained in rats and mice be interpreted in terms of human health risks? And how can scientists account for the fact that these studies sometimes expose animals to RF almost continuously—up to 22 hours a day—and to whole-body radiation, unlike people’s head-only exposure?

- While studies generally have shown no link between cell phones and brain cancer, there is some conflicting scientific evidence that may be worth additional study, according to FDA. (See “Studies So Far” on page 23.)

Based on the evidence so far and possible limitations in some studies’ research methods, FDA is closely following ongoing research into whether there might be any association between cell phones and cancer, according to the agency’s Feigal.

A long-term study by the government’s National Cancer Institute is already under way to examine possible risk factors for brain cancer. It compares past usage of mobile phones (as well as other environmental, lifestyle, and genetic factors) by 800 people with brain tumors compared with 800 others who don’t have tumors.

The study, the first part of which is expected to be published early next year, will provide a “snapshot” of what the risks from cell phones could be, says Peter Inskip, Sc.D., one of the study’s principal investigators. But this research, he cautions, has its own limitations. For one thing, the study was started in 1994 and it considers radiation exposures from cell phones that (Continued on page 23)
Within the range of radiation frequencies, called the electromagnetic spectrum, cell phones fall between TVs and microwave ovens. At that level, many scientists believe the radiation from cell phones couldn’t conceivably impair human health.
Epidemiological and animal studies undertaken by the U.S. cell phone industry and others have yielded mixed results.

- In a study published in 1999, investigators at the Orebro Medical Centre in Sweden compared the past mobile phone use of 209 Swedish brain tumor patients and 425 healthy people. Conclusion: The study found no mobile phone/brain cancer link “in virtually all respects,” cancer researcher John E. Moulder, Ph.D., says in the August 2000 issue of IEEE Spectrum, the official magazine of the Institute of Electrical and Electronics Engineers. Investigators did find that mobile phone users who got certain types of brain tumors tended to report using the phone on the side of the head where they developed the tumor. The study’s limitations, according to Moulder, include a weak association between cell phone use and tumor development, as well as a possibility that the cancer patients’ recollections were biased by already knowing on which side of their head the brain cancer developed.

- In a yet-unpublished study presented at a 1999 scientific meeting, researcher Joshua Muscat looked for an association between mobile phone use and a type of brain cancer called glioma. Muscat did not find evidence that cell phone use increased people’s risk of this type of brain cancer generally. He did, however, observe an increase in one rare kind of glioma, which FDA scientists say might have occurred by chance. Interestingly, with increased hours of mobile phone use, the risk tended to decrease rather than increase as might be expected.

- A few animal studies have suggested that low levels of RF exposure could speed up development of cancer in laboratory animals. In one recent Australian study, for example, mice genetically altered to be predisposed to developing lymphoma got more than twice as many of these cancers when exposed to RF energy compared to mice not exposed to the radiation.

(Continued from page 21)

Fear Factor

The new studies may bolster current scientific knowledge, but they will never be able to prove cell phones to be absolutely safe. Proving that cell phones don’t cause cancer presents the insurmountable scientific obstacle of trying to prove a negative, Moulder explains. “The closest thing to proving that something is safe—that it doesn’t cause cancer—is to try to prove that it does, and fail, and fail enough times and in enough different ways.”

Even when scientists are convinced of the safety of a technology—be it the technology of cell phones or of televisions, radios, computers, or microwave ovens—it doesn’t necessarily follow that public fears will be put to rest. Lay people interpret scientific evidence differently from scientists, according to risk experts, and the general public may be more likely to be frightened when preliminary research shows a mere possibility of harm.

Scientist Moulder is already confident that cell phone use doesn’t increase a person’s chance of getting brain cancer—so confident, in fact, that he sees nothing wrong with using a cell phone for even hours each day. “Go right ahead,” the cancer researcher says, “but please-please-please don’t use it while driving. That’s dangerous.”

Tamar Nordenberg is a former staff writer for FDA Consumer, and now writes for FDA’s Food Safety Initiative program.
Prescriptions For Healthy Animals

Pets And People Frequently Fight Disease With Similar Drugs

By Linda Bren

Much as they do in managing their own healthcare, people need to weigh the benefits and risks of a drug prescribed for their pet.

Tina and Baron have both seen better days. Tina Gilliam, of Gaithersburg, Md., slowly gets out of bed in the morning and carefully pulls on her socks to avoid the pain she feels when she tries to move too fast. Her golden retriever, Baron, also lifts himself slowly from the floor next to her bed. As he limps after her to the medicine cabinet, his gait is much like hers—slow, stiff and deliberate—for like Gilliam, Baron suffers from arthritis.

Gilliam shakes a pill out of a bottle, and swallows it with a few sips of water. She shakes another pill out of a different bottle, pops it into Baron’s mouth, and massages his throat while he swallows it. Soon, the pain and stiffness for both will lessen, and the two companions will go out for their morning walk.

Gilliam has just taken Lodine, and Baron has taken EtoGesic. The pills are different sizes, shapes, and colors. But if Gilliam were to check the label on each, she would find the same active ingredient: etodolac.

Gilliam and Baron are part of an increasingly common phenomenon in which humans and animals often take similar drugs for similar diseases.

Admittedly, the animal drug’s active ingredient may be in a concentration different from that found in the human drug. The animal drug might even have different inactive ingredients. But that drug can alleviate the same pain, eliminate the same
Drugs That Do Double Duty

Some FDA-approved animal drugs have the same active ingredient as human drugs

<table>
<thead>
<tr>
<th>Generic drug name</th>
<th>Human drug brand name</th>
<th>Animal drug brand name</th>
<th>Use in Humans</th>
<th>Use in Animals</th>
</tr>
</thead>
<tbody>
<tr>
<td>Clomipramine hydrochloride</td>
<td>Anafranil</td>
<td>Clomicalm</td>
<td>Obsessive-compulsive disorder</td>
<td>Separation anxiety in dogs</td>
</tr>
<tr>
<td>Selegiline hydrochloride</td>
<td>Edepryl</td>
<td>Anipryl</td>
<td>Parkinson's disease</td>
<td>Cognitive dysfunction syndrome in dogs; Cushing's disease in dogs</td>
</tr>
<tr>
<td>Enalapril maleate</td>
<td>Vasotec</td>
<td>Enocard</td>
<td>Hypertension</td>
<td>Heart failure in dogs</td>
</tr>
<tr>
<td>Omeprazole</td>
<td>Prilosec</td>
<td>GastroGard</td>
<td>Gastroesophageal reflux disease</td>
<td>Gastric ulcers in horses</td>
</tr>
<tr>
<td>Propofol</td>
<td>Diprivan</td>
<td>Rapinovet</td>
<td>Injectable sedative to maintain anesthesia during surgery</td>
<td>Injectable sedative to maintain anesthesia during procedures or surgery in dogs</td>
</tr>
<tr>
<td>Etodolac</td>
<td>Lodine</td>
<td>EtoGesic</td>
<td>Pain and inflammation from osteoarthritis and rheumatoid arthritis</td>
<td>Pain and inflammation from osteoarthritis in dogs</td>
</tr>
</tbody>
</table>

"As people are seeing more complex and sophisticated drugs for themselves, they want that same quality for their pets."

—Melanie Berson, DVM, FDA's Center for Veterinary Medicine

symptoms, and cure the same illness in pets as its counterpart can in people.

Veterinarians have been prescribing approved animal drugs that are similar to human drugs for years. And, since the passing of the Animal Medicinal Drug Use Clarification Act of 1994 (AMDUCA), it has been legal for vets to treat pets with human drugs that have not been approved for animals. Veterinarians also prescribe drugs not approved for humans, such as flea control medications.

Veterinary science is working doggedly to keep up with the expectations of pet owners, who represent the majority of Americans. More than 37 percent of American households own dogs, 34 percent own cats, and 16 percent own both, according to consumer marketing firm NPD Group Inc.

These guardians of 58 million dogs and 72 million cats want first-rate treatment for their four-legged friends. "As people are seeing more complex and sophisticated drugs for themselves, they want that same quality for their pets," says Melanie Berson, DVM, director of the Division of Therapeutic Drugs for Non-Food Animals within the Food and Drug Administration’s Center for Veterinary Medicine (CVM).

Recognizing this need, animal pharmaceutical companies continue to submit applications to CVM, the organization within FDA that approves drugs designed for animals. The applications fall into three drug categories: an existing animal drug to be used for a different illness, an existing animal drug to be used for a different type of animal, and an entirely new animal drug.

**Drugs Approved for Animals**

Nearly 300 drugs currently on the market have been approved by FDA for dogs, cats, and horses—otherwise known as companion animals. Many of these have the same active ingredient found in their human drug counterparts.

Drugs for animals are given new trade names to distinguish them from the human drugs, and different companies may (Continued on page 28)
Vet Medicine Promotes Progress in Human Medicine

While advances in human medicine can mean new drugs to treat pets, veterinary medical advances can also benefit humans. The creation of a blood substitute is an example of this potential. Scientists have been searching for an effective oxygen-carrying blood substitute for more than 50 years.

In 1998, FDA approved Oxyglobin, the first blood substitute to reach the market, for the treatment of anemia in dogs. Anemia, a deficiency of red blood cells or the protein hemoglobin within red blood cells, kills millions of dogs each year. Treatment for canine anemia is difficult because of the lack of donated dog blood, the resources required to refrigerate the blood for storage and warm it prior to use, and the need to use it within its 35-day shelf life. Also, typing and cross-matching must be done to accommodate the eight blood types of dogs.

Oxyglobin is the first alternative solution to donated blood. A chemically modified bovine hemoglobin solution, Oxyglobin picks up oxygen in the lungs and carries it to cells throughout the body. “The product quickly delivers oxygen into tissue and organs and buys time for the dog’s own regenerative red blood cells to come back,” says Robert Murtaugh, DVM, principal investigator for the canine clinical trials at Tufts University School of Veterinary Medicine.

Biopure Corp., the manufacturer of Oxyglobin, along with Tufts University, is testing a similar blood substitute, Hemopure, for humans as a treatment for sickle cell anemia and as a replacement for donated blood during surgery. Unlike stored blood, Hemopure requires no refrigeration, is compatible with all blood types, and has minimal potential to transmit viruses or bacteria.

FDA’s Center for Biologics and Evaluation (CBER) is currently evaluating this human blood substitute to determine its safety and effectiveness. “Hemopure is subjected to a higher level of scrutiny,” says Abdu Alayash, Ph.D., a research chemist in CBER, “particularly in light of recent clinical failures with other hemoglobin-based products intended for human use.”

The implications of a human blood substitute are significant: Emergency medical personnel can carry out transfusions in the field, for example at the site of an accident or in a war zone, without the worry of blood-typing, cross-matching, or transmitting infectious diseases.

—L.B.
“Success in treating a behavioral problem ... can mean the difference between having to put an animal to sleep or being able to live with the pet.”
—Stephen Sundlof, DVM, director of FDA’s Center for Veterinary Medicine

(Continued from page 26)

manufacture them. GastroGard, for example, used to treat stomach ulcers in horses, has the same active ingredient as Prilosec, used to treat severe and persistent heartburn in people. GastroGard is made by Merrial Limited in London, while Prilosec is a product of AstraZeneca PLC, also in London.

“The approval process for a new companion animal drug is similar to the approval of a new human drug,” says Berson. “The major difference is that the size of the clinical trials for animal drugs is many times smaller.” A human clinical trial typically involves thousands of test subjects, but an animal trial involves only hundreds, according to Berson.

Despite their smaller clinical trials, pet drugs must meet standards similar to those for human drugs. And pet drug manufacturers “must apply the same rigorous scientific standards to studies and the manufacturing processes must be in accordance with Good Manufacturing Practices,” says Ann Stohlman, VMD, a veterinary medical officer at CVM.

Drugs Used But Not Approved for Animals

The practice of giving animals drugs that have been approved for humans but not for animals is known as prescribing “off-label,” or “extralabel.” Extralabel use can also mean prescribing a drug to a different species, for a different condition, or in a different dosage than that for which the drug was approved. For example, a veterinarian may prescribe a lower dose of an arthritis drug approved for dogs to a feline with an inflamed joint.

FDA restricts extralabel use of human drugs in food-producing animals. This precaution is taken to prevent drug residues in animals from entering the human food chain and threatening public health. But extralabel use of human drugs in companion animals is not as restricted.

While these human drugs have been tested in some animals before being tested in humans, they have not gone through the comprehensive studies FDA requires to approve them for use in animals. And drug manufacturers cannot advertise to veterinarians or pet owners a drug that has not been approved for animals.

Even so, it is a long-standing veterinary practice to treat pets with the latest human drugs. “In vet medicine we’ve relied on human drugs for years,” says Michael Bassett, DVM, owner and medical director of Pet Dominion Animal Hospital in Rockville, Md. “They don’t develop new drugs for animals fast enough.”

Veterinarian Daniel Negola tries to rely on the animal drugs when possible. “We use the drugs approved for animals first,” says the owner of Negola’s Ark Veterinary Hospital in Gaithersburg, Md. “Only when they’re not working or if they’re not available for a specific problem do we go to the next source—human drugs.”

How do vets know how much of a human drug to prescribe to an animal when it is not approved for animal use? The veterinary research community shares study results through published papers, seminars, and books, says Neal Bataller, a veterinarian in CVM’s Office of Surveillance and Compliance. Formulations found to be effective are documented in numerous veterinary drug handbooks and textbooks.

The handbooks provide such information as the drug’s indications and usage, contraindications, dosage, precautions, and adverse reactions. There are also veterinary handbooks and texts that explain what drugs to use to treat other pets—such as lizards, rabbits, and birds—for which specific FDA approvals do not exist, adds Bataller.

Informed Consent

Much as they do in managing their own health-care, people need to weigh the benefits and risks of a drug prescribed for their pet. It’s the veterinarian’s responsibility to explain the risks and benefits of each drug to clients and give them printed information, particularly for the drugs that aren’t approved for animal use, says Karen Overal, VMD, Ph.D., professor of behavioral medicine and director of the small animal behavior clinic at the Veterinary School of the University of Pennsylvania. “It’s important that we have the informed consent of our clients.”

Pet owners should ask their vet questions about any drug being prescribed for their animal—especially in the absence of printed information. Although manufacturers provide a label, or printed information, with each drug they give to veterinarians, says Bataller, “in repackaging the drug at a veterinary facility, the label often does not get passed on to clients. And if the drug is prescribed extralabel, the label would be of limited value to the pet owner.”

FDA has helped two animal pharmaceutical companies develop consumer-friendly labels that explain the benefits and risks of their osteoarthritis drugs for dogs. Fort Dodge Animal Health of Overland Park, Kan., distributes a “client information sheet” with EtoGesic (the generic drug etodolac). Pfizer Animal Health, Inc., of Exton, Pa., gives out a client information sheet with Rimadyl (carprofen). Both drugs are non-steroidal anti-inflammatory drugs (NSAIDs).

Pfizer provided the Rimadyl information at CVM’s request following a high volume of adverse events, including deaths, reported by owners whose dogs were treated with the drug. The angry owners, who were not properly informed of the drug’s risk, prompted the new labeling that will better help other pet owners decide if the drug is appropriate for their dogs.

Although pet owners are becoming better educated and informed about animal treatments, it is still unwise for them
to medicate their animals without veterinary supervision, warns Bataller. “Different species metabolize drugs differently. A dog is not a small human, and a cat is not a small dog,” he says. “Some drugs may be better tolerated in a dog than in a human, while other drugs may have the reverse effect. Dogs are generally more sensitive to aspirin than humans, and Tylenol (acetaminophen) can readily kill a cat.”

A Brave New Behavioral Frontier

“Behavior is an emerging area of vet medicine,” notes CVM’s Berson, and “improving the quality of life for geriatric pets” is an area of strong veterinary and public interest.

In 1999, the veterinary community and pet owners celebrated the introduction of the first FDA-approved drugs for behavioral conditions in pets: Clomicalm to treat separation anxiety in dogs, and Anipryl to treat the symptoms of canine cognitive dysfunction syndrome (CDS).

Anipryl has the same active ingredient as Eldepryl (selegiline hydrochloride), which FDA approved in 1989 to treat Parkinson’s disease in humans.

Clomicalm has the same active ingredient as the human anti-depressant Anafranil (clomipramine hydrochloride), which was approved by FDA in 1989 to treat obsessive-compulsive disorders in humans.

Aging Dogs and Cognitive Decline

FDA first approved Pfizer’s Anipryl in 1997 to treat canine Cushing’s disease, a common endocrine disorder, and in 1999 approved it to treat canine CDS. This age-related decline of cognitive ability can cause a dog to become disoriented, appear confused or lost in the house or yard, be unresponsive to familiar people, forget previous learned behavior (such as housetraining), bark and whine more, and change its sleep-wake cycle.

“Anipryl really made a difference in my dog’s life,” says Bobbi Wallace of northern California. Wallace’s lively little 10-pound dog, dubbed Miss Piggy because of her pudginess, had a sudden onset of confusion at age 15. “She didn’t know what to do with her food,” says Wallace, “and she would go under a table and couldn’t figure how to get out.” After starting on Anipryl, Miss Piggy improved in just three to four days, according to Wallace. “She knew where her food was and how to eat it again. It seemed to clear her head.”

Although Wallace was warned by her veterinarian that Anipryl doesn’t work in all cases, she calls it a “miracle drug” because it brought her dog’s quality of life “almost back to normal.”

“[Anipryl] can work a miracle in about one-third of cases, says Nicholas Dodman, BVMS. “It can be useful in about one-third, and it doesn’t work in one-third,” adds the professor and director of the Behavior Clinic at Tufts University School of Veterinary Medicine.

Some researchers liken the brain of an older animal with CDS to that of an older human. A loss of neurotransmitters has been found in both. And amyloid plaques, or lesions, similar to those that cause damage in the geriatric human brain, have been found in the brains of older dogs and cats. Animal behaviorist Overall says that Anipryl “won’t fix the existing plaques, but it will improve the effectiveness of the neurons wrapped up in plaque.”

As in diagnosing age-related cognitive decline in people, CDS in dogs should not be diagnosed until all other medical problems have been ruled out. Anipryl cannot cure CDS, but it can alleviate the symptoms and enhance the pet’s quality of life.

Distressed Dogs and Separation Anxiety

The only other FDA-approved drug for animal behavioral problems currently on the market is Clomicalm, manufactured by Novartis Animal Health US, Inc., of Greensboro, N.C. Clomicalm is to be used as part of a behavior modification program to treat separation anxiety in dogs older than six months.

Although not a tranquilizer, Clomicalm can lessen anxiety by increasing the serotonin levels in the brain. Increased serotonin can make a dog more receptive to positive behavior modification and less likely to overreact to an owner’s absence.

While few dogs are happy when their owners leave, some show extreme anxiety, resulting in destructive behavior, soiling the house, excessive salivation, or constant barking and whining. In severe cases, dogs mutilate themselves, eat furniture, jump through windows, or claw through walls.

“If your dog is tunneling through your wall, that dog is going to be dead soon,” says Overall, who sees many rescued
dogs with separation anxiety in her clinic. She attributes these cases in part to the “pet recycling” process. “Cute animals get adopted, they go home, they don’t behave as expected so they go back, get readopted, and go home again. As they get recycled, separation anxiety increases.”

Overall cautions owners that they cannot simply pop a pill in their pet’s mouth and expect to come home to a perfectly calm dog and intact house. Treating a dog for separation anxiety requires hard work on the part of the whole family to modify the pet’s behavior. “I know everybody wants magic from science, but I try to get across to my clients that you’re not going to solve anything with just a pill,” says Overall. “The people who work the hardest get the biggest change—regardless of the severity of the condition.”

Whitley, a mixed terrier-poodle, is a testimony to the success of behavior modification combined with medication. The 10-year-old dog, known for her spirited but sweet disposition, suddenly became anxious and destructive after her owner left for work. “She chewed up clothes, doors, furniture, and electrical cabling—to the point where her gums were bleeding,” says owner Mark Oumeedian of Livonia, Mich.

Under the supervision of his veterinarian, Oumeedian put Whitley on Clomicalm. At the same time, he practiced behavior modification techniques—exercises to help learn positive behaviors—with Whitley. But Whitley went through an entire bottle of Clomicalm with no effect. Oumeedian’s initial discouragement turned to delight when halfway through the second bottle—about 45 days after the dog began taking the drug—Whitley started to show results. Soon after, he became a happy, well-adjusted pooch once again.

And Oumeedian was relieved that his spunky dog’s character remained unchanged. “It was so amazing to me that there were no personality changes or side effects,” he said. “It would have broken my heart if there were.”

Animal behaviorist Dodman emphasizes the grim consequences of behavior problems. “Behavior problems are probably the leading cause of mortality in the canine population,” he says. “It’s estimated that at least one-and-a-half million dogs are needlessly euthanatized each year because of behavior problems, which is three times as many as die of cancer.”

Some veterinarians predict that the use of drugs for behavioral problems will result in a decrease in the number of animals euthanatized or relinquished to shelters. “Oftentimes, success in treating a behavioral problem like separation anxiety can mean the difference between having to put an animal to sleep or being able to live with the pet,” says Stephen Sundlof, DVM, director of FDA’s CVM. “Having drugs like this available can really make a tremendous difference.”

New psychotropic drugs to treat animal behavioral problems and geriatric conditions may be just ahead. Meanwhile, pets can continue to have the best of both worlds—a host of human and animal drugs to treat their ailments and keep them healthy and active for many years.

Linda Bren is a staff writer for FDA Consumer.
Planning To Look Flab-u-less?

Know The Facts About Liposuction

By Alexandra Greeley

A self-described athlete, thirty-year-old Jeanne Smith of Washington, DC, is fit, active, and happy. But like many young women, she has felt dissatisfied with her looks. Because she works in the medical field, Smith knows about its latest trends and techniques. So when friends talked about their satisfaction with liposuction, Smith already knew about the procedure and readily considered its pros and cons. She decided it suited her.

She wanted some body sculpting and knew what she was getting into. “I had basically the lower half of my body done, and it was pretty targeted surgery,” she says. “I experienced drainage afterwards and that’s normal. I stayed out of work for about one week, though I was active during that time. I went to movies, out to dinner … but was not up to my 100-percent best.”

That was more than one year ago, and Smith says she is happy with her new trimmer look.

Or consider the case of Robert F. Jackson, M.D., board-certified cosmetic surgeon of Marion, Ind., and chairman of the liposuction committee of the American Academy of Cosmetic Surgery. Himself a liposuction patient, Jackson had excess tummy fat—a potbelly, he calls it—removed. “The day after the surgery, I felt sore,” he says, “but the pain was minimal.” His surgery took place on Friday morning, and by Monday, Jackson was back at work.

These cases represent two of the many individuals who have helped make liposuction the most popular form of cosmetic surgery today. An estimated 287,000 procedures were performed in 1999, according to the American Society for Aesthetic Plastic Surgery.

Liposuction has become the technique of choice for people who want an improved body shape, a body sculpted to reflect their own—and society’s—ideals of physical beauty. Moreover, liposuction may be used in conjunction with facelifts, for chin and tummy tucks, and to reduce the size of abdomens, hips, and thighs.

“Most liposuction procedures are done for purely cosmetic reasons,” says Lori Brown, Ph.D., an epidemiologist in the Food and Drug Administration’s Center for Devices and Radiological Health, or CDRH. But she adds that some medical conditions, such as large breasts in men, lipomas (fatty lumps), or fatty deposits like the buffalo hump—caused by hormonal imbalances that grow masses of fat on and around the neck—may be treated with liposuction.

But the rise in its popularity and changes in the techniques doctors use to perform liposuction have raised concerns within FDA. There is growing evidence that the increased aggressiveness with which the procedure is performed—especially the amount of tissue sucked from the body, the venues in which the procedures are performed, and the amount of anesthesia used to sedate patients during increasingly lengthy procedures—may be increasing the risk of post-surgical complications and even death.

How Liposuction Works

Conceptually, liposuction (or lipoplasty) is a straightforward technique in which excess fatty tissue is suctioned from beneath the skin. Prior to surgery, doctors flush the targeted area or areas with a solution composed of lidocaine (a local anesthetic similar in its numbing effects to novocaine), saline, and epinephrine (a drug that constricts blood vessels and thus reduces bleeding during surgery).

Then doctors insert a hollow wandlike device called a cannula through incisions in the skin. They push and pull the cannula around through fatty deposits, breaking up the cells, which, along
with other body fluids, are suctioned out by an attached vacuuming device.

It’s a simple system, says Stephen Rhodes, chief of the plastic and reconstructive surgery devices branch in FDA’s CDRH. “It’s essentially just a cannula and a vacuum.” However, these products have only been approved for body contouring, and are not intended for large-scale fat removal, an increasingly popular use of liposuction.

There are several liposuction techniques available today. The amount of injected fluid determines the technique used, explains Peter B. Fodor, M.D., chief of plastic surgery at Century City Hospital in Los Angeles and spokesman for the American Society for Aesthetic Plastic Surgery.

In the “dry” technique, which few doctors use anymore, no fluid is injected into the targeted area.

For “wet” liposuction, the surgeon injects only a small amount of fluid, about six to eight ounces and usually containing small amounts of epinephrine, regardless of how much tissue is subsequently removed.

The “superwet” technique evolved, says Fodor, because doctors found that the more fluid they injected—up to a point—the less blood was lost. “We found that by injecting one cc of solution for each cc of aspirate [amount of tissue and fluid removed], the blood loss was negligible.” Although lidocaine is sometimes added when performing wet or superwet liposuction, patients will also receive general or epidural anesthesia.

In the tumescent technique, doctors inject up to five times as much fluid as aspirate. Because the injected fluid also contains large amounts of lidocaine, tumescent liposuction is generally performed with only a local anesthetic.

Many doctors are offering a modified version of the procedure that calls for using ultrasound in addition to the injected solution and the suctioning. Rhodes and others at the FDA are especially concerned about this practice, which calls for using devices not approved for liposuction—that is, special cannulas that vibrate at high rates and emulsify fat tissue before its removal. The wand generates a great deal of heat, and if doctors don’t move it constantly, it can cause severe burns. As Roxolana Horbowyj, M.D., senior medical officer in CDRH, points out, a temperature increase of 20 degrees Celsius (about 36 degrees Fahrenheit) may encourage cell death. And, as FDA epidemiologist Brown notes, “We don’t really know the long-term effects of ultrasound on tissues.”

Understanding the Benefits vs. the Risks

In a society in which beauty is often measured by slender bodies and youth, it is no wonder that thousands of Americans chase the “perfect” look by means of liposuction. Portrayed in upbeat tones and associated with Hollywood glamour, liposuction seems to offer instant help for unsightly bulges. Consumers checking out liposuction Web sites on the

Dr. Steven B. Hopping (left) of Washington, D.C., works to remove a client’s “love handles.” The anesthesiologist (center background) monitors the patient while a nurse (right) assists the surgeon.
Internet are further assured by the positive information they find.

"There are probably hundreds of thousands of patients who have had body sculpting without complications," says Ann Graham, senior nurse consultant in CDRH's Office of Surveillance and Biometrics. "But we are concerned about the published reports of patients who have not had a good outcome. They have undergone liposuction for weight reduction, not just body sculpting.

Liposuction, in general, is a purely elective procedure. As such, our tolerance for an unsafe or harmful outcome is extremely low."

Although many consumers think of liposuction as a quick and permanent fix, it's likely that few understand its risks and frequently temporary results. There is no national group of consumers, nor one group representative of all clinicians, that is organized to oversee liposuction procedures and results. Although FDA is aware of problems published in medical literature and described by other sources, "very few adverse event reports are coming into the agency through its formal reporting channels" according to Anita Kedas, a nurse consultant in CDRH's Office of Surveillance and Biometrics. But the small number of reports may simply mean that negative outcomes aren't being reported.

Office-based procedures may present the greatest reporting problem. There's no requirement that adverse events from office procedures be reported, and most procedures are done in offices, according to Graham. Even if offices are well equipped, she adds, patients often need days of continuous support such as rehydration, pressure dressings, and good nursing care, while others actually need resuscitation and hospitalization to recover. And if a patient goes to the emergency room for care, FDA doesn't hear about it, adds Graham.

Whether reported or not, liposuction problems are real enough—though some, such as wavy or uneven skin after fat removal, are not medically serious.

But others are. Overworking the heart can be a serious side effect of the tumescent technique. "Let's say they plan to remove 5,000 cc's of aspirate," says plastic surgeon Fodor, "so they inject a dangerously large amount of fluid. The patient would be practically 'drowning' in fluids. The heart can't handle this fluid overload."

Another potential complication is infection, says Brown. Infections can occur after any surgery. Sometimes, infections may be serious or life threatening such as in cases of necrotizing fasciitis (when bacteria eat away at tissue) or toxic shock syndrome, a serious infection which has been associated with tampon use but may also be associated with surgery, says Brown.

Other possible problems Brown lists are burns, embolisms, cardiac arrhythmia, edema, and nerve compression, which are all reported in the medical literature. Often, too, Graham notes, cannulas are inserted in several different locations, resulting in puncture wounds that need to heal.

A condition called seroma, or an oozing or pooling of serum, or body fluid, may be a problem after the more aggressive ultrasound techniques during which some skin is detached from underlying tissue and fluid accumulates in a subcutaneous pocket.

Deaths and Liposuction

According to a survey conducted by the American Society of Plastic Surgeons (ASPS) of more than 1,500 plastic and reconstructive surgeons in January, 1999, the death rate of one in every 5,000 (or 20 out of 100,000) liposuction patients between 1994 and 1998 was much higher than anyone anticipated—higher even than death rates from traffic accidents. And higher than acceptable

Liposuction uses a vacuum and a small metal tube to literally pull fatty tissue out of the body. A plastic hose connects the metal tube to a vacuum device (left), where the tissue is collected in a plastic cylinder.
Reporting Problems

Health professionals or consumers should report serious adverse reactions or other problems related to equipment or medications used for liposuction through FDA’s MedWatch program (See “Serious Product Problem? Report It” on page 6). The Safe Medical Devices Act of 1990 requires hospitals and other user facilities to report deaths, serious illnesses, and injuries associated with the use of medical devices. Questions about mandatory reporting can be answered by the Division of Surveillance Systems, Reporting Systems Branch, by phone on 301-827-0361, or write to FDA, CDRH, MDR User Reporting (HFZ-531), PO Box 3002, Rockville, MD 20847-3002.

dearth rates from other kinds of surgeries, admits Jack Bruner, M.D., associate clinical professor of plastic surgery at the University of California, Davis, and chairman of the task force on liposuction for ASPS. Although the survey data are not considered scientific information, they are useful when establishing practice guidelines, and they led ASPS to recommend some practice changes when performing liposuction.

It is encouraging, Bruner says, that more recent statistics from The Doctor’s Company, an insurance company located in California, show that no liposuction-related deaths have been reported there in the last 18 months. However, he notes, this survey only addresses what’s happening among board-certified plastic surgeons, not with other doctor groups performing liposuction.

Deaths among liposuction patients can happen for a number of reasons, Bruner says, including thromboembolism, or a blood clot that forms in the deep veins of the pelvis or legs. “That can happen during any surgery,” he adds, “and I wish I could say that it is always preventable, but it is not.” Next, he cites perforation of the abdominal wall or bowels, the latter being especially serious. “If you perforate the bowel, there’s a high mortality rate if it’s not fixed in the first 24 to 48 hours,” he says. Physicians are essentially blind as they perform liposuction because they can’t see what is in front of the cannula, notes FDA’s Horbowy.

Finally, Bruner notes that shock and hemodilution, or diluting of the blood, may lead to a patient’s death. This can occur when patients have had large amounts of fluids injected and then both fat and fluids removed, about 11 pounds worth in all during a larger-scale procedure.

Further, although virtually no hard data exist, says Bruner, he and others worry that too much lidocaine may also lead to death. Lidocaine use poses particular hazards, especially since experts do not agree on safe injectable levels. “If you get too much lidocaine for too long,” says Bruner, “the heart muscles become lazy. On the other hand, the brain becomes very agitated at first, which may cause a seizure, before coma sets in.”

At least one study links possible lidocaine toxicity to liposuction deaths, says Horbowy, adding that people with less than normal liver function or those who have been drinking alcohol may not be able to metabolize lidocaine well.

After Surgery

Patients should expect discomfort post-surgery, says Graham. “Patients are bloated, have wounds all over, and are feeling distended.”

Surgeons, says Bruner, should discuss such conditions with their patients beforehand. “We talk about excessive bruising and chronic and prolonged swelling,” he says. Anytime there’s an injury—and liposuction surgery is really a controlled injury—body fluid rushes to the site and the injured tissue becomes like a sponge, he explains. With liposuction, doctors have gone under the carpet of skin and have taken away the fat undercoating, so the raw surface oozes serum on the inside.

To control the swelling, Bruner has his patients wear a garment with elastic pressure, reaching from below the breast area to mid-thigh. “This gives good compression, and if we don’t do that, the body swells up like the Michelin man,” he says. The skin sticks to the undersurface, and as it starts to heal the fluid stops oozing and the swelling goes away. “At the end of three weeks, 90 percent of the swelling and bruising are gone,” he says, although patients may wear the elastic garment for up to six weeks.

Is Liposuction for Everyone?

Many people develop stubborn fatty deposits—in the buttocks or upper thighs, or the so-called “love handles”—that are resistant to dieting and exercise. And although most people would admit to wanting to reshape their body in some way, not everyone makes an ideal liposuction candidate, says Daniel Morello, M.D., president of the American Society for Aesthetic Plastic Surgery. Morello stresses that liposuction is for body contouring, not weight reduction. “It is designed for removing localized areas of fatty tissues—not as a substitute for proper dietary management and exercise.”

But what happens to the mildly to seriously overweight people who want and get liposuction? Sometimes after the surgery, these people may face yet another unwanted—and possibly unexpected—complication: the return of fatty deposits, but probably in other areas of the body, says C. Wayne Callaway, M.D., an associate clinical professor of medicine at George Washington University. Callaway, who is also an internist, endocrinologist, and obesity specialist in Washington, D.C., sees post-liposuction patients complaining of renewed accumulations of fat.

Animal studies have shown that if you remove significant amounts of fat from one area, body fat increases elsewhere, according to Callaway. “The signal is leptin, a hormone made in fat cells,” he says. “The more fat you have, the more leptin is made ... and if a large amount of fat is removed, there is a drop in leptin levels.” In animal studies, this drop in leptin levels results in an increase in food intake and a decrease in activity until the leptin levels are up again, according to Callaway.

Callaway says that the people who have the most trouble after a liposuction procedure are the really obese who have had large amounts of fat removed. “They have a compensatory increase in new fat cells,” Callaway says. “And fat
Making the Decision

The American Society for Aesthetic Plastic Surgery offers some guidelines for consumers considering liposuction:

- **Have realistic expectations.** Liposuction is for body contouring, recommended for people who want to remove small amounts of fatty deposits. As a general rule, this means the mildly overweight who are within 30 percent of their ideal body weight.
- **Select a surgeon certified by the American Board of Plastic Surgery.** Ask for verification in writing of the doctor’s privileges to perform lipoplasty in an accredited acute care hospital. (Doctors may have privileges to perform other types of surgeries, but not necessarily liposuction.) If the doctor does the surgery in an office, ask for proof of the facility’s accreditation.
- **Give an accurate medical history** and be sure to report all medications you take, even dietary and herbal supplements.
- **Discuss the procedure thoroughly** with your doctor, and make sure you understand the differences between the various types of liposuction. Ask questions. If your doctor can’t answer them, or dismisses them as unimportant, find another doctor.
- **Understand which type of anesthesia** is recommended and if that includes deep sedation, be sure that certified staff who have appropriate training will administer it.
- **Discuss pre- and post-operative care**, and make sure you understand any possible risks.

—A.G.

goes to areas where there are still a lot of fat cells. So that means to the neck, above collar bones, and the upper abdomen.” Besides, he adds, abdominal obesity is controlled by a whole other set of signals, so that even after liposuction, the underlying causes for obesity remain. “Those causes are not addressed by taking out fat cells.” He points out that, contrary to recent theories, “One can keep making new fat cells throughout life, so little can be gained by liposuction.”

Liposuction for obese patients is “a prescription for disaster,” according to Gerald Imber, M.D., a plastic surgeon in New York City and clinical assistant professor of plastic surgery at Cornell-Weill Medical College. The greater the volume of fat and tissue fluids, including plasma, that are sucked out, the greater the chance of severe dehydration and electrolyte imbalances. “When you remove six, eight, or ten liters of mixed fat and water, you are courting disaster,” he says. “Liposuction is not meant to change a size 16 to a size 8.”

According to a consensus of the experts, the ideal liposuction candidate is a mature adult between the ages of 30 and 50 years old, male or female, in good health, who has dieted and exercised to lose unwanted pounds, with good skin tone, with a set of realistic expectations, and who wants a limited procedure for body contouring.

**Buyer Beware**

Anyone considering liposuction should consider all the options, and consumers need to be very careful when selecting a doctor. The saying “caveat emptor” (buyer beware) has never been truer, says Morello. Liposuction sounds so deceptively simple, but in the hands of unskilled doctors, it poses a real threat to people’s health, he adds. To complicate matters, anyone with a medical degree can perform liposuction, even with only the briefest weekend training period.

Fighting fat may be the number one battle for many Americans, but liposuction may not be the best weapon to win that slimmer, trimmer body.

Alexandra Greeley is a writer in Reston, Va.

FDA Consumer / November-December 2000 / 35
Site Opens Gate to Fed, Local, State

Information on topics ranging from immunizations to starting a small business to obtaining student financial aid is available on “Workers.gov” (www.workers.gov), a Web site launched in July as a gateway to more than 1,000 federal, state and local government resources. Through the site, users can scan Web sites for the latest medical information, check out job listings, acquire new skills through distance learning, and explore resources available for people with disabilities. The site also has information on money management, travel, tourism, and citizenship issues such as voting. Workers.gov is a joint venture between the Labor Department and the National Partnership for Reinventing Government.

Preventing Seafood Hazards

It started as a way to keep astronauts from getting sick to their stomachs in outer space. Now the technique has come down to earth to help ensure that seafood is safe to eat. Called Hazard Analysis and Critical Control Point (HACCP, pronounced “hassip”), the system identifies and prevents illness-causing hazards rather than relying on spot checks and random samplings of food. By going to www.cfsan.fda.gov/~lrd/haccp.html, you can learn more about how HACCP is doing its part to curb foodborne sickness. FDA has required seafood producers to use HACCP since 1997, and the site discusses proposed rules for adopting HACCP to regulate fruit juice safety.

Keeping Fit in Those Middle Years

So you’ve hit the half-century mark—now what? Well, you might want to check out “Staying Healthy at 50+” (www.ahrq.gov/ppip/50plus), an online guide loaded with solid information about keeping fit and staying well in the middle-aged years. Though some of the advice is familiar—such as quit smoking, stay physically active and reduce dietary fat—the site also has helpful tips on disease prevention, health screening tests, and ways to fit exercise into a busy schedule. Also included are “personal prevention charts,” such as ones that keep track of flu, tetanus and pneumonia shots. The guide also is available in hard copy by calling 1-800-358-9295; ask for publication AHRQ 00-0002. The “Staying Healthy” Web site is hosted by the Agency for Healthcare Research and Quality (AHRQ).

Spelling H-E-L-P for the Typographically Challenged

Let’s face it, for some of us, spelling is not our strong suit. But that’s okay when it comes to getting medical information—thanks to a new “spell-check” mechanism built into the search engine on the National Institutes of Health’s Web site (http://search.nih.gov). It allows users to conduct searches on terms even if words are misspelled. For example, let’s say you forget that the word “pneumonia” begins with a “p” and you do a search on “neumonia.” No problem. A pull-down menu will appear with the correct spelling, which you can choose and continue the search. Developer Dennis Rodriguez and his NIH team plan to refine the spell-check mechanism even further in the near future with interfaces that engage users in actual dialogue and direct them to what is likely the best response.

Update

In our last issue, we published a Web address for the Government Printing Office’s “GPO Access” site, which links to more than 100,000 federal publications for easy access. Though that address will get you to the site (with a few extra clicks), the good folks at GPO tell us there’s an even better address that will take you directly to the site: www.gpo.gov/gpoaccess.

John Henkel is a member of FDA’s Web management staff.
**SUMMARIES OF COURT ACTIONS**

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

Summaries of Court Actions are prepared by the Office of the Chief Counsel, Food and Drug Administration. Published by direction of the Secretary of Health and Human Services.

**SEIZURE ACTIONS**

**Food/Contamination, Spoilage, Insanitary Handling**

**PRODUCT: Cases of Canned Straw Mushrooms** at San Francisco, Calif. (N.D.Cal.); Civil Action No. 99-3733. CHARGED 8-5-99: While held for sale after shipment in interstate commerce at Superhuck Co., San Francisco, Calif., the article of food was misbranded in that its labeling was false and misleading because the invoice falsely represented that it had been packed by Kepper Food Processor Co.—343(a)(1). The article of food was adulterated in that it had been prepared and packed under conditions whereby it may have been rendered injurious to health because of inadequate processing—342(a)(4).

DISPOSITION: The article was destroyed. (F.D.C. No. 67275; S. No. D53-0029148-6; S.J. No. 1)

**Drugs/Human Use**

**PRODUCT: Dyconine HCL HSP 19/25 Kilogram Drums, more or less, at Titusville, Fla. (M.D.Fla.); Civil Action No. 99-415.**

CHARGED 4-7-99: While held for sale after shipment in interstate commerce at Pharmco Laboratories, Inc., in Titusville, Fla., the articles of drug were adulterated in that the methods used for their manufacture, processing, packing, and holding did not conform to, and were not operated and administered in conformity with, good manufacturing practice to assure that such drugs met the safety requirements of the Food, Drug, and Cosmetic Act and had the identity and strength and met the quality and purity characteristics which they purported, and were represented to possess—501(a)(2)(B).

DISPOSITION: The articles were destroyed. (F.D.C. No. 67263; S. No. 37132; S.J. No. 2)

**PRODUCT: Oxygen, U.S.P., at Cincinnati, Ohio (S.D.Ohio); Civil Action No. 99-1083.**

CHARGED 2-7-00: While held for sale after shipment of one or more of their components in interstate commerce at Wright Brothers, Inc., Cincinnati, Ohio, in that methods used in, and the facilities and controls used for, their manufacture, processing, and packing do not conform to and are not operated or administered in conformity with current good manufacturing practice to assure that such articles of drug meet the safety requirements of the Food, Drug, and Cosmetic Act, and have the identity and strength and meet the quality and purity characteristics which they purport and are represented to possess—351(a)(2)(B).

DISPOSITION: The articles were destroyed. (F.D.C. No. 67279; S. No. 98-796-236; S.J. No. 3)

**PRODUCT: Phenylbutazone Powder** at Jackson, N. J. (D.N.J.); Civil Action No. 98-4218. CHARGED 8-5-98: The articles of drug were misbranded at A&G Pharmaceuticals, Inc., Jackson, N.J. The phenylbutazone was an unapproved new drug and, therefore, the defendant articles of drug were subject to forfeiture and condemnation pursuant to 21 U.S.C. § 334, and having noted that, the United States Marshal's Service seized the defendant articles.

DISPOSITION: The articles were destroyed. (F.D.C. No. 67245; S. No. 98-087-136; S.J. No. 4)

**INJUNCTION ACTIONS**

**DEFENDANT: Stewart Sandwiches, Inc., at Norfolk, Va. (E.D. Va.); Civil Action No. 90-1344-N.**

CHARGED 7-10-97: United States notified America's Foods, Inc. (AFI) in early 1997 that firm was successor and assign of Stewart Sandwiches, Inc. (Stewart) and operating out of compliance with consent decree. In July 1997, AFI agreed file together with United States, a Joint Motion to Grant Permissive Joiner and To Modify Consent Decree of Permanent Injunction.

DISPOSITION: Modified consent decree was entered on July 15, 1997. Thereafter, the sandwiches were destroyed, the firm shut down, and all assets were sold in bankruptcy. (Inj. No. 1233; S.J. No. 5)

**MISCELLANEOUS ACTIONS**

**ACTION: Satish R. Shah v. FDA, at the District of Columbia Court of Appeals, DC (D.C. Cir); Civil Action No. 99-1191.**

CHARGED 7-9-99: Satish R. Shah was debarred in 1994 following his felony convictions for conspiracy and making a false statement to a federal agency. In 1997 and 1998, Shah applied to the agency for special termination of his debarment, contending that he had provided substantial assistance in the investigation of other offenses within FDA's jurisdiction. FDA denied his petition because, based on the record before FDA, the agency could not find that Shah had provided such substantial assistance. The agency is statutorily required to make a determination of substantial assistance prior to granting an application for special termination of permanent debarment.

DISPOSITION: On Nov. 19, 1999, a three-judge panel of the Court of Appeals for the District of Columbia Circuit denied Shah's Application For Special Termination of his permanent debarment. The court found that FDA's denial of Shah's application was reasonable and supported by the record and, therefore, was not arbitrary and capricious. (Misc. 1230; S.J. No. 6)
Statement of Ownership, Management, and Circulation  
(Required by 39 U.S.C. 3685)

*FDA Consumer*, ISSN 0362-1332; owner and publisher: Food and Drug Administration (HFI-40), 5600 Fishers Lane, Rockville, MD 20857; editor: Larry Thompson.

Date of filing: October 2000, issued 6 times annually (bi-monthly); annual subscription price $12 ($15 foreign).

### Extent and Nature of Circulation:

<table>
<thead>
<tr>
<th>Description</th>
<th>Average No. Copies Each Issue During Preceding 12 Months</th>
<th>Actual No. Copies of Single Issue Published Nearest to Filing Date</th>
</tr>
</thead>
<tbody>
<tr>
<td>A. Total number of copies (net press run)</td>
<td>26,873</td>
<td>26,775</td>
</tr>
<tr>
<td>B. Paid and/or requested circulation</td>
<td></td>
<td></td>
</tr>
<tr>
<td>1. Paid/requested outside-county mail subscriptions</td>
<td>23,966</td>
<td>23,800</td>
</tr>
<tr>
<td>2. Paid in-county subscriptions</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>3. Sales through dealers and carriers, street vendors, and counter sales (not mailed)</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>4. Other classes mailed through the USPS</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>C. Total paid and/or requested circulation (sum of B1, B2, B3 and B4)</td>
<td>23,966</td>
<td>23,800</td>
</tr>
<tr>
<td>D. Free distribution by mail (samples, complimentary, and other free)</td>
<td>2,087</td>
<td>2,058</td>
</tr>
<tr>
<td>E. Free distribution outside the mail (carriers or other means)</td>
<td>609</td>
<td>622</td>
</tr>
<tr>
<td>F. Total free distribution (sum of D and E)</td>
<td>2,696</td>
<td>2,680</td>
</tr>
<tr>
<td>G. Total distribution (sum of C and F)</td>
<td>26,662</td>
<td>26,480</td>
</tr>
<tr>
<td>H. Copies not distributed</td>
<td>211</td>
<td>295</td>
</tr>
<tr>
<td>I. Total (sum of G and H)</td>
<td>26,873</td>
<td>26,775</td>
</tr>
<tr>
<td>Percent paid and/or requested circulation (C / G x 100)</td>
<td>90%</td>
<td>90%</td>
</tr>
</tbody>
</table>

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

Larry Thompson, editor
Counterfeiting Couple Pays High Price for Baby Formula Fraud

By Tamar Nordenberg

Some parents who paid extra money to feed their dairy-sensitive babies a special infant formula instead unwittingly fed them a potentially dangerous milk-based formula. Two southern Californians recently pleaded guilty to the crime of trafficking counterfeit goods and are paying back an infant formula manufacturer more than $200,000 for a scheme that landed mislabeled baby food in grocery stores in their state.

Shane Thompson, who also went by the last name Devisser, and Margaret M. Thompson, who sometimes used the last names Devisser and Bell, bought regular infant formula called “Next Step,” which cost $7 to $9 per can, and replaced the cans’ labels with glued-on photocopies of labels from the hypoallergenic “Enfamil Nutramigen” that cost three times as much. The husband-and-wife team milked their profits by returning the disguised cheaper baby food for the high-end refund.

“Here were two individuals presumably out to make a quick buck,” says Jud Bohrer, a special agent in charge with the Food and Drug Administration’s Office of Criminal Investigations (OCI). “And the victims were the most vulnerable population, babies who had no choice in the matter.”

Feeding a milk-based formula to infants who are sensitive to cow proteins can cause fever, vomiting, skin rash, and diarrhea. Says Bohrer. “Several mothers who unknowingly fed their infants the wrong formula had to rush their babies to the emergency room.”

OCI special agents began investigating the sale of counterfeit Nutramigen infant formula in October of last year after getting complaints from Mead Johnson Nutritional, Evansville, Ind., which makes both Nutramigen and Next Step. Consumers had reported to the company that the so-called Nutramigen looked different than in the past and appeared to be making their babies vomit or refuse to eat.

That October, OCI agents interviewed more than 100 duped consumers and store employees who had encountered the mislabeled product. The agents collected the counterfeit cans, which could be identified because they lacked the marking “NUTRAM” that was embossed on the bottom of the genuine cans.

Meanwhile, Mead Johnson notified major grocery store chains in southern California and area consumers to look out for the counterfeit cans, and FDA asked stores to check the driver’s license or other photo identification of anyone who requested a refund for Nutramigen formula.

Within a month, the manager of a grocery store in Anaheim Hills, Calif., told FDA about a woman who had sought a refund for three suspect cans of Nutramigen. The woman’s driver’s license identified her as Anaheim resident Margaret M. Thompson.

The mere fact that Thompson was returning Nutramigen cans did not incriminate her because many concerned consumers were returning the counterfeit formula as well, Bohrer points out, adding, “We had already gotten dozens of ghost leads that led nowhere.”

But this time, the I.D. checks yielded their reward when the U.S. Secret Service’s forensics laboratory found fingerprints on the returned Nutramigen cans, underneath the fake label, that matched Margaret Thompson’s fingerprints on file with the government in connection with a prior job application. “It certainly helped the Secret Service in quickly identifying the prints that Thompson had shown her real I.D.,” Bohrer says.

Store employees who had seen Margaret Thompson trying to return the counterfeit product were also able to pick her out of a photo line-up of similar-looking women.

Other fingerprints lifted from the cans collected during FDA’s investigation proved to be a match with those of Margaret’s husband, Shane Thompson, who had committed crimes in the past.

“Many of the hundreds of cans we had picked up from stores had carried the Thompsons’ fingerprints,” Bohrer says.

In November 1999, OCI agents arrested Shane Thompson as he picked up his mail from a North Hollywood post office box. The following month, his wife voluntarily surrendered to OCI agents.

Based on their guilty pleas to three counterfeiting-related counts, a judge in the U.S. District Court for the Central District of California in July of this year handed down the Thompsons’ sentences: seven months in prison for Shane Thompson, which he has served out, and five years probation for him and Margaret Thompson. The two are jointly responsible for the restitution amount of just over $203,000. ■
The Public’s Right To Know

By Lawrence Bachorik, Ph.D.

“Our government,” wrote Supreme Court Justice Louis D. Brandeis in <em>Olmstead</em> v. U.S., “is the potent, omnipresent teacher.” That was in 1928, the year of the discovery of penicillin—16 years before the invention of synthetic cortisone, 45 years before the first gene was spliced, and 69 years before the cloning of Dolly, the celebrity sheep in Scotland. And it was 11 years before the introduction of commercial television, and about 60 years before the onset of the Age of the Internet.

As in the 1920s, government agencies have the obligation of providing valid and useful facts, although the job has become much more demanding. Knowledge about nutrition, medications and medical devices has become enormously more complex, all the while multiplying at an exponential rate. The audience has also changed, and so have the sources of its information.

In 1920, the United States population was just over 100 million, less than 40 percent of today’s 275 million; one out of every two Americans lived in a small town or on a farm; and life expectancy, education level, and cultural diversity were a fraction of what they are now. Health-related information, which used to be severely limited, now saturates the airwaves and the World Wide Web and fills countless columns of print.

Unfortunately, much of this abundance is far from objective. Stories of health fraud abound; the Internet, in particular, allows anyone to claim expertise. The resulting cacophony is blamed for confusion that adds to the reported public skepticism about authorities and purveyors of news.

At FDA, we are encouraged by signs that when it comes to public health information, this distrust has been exaggerated. The most recent heartening evidence comes from last year’s poll by the prestigious Pew Research Center, which measured constituent opinions about FDA and other federal agencies.

Asked whether they “trust FDA to do what is right,” 72 to 85 percent of medical professionals, consumer advocates, industry officials, and patients answered, “Yes.” Asked if “FDA’s decisions use good science,” 74 to 87 percent of respondents expressed the same approval.

There is good news in recent polls also for the cutting-edge research of our nation’s scientists. In January, a National Science Foundation report showed undiminished U.S. public support for genetic engineering, despite the widespread speculation about human cloning that followed the publicity about Dolly.

In Europe, where public support for biotechnology is substantially weaker, some of the difference is attributed to the public trust enjoyed by FDA. We’re frequently asked by European officials how FDA keeps its credibility. A big part of the answer is our agency’s 94-year record of integrity: insistence on high public health standards, fair and science-based decisions, and dedication to the protection of consumers. But another part of the answer is FDA’s culture of transparency and disclosure.

This takes many forms, including the open discussions of the pros and cons of product submissions in FDA’s advisory committee meetings, the publishing of FDA’s proposed rules for public comment, the public exchanges with stakeholders about FDA guidelines and policy changes, and the scrutiny of the agency’s processes in open congressional hearings.

At FDA’s Office of Public Affairs, we bring the agency’s public health information to all who need it. One major transmission belt is the 100-odd press releases, backgrounders and talk papers we publish each year. Rigorously factual, they are widely picked up by the media, and they give new product approvals and public health alerts nationwide resonance.

Since the start of this year, for example, FDA has warned the public against potentially contaminated dips and smoked fish, and alerted consumers to a recall of frozen cheeseburgers. In addition, <em>FDA Consumer</em> discusses consumer-oriented issues in longer articles, many of which we translate for Spanish-speaking communities.

We also serve the needs of health-care professionals, academicians, and industry by providing FDA data for their specialized publications. Another prodigious source is our Freedom of Information staff, which annually answers more than 25,000 requests for data, much of which is sensitive. Our staff’s effort to be forthcoming without divulging trade secrets is a daily testimony to FDA’s commitment to openness.

And currently, we are opening the information floodgates still wider by augmenting FDA’s Web site and making it more user-friendly. By logging onto www.fda.gov, anyone can find data as simple as the address of the nearest certified mammography facility and as complex as dosage guidelines for oncology drugs.

FDA’s Web site is already averaging 50,000 visitors a day. People depend on us for the right answers, and we are trying to live up to Justice Brandeis’ compliment.

Lawrence Bachorik, Ph.D., is FDA’s Associate Commissioner for Public Affairs.
"IT'S SAFE TO BITE WHEN THE TEMPERATURE IS RIGHT!"

**Temperature Rules!**

- **145 °F**  
  Beef, lamb & veal steaks & roasts, medium rare (medium 160 °F)

- **160 °F**  
  Ground beef, pork, veal & lamb  
  Pork chops, ribs & roasts  
  Egg dishes

- **165 °F**  
  Ground turkey & chicken  
  Stuffing & casseroles  
  Leftovers

- **170 °F**  
  Chicken & turkey breasts

- **180 °F**  
  Chicken & turkey  
  whole bird, legs, thighs & wings

**FSIS Meat and Poultry Hotline**  
1-800-535-4555 • TTY: 1-800-256-7072  
E-mail: mphotline.fsis@usda.gov