Salmonella Enteritidis: From The Chicken To The Egg

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Modified Fast: A Sometime Solution to a Weighty Problem
Very low calorie formula diets are enjoying renewed popularity. Though less dangerous than their '70s forerunners, these newer products may not be risk-free.

Bovine Growth Hormone: Harmless for Humans
How can FDA say that milk containing bST is safe for humans when the hormone is still being tested for safety and effectiveness in cattle? Differences in bST’s activity in people and in animals are among the reasons.

On the Trail of the Alaskan Oil Spill
More than two dozen FDA investigators and scientists went to Alaska to help clean up last year’s oil spill from the Exxon Valdez. Sniffing for oil, negotiating slippery ladders, and flying in seaplanes were all in a day’s work.

Lactation Suppression: Safer Without Drugs
When a woman decides not to breast-feed her newborn, it’s more comfortable if breast milk production can be suppressed. But due to safety and effectiveness concerns, FDA recently asked manufacturers of drugs used for lactation suppression to stop including this as an approved use in the labeling.

Pet Ownership—Risky Business?
Tabby and Fido may be giving you more than companionship. Though fortunately not commonplace, there are a number of diseases that can be transmitted from pets to people.
No Antibiotic Residues in Milk, FDA Finds

An FDA nationwide survey of milk revealed no residues of any antibiotics, including sulfa drugs, the agency announced Feb. 5. The findings, based on the most current technology, contradict earlier conclusions of a screening test sponsored by a national newspaper.

Specifically, no sulfamethazine (a drug suspected of causing cancer that is no longer permitted for use in milk cows) or other potentially dangerous drug was found in the 14-city survey of milk, FDA said. Using testing methods perfected for the study, FDA was able to confirm earlier negative findings for antibiotics from tests regularly carried out by states under the National Conference of Interstate Milk Shippers. The new testing methods, FDA said, will be available for use by states as well as the federal government.

The accuracy of the National Conference testing program was challenged by The Wall Street Journal in articles published Dec. 29 and Jan. 2. The newspaper said it had asked a laboratory to test milk using the Charm II method, on samples collected before Christmas in 10 cities, 38 percent were found to be contaminated with antibiotics or sulfa drugs—including sulfamethazine, a suspected carcino-gen.

FDA’s recent results indicate, however, that the “positives” in the newspaper’s tests may have been false positives. The newspaper published the Charm II results without confirmation by other methods. FDA said at the time of the newspaper report that Charm II could detect only classes of drugs, and that the test was not specific for sulfamethazine. The agency also said the levels reported would not constitute a health threat. Nevertheless, FDA said it was beginning its own tests.

In doing so, the agency duplicated the testing methodology—Charm II—and got “positives” similar to those reported by The Wall Street Journal for drugs overall. However, in confirmatory tests, FDA found no sulfamethazine. Nor was chloramphenicol—a compound not approved for use in any food-producing animal—detected. The testing also specifically targeted penicillin, as it can cause allergic reactions at some levels. None was found.

“Since one error with one milk cow can cause a detectable residue of sulfamethazine in the pooled milk of 70,000 cows, our study indicates that the American dairy farmer is using animal drugs carefully and conscientiously, and that the milk supply does not contain unsafe drug residues,” FDA’s Center for Veterinary Medicine Director Gerald Guest, D.V.M., said.

To further ensure the wholesomeness and safety of the nation’s milk, FDA plans to:

• regularly monitor pasteurized milk for drug residues. This would supplement the testing carried out by the states under the National Conference of Interstate Milk Shippers.
• work through the conference to have the states institute new test procedures, continue to educate farmers about proper drug use to prevent residues, and penalize farmers who violate the laws. (Such economic penalties now include dumping contaminated milk without providing compensation.)
• further ensure the wholesomeness and safety of pasteurized milk, FDA plans to:

In addition, FDA said it will continue research, development and validation of new analytical methods.

For more information on milk safety, see “Bovine Growth Hormone: Harmless for Humans,” on page 16.

New Rule Proposed For Food Health Claims

A new health messages regulation to replace FDA’s 1987 plan allowing health claims on food product labels has been proposed by the agency.

Under the policy FDA will consider health claims about:

• calcium and osteoporosis
• sodium and high blood pressure
• fat and heart disease
• fat and cancer
• fiber and cancer
• fiber and heart disease

The proposal, published in the Federal Register Feb. 13, 1990, takes a more cautious approach to health messages than was defined in a 1987 proposal issued by the
agency. Many respondents to the earlier proposal commented that it was too broad and allowed label claims that may not be justified by scientific research.

"In hindsight," said HHS Secretary Louis Sullivan, "the 1987 proposal has proved to be too permissive," adding that "We need an interim policy to serve as a mid-course correction and provide guidance to industry on what health messages will and will not be allowed."

The claims must be supported by scientific evidence accepted by FDA, and the agency will have legal authority to act against misleading claims.

Comments on the new proposal may be sent to FDA, Dockets Management Branch, 5600 Fishers Lane, Rockville, Md. 20852 by April 16, 1990.

**New Recommendations For Measles Immunizations**

Concerned about the growing number of measles cases in the United States, the Public Health Service recently recommended that two doses of measles vaccine be given to all children, preferably as combined MMR (measles, mumps, rubella vaccine). Previously, only one dose was recommended routinely. (See "Mumps Makes a Comeback ... And Measles, Too" in the July-August 1989 FDA Consumer.)

While the tally is not yet complete for 1989, about 14,000 measles cases were reported to the federal Centers for Disease Control in the first 48 weeks of the year, compared with the previous post-vaccine era high of 6,282 cases for all of 1986.

The new PHS recommendations specify that in most localities, the first dose of vaccine should be given at 15 months of age and the second one at 4 to 6 years, when the child starts school. However, in counties with more than five cases among preschool-aged children during each of the preceding five years, with recent outbreaks among unvaccinated preschool-aged children, or with large inner-city populations, the first dose should be given at 12 months.

Students entering college and medical personnel with direct patient care who are beginning employment should present documentation of having received two doses of measles vaccine no less than a month apart after their first birthday, or other evidence of immunity. If resources are available, PHS suggests that institutions may want to extend this recommendation to all medical personnel. Because some medical workers born before 1957 have acquired immunity in medical facilities, institutions may consider also requiring at least one dose of measles vaccine for older employees who may be exposed to the disease during their work.

In outbreaks involving children under 1 year, children as young as 6 months of age can be vaccinated. However, children initially vaccinated before their first birthday should be revaccinated at 15 months. In institutional outbreaks, all students and their siblings and all school personnel born after 1956 who do not have documentation of immunity should be revaccinated.

Persons who received immune globulin at the same time as live "further attenuated" (Swarz or Moraten) vaccine should consider themselves unimmunized. The practice of giving immune globulin with measles vaccine was particularly common in 1967-69 when both the live "attenuated" (weakened) Edmonton B vaccine, recommended to be used with immune globulin, and the newer "further attenuated" vaccines, not requiring immune globulin, were in use. People vaccinated in 1967-69 who know they also received immune globulin but don't know which vaccine they received should consider themselves unimmunized and should receive two vaccinations more than one month apart.

**Partial Ban of Red No. 3 Proposed**

FDA has proposed banning the "provisional" uses of color additive FD&C Red No. 3. This would include uses in cosmetics, externally applied drugs, and as a pigment form called "lakes" in foods, drugs and cosmetics.

The decision is based on studies showing that high doses of the color additive may cause thyroid tumors in male rats. Under the Delaney Clause of the 1960 Color Additive Amendments, products shown to cause cancer in laboratory tests, even at very low doses, cannot be approved.

These 1960 amendments placed color additives already in use on a provisional list to permit continued use while safety studies were conducted. If studies submitted by the manufacturer showed that specific uses of the color were safe, FDA then permanently listed these uses.

In response to a petition submitted by the Certified Color Manufacturers Association in 1969, FD&C Red No. 3 was permanently listed for uses in drugs and foods, including baked goods, cherries, dairy products, dessert powders, dietary supplements, seasonings, jellies, jams, and vegetable products.

After delisting the provisional uses, FDA will follow the mandate of the Delaney Clause and will take steps to eliminate the rest of the color's uses.

**87 New Drugs Approved in '89**

By the close of 1989, FDA had approved 87 new drugs, 113 biological products, and 265 generic drugs.

Of the 87 drugs approved, 23 were new molecular entities (drugs distinctly different in chemical structure from those on the market). Four of the 23 were classed 1A, meaning they provided significant therapeutic gains. These were Lariam (mefloquine), an antimalarial manufactured by Hoffmann-La Roche; Cytovene (ganciclovir), used to treat cytomegalovirus, manufactured by Syntex Labs; Clozaril (clozapine), a drug for treating schizophrenia, manufactured by Sandoz Pharmaceuti-
cals; and Anafranil (clomipramine hydrochloride), used to treat obsessive-compulsive disorder, manufactured by Ciba-Geigy Corp.

Among the biologicals approved were:
- Epogen, a treatment for anemia in patients with chronic renal failure, manufactured by Amgen, Inc.
- Oculinum, a treatment for the eye disorders blepharospasm and strabismus, manufactured by Oculinum, Inc.
- two cardiovascular products—Emine (a clot dissolver manufactured by Beecham-Wulffing) and Fluosol (used in balloon angioplasty procedures)
- three vaccines—one for hepatitis B, one for Haemophilus B influenza, and one for typhoid
- four diagnostics, including three to detect the AIDS virus (HIV-1) or HIV-1 antibodies.

In addition, the agency also approved a liquid form of Retrovir (zidovudine), the AIDS drug commonly known as AZT; a new use for the cholesterol-lowering drug Lopid (gemfibrozil) to treat coronary heart disease in some patients; and a nonprescription version of Schering-Plough Corp.'s Lotrimin (clotrimazole), a topical anti-fungal product used to treat conditions such as athlete's foot.

Typhoid Vaccine with Fewer Side Effects
An oral typhoid vaccine in capsule form that produces fewer side effects than the injectable ones was approved by FDA last January.

The new product—which contains live bacteria in a coated capsule—is taken every other day for four days. Routine immunization for travelers is not recommended, except for those traveling to Central and South America, Africa, India and Southeast Asia, where typhoid is common. A booster dose every four years is recommended for people who are continuously or repeatedly exposed to Salmonella typhus, the bacterium that causes the disease.

Typhoid is rare in the United States, and most of the 400 to 500 cases reported annually here are contracted in other countries in areas with poor sanitation. Symptoms include sustained fever, headache and malaise. About 10 percent of cases are fatal, whereas less than 1 percent of patients treated properly with antibiotics die. The recent emergence of drug-resistant strains of S. typhus can complicate therapy.

The vaccine was tested in more than a half million children and adults in the United States, Egypt, Chile, Indonesia, and Switzerland. Assistant Secretary for Health James O. Mason, M.D., Dr.P.H., said that "In most of the efficacy studies, the oral vaccine was shown to be of comparable efficacy to that previously reported for injectable typhoid vaccines without the severe side effects, such as fever, which can temporarily incapacitate many recipients of the injected vaccine."

The vaccine, developed and manufactured by the Swiss Serum Vaccine Institute in Berne, Switzerland, will be distributed in the United States by Berna Products Corporation of Coral Gables, Fla., as Vivottif Berna Vaccine.

Legionnaires' and Misters
A recent outbreak of Legionnaires' disease in Louisiana has been linked to a supermarket's vegetable misting machine, according to the Louisiana Department of Health and Hospitals and the federal Centers for Disease Control.

There were 34 confirmed cases of Legionnaires' disease, a type of pneumonia, last October and early November in Bogalusa, La. At least two people died from the disease. Legionella pneumophila, the bacteria that causes Legionnaires' disease, was found in a cultured sample from the machine's mist.

Louisiana public health officials say the mist machine found in the Bogalusa store was connected directly to a water supply line and had a small water reservoir tank. In a notice to all state health departments in January, FDA said reservoir tank-type misters should be checked immediately for contamination and then thoroughly cleaned and sanitized once a week.

Legionnaires' disease is transmitted by inhaling small droplets of water containing L. pneumophila bacteria. It cannot be transmitted from one person to another, and there is no evidence that the disease can be transmitted through food.

The disease got its name when American Legion members became ill while attending a 1976 convention in Philadelphia. That outbreak was traced to bacteria growing in standing water in an air-conditioning system and involved 221 illnesses, including 34 deaths.

(For more information on Legionnaires' disease, see "Still a Killer: Pneumonia Targets the Ill, the Elderly" in the June 1987 FDA Consumer.)

New Edition of FD&C Act Available
The newest edition of the Federal Food, Drug, and Cosmetic Act—complete with all of its most recent amendments—is available for purchase.


Copies are $7.50 each and can be ordered from the U.S. Government Printing Office, Superintendent of Documents, Washington, D.C. 20402; (202) 783-3238. Ask for publication number 017-012-00347-8.
Long-Term Dose Of AZT Halved

Revised labeling for the anti-AIDS drug zidovudine, commonly known as AZT, recommends a long-term dosage half that previously given.

Approved last January, it is expected that the new dosage will enable patients who are on long-term therapy with zidovudine to tolerate the drug longer without developing severe side effects—including anemia and low white blood cell counts—that formerly required the drug to be stopped in some patients.

In addition, HHS Assistant Secretary for Health James O. Mason, M.D., Dr.P.H., noted that “Since the new approved dose will require only half the amount of zidovudine used at the previously recommended dose, the cost of...therapy should be halved for many patients.”

The long-term regimen of 600 milligrams (mg) daily may be started after the patient has received treatment with the drug for one month at the previously recommended dose of 1,200 mg per day.

A two-year study sponsored by the National Institute of Allergy and Infectious Diseases compared the effects of zidovudine in two groups of 262 patients; one group was given 600 mg per day of the drug, the other 1,500 mg. The lower dose proved just as effective in prolonging survival and preventing infections associated with AIDS as the high dose. Moreover, nearly half the patients in the high-dose group had to stop treatment at that dosage because of serious adverse reactions. The effectiveness of the lower dose in improving neurologic problems caused by the AIDS virus is unknown, however.

FDA’s approval of the new recommended dose for zidovudine applies both to capsule and syrup forms of the drug. Physicians may prescribe the drug at higher or lower dose levels when warranted.

New Drug Approved For AIDS Complications

AIDS patients and others with weakened immune systems have access to a new treatment for two serious infections, one of which is life-threatening.

FDA recently approved the drug Diflucan (fluconazole) for treating candidiasis, a fungal infection most often seen as sores in the mouth and throat, and cryptococcal meningitis, an inflammation of the brain and nervous system. Current treatments for these infections have limited use.

For example, the drug amphotericin B, marketed as Fungizone and Amphotericin B, usually is effective for an initial episode of cryptococcal meningitis but can result in serious adverse reactions, including impaired kidney function and bone marrow suppression. In addition, many patients relapse within months and must take the drug for the rest of their lives. Although lifetime treatment with Diflucan is recommended for cryptococcal meningitis in AIDS patients who have relapsed, in clinical studies Diflucan provided effectiveness comparable to Fungizone with fewer side effects.

In a study of AIDS patients with esophageal candidiasis, Diflucan was as effective as the drug Nizoral (ketoconazole). Results were similar in trials comparing Diflucan with the drug Mycelex (clotrimazole) in treating candidiasis in people with AIDS and people with cancer.

While Diflucan appears to be well tolerated by most patients, it has been associated with abdominal discomfort and nausea. Less commonly, it has been linked to signs of liver damage and, in rare instances, to severe skin rashes and liver failure.

The drug will be marketed in both a tablet and intravenous form by Pfizer Inc. of New York City.
SALMONELLA ENTERITIDIS

From the Chicken to the Egg

by Dale Blumenthal

White, shining, unmarred—a Grade A mystery now lies in the uncracked egg. Is it safe to eat?—9,999 times out of 10,000, yes. But...

- In May 1989, six nursing home patients in Pennsylvania died from Salmonella enteritidis poisoning after eating stuffing that contained undercooked eggs.
- In July, 21 guests at a baby shower in New York became ill after eating a pasta dish made with a raw egg. One victim was 38 weeks pregnant and delivered her baby while ill. The newborn infant developed Salmonella enteritidis blood poisoning and required lengthy hospitalization.
- Last August, a healthy 40-year-old man died, and 14 others were hospitalized, after eating egg-based custard pie contaminated with Salmonella enteritidis, which was served at a company party in Pennsylvania. The list goes on.

Public health officials are concerned. More than 49 outbreaks of Salmonella enteritidis poisoning took place in nine states and Puerto Rico last year, resulting in at least 13 deaths and more than 1,628 illnesses. According to the Jan. 5, 1990, issue of the Centers for Disease Control’s Morbidity and Mortality Weekly Report, from January 1985 through October 1989, 189 Salmonella enteritidis outbreaks in the United States caused 6,604 illnesses and 43 deaths. Many more illnesses probably went unreported, says Joseph Madden, Ph.D., deputy director of FDA’s division of microbiology.

Health investigators suspect that contaminated shell eggs caused nearly half of these outbreaks. The egg connection in these cases was determined by tracing the food eaten by the victims and taking cultures both from patients and foods.

Especially at risk for Salmonella poisoning are the elderly, the very young, pregnant women (because of risk to the fetus), and people already debilitated by serious illness, malnutrition, or weakened immune systems. Symptoms of Salmonella enteritidis infection usually include diarrhea, vomiting, abdominal pain, chills, fever, and headache. The bacteria can invade organs outside the gastrointestinal tract, causing complications that require lengthy hospitalization, even in healthy people.

Symptoms usually develop 12 to 36 hours after eating the contaminated food. The initial illness also can bring about serious chronic complications.

In 1985, in an incident in Chicago, more than 16,000 people contracted food poisoning from low-fat milk contaminated with Salmonella bacteria. Within two weeks, about 2 percent of these patients developed a chronic reactive arthritis condition linked to the infection. Although the Salmonella bacteria that made these people ill was not Salmonella enteritidis, researchers have found that rats infected with Salmonella enteritidis may develop the same arthritic condition. Researchers are concerned that Salmonella enteritidis may also cause this complication in humans.

Since 1976, says Robert Tauxe, M.D., a CDC expert on the spread of the disease, the reported rate for Salmonella enteritidis infections from food “has increased more than sixfold in the northeastern part of the United States.” First noted in the New England states, the infections also appeared in the mid-Atlantic region by 1983, and now have become a problem in the south Atlantic states as well. Recently, outbreaks were reported in Minnesota, Ohio and Nevada.

The problem also has become an international egg to crack. “The U.S. Salmonella epidemic,” says Tauxe, “is dwarfed by dramatic increases that have been reported from Yugoslavia, Finland, Sweden, Norway, and the United Kingdom.” In Britain alone, the number of confirmed Salmonella enteritidis cases reported for January through July 1988 (4,424 cases) was more than double the number (2,000) for the same period in 1987.

Source: Intact Eggs

At first, says Tauxe, “we did not have an explanation for this striking increase.” The first real clue that intact eggs were a source of the problem came in 1983, when CDC traced a large outbreak caused by Salmonella enteritidis to a commercial stuffed pasta product made with raw eggs.

Investigators then reviewed reports of past outbreaks and determined that at least since 1973, Salmonella enteritidis outbreaks appeared to be caused by the bacteria in clean, uncracked, Grade A eggs.

“In the 1960s,” Tauxe says, “salmonellosis [the disease caused by the Salmonella bacteria] associated with chicken eggs was epidemic in the United States. At that time it was determined that eggs were being contaminated by Salmonella in chicken feces on the outside of the egg shell, which penetrated into the eggs through cracks in the shell.” That led to strict rules, established and enforced by the U.S. Department of Agriculture, for washing and sanitizing shells of commercial eggs.

(Continued on next page)
The Transovarian Transmission Hypothesis

But this new epidemic is associated with *Salmonella enteritidis* in inspected, uncracked and sanitized Grade A eggs. “The infected egg may appear normal,” says Tauxe. The contamination comes from the *inside*, not the *outside*, of the egg.

**How Does Contamination Occur?**

No one knows how some intact eggs become contaminated with *Salmonella enteritidis*. Poultry researchers, however, suggest that the egg yolk becomes infected before the shell forms.

In fact, Charles Benson, Ph.D., of the University of Pennsylvania, says that in his experiments the bacteria were found not in the white, as when organisms penetrate the egg shell, but only in the yolk. This occurred even though Benson added iron to the white to encourage the bacteria to grow in the albumen, which has antibacterial properties.

Madden believes that in the past 10 years a new strain of *Salmonella enteritidis* that can live in chickens may have evolved. Other researchers are finding that *Salmonella enteritidis* bacteria migrate from the yolk to the white of the egg, where they can survive up to 12 hours. However, it is in the yolk where the bacteria multiply and thrive.

These and other findings, such as ovarian infections in egg-laying chickens, have led to the concept of “transovarian transmission.” According to this theory, the infection occurs first in the chicken and is transferred to the egg before the shell is formed.

Researchers also speculate that the infection may be passed from bird to bird in the same flock. For instance, Madden notes that several birds might pick up *Salmonella enteritidis* from the droppings of rodents and sparrows (known carriers of the organism) and spread it among the others. There are also reported cases, Madden adds, of workers picking up the bacteria on their clothing and transmitting *Salmonella* from one chicken house to another.

Only after scientists understand how *Salmonella* is transmitted will they know how to control it. Right now the proposed solution is a long-range plan to prevent spread of the disease by testing flocks and replacing infected ones.

**The Voluntary Model State Program**

The Northeastern Conference on Avian Diseases in 1987 proposed a voluntary model state program, which FDA and USDA then modified. The program calls for state agriculture, veterinary and health officials to work together to test the poultry flocks in their states for *Salmonella enteritidis*.

There are different levels of flocks in the poultry industry, starting with the grandparents. Only 800,000 birds in the United States, owned by five companies, make up these primary breeders. They produce the multiplier, or parent, flocks, which in turn produce the 230 million commercial, egg-laying hens.

The main targets of this massive, nationwide testing effort are the grandparent and parent birds, based on the theory that the infection is passed from mother to chick. Egg-laying hens that have produced eggs implicated in outbreaks or that are offspring of infected parent birds also should be tested.

Under the plan, blood samples are taken from 300 birds per age group in a flock. (The number of birds in a flock can vary from a few thousand to a hundred thousand.) If blood tests from any of the chickens are positive, state officials must take cultures from birds in that flock. The plan calls for destruction of infected flocks.

Another provision in the plan calls for routine culturing of the hens’ cages and litter. Sometimes fertilized eggs don’t hatch, and, under the program, every three months 30 embryos from such eggs should also be cultured.

Under the voluntary plan, eggs from infected flocks are to be pasteurized (broken and heat processed) to destroy the bacteria. There is no evidence that *Salmonella enteritidis* survives pasteurization. Pasteurized eggs are used in many commercial food products, such as baked goods.

**Making Testing Mandatory**

The effectiveness of the voluntary program depends upon producers’ willing-
ness to test and, if necessary, replace infected flocks. However, according to Madden, the increase and spread of the problem suggest that producers and states are not following the program.

Because of this concern, Madden announced at the annual meeting of the U.S. Animal Health Association on Oct. 31 that FDA is working on a regulation to require mandatory testing. The United States would not be the first to have such a program; the United Kingdom instituted a mandatory plan in March 1989.

The testing program that FDA is reviewing would target both breeder and commercial egg-producing flocks. In addition, the proposed regulation under consideration when this article went to press would tighten requirements of the current program by specifying organ specimen size and culturing media used.

"It would leave little room for discretion," says Madden.

Under the voluntary program, producers could choose to send their samples to industry-owned laboratories certified by state agriculture departments under the National Poultry Improvement Program. (NPIP is a cooperative state-federal agriculture program, established in 1935, that already has in place the mechanism for reporting diseases spread by poultry.) Or, producers could choose to send culture samples to private laboratories certified by USDA under the voluntary model program.

USDA responded to the increasing concern over the Salmonella enteritidis problem by passing an interim rule on Feb. 16. The regulation, which allows for a 60-day comment period but went into effect immediately, makes testing of primary and multiplier flocks mandatory. Much of the work will be done through NPIP.

**Backing of Law**

FDA also has the backing of law to attack the Salmonella enteritidis problem. The Public Health Service Act authorizes FDA to take steps to "prevent the introduction, transmission, or spread of communicable diseases." Under this provision, the agency can issue regulations requiring flock testing and certification before the eggs can be shipped in interstate commerce.

Another law supports the mandatory program. Under the Food, Drug, and Cosmetic Act, the agency can seize products of a diseased animal. If an egg producer does not want the eggs destroyed, FDA can request a court order requiring that the eggs be pasteurized.

**Egg Industry Cooperation**

At the same time that FDA and USDA have been working on regulations for mandatory testing, the egg industry has been developing its own quality assurance program. Ken Klippen, vice president of the United Egg Producers (a federation of regional cooperatives representing most of the laying-hen producers in the United States), says that UEP is drafting a new food safety plan. The program will address the Salmonella enteritidis problem and will be "a brand new thrust for the industry," says Klippen.

To the producers of the 67 billion eggs marketed in the United States every year, Salmonella enteritidis is an economic as well as a public health issue, as FDA acknowledged at the September 1988 public hearing on Salmonella and eggs.

Resolving the economic issue will be difficult. Most breeders and egg producers have been seeking USDA indemnification, or reimbursement, for flocks that are destroyed. USDA's responsibility, however, is limited to protecting agriculture, livestock and poultry. For instance, while hens infected with Salmonella enteritidis often do not become noticeably sick, in the 1983 avian influenza outbreak sick hens died and there was a significant mortality in the infected flocks. In the avian flu case, says USDA, indemnification was the appropriate response.

**67 Billion Eggs**

Despite the hard times egg producers are facing, eggs continue to be an inexpensive and important source of protein. According to UEP, the average American eats 250 eggs a year. A survey from the market research group Technical Assessment Systems finds that 90 percent of the population eat eggs in some form each day. (This includes eggs contained in foods like baked items and egg noodles.)

Nearly 5 percent of Americans surveyed said they either ate raw eggs daily or could not specify whether the egg consumed was raw or cooked. Raw and lightly cooked contaminated eggs are causing the illnesses. Thorough cooking kills the bacteria. (See accompanying article, "Safe Egg-Cooking Tips.")

According to Madden, a person can become ill after eating only a small amount of a contaminated egg. For instance, he says, one New York incident involved a family who cooked three eggs sunny side up. The yolk of one egg broke onto the other eggs during cooking, and all three family members became ill.

Madden explains that the one broken egg was probably responsible for all three illnesses, as it is extremely unlikely...
**Safety Tips**

**Egg Cooking**

The elderly, patients already weakened by serious illness, and people with weakened immune systems (such as persons with AIDS) are at high risk for death or serious illness from *Salmonella enteritidis*. Nursing home, hospital, and other food institutions serving those in high-risk groups should *strictly* follow these safe egg guidelines, which also apply to all home preparation.

You can't tell a good egg from a bad egg by the way it smells, tastes or looks. But, these precautions can help minimize risks:

- Review recipes, and consider using pasteurized eggs instead of shell eggs whenever possible.
- Avoid serving raw eggs and foods containing raw eggs. Caesar salad, Hollandaise sauce, homemade ice cream, homemade eggnog, and homemade mayonnaise are possible carriers of *Salmonella enteritidis*.
- Lightly cooked foods containing eggs, such as soft custards and French toast, may be risky for those in high-risk groups.
- Cook eggs thoroughly until both the yolk and white are firm, not runny. These cooking times are now recommended by researchers at Cornell University:
  - Scrambled—1 minute at 250 degrees Fahrenheit
  - Poached—5 minutes in boiling water
  - Sunny side—7 minutes at 250 F or cook covered 4 minutes at 250 F
  - Fried, over easy—3 minutes at 250 F on one side, then turn the egg and fry for another minute on the other side
  - Boiled—7 minutes in boiling water.

**Handling Practices**

- Wash hands with hot, soapy water, and wash and sanitize utensils, equipment (such as blenders), and work areas before and after they come in contact with eggs and uncooked egg-rich foods.
- Use only Grade A or better eggs. Avoid eggs that are cracked or leaking.
- Discard the egg if any shell falls into the egg.
- Leave eggs in their original carton, and store them in the main section of the refrigerator—not the egg section in the door, as the temperature in the door is higher.
- Never leave eggs or egg-containing foods at room temperature for more than two hours, including preparation and serving (but not cooking) times.
- When refrigerating a large amount of a hot egg-rich dish or leftover, divide it into several small shallow containers so it will cool quickly.
- Cook scrambled eggs in batches no larger than three quarts. Hold for serving at 140 F or hotter, such as on a steam table. Do not add a batch of just-cooked scrambled eggs to leftover eggs held on a steam table. —D.B.

that more than one egg per container would be contaminated. In fact, only 1 in 200 eggs from an infected flock may be contaminated. The risk is even lower for all eggs—only 1 in 10,000 eggs on the supermarket shelves are likely to be contaminated with *Salmonella enteritidis*.

*Salmonella enteritidis* grows quickly, presenting another danger for spread of the disease when a contaminated egg is mixed with clean eggs, such as when eggs are pooled to make scrambled eggs for a group of people. One organism can multiply into millions in an egg stored at 60 degrees for two days. Eggs should always be stored in the refrigerator and only taken out just before use.

Scientists around the country are trying to find out what refrigeration temperatures are most effective for stopping the growth of *Salmonella enteritidis* in eggs. They are also investigating the cooking times and temperatures required to destroy the bacteria.

FDA and USDA officials are conducting a public health campaign to spread information on what they know so far about safe cooking and handling of eggs. Over 50,000 bulletins have been distributed to consumers, food service establishments, and institutions that take care of people particularly vulnerable to *Salmonella enteritidis* infections. For copies of the materials, contact USDA, Agricultural Marketing Service/Information Staff, P.O. Box 96456, Washington, D.C. 20090-6456.

Cold weather seems to slow the growth of *Salmonella enteritidis*. Jack Guzewich, the New York state health department’s chief of food protection, notes that in New York 75 percent of outbreaks and 95 percent of illnesses have occurred in the summer. Scientists are working now to solve some of the microbiological mysteries, and officials are trying to resolve the administrative issues before warm weather sets in.

"Are we going to wipe out *Salmonella enteritidis* from the face of the United States?" asks USDA researcher Charles Beard, Ph.D. "I doubt it," he says. "I don’t think the rodents and birds would agree to that." Eradicating the bacteria may be impossible, but joint efforts of FDA, USDA, CDC, and industry are aimed at controlling the spread of this newly recognized danger.

Dale Blumenthal is a staff writer for FDA Consumer.
Overweight is a hefty problem in the United States. It's estimated that 24 percent of men and 27 percent of women in this country—about 34 million adult Americans—are obese. And sometimes it seems that there are 34 million different diets or diet products promoted to combat the problem. The latest to win the nation's fervent attention is a revival of a sort—a return to very low calorie diets, generally 400 to 800 calories per day.

Very low calorie, or "modified fasting," diets, as they are sometimes called, are not a new concept. Protein formula products (either liquid or powdered) were popular more than a decade ago until serious health effects—including several deaths—dampened the public's enthusiasm and led to new federal requirements for labeling of these products (see accompanying article, "Protein Diet Warning").

New Product, New Program

The modified fast regimen is enjoying renewed popularity, but today's very low calorie diet products differ markedly in both content and use from those of the past. While many of the formulas of the '70s were directly available to consumers through supermarkets and other retail outlets, the newer products are sold only to doctors or hospitals for use in medically
supervised programs that include frequent medical examinations and behavior modification training.

Some dieters using the old products subsisted on as few as 300 calories per day of a nutritionally deficient product consisting primarily of a poor-quality protein (usually a hydrolyzed gelatin). Unlike the old diet formulas, today's Optifast, Medifast, HMR, and similar products contain a high-quality protein (egg white- or milk-based), carbohydrates, and some fat and are supplemented to meet recommended dietary allowances for vitamins, minerals and electrolytes. They are not a panacea, however, and, as the American Dietetic Association recently warned, they are not for everyone.

The comeback of very low calorie diets had been fairly quiet until last winter, when they were catapulted into the limelight by talk show host Oprah Winfrey. With some flair, Winfrey demonstrated on national television how she won the battle of the bulge with Optifast. Carting 67 pounds of animal fat on the television set to dramatize how much extra weight she had been carting around in her body pre-Optifast, Winfrey made quite an impact on her viewers—and many more of the nation's dieters who learned about her transformation from newspapers, magazines, television, and radio.

That Lean and Healthy Look

Shedding that 67 pounds not only took inches from Winfrey's torso, it may add years to her life as well. For the problem of obesity is not simply a matter of whether a "slim, svelte" look is or is not more appealing than one that's "pleasingly plump." Observations from the famous Framingham Heart Study, in which several thousand members of the small Massachusetts town have been followed medically since 1948, have shown that a 20 percent excess over ideal weight constitutes a health risk.

Overweight has been linked to a long list of health problems—high blood pressure, respiratory problems, nighttime sleeplessness and (resulting daytime sleepiness), heart disease, diabetes mellitus, elevated blood lipids, gallstones, arthritis, and some cancers—including that of the breast, endometrium and gallbladder in women, and colon, rectum and prostate in men.

Like Winfrey, "Karen," who asked that her real name not be used, has been battling the bulge for years. A 41-year-old registered nurse, Karen has been on one diet or another almost continuously since she was 15 years old, losing and regaining pounds for 26 years.

The Program

And, like Winfrey, Karen lost 67 pounds on Optifast. Hers was a 20-week program that consisted of 12 weeks of "fasting," six weeks of "reefing," and two weeks of maintenance. During the fasting phase, Karen subsisted on five packets a day of an 85-calorie powder formula reconstituted with water or a very low calorie diet beverage with no sodium or caffeine. She also took a potassium supplement daily. (An 800-calorie diet is prescribed for some people—for example, for medical reasons or for very active overweight men who require more calories to get through the day.) Solid food was gradually introduced over the next six weeks, and the final two weeks were devoted to maintaining weight. Karen had blood tests done every other week throughout the program to check sodium, potassium, and other blood chemistries, and an electrocardiogram once a month to check for heart abnormalities.

Also integral to the program—and mandatory—was nutrition education and behavior modification training with a psychological component to help overeaters examine why they overeat and how they can replace their food dependency with other pleasurable activities, such as exercise, reading, or listening to music. The program has been modified slightly since Karen took it three years ago, but it and other medically supervised very low calorie diet programs remain similar in content, calories, recommended length of use, and cost.

A 67-pound weight loss in 20 weeks sounds pretty good, doesn't it? But before you lace up your running shoes to dash out and sign yourself up, consider the following—the program may not be for you. To begin with, you may be screened out. You must be a certain amount overweight; in Karen's program, entry criteria are at least 50 pounds or 30 percent over ideal weight. People with a history of certain medical problems—such as liver or kidney disease, heart
failure, cancer or Type I (insulin-dependent) diabetes—may not be accepted. Even if you qualify, when you learn the cost, you may want to screen yourself out—the range is generally from $100 to $150 a week. This includes all aspects of the program—the formula, supplements, medical exams, and behavior modification training.

And then there’s the “C” word—commitment. In a recent issue of the International Journal of Obesity, Marvin A. Kirschner, M.D., and his colleagues at Newark Beth Israel Medical Center, N.J., reported that of 4,026 morbidly obese patients (at least 100 pounds over ideal weight) who began the Optifast program, one-fourth dropped out within the first three weeks.

Results: Good and Bad

What about the 3,020 men and women who stuck it out? Sixty-eight percent lost considerable weight but did not reach their goal, and only 5 to 10 percent of them had maintained the weight loss after 18 months. The 32 percent who attained their goal by program’s end proved to have greater staying power; 30 percent of the women and 58 percent of the men kept off the pounds for at least 18 months.

Kirschner and colleagues reported lightheadedness and tiredness as the most common complaints among dieters early on in the fast. The most common late complaint was a mild transient hair loss, experienced by about 10 percent of the participants. There were two cases of acute gout; two cases of foot drop, which the authors speculate were due to sciatic nerve compression from leg crossing during or after weight loss; and four cases of acute psychosis. One patient developed a rapid heartbeat due to low blood sugar, which was corrected with intravenous glucose, and two patients were hospitalized for irregular heartbeats.

Other known adverse side effects of rapid weight loss include cold intolerance, dry skin, constipation, potassium deficiency, excess uric acid in the blood, gallbladder inflammation, and psychological changes ranging from elation to depression.

On the positive side, Kirschner and colleagues found that complications of obesity among the group—including high blood pressure, Type II diabetes mellitus, and elevated blood lipids—improved markedly. Unexplained sudden deaths, such as occurred with use of protein products in the 1970s, have not been reported with use of the improved formulas.

The American Dietetic Association is cautious about fasting diets, nevertheless. In a statement released in May 1989, the association noted the serious health hazards posed by very low calorie diets and warned that they should be undertaken “only with the supervision of a multidisciplinary health team that includes monitoring by a physician and nutrition counseling by a registered dietitian.”

According to the association, very low calorie diets have poor long-term results: “Evidence shows that a high percentage of dieters regain over half the weight lost in the program.” To improve these statistics, the association encourages follow-up with continued nutrition counseling, increased aerobic exercise, relaxation techniques, and behavior modification.

Behavior Therapy—Key to Success?

In a study of 59 subjects, Thomas A. Wadden, M.D., and Albert J. Stunkard, M.D., of the University of Pennsylvania School of Medicine compared the effectiveness of three different weight-loss regimens: very low calorie (400 to 500 calories) diet alone, behavior therapy with a 1,000- to 1,200-calorie diet, and very low calorie diet plus behavior therapy. After following the dieters for one year, they concluded that:

• Weight is regained rapidly after treatment by very low calorie diet alone.
• Behavior therapy produces favorable long-term results when used with either a conventional 1,200-calorie diet or a very low calorie diet.
• Weight lost in behavioral treatment is associated with improved psychological functioning.

Karen knows well the problem of regaining weight. According to her, getting the weight off is not the issue. “Most very heavy people have gained and lost weight millions of times,” she says. They know how to lose weight. They don’t know how to maintain weight.”

She describes the “refeeding” phase of the Optifast program as a type of re-entry process. “Okay, now you’re allowed a
Protein Diet Warning

WARNING: Very low calorie protein diets (below 400 Calories per day) may cause serious illness or death. Do Not Use for Weight Reduction in Such Diets Without Medical Supervision. Not for use by infants, children, or pregnant or nursing women.

In the spring of 1984 the Food and Drug Administration published a final rule in the Federal Register requiring that the above warning appear on protein products promoted for weight reduction.

The new regulation grew out of numerous reports of deaths associated with the use of very low calorie weight reduction regimens beginning in the late 1970s. An investigation by FDA and the federal Centers for Disease Control revealed a pattern of sudden death or death from irreversible abnormal heart rhythms in people who had been dieting for prolonged periods and had lost large amounts of weight.

Of the first 58 reports, 17 deaths were of relatively young people (average age 35 years) who had no underlying disease to which the deaths could have been attributed. Six of the dieters died suddenly, six died in the hospital (having been admitted after fainting), and five nonhospitalized dieters suffered cardiac arrest.

In 13 of the cases, the dieters' total caloric intake came solely from a liquid collagen or gelatin protein solution. Two patients supplemented their liquid protein once a day with a high-quality protein food. The remaining two used powdered products of a high-quality protein, one containing mineral supplements.

No single brand product was used by more than two individuals. The daily caloric intake for all dieters was from 300 to 400 calories, and all took a vitamin or vitamin-mineral supplement. Twelve of the dieters were under some form of medical supervision, ranging from thorough to infrequent follow-ups without laboratory tests.

In December 1977, FDA first proposed to require warnings on the labels and labeling of protein products for weight reduction, and the following December a tentative final rule was published in the Federal Register. The final rule, requiring three different warnings for protein products deriving more than 50 percent of their total caloric value from protein, was published in April 1980.

A month after publication, the Council for Responsible Nutrition—a trade association whose membership includes manufacturers of dry, whole-protein products—filed suit to invalidate the labeling regulations. Although the court upheld FDA's overall labeling plan, it decided against the agency, finding insufficient evidence to support FDA's finding that diets between 400 and 800 calories per day may cause serious illness or death. So, the court ordered the regulation back to FDA for further study and reformulation.

In the Federal Register of June 11, 1982, FDA proposed a revised rule for protein product labels. After reviewing comments received in response to the new proposal, a final rule was developed. It became effective Aug. 6, 1984. The rule concerned label requirements for "any food product in liquid, powdered, tablet, capsule, or similar form that derives 50 percent of its total caloric value from either whole protein, protein hydrolysates, amino acid mixtures, or a combination of these, and that is... promoted for use to reduce weight."

Protein products are exempt from the labeling requirements if the product is represented as part of a nutritionally balanced diet plan providing 400 or more calories per day and the label specifies the diet plan in detail or briefly describes the plan and provides information on where it can be obtained. In this case, the label must bear the following statement: "NOTICE: For weight reduction, use only as directed in the accompanying diet plan (the name and specific location in labeling of the diet plan may be included in this statement in place of 'accompanying diet plan'). Do not use in diets supplying less than 400 calories per day without medical supervision."

FDA, as a regulatory agency, does not formally approve diet plans. Unlike drugs, foods do not require pre-market approval. An agency talk paper released Dec. 30, 1982, in response to inquiries about the safety of extremely low calorie diets, stated that "There is a general consensus among nutrition and obesity control experts that extremely low calorie diets—diets providing less than 400 calories per day—are physiologically unsound regardless of their overall nutrient composition."

The paper further stated that there is also a consensus among these experts that diets providing less than 800 calories per day should be used only under proper medical supervision, and that "FDA concurs with the consensus."
Going It Alone

FDA's division of nutrition deputy director Victor Frattali, Ph.D., is wary of fasting diets in general. He is especially concerned, however, about dieters who use very low calorie diet products without medical supervision. He says there are two critical factors to consider in very low calorie diets: the quality of the product and the directions for use. "The powder or liquid in the newer products that are sold directly to consumers may or may not provide all the nutrients you need," says Frattali, "but even if they do, I have serious concerns about diets of less than 800 calories per day."

FDA's position is that diets of less than 800 calories a day should be undertaken only with proper medical supervision, and Frattali maintains that, in fact, almost anyone can lose weight on 1,200 calories a day.

Nutritionist Marilyn Stephenson of FDA's Office for Nutrition and Food Sciences says a reasonable goal for weight reduction is to lose a pound or so a week. To lose one pound of fat a week, food consumption must be reduced by 500 calories a day.

"A 1,000- to 1,200-calorie-per-day diet should be combined with increased physical activity, which raises your metabolism, [burns more] calories, and improves physical fitness," Stephenson advises. "For many people, simply eating smaller portions of the foods usually eaten, keeping fried and other fatty foods and rich desserts to a minimum, and exercising more is an appropriate approach to weight loss and weight maintenance."

Stephenson also advises consulting a physician and then, if possible, a nutritionist or dietitian before beginning a diet. This is especially prudent for people who have a medical condition or have many pounds to lose. Certain diets pose serious health hazards for people with some diseases such as diabetes or intestinal disorders. (For more on diets and weight loss, see "Diet Books Sell Well but..." in the March 1982 FDA Consumer.) —M.S.
Bovine Growth Hormone Harmless for Humans

by Beverly Corey, D.V.M.

Generations of Americans have been told that "Milk is nature's most perfect food," and the nutritional value of milk supports this claim. Milk sustains infants and is also beneficial to adults, including the elderly. Many people begin the day with it—by the glass, in cereal, coffee, and in baby's bottle. And because it is perceived as perfect and essential, some consumers and processors of milk products are highly uneasy about the decision of the Food and Drug Administration to allow marketing of milk from experimental herds injected with bovine growth hormone, also known as bovine somatotropin, or bST.

Some consumers suspect that this hormone, even if not harmful, at least detracts from the "purity" of milk. Such skepticism has many sources, ranging from a desire to protect children and an uneasiness about "nature-altering" biotechnology, to the underlying apprehension that life-sustaining gifts of agriculture are becoming polluted by chemistry. (See "Perspective on Food Biotechnology" in the March 1990 FDA Consumer.)

Writing not long ago about chemical firms that want to market bST, Milwaukee Journal columnist Joel McNally captured the public's wary state of mind: "Consumers," he wrote, "might have second thoughts about... milk enhanced by the same companies that gave us such taste treats as vinyl chloride and polystyrene."

Adverse publicity has made bST a hot political issue among dairy farmers, particularly in Wisconsin, Minnesota and Vermont, many of whom demand that the hormone be banned. At a meeting in Washington, D.C., last summer, Jeremy Rifkin, president of the Foundation on Economic Trends and a frequent critic of biotechnology, launched a campaign (the second in three years) against bST as a potentially dangerous drug "with no redeeming social value." He was joined by consumer, animal welfare, and environmental groups, as well as 40 public officials. The grass-roots pressure resulted in a partial boycott of milk produced by experimental herds that receive injections of the growth hormone in clinical animal studies being performed by commercial sponsors of the drug.

Subsequently, the supermarket chains of Safeway, Kroger, Stop & Shop, and Vons last August said they had agreed to not market milk from the bST-supplemented cows, and Kraft USA, Borden's, and Ben & Jerry's Homemade (the Vermont ice cream maker) announced they would not use it in their products. The country's largest dairy cooperative, Associated Milk Producers Incorporated, issued a statement that its 21,000 members will not give the hormone to their cows.

"People are nervous about this substance," says Alan Parker, the Ben & Jerry's spokesman. Coming on the heels of the widely publicized concerns about Alar—the growth regulator for apples whose cancer-causing metabolites resulted in the manufacturer withdrawing it from the market—the experiments with bST, in Parker's view, made many "consumers feel that they're losing contact with their food."

Unfounded Fears

BST is biologically inactive in humans. FDA concluded almost five years ago, based on extensive scientific investigation, that milk and meat from bST-supplemented experimental dairy cows may be used for human consumption without causing a risk to the public health. Fears about the growth hormone's effect on human health do not withstand close scrutiny.

Furthermore, talk about "natural" milk in the American marketplace is a piece of nostalgic fiction. Gone are the days when one consumed milk in the "natural" state in which it was drawn from the udder. Milk that is pasteurized to destroy bacteria, homogenized to evenly distribute fat, and fortified with vitamin D to improve nutritional qualities is the result of technological advances. Skim and low-fat milk are supermarket best sellers. Even the recent introduction of unrefrigerated ultra-long-life milk, yet another type of processed milk, represents the application of current technology to milk, and it has met little consumer resistance.

Some scientists believe that bST will ultimately benefit the dairy industry—as have the application of other technologies—by increasing the efficiency of milk production and controlling the retail prices of milk and dairy products to consumers.

BST is a natural product of the pituitary gland of cattle. It stimulates growth in immature cattle and, as a Russian scientist first noted in 1937, it increases milk yield in lactating cows. Research on the substance until the early '80s was stymied by shortages of bST, which could only be extracted from slaughtered animals and varied in purity. In recent years, however, newly perfected genetic engineering techniques have enabled sci-
entists to produce the hormone in sufficient quantity and quality for intensive study. The early findings that bST increases milk production 10 to 25 percent gave the hormone such economic potential that four firms—Monsanto, American Cyanamid, Upjohn, and Elanco—applied to FDA for marketing approval for their brands of genetically produced bST.

Grounds for Decision

Before FDA allows the full-scale commercial marketing of bST—or any new animal drug—the manufacturer must provide sound scientific data showing that its bST product is effective for the proposed use (increasing milk production) and causes no safety concerns for human or animal health. The sponsor must also provide adequate data on the environmental impact of the drug’s use. However, in the meantime, FDA has allowed the marketing of meat and milk from bST-supplemented cows in experimental herds because it has determined that these foods meet the requirement of federal law. Federal law permits the commercial sale of food products from animals in investigational studies only when the sponsor has demonstrated that they present no public health risk. Some of the main scientific grounds for FDA’s decision are:

• Bovine somatotropin is a protein hormone, and this means that when a product containing bST is eaten, it breaks down during digestion in the gastrointestinal tract into inactive fragments without any effect on the person (or cow) who ate it. That is why cows must be injected with bST for it to be effective.

• Experiments with rats have shown that they are unaffected by oral administration of bST. Rats are an appropriate model because bST is biologically active in rats when injected. Thus, any bST escaping digestion in the rat would have biological effects, such as effects on growth.

• Studies indicate that bST is not effective in humans and other primates even if injected. In the 1950s, physicians tried to treat human dwarfism in children by injecting them with bovine somatotropin, but it had no effect because the amino acid structure of human somatotropin is 35 percent different than bST.

• BST is a natural constituent of milk. It is produced by the pituitary gland and has always been present in the meat and milk of cows. The bST injected to increase milk production merely increases the amount to which the cow is exposed.

• Supplementation with bST does not significantly affect the nutritional qualities of milk or interfere with milk processing. Subtle changes, primarily in the milk fat, occur in the first few weeks of bST supplementation due to metabolic adjustments in the cow. However, this is temporary, and because it occurs to some degree during early lactation in untreated cows the milk contains milk fat well within the normal composition range.

Other studies have shown that bST has minimal, if any, effect on the remaining components and characteristics of milk, including protein, minerals, protein coagulation, cholesterol, starter cultures, and flavor. In fact, FDA scientists are not aware of any technology that can detect a difference between milk and dairy products from bST-supplemented cows and similar products from untreated cows.

Other Considerations

There is, however, at least one area of controversy concerning bST that, under the law, FDA may not consider in making its approval decision: the potential social and economic impact of the growth hormone on the nation’s dairy farmers. According to the drug’s opponents, the lower prices of a more plentiful milk supply will adversely affect thousands of small dairy farms in an already precarious economic situation.

Fear for the continued existence of family farms has fueled the opposition to the growth hormone in the dairy states and increased support for activist Rifkin’s anti-bST campaign. Rifkin was back in Washington this past January once again to claim that bST is, among other things, bad for farmers, cows and taxpayers. In support of family farms, Ben & Jerry’s Homemade, which buys milk from small Vermont producers, last August placed on its ice cream containers a sign opposing the hormone and calling for the preservation of small farms. Since then, the firm has received more than 1,000 requests for more information on the issue.

On the other hand, many bST supporters realize that dairy farming has changed a great deal since the 1950s—largely as a result of technological innovation—and believe that further changes in the industry are inevitable due to emerging technologies.

It does appear that even after FDA answers all scientific questions about bST and reaches a decision about its approval for general use in the nation’s dairy cattle, it may continue to be a controversial topic. However, one thing is certain. Bovine somatotropin will not be approved for commercial use unless, and until, FDA is completely satisfied that scientific data show that it meets all safety and efficacy requirements for commercial marketing.

Beverly Corey is a member of FDA’s speechwriting staff.
BY JEFFREY P. COHN

Duzenack looked down and grimaced. It was 5 o'clock in the morning on a dark, dreary day in Valdez, Alaska, last July. And it was a good 30 feet down a wet, slippery metal ladder from the weathered dock where a tired Duzenack stood to the pitching deck of the fish tender below. Duzenack had worked until midnight the previous day and would have liked to get more sleep, but the tender's load of freshly caught salmon was waiting his inspection.

PHOTOS: BLACK STAR, INC. (Continued on page 21)
A B O A R D  T H E  F I S H
T E N D E R S ,  F D A
I N V E S T I G A T O R S  H E L P E D
A L A S K A N  O F F I C I A L S  K E E P
C O N T A M I N A T E D  F I S H  F R O M
R E A C H I N G  T H E  M A R K E T .
O P P O S I T E ,  F D A ' S  B R U C E
S T E R L I N G  ( L E F T )  A N D
D E B R A  D E V L I E G E R  S E L E C T
F I S H  F O R  O R G A N O L E P T I C
A N A L Y S I S .  B E L O W ,  L E F T,
D E V L I E G E R  S N I F F S  S A L M O N
B E L O W ,  R I G H T ,  S A L M O N  I S
P L A C E D  I N  A  H O L D I N G
T A N K  O F  R E F R I G E R A T E D
S E A  W A T E R .

(Continued from page 19)

So, wearing awkward rubber boots and a two-piece rubber rain suit as protection from the steady drizzle, down the ladder Duzenack went, onto the tender’s slick deck, and, after a quick look around, down yet another wet metal ladder into the ship’s hold. There, he looked over the walls and floor of the now-empty hold for signs of contamination. “Fine,” Duzenack yelled, “there’s no oil here.”

Duzenack was one of more than two dozen investigators, scientists and advisors the U.S. Food and Drug Administration sent to Alaska in 1989. Their job was to help state officials ensure that no fish or shellfish contaminated by the March 24 oil spill in Prince William Sound near Valdez got into food intended for human consumption.

“Our role was primarily that of assisting the Alaskans,” says Roger Lowell, director of FDA’s district office in Seattle, Wash. “We also wanted to assure consumers that there was nothing of concern about the quality of seafood from Alaska.”

New Twist to Old Job

Inspecting seafood and cannery operations in Alaska is nothing new for FDA. The agency maintains a one-person office in Anchorage, which is under the Seattle office’s jurisdiction. Both offices regularly send investigators to visit seafood processing plants in the nation’s largest state during the commercial fishing season. Their job is to ensure compliance with FDA’s wholesomeness, cleanliness and labeling requirements under the Food, Drug, and Cosmetic Act.

But 1989 was different. The oil tanker Exxon Valdez altered the focus of FDA’s routine seafood inspections when it ran aground on Bligh Reef off Alaska’s southern coast a few minutes after midnight that early spring morning. Within hours, more than 10 million gallons of crude oil had washed into one of the state’s richest fishing grounds. And it happened only weeks before the anticipated start of Alaska’s commercial fishing season—April for herring, early May for halibut, and June through September for salmon.

Recognizing the need for a coordinated effort by federal and state agencies to make sure no oil-contaminated seafood reached consumers, Lowell and other FDA officials met with their counterparts from the National Marine Fisheries Service (NMFS) and from the Alaska Departments of Environmental Conservation (ADEC) and Fish and Game. Separately, the U.S. Coast Guard, Environmental Protection Agency, Fish and Wildlife Service, and other federal agencies helped Alaska oversee Exxon’s cleanup efforts and monitor the oil spill’s effects on the environment.

The federal and state officials quickly agreed that a completely open fishing season would soon overwhelm the ability of investigators to keep up with the catch, says Douglas Donegan, ADEC’s director of environmental health. Instead, they decided to ban commercial fishing in obviously contaminated waters. The Alaska Department of Fish and Game, along with NMFS, was charged with judging which waters to close or open for fishing.

Fishing Limited

In all, one-third of Prince William Sound was closed to commercial fishing by the state in 1989. Even greater restrictions were placed on fishing around Kodiak Island off Alaska’s southwestern coast, where only one-eighth of the waters normally fished were opened.

In large part because of those restrictions, less than 50,000 pounds of oil-contaminated fish were found in 1989, Donegan says. That compares with 696 million pounds of salmon caught in 1989 alone, a state record according to Alaska Department of Fish and Game data.

Further, federal and state officials decided to destroy all oil-contaminated fish caught in waters where fishing was allowed. They also designated ADEC to oversee and coordinate all seafood inspections. But, since ADEC’s work force was already stretched thin by the oil spill,

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ABOVE, OIL PATTERNS THE WATER OF PRINCE WILLIAM SOUND NEAR THE SITE OF THE SPILL. ON THE LEFT, OIL-DISCOLORED ROCKS IN HERRING BAY NEAR ELEANOR ISLAND, AN AREA HEAVILY AFFECTED BY THE SPILL.

WORKERS USE HOSES DURING CLEANUP EFFORTS ON ELEANOR ISLAND IN PRINCE WILLIAM SOUND.
and its aftermath, Lowell says FDA agreed to supply additional investigators, train inexperienced ones, conduct inspections usually done by Alaska officials, and assist ADEC and NMFS with laboratory analyses.

FDA sent 22 investigators to Alaska in 1989, says James Davis, director of investigations for FDA’s Seattle district office. They spent a total of about 90 weeks in the state last year, more than double the time usually allotted. And their expenses ran to $100,000, triple the amount budgeted.

“We assigned people to Alaska who normally would not have gone,” Davis says. “We had them stay in towns for days and weeks at a time rather than [conduct] their usual one- or two-day inspections. Our people worked night and day. They were on site around the clock.”

Alaskan Adventures

For Al Duzenack, a 58-year-old compliance officer who has been with FDA since 1960, there were times when he wondered “what in the world is an old man like me doing here?” He had been to Alaska for FDA before, but not since 1986 and never for four weeks at a time. And, as Gerald Eastwood, FDA’s resident investigator in Alaska, says: “You find out how resolute you are up here.”

Duzenack’s day typically began at 4 or 5 a.m when the first fish tenders, vessels that collect the catches of several smaller fishing boats, arrived at the dock. The tenders continued coming throughout the day and well into the evening, sometimes even up to midnight. Fortunately, Duzenack usually knew hours in advance when the tender was due because they were tightly scheduled according to the freshness of their load, weather conditions, and prevailing tides.

After examining the tender and its equipment and hold, Duzenack watched as some 40,000 to 200,000 pounds of fish were unloaded onto conveyer belts for processing. He sampled 200 fish from each tender using sight, smell, touch—but especially smell—to check for signs of oil contamination. If clean, the fish were processed except for three from each tender; these Duzenack sent for chemical analysis to ADEC’s laboratory in Palmer, Alaska, about 30 miles northeast of Anchorage.

If any fish tested by such sensory means, known collectively as organoleptic analysis, seemed contaminated, Duzenack could order the entire tender load detained under authority usually held by the state, but granted FDA last year by Alaska. The seafood processor could still accept and process the suspect load, but had to separate the fish from other tender loads and hold them pending analysis at Palmer. If chemical tests confirmed what Duzenack sensed, the whole load had to be destroyed. If no contamination was found, however, the fish could be shipped for consumption.

Duzenack never found any confirmed cases of oil contamination, but he did manage to “lose” a fish tender once. When he examined the tender, he noticed an oil sheen on its brine, water in the ship’s hold chilled to keep fish fresh until processing. When Duzenack pointed out the sheen, the processor refused the load, and the tender pulled away from the dock. Duzenack went on to inspect other loads, intending to collect samples later that day from the tender, which was supposed to tie up in the harbor.

When he returned to the harbor, however, the tender was nowhere to be seen. After the harbor master tried to contact the tender but got no response, the Alaskan Department of Fish and Game began looking for the vessel and Exxon sent out its search planes.

Hours later the tender reappeared, this time with no visible oil sheen. Duzenack suspects the oil came from leaky hydraulic equipment, rather than contaminated waters, and the tender simply flushed and refilled its hold with fresh brine at sea to eliminate the sheen.

Flying the Sea Route

Unlike Duzenack, who spent nearly all his time in Valdez, Seattle-based investigator Debra DeVlieger traveled from one Alaskan fishing village to another in 1989 to conduct normal one- and two-day inspections at one processing plant after another. She spends at least two weeks in Alaska every summer, but last year was there for eight.

In addition to Valdez, DeVlieger’s 1989 itinerary included stops at Cordova, Dillingham, Clark’s Slough, Kenai, Eek, Ninilchik, and a host of other places, some more than once. Some of the towns are not even on standard road maps. Indeed, most have no permanent roads and the only way to get there is by air.

“I go in anything that flies,” DeVlieger claims. Sometimes that means regularly scheduled flights aboard four- and six-seater airplanes, but more often she has to charter her own. Moreover, some villages DeVlieger visits have no runways. “Float planes are great,” she says, adding: “There’s a lot more water than land where I go in Alaska.”

Occasionally, flying in Alaska can get scary. Flights are often delayed or cancelled due to bad weather or low ceilings, making travel schedules meaningless. Once when flying into Clark’s Slough on Alaska’s west coast, DeVlieger’s plane landed short of the dirt runway, shearing off its landing gear. The plane continued down the dirt strip on its belly and hit an embankment, tearing apart a wing tip and rupturing both fuel tanks. DeVlieger escaped unhurt, conducted her inspection, and left at 10 o’clock the next evening by fishing boat.

She arrived at Dillingham across Bristol Bay, her next stop, at 1 o’clock in the morning. Luckily, the town’s only hotel had a vacancy. DeVlieger often has to scramble at the last minute for sleeping accommodations. Sometimes she winds up in bunkhouses maintained by seafood processors for their work crews, a pretty rough and rowdy crowd. “You learn to travel light and make arrangements as you can,” DeVlieger says of her life on the road in Alaska.

Beyond inspecting fish tenders and their load, FDA compliance officers and investigators like Duzenack and DeVlieger also look carefully at processing plants and their equipment. They
Sniffing for Oil

Such inspections, the normal fare of seafood investigators in Alaska and elsewhere in the United States, call for observational skills and knowledge of FDA regulations. But spotting signs of oil contamination, the major focus of the 1989 inspections in Alaska, requires using one’s senses of sight, smell, touch and sometimes taste, says Richard Throm, FDA’s leading trainer in organoleptic techniques.

“Organoleptic methods are subjective analysis,” Throm says. “You have to learn to eliminate the biases most people associate with fishery products. Good fish don’t smell bad. A well-trained nose can correctly detect low levels of oil contamination more than 90 percent of the time.”

Throm’s job in Alaska in 1989 was to train the many federal, state and industry inspectors assigned to fishing and seafood processing operations. Nearly all were already experienced investigators, but many usually investigated meat and poultry plants or restaurants, not seafood. Others who sometimes examined seafood were rusty and needed their organoleptic skills refreshed. And most had little or no experience with oil spills.

Throm, who usually goes to Alaska once or twice a summer, went there eight times in 1989. He and his staff gave 12 full-day training sessions in Alaska, plus one in Seattle. At each, Throm had his pupils examine various fish, fishing equipment, and crude oils to show how each changed over time and place following a spill. He also contaminated live fish with varying amounts of crude oil so trainees could see, feel and smell contaminated fish.

The 13 sessions drew from 15 to 40 people each, 330 in all, Throm says. Some were held in Anchorage, but most were in Valdez and other small fishing villages. The latter were designed for individual fishermen, tender operators, and seafood processors rather than federal and state inspectors.

“We wanted to give people we trained a greater confidence in their ability to detect oil-contaminated fish,” Throm explains. “They didn’t know what to expect at first, but some became quite good at detecting low levels of contamination. We felt we were helping Alaska prevent contaminated fish from reaching consumers.”

That was also the goal of much FDA work outside Alaska in 1989. The agency’s Seattle laboratory, for example, added $45,000 worth of new scientific equipment to test fish and shellfish sent from ADEC’s Palmer lab. “We needed to be able to confirm organoleptic and chemical analyses done in Alaska,” says John Wiskerchen, director of FDA’s Seattle lab.

Using methods developed by the nearby National Marine Fisheries Service laboratory in Seattle, FDA and other scientists found few fish with any more than minute traces of oil-derived hydrocarbon chemicals in their tissues in 1989. All contaminated fish that were found had been caught by subsistence, rather than commercial, fishermen, ADEC’s Donegan says.

In addition to obviously contaminated waters being closed to commercial fishing, the main reason so few fish were found to be contaminated was that most fish quickly break down any ingested oil in their gallbladders and excrete the resulting chemicals from their bodies, says Usha Varanasi, director of NMFS’s Seattle lab.

Nevertheless, FDA, NMFS, and other scientists are concerned that lingering oil in Prince William Sound will pose a future threat to fish and, eventually, consumers. “We are developing the baseline data we will need to test for bioaccumulation of oil-derived hydrocarbons in fish tissues” in 1990 and subsequent years, FDA’s Wiskerchen says.

Shellfish Contamination

Of greater immediate concern is oil contamination levels in crabs, shrimp, mussels, clams, and other shellfish. Unlike fish, most shellfish are sedentary, rarely moving far or fast. Thus, they are more susceptible to contamination. More importantly, they do not break down or excrete any oil they ingest the way fish do, Varanasi says.

NMFS does not yet have complete data on shellfish contamination because the main commercial season began only in December, but preliminary findings show marked elevation in oil levels in mussels and clams taken from highly contaminated waters in Prince William Sound. Of particular concern are the effects on Alaska’s subsistence fishermen and their families, many of whom get 80 percent of their diet from seafood.

Based on the preliminary data, an expert panel, created by Alaska’s Department of Health and Social Services in 1989 to assess the oil spill’s effects on Alaskan natives, advised the state that shellfish taken from obviously contaminated waters should be considered unfit for consumption, says P. Michael Bolger, a toxicologist in FDA’s Center for Food Safety and Applied Nutrition. Bolger serves as one of two agency representatives on the panel.

Meanwhile, FDA laboratories are testing different screening methods for examining fish and shellfish for oil contamination, says Gregory Diachenko, chief of the food formulation branch in the Center for Food Safety and Applied Nutrition. “We want to be able to confirm organoleptic, chemical and other analytical results,” Diachenko says.

For now, though, the FDA scientists and investigators who helped Alaska respond to the 1989 oil spill have good feelings about their role in its clean up. “It was a pretty incredible summer,” DeVlieger says. Duzenack agrees, adding: “It was a great experience and I was glad to be a part of an important event.”

As for the future, most sense a need for continuing FDA vigilance. “I expect 1990 to be more of a normal year for us,” Seattle district director Lowell says. “But we will be watching to make sure there is nothing we don’t know about.”

That spirit is also voiced by DeVlieger. Speaking for herself and other FDA inspectors, she says: “The oil spill is not over for us by any means.”

Jeffrey P. Cohn is a free-lance writer in Washington, D.C.
Rosellen Bowen was having a tough time completing her master's thesis. The graduate nursing student was researching whether breast massage would help relieve the pain and discomfort some new mothers experience when they don't breast-feed their babies. But she had trouble finding participants.

During the year she worked on her thesis, over 3,000 babies were born at the University of Rochester Medical School Hospital, where she worked, and the Rochester Community Hospital. But out of the 800 women at these two hospitals who didn't breast-feed their babies, Bowen could only find 46 who said they felt pain when their breasts filled up with milk.

Determining pain is subjective, experts say. But on a 10-point pain scale that Bowen provided for the participants, no mother, at any time, scored pain above a 6.

"She had a lot of trouble completing her thesis with a valid number of patients because [pain] was not a common complaint," says Ruth Law-
ence, M.D., a pediatrician who worked with Bowen. Bowen found that although breast massage did help some new mothers, for most, the long-standing traditional treatment of pain relievers, ice packs, and a well-fitting bra or specially made breast binder was sufficient.

Because other studies have also shown that these traditional treatments provide enough help for the minority of women who do experience pain, and because the drugs used to suppress lactation carry risks, the Food and Drug Administration’s Fertility and Maternal Health Drugs Advisory Committee recently recommended that drugs to prevent milk production not be used. Following the committee’s recommendation, FDA has asked the manufacturers of these drugs to stop including lactation suppression as an approved use.

The major drug used for suppressing lactation is a non-hormonal substance called bromocriptine. It is also used to treat Parkinson’s disease, but because this is a serious disease, the risks associated with the drug’s use do not outweigh its benefits. The other lactation-suppressing products all contain the female sex hormone estrogen, alone or in combination with the hormone testosterone.

Sending a Message
Even when a woman knows long before her baby is born that she isn’t going to breast-feed, her body needs a few non-breast-feeding days after the baby is born to get the message.

In the meantime, milk production begins. First, levels of the hormones estrogen and progesterone, which are very high during pregnancy, drop abruptly after birth. This drop signals another hormone, prolactin, to stimulate milk production in the breast. The milk is produced in cells throughout the breast and then travels through the milk ducts to the openings in the nipple. In a mother who breast-feeds, her baby’s suckling signals the prolactin to keep the milk coming. But when a woman doesn’t breast-feed her baby, the prolactin levels drop, and milk production ceases.

In the few days it takes before lactation...
stops, the mother's breasts can fill up with milk. For some non-nursing women, this engorgement is uncomfortable, and occasionally even painful.

Lactation suppression drugs prevent engorgement and, in fact, prevent lactation before it begins. The most commonly prescribed drug, bromocriptine, acts by cutting the production of prolactin. In contrast, the sex hormones keep the estrogen at pre-birth levels, tricking the body into thinking it is still pregnant.

**Do They Work?**

The National Academy of Sciences/National Research Council (NAS/NRC) reviewed the effectiveness of estrogens and androgens such as testosterone as lactation suppressants approximately 20 years ago as part of a review of all drugs approved before the 1962 drug amendments. (The amendments required, for the first time, that drugs must be effective as well as safe.)

NAS/NRC explained that it did not know of any satisfactory evidence that these drugs could effectively prevent lactation. Nevertheless, since the drugs were commonly used for lactation suppression, the panel decided the indication could be continued.

Evidence on the safety of the sex hormones for lactation suppression is also lacking. (Since the safety problems connected with other uses of these hormones had not surfaced in the 1950s, the indication was allowed at that time.) The risk of thromboembolism has been connected with estrogens used as oral contraceptives. But, according to FDA's Diane Wysowski, Ph.D., "there is a paucity of good, definitive data on the acute and long-term effects of sex hormones used for prevention of postpartum breast engorgement. The bottom line is, nobody really knows."

The same uncertainty about safety and effectiveness surrounds bromocriptine. When FDA approved this drug for lactation suppression, clinical trials had not uncovered any serious side effects and the results of several studies showed that the majority of women given the drug did not experience engorgement. However, what was impossible to determine with these studies was whether engorgement was actually prevented. There is no way to predict whether a woman's breasts will become engorged or, if they do, whether the engorgement will cause pain.

In addition, even when bromocriptine seems to work, the drug's success may be short-lived. According to the official labeling, up to 40 percent of the time, rebound engorgement occurs after the two-week course of treatment with bromocriptine ends.

According to FDA's division of metabolism and endocrine drug products, bromocriptine has been associated with seizures, strokes, and heart attacks, but the connection has not been firmly established. What has been established are bromocriptine's less severe side effects—nausea, dizziness, and drop in blood pressure.

**Benefit vs. Risk**

Based on several different studies, FDA estimates that only a very small minority of women given lactation suppressants may possibly benefit from the treatment. For the majority, taking the drug only exposes them to possible side effects. In August 1989, the Health Research Group, a consumer organization, requested action against the use of lactation suppressants. In its response, FDA said that because the drugs are not therapeutically required, any risks are unacceptable.

What about the side effects from doing nothing to stop milk from coming in? "The side effects of letting nature take its course—breast engorgement, leakage, discomfort—are short-lived," says Lisa Rarick, M.D., an obstetrician with FDA's division of metabolism and endocrine drug products. "Doing nothing is 100 percent effective. It's an issue similar to any physiological problem that resolves on its own, like painful [menstrual] periods."

When you have an adolescent come to your office and she hasn't had a period yet, you don't just automatically give her a prescription to prevent painful cramps. If somebody comes to you and she has the pain, then you treat her."

Where does that leave women who decide not to breast-feed? First, the symptoms can be treated by other means if they occur. According to the University of Rochester's Lawrence, who has written a book for physicians on all aspects of breast-feeding, nonprescription pain relievers such as acetaminophen "seem to take care of women's discomforts. Only rarely is something [stronger] needed."

Second, except for two estrogen drugs that are only used for lactation suppression, all the other products will still be on the market. FDA does not regulate the practice of medicine. Physicians are free to use approved drugs in any way they feel is medically necessary.

Lawrence adds that the risks of letting lactation end naturally "seem to be close to zero. I think in some respects we've assumed that women would rather be medicated than experience any discomfort at all, and that is probably not true." ■

*Dori Stehlin is a staff writer for FDA Consumer.*
Pet Ownership Risky Business?
Sharing homes with pets is a way of life for many Americans—at least 60 percent by some estimates. And the companionship, affection and trust of pets can provide distinct health benefits for their owners.

Studies described at a 1987 National Institutes of Health workshop linked life with a pet with:
• higher survival rates in patients with heart disease
• increased self-confidence and independence in psychiatric patients
• improved ability of children to interact with others.

But if you're a pet owner—or thinking about becoming one—you need to consider that these trusted companions can also present some very real health risks. In addition to giving affection, the millions of household cats, dogs, birds, reptiles, and other small animals can impart diseases to their owners as well.

Zoonosis is a disease communicable between vertebrate animals and humans, and between different species of animals. Some of these diseases have been known for a long time. The ancient Greeks, for example, were aware that rabies could be transmitted through dog bites. And the bubonic plague that decimated the population of Europe in the 15th century bridged the gap from animals (mainly rodents) to people by way of fleas.

Growing List

The list of known animal-transmitted diseases constantly changes, as improved diagnostic techniques identify zoonoses previously mistaken for more common exclusively human diseases. For example, in the 1960s, the role of felines in transmitting toxoplasmosis in their feces was discovered. In addition, travel to more remote parts of the world by people and the increased international commerce in exotic animals have added to the list of zoonoses.

Fortunately, most zoonoses are rare, and almost all can be treated once a diagnosis is made. Here's a list pet owners should be familiar with:

**Toxocara canis**, or roundworm, is a parasite that is carried most often by nursing dogs and their puppies, and less often by cats. Scientists estimate that virtually all puppies have roundworm.

Because children like to play in the dirt, they are most vulnerable to picking up roundworm; and the disease is transmitted through contact with the dog's feces or soil contaminated with it. Symptoms of roundworm in humans are fever, headache, cough, and poor appetite.

So prevalent and well-established is the dog roundworm in our pet population that roundworm-free puppies can only be obtained by raising several generations in isolation or administering repeated high doses of anthelmintics (a type of drug that gets rid of intestinal worms) to the pregnant mother dog.

Diana Post, V.M.D., a veterinarian with the Food and Drug Administration, explains that much of the roundworm infection of the mother dog is non-egg-producing and does not contaminate the environment. However, it is more resistant to elimination with anthelmintic drug treatment than the egg-producing contagious type of infection found in the puppies. Egg-producing infections may be found in adult dogs, although less frequently than in puppies.

For this reason, many parasitologists recommend that veterinarians consider treating very young pups two to three weeks after birth (the time they would be expected to pass infected eggs in their stool). This can be risky, though, because immature animals, including dogs, are very sensitive to any drug therapy. Such treatment should only be undertaken if it is recommended by a veterinarian.

Both puppies and people can be treated with anthelmintics, a class of drugs used in both human and veterinary medicine.

**Toxoplasmosis** is a disease produced by infection with the one-celled animal *Toxoplasma gondii*, a parasite capable of surviving in many different animal species. It is sometimes spread to humans through cat feces or dirt contaminated with cat feces. All breeds of felines, even wild jungle cats, can become infected with *Toxoplasma gondii*. The cat becomes infected by killing and eating small rodents. But most people contract toxoplasmosis not from cats but from eating raw or poorly cooked meat. Meat becomes infected because cows and sheep graze in pastures that have been contaminated by infected cats.

Toxoplasmosis infection is common and can infect almost all species of warm-blooded animals. But most infected people do not develop symptoms because, according to most estimates, about one-third of the world's population has antibodies to the disease. (Infected persons with immune system defects or those receiving immunosuppressive therapy may develop a serious form of the disease.)

Symptoms in humans are fever, headache, swollen lymph glands, cough, sore throat, nasal congestion, loss of appetite, and skin rash. The disease can be treated with antibacterial drugs.

Expectant mothers—especially those in the first three months of pregnancy—should be especially alert to the possibility of this disease because toxoplasmosis can cause miscarriage, premature births, or blindness in unborn children. For this reason, pregnant women should not clean a cat's litter box and should avoid eating raw or poorly cooked meat.

**Ringworm** is a skin disease caused by a fungus, not by a worm as the name would imply. Dogs, horses, cows, and most commonly cats pass the disease on to humans. Only children pick up ringworm. "Long-haired kittens seem especially prone to ringworm," says Post. The fungus infects cat hair, and a younger can contract the disease by petting the kitty. Ringworm can be diagnosed by exposing the animal to a Wood's lamp, an ultraviolet light in which the infected hairs look green. Treatment for ringworm should be prescribed by the veterinarian caring for the pet.

In humans, infection usually occurs on exposed parts of the body, particularly the scalp, appearing as an inflamed, scaly lesion. Iodine-based soap or antifungal drugs cure the problem in humans.

**Psittacosis (parrot fever)** is a bacterial disease that affects 130 species of domestic and wild birds, most commonly pigeons, ducks, turkeys, chickens, and parrots. Humans can get the disease from parrots or parakeets through contact with their feces and the dust from their feathers that accumulates in cages.

In humans, respiratory symptoms of cough and chest pain usually predominate, but other symptoms may include fever, chills, malaise, vomiting, and muscular pain.

Typical symptoms in an infected bird may include poor eating habits or droopy feathers. On the other hand, the bird may show no symptoms. Wearing a surgical or dust mask and rubber gloves while cleaning the bird's cage will help protect against contracting psittacosis. A blood test can confirm the diagnosis of psittacosis, and antibiotics are an effective treatment for the disorder in both humans and birds.

**Lyme disease** was first identified in the mid-1970s in the town of Old Lyme,
Wood engraving from Harper's Weekly, Aug. 2, 1879, of the shooting of a “mad” dog. The term “mad” was used in the 19th century to describe rabid animals. (Courtesy of the National Library of Medicine)

Conn. (See the July-August 1988 FDA Consumer, “Ticks Carry Lyme Disease Across U.S.”) According to the U.S. Centers for Disease Control in Atlanta, the disease has been reported in all but seven states, but is most prevalent on the East Coast.

Lyme disease is caused by a bacterium called Borrelia burgdorferi, which is transmitted to humans and other animals by tiny deer ticks. These ticks pounce on white-tailed deer, field mice, and other wild animals whose bodies are full of these bacteria. The tick sucks blood from these animals, becomes infected with the bacteria, and moves on to other animals or humans, biting and infecting them. You may also catch the disease from the family pooch, which can act as a tick trolley if an infected tick being transported by the dog latches on to you. However, keep in mind that only a small percentage of these pinhead-sized ticks are infected with the bacteria.

Because Lyme disease symptoms are vague and numerous and may mimic the symptoms of other diseases, doctors are increasingly relying on two blood tests to help with diagnosis—the ELISA and Western Blot test. The first sign of the disease is usually a bull’s-eye insignia—a small red pimple that later expands to form a ring-shaped rash. Other symptoms include flu-like aches in the joints, chronic fatigue, dizziness, shortness of breath, and a rash. Treatment with antibiotics in early stages is imperative to prevent the disease from progressing to more serious states linked to arthritic, cardiac and neurological disorders.

Rocky Mountain Spotted Fever—now found in all parts of the country despite its name—is primarily transmitted by the American dog tick. You can pick up the disease if bitten by an infected tick—either from your dog or in the woods. Symptoms include headache, fever, and skin rash. As with Lyme disease, early diagnosis and treatment with antibiotics is crucial to prevent development of more serious consequences.

Rabies currently is common in certain wild animals, including raccoons, skunks, foxes, bobcats, and bats. (See September 1983 FDA Consumer, “Raccoon-Borne Rabies Spreads.”) Rabbits and rodents, including squirrels, are seldom infected with rabies. Worldwide, people most commonly are infected with rabies through bites from unvaccinated dogs. On the east coast of this country, where canine rabies has been controlled, the main source of infection is wildlife or cat bites.

Though rabies is most often transmitted by a bite from an infected animal it can also be spread through contact of an animal’s saliva with an open wound. Animals can harbor and transmit the rabies virus long before the animal itself shows signs of illness.

Rabies is almost always fatal. Vaccination of pet cats and dogs is imperative to keep the disease from spreading both to humans and to other animals.

If you are bitten by a cat or dog, check with the owner to make sure the animal’s rabies vaccine is current. Most states require that, regardless of their vaccination
status, the dog or cat be quarantined for a number of days to double-check for signs of rabies. In the case of a bite by a wild animal, a rabies vaccine should be administered as a precaution.

To try to prevent infection after a bite, clean the wound immediately with a strong jet of water, soap or detergent, and a solution of alcohol or iodine. In some cases, this cleansing will get rid of the virus, but it is always necessary to consult with a physician immediately to see if you need a series of rabies shots.

**Cat Scratch Fever.** The cause of this disease has not been positively identified, but the source of infection is a cat scratch or bite. The resulting sore at the site of the scratch is slow to heal, and after one to three weeks, lymph nodes may swell and become tender and painful. Although uncomfortable, the disease is rarely serious. If it lingers, however, check with a physician, who may prescribe antibiotics.

**More Familiar Infection**

Animals also can be the source of some more familiar infections. Isadore Rosenfeld, M.D., clinical professor of medicine in the cardiology division of New York Hospital-Cornell Medical Center and author of Modern Prevention: The New Medicine, offers this example: Children in a particular family are plagued by sore throats, which, cultures show, are caused by streptococcal bacteria. Penicillin is administered and the infections are cured, only to reappear after a few weeks. There must be a carrier in the family, but who is it? Finally, someone thinks to look at the throat of the family dog, and the culprit is found.

Similarly, *Salmonella* bacteria may be transmitted to humans by animals. *Salmonella* infections cause mild to severe gastroenteritis, inflammation of the stomach and intestine that may cause diarrhea and vomiting. But such an infection can have much more serious consequences in very young children and the elderly, as well as in those whose immune systems are compromised, such as AIDS patients.

*Salmonella* can be carried by dogs and birds, but turtles present a special risk, so much so that in 1975 FDA banned the sale of “pet-sized” turtles with a shell length of less than 4 inches. (See December 1987-January 1988 FDA Consumer, “Risky Shell Game: Pet Turtles Can Infect Kids.”) A turtle from the wild is just as likely to have *Salmonella* as is a domestically bred one; thus, any turtle should be ruled out as a pet.

For that matter, *any* wild animal should be ruled out, says veterinarian Post. The fact that a wild animal would allow humans to approach it is reason enough to suspect impairment, perhaps due to disease. If for no other reason, the prevalence of rabies should discourage the notion of a pet skunk or raccoon.

**Choosing a Pet**

Despite these risks, the companionship of many kinds of pets can be safely enjoyed with the exercise of common sense and some reasonable precautions. The first rule of thumb is to be certain that the pet you choose is healthy. A dull coat or drooping feathers and lethargic behavior are not good signs. You may want to check with a veterinarian or animal welfare organization for further tips on the physical appearance of the kind of pet you are considering.

In addition to looking over an animal with care, check out its surroundings. Are they clean? Are cages and pens kept free from animal feces? And, if you are dealing with a pet store, do the other animals appear clean and healthy? Once again, a veterinarian or local animal welfare organization can be a good source of information on reputable stores and breeders in your area.

Even if you don’t consult with a veterinarian before obtaining a pet, you will want to line one up to treat and care for your animal. This is an especially good idea if you have chosen a bird or more unusual animal. Some vets may specialize in the care of these animals; others may not include them in their practice.

An initial check-up is definitely recommended to be sure there are no problems that may have escaped the untrained eye. For dogs and cats, puppies and kittens, you will need to provide the vet all available information on inoculations and worming treatments.

Determine whether your vet has a procedure for reminding you when it is time for new inoculations. If not, set up a schedule and follow it carefully. You should also keep in mind that dogs and cats may be exposed to parasitic worms and need to be routinely checked and possibly dewormed regularly.

Here are some other tips for protecting your pet and your family:
- Keep cages or pens scrupulously clean and free from droppings.
- Remove solid waste from the cat litter box daily.
- Keep household pets clean and free of ticks and mites.
- Do not feed your pets raw meat.
- Discourage children from attempting to pet or handle unfamiliar animals because there is no way of knowing whether they are healthy. Moreover, some animals do not recognize such attempts as friendly and respond by biting.
- Never allow children to pet or handle a sick animal. And teach children to wash their hands routinely after handling any animal.
- Do not adopt wild animals as pets if they are injured. Call the local humane society or a wildlife rehabilitator who will take care of the injured animals.
- Avoid walking dogs in tick-infested areas during the summer months.
- Never use pet waste as fertilizer. This material actually has little fertilizer value, but can spread disease.
- Keep children’s sandboxes covered when not in use. Otherwise, they make tempting outdoor litter boxes for neighborhood cats.
- If your dog or cat has access to a wooded area, check the pet daily for ticks. If you find ticks, remove them carefully to avoid being bitten. Deer ticks, associated with the transmission of Lyme disease, are much smaller than dog ticks. Roller-type lint removers are effective in removing non-attached ticks.

Writing in the *Journal of Pediatric Infectious Disease*, Philip Goscienski, M.D., notes that animal-transmitted diseases are all too often unsuspected and unrecognized. He adds that a physician treating a veterinarian or a zookeeper who is ill will be apt to suspect an animal-transmitted disease at once, but a pediatrician treating a child who recently received a puppy as a birthday present may not. When any family member is ill, therefore, it is important to mention to the treating physician the number and kinds of pets in your home.

Being alert to the possibility of animal-transmitted disease and following some simple and sensible steps can do a good deal to remove the risks from pet ownership and permit you and your family to enjoy the pleasures.
The Notebook: a potpourri of items of interest gathered from FDA news releases, other news sources, and the Federal Register (designated FR, with date of publication). The Federal Register is available in many public libraries.

■ Food labeling regulations published in the Federal Register after Jan. 1, 1990, and before Jan. 1, 1992, must be adopted by industry by Jan. 1, 1993. FDA has established this uniform compliance date to give manufacturers time to make required changes. For further information, contact Raymond W. Gill, Center for Food Safety and Applied Nutrition (HFF-300), FDA, 200 C St. S.W., Washington, D.C. 20204, telephone 202-485-0162 (FR Jan. 4).

■ Irradiated foods should continue to be labeled “treated with radiation” or “treated by radiation,” and carry a representative logo, according to a new FDA proposal. The proposal would eliminate the April 8, 1988, expiration date for the required wording, established in an April 1986 rule. For further information, contact Clyde A. Takeguchi, Center for Food Safety and Applied Nutrition (HFF-330), FDA, 200 C St. S.W., Washington, D.C. 20204, telephone 202-472-5740 (FR Jan. 8).

■ Abbreviated new drug applications for generic drugs should include new provisions to expedite the review process, according to a July 10, 1989, FDA proposal. FDA has proposed extending to April 9, 1990, the comment period for this proposal. For further information, contact Philip L. Chao or Wayne H. Mitchell, Center for Drug Evaluation and Research (HFD-362), FDA, 5600 Fishers Lane, Rockville, Md. 20857, telephone 301-295-8049 (FR Jan. 16).

■ Pesticide tolerances and regulations for residues on various agricultural products are the subject of 23 initial filings, amendments and withdrawals of petitions at the Environmental Protection Agency. For information, contact Registration Division (TS-7676C), Office of Pesticide Programs, EPA, 401 M St. S.W., Washington, D.C. 20460 (FR Jan. 9).

■ Pesticide use for experimental purposes has been authorized by EPA for seven chemicals. For information, contact Registration Division (H7505C), Office of Pesticide Programs, EPA, 401 M St. S.W., Washington, D.C. 20460 (FR Jan. 10).

■ Color additive regulations should be amended, according to a petition filed by the Warner Jenkinson Co. The amendments would provide for the safe use of EDTA (disodium ethylenediaminetetraacetate) and calcium sodium EDTA (calcium disodium ethylenediaminetetraacetate) as diluents for use in color additive mixtures in food and ingested drugs. For further information, contact Catherine J. Bailey, Center for Food Safety and Applied Nutrition (HFF-334), FDA, 200 C St. S.W., Washington, D.C. 20204, telephone 202-472-5690 (FR Jan. 10).

■ Child-resistant packaging would be required for household glue removers containing acetonitrile and home cold-wave permanent neutralizers containing sodium bromate or potassium bromate, according to a rule proposed by the Consumer Product Safety Commission. Acetonitrile is often contained in glue remover for sculptured fingernails, and accidental ingestion has caused death and injury to children. Bromate poisoning can damage kidneys and hearing. At least one child has died from accidental ingestion, and 16 others have been injured since 1984. Submit comments to the Office of the Secretary, Consumer Product Safety Commission, Washington, D.C. 20207 (FR Jan. 16).
Investigators' Reports

FDA Battles Against "Regulatory Anarchy"

by Dixie Farley

A federal district court has banned an unproven, potentially life-threatening dialysis filter.

Without such action, said Judge Charles Schwartz Jr. of the U.S. District Court for the Eastern District of Louisiana, "immediate and irreparable damage or injury" may result to patients and to FDA's ability to protect them.

Despite repeated warnings from FDA that the blood filter, known as the Al/Fe Clark Specific, was illegal and could be hazardous, Clark Research and Development, Inc., of Folsum, La., continued to sell the device, causing the agency to seek a restraining order.

"Loosing a novel... device intended for life-sustaining purposes... without solid study data upon which FDA can evaluate its safety and effectiveness is a serious violation of law that threatens the public health," wrote FDA attorney Mark Heller in a court brief dated July 20, 1989. "Were one to follow Clark Research's path," he stated, "regulatory anarchy would occur."

Judge Schwartz issued a temporary restraining order against the firm on July 26, ruling that Clark was marketing the filter illegally and was likely to continue to do so. FDA and Clark agreed to an order of preliminary injunction, which the judge signed on Aug. 1.

The Al/Fe Clark Specific filter is intended to remove excess iron and aluminum from the blood of patients suffering from metal toxicity, as can occur after repeated dialysis or many blood transfusions. It contains deferoxamine mesylate (DFO), a substance that binds the metals. The traditional treatment for this condition is to administer the DFO and then filter the combined DFO-and-metal complex from the blood.

Firms planning to market a medical device must submit information for FDA's review at least 90 days before marketing—the "review clock" starting anew with each submission. The device may be marketed if FDA determines it is substantially equivalent to a Class I or II device or to a Class III device marketed before the Medical Device Amendments of 1976. (Devices are classified on the basis of risk to the patient. Class I devices pose the least risk, and Class III devices pose the greatest.) A post-amendments (or "new") device deemed not to be equivalent is automatically placed in Class III and requires pre-market approval before distribution. A firm wishing to test a new Class III device must have approval to do so, obtained through an application for an investigational device exemption (IDE). The law does not require FDA to complete its classification of new devices by a certain time, though the agency generally does this within 90 days.

Clark claimed FDA "missed the opportunity to interrupt marketing" because of an allegedly late response to the firm's pre-market notification submission. This is the first time FDA's pre-market notification program has been challenged in court.

In a pre-market notice CDRH received on Nov. 10, 1988, Clark claimed the Al/Fe Clark Specific was substantially the same as a Clark filter already on the market. But FDA found the submission did
not provide enough data to determine whether the new filter was as safe and effective as a pre-amendments device. The agency wrote Clark on Feb. 6, 1989, asking for more information about how the device worked. The firm received FDA’s letter on Feb. 13, 96 days after the November submission, but had begun marketing its unapproved filter a week earlier, at the end of the 90-day period.

On Feb. 14, Clark sued FDA and individuals within the agency, charging harassment—among other allegations—and claiming that FDA had no right to interfere with the marketing of its device. On the same day, Clark sent FDA a letter responding to the agency’s request for scientific data. Judge Schwartz dismissed Clark’s suit on May 10.

With continuing advice from outside experts, FDA reviewed Clark’s letter and all the information the firm had submitted and determined that the device was not substantially equivalent to a pre-amendments device. On May 10, FDA placed the filter into Class III, requiring pre-market approval.

Writing back on May 16, Clark stated that FDA’s position was wrong as well as “untimely, malicious, and illegal” and that the firm would continue to market the device. Clark also provided some information on rudimentary laboratory tests, as well as limited data on patient experience with the device. Despite several letters from FDA and meetings in which FDA explained that continued marketing was illegal and that an approved pre-market approval (PMA) application or IDE was required, Clark continued its sales. Clark alleged FDA had no jurisdiction to classify the filter because the firm hadn’t received the classification notice until Feb. 13, six days after the 90-day period. FDA again pointed out that this legal time frame is a restriction on the manufacturer, not FDA.

After the May 16 letter, Clark gave FDA some additional limited patient information, but FDA found none to be relevant to the classification order. Further, none of the firm’s information showed the filter to be safe and effective, according to experts Richard Swartz, M.D., director of the dialysis unit at the University of Michigan in Ann Arbor, and J. David Wallin, M.D., chief of nephrology at Tulane Medical School in New Orleans.

Paradoxically, Clark claimed both that the filter was substantially equivalent to a pre-amendments (or “old”) device, and therefore needed no approved PMA or IDE, and that the device was unique (or “new”) because it was the first dialysis filter to contain the drug DFO. “Now, for the first time,” Clark wrote in its promotional literature, “new technology, available only in the Al/Fe Clark Specific, makes it possible to directly remove selected, previously inaccessible specific toxins.”

As a result, FDA asked for the court’s help in getting the Al/Fe Clark Specific filter off the market. The July 26 temporary restraining order stated that patients treated with the filter before the May 10 classification could continue to receive this treatment, but the preliminary injunction prohibited any further distribution of the device unless Clark obtained an approved PMA or IDE.

Then, on Sept. 15, Clark attorney James Perdigao telephoned Judge Schwartz, asking that the judge allow the filter to be used on a patient said to be dying of sickle cell anemia. The judge verbally granted this use as an exemption to the preliminary injunction.

But FDA and the U.S. Attorney’s Office in New Orleans, on Oct. 12, 1989, requested sanctions against Perdigao, alleging that virtually all of his statements in the September telephone conversation with Judge Schwartz were “palpably false.” An affidavit by the patient’s physician stated that the physician had never treated the patient with the Clark filter and that the patient was in fact stable and thriving and hadn’t been hospitalized since Aug. 24.

“The court was misled,” stated Judge Schwartz in a verbal order on Nov. 8, 1989, subsequently filed Nov. 13. Under this order, Perdigao must pay all costs incurred by the government in its motion for the sanctions. The government submitted costs exceeding $5,000.

While Clark has recalled the unused filters from its 25 consignees—mostly hospitals and dialysis centers—FDA is not certain all devices are accounted for. The agency will monitor the recall to completion.

Dixie Farley is a staff writer for FDA Consumer.

Flawed Gloves Lead To New Proposal

Recent seizures of more than 47 million imported latex medical gloves with defect rates as high as 91 percent led FDA to propose for the first time a regulation setting a maximum defect level for patient examination and surgeons’ gloves, instead of acting on a case-by-case basis.

Concern about the quality of patient examination and surgeons’ gloves has heightened since the advent of AIDS. Health-care workers rely on latex as a protective barrier against possible transmission of the AIDS virus. In response to this concern, FDA in September 1988 began a five-month survey and sampling program for medical gloves.

An FDA investigation in Cleveland, Ohio, and in Indianapolis, Ind., led to seizure of 1.72 million imported patient gloves valued at more than $85,000. Cincinnati district investigator Frederick Lochner says that since the demand for medical gloves has increased, the number of shipments of imported gloves has burgeoned.

FDA issued an import alert on foreign companies whose products the agency found defective in its survey. Lochner traced a shipment from one of these companies—P.T. Indotama Megah Indah Rubber, Indonesia—to Cypress Corporation, a Cleveland distributor. FDA visited Cypress and took 100 gloves to sample for defects; 21 had pinholer-sized leaks. Cypress told the agency that another lot of 500 cases—totaling 1 million gloves—from Indonesia had been sent to Midwest Hospital Supply in Indianapolis. Patricia Cochran, an FDA inspector in the Indianapolis office, sampled the gloves at Midwest Hospital Supply and found a 25 percent defect rate. U.S. marshals immediately seized and destroyed...
In Los Angeles, a complaint to FDA in May 1989 from American Consolidated Products, Inc., led investigators to a warehouse full of exam gloves imported by Medi-Pure Corporation of El Monte, Calif., from a Taiwanese manufacturer. Sampling showed that approximately 25 percent of the gloves were defective. As a result, 12,370 gloves, valued at $62,000, were seized. FDA investigators Robert Brett and Martha Vera-Tudela launched other investigations that turned up defect rates from 20 to 91 percent.

By the end of October, Los Angeles officials had seized more than 46 million suspect leaky exam gloves, valued at $801,000. The investigations led to eight different importers and involved seven different manufacturers—six from Taiwan and one from the Peoples’ Republic of China.

The millions of defective gloves seized as a result of these investigations were all from foreign manufacturers. No health-care problems have been directly linked to specific shipments of gloves.

FDA’s proposed new rule would establish a 4 percent defect level for patient examination gloves and a 2.5 percent level for surgeons’ gloves. The new rule, which FDA officials expect to become effective by the summer of 1990, also would allow the agency to seek injunction or criminal prosecution of manufacturers and individuals responsible for adulterated gloves.

Too Toxic to Handle

FDA’s Phoenix resident post-consumer safety officer Randall Johnson last October put FDA seals on three containers of a toxic chemical destined for hazardous waste disposal, capping an agency investigation that stemmed from a local probe of a Maricopa County health official in Phoenix.

The chemical, nicotine alkaloid, is a pesticide approved by the Environmental Protection Agency that the county’s Rabies Animal Control Center was reformulating, repackaging, and using illegally as an animal tranquilizer. It has never been approved by FDA for that use.

FDA learned of the county’s use of the nicotine alkaloid product during a local probe of veterinarian Thomas Kelly, then-director of the Rabies Animal Control Center. Kelly, according to a report in The Phoenix Gazette, “admitted using his workers and county vehicles to run errands for his woodworking business and conducting his private business from his county office.” The newspaper also reported that Kelly’s workers said they had been using the illegal nicotine product since about 1982 on Kelly’s orders.

In early March 1989, FDA’s Johnson visited Randy A. Baca at the Rabies Animal Control Center. Baca was acting director of the center, having replaced Kelly after allegations against the veterinarian had appeared in the local papers early in February. Baca told Johnson that one of the first steps she had taken as acting director was to instruct field personnel to stop using the chemical and return it to headquarters. Harvel Althouse, D.V.M., air quality advisor with the county health department, created a new warning label for the product and reissued it to the field, claiming the new labeling was considered adequate by animal control and no substitutes were immediately available.

Johnson then inspected the facility, inventoried and photographed the bulk

all remaining boxes of gloves.
product on hand, collected a sample of each of four dilutions of the product, and explained to Baca that the chemical is not approved for any anesthetic uses. Johnson also explained FDA's animal drug approval process and outlined the agency's good manufacturing practices and registration requirements for drug repackagers and manufacturers.

In his inspection report, Johnson noted that he «advised [Baca] that the product is too toxic to safely handle and that there is no antidote» and that «her department's use of this product contrary to its labeled indicated uses and directions for use violates Environmental Protection Agency regulations.» Johnson gave Baca a source to call for information on possible substitutes.

Three weeks later, Johnson interviewed Daniel A. Shriek, an animal control officer at the center who, along with Kelly, had been involved in manufacturing the tranquilizer. Also present at the interview were an attorney with the Maricopa County Attorney's Office and Susan L. Svitak, who had by then replaced Baca as acting director at the center.

According to Johnson's report, Shriek said he didn't know when the bulk product used to make the tranquilizer had been purchased, but that the center had made formulations of various strengths of the substance three or four times in the past six or seven years, the last time being January 1988. He said the product was always made at the Maricopa County's Air Pollution Control Department using basic lab equipment; that Kelly used a piece of yellow paper with some handwritten calculations "scratched" on it as a dilution procedure for preparing the final product; that no assays were done on the raw material or final product; and that sterile conditions were not maintained. No records had been kept on the manufacture or packaging of the product.

At the end of this second inspection, Johnson gave Svitak a written report of general deficiencies in manufacturing practices and record-keeping, noting that the report was far from all-inclusive. Svitak informed Johnson that Rabies Animal Control had stopped using the product and was looking for substitutes. In May, the county sent letters to the con-
signees who received the nicotine alkaloid solution, advising them that the product is not approved by FDA as an animal tranquilizer and instructing them to return their supply to the Maricopa County Rabies Animal Control Center for disposal. The recall was completed in September. In October, the product was prepared for transfer to Marine Shale Processors in Louisiana for incineration.

During his inspection in March, Johnson had not been told of any injuries reported from handling or use of the tranquilizer. Following up on information from a July 21 Phoenix Gazette article, however, Johnson learned from Roland Bergen of the County Health Services Department that an industrial accident claim involving the chemical had been made three years earlier. Dan Thomas, an employee with the county's Rabies Animal Control Center, had reported that a diluted nicotine alkaloid dart accidentally discharged in his vehicle, blinding him for several hours. Although his finger was also punctured by the dart, he had no other ill effects. Bergen said no other injuries or incidents were reported for the nicotine product.

Unapproved Analgesic Sales Stopped

The federal government has told a drug manufacturer to stop selling a prescription painkiller because it is an unapproved new drug. The analgesic, Esgic with Codeine, manufactured by Forest Pharmaceuticals, Inc., St. Louis, Mo., contains acetaminophen, caffeine, codeine, and butalbital (a barbiturate). Although FDA has approved each of these drugs individually, their combination in one product constitutes a new drug. Under FDA regulations, a new drug can't be marketed until the company submits—and FDA approves—a new drug application.

Forest Pharmaceuticals never sought or received approval for Esgic with Codeine, which the company began selling on April 15, 1987. FDA immediately advised Forest to take Esgic with Codeine off the market. When Forest didn't comply, the agency considered requesting permission from federal court to seize the product, but de-

On July 10, 1989, the court ordered Forest to stop distributing Esgic with Codeine until the drug is approved by FDA. Forest appealed the court's decision on Oct. 26, 1989. As of this writing, Forest's appeal is being considered by the U.S. Court of Appeals for the 8th Circuit. Both the District Court and the Appeals Court have denied Forest's request to allow the drug to stay on the market during the appeal.

—This small sample of reports from the field was prepared by Dale Blumenthal, Marian Segal, and Dori Stehlin.
Summaries of Court Actions are given pursuant to section 705 of the Federal Food, Drug, and Cosmetic Act. Summaries of Court Actions report cases involving seizure proceedings, criminal proceedings, and injunction proceedings. Seizure proceedings are civil actions taken against goods alleged to be in violation, and criminal and injunction proceedings are against firms or individuals charged to be responsible for violations. The cases generally involve foods, drugs, devices or cosmetics which were alleged to be adulterated or misbranded or otherwise violative of the law when introduced into and while in interstate commerce or while held for sale after shipment in interstate commerce.

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

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

SEIZURE ACTIONS

Food/Contamination, Spoilage, Insanitary Handling

PRODUCT: Beverages, carbonated, bottled, Oscar’s (club soda, grapefruit soda, and cherry soda), at Buffalo, W. Dist. N.Y.; Civil No. 88-0501-C.
CHARGED 5-13-88: While held by Empire Water Co., Inc., Buffalo, N.Y., the articles had been prepared under insanitary conditions—402(a)(4); and one lot each of club soda and grapefruit soda contained mold—402(a)(3).
DISPOSITION: Consent—authorized release to the dealer for bringing into compliance (i.e., bottles salvaged by emptying and destroying contents). (F.D.C. No. 65444; S. No. 88-543-348 et al.; S.J. No. I)

CHARGED 10-26-87: While held for sale, the article contained insects, animal and insect filth, and moldy cocoa beans, and had been held under insanitary conditions—402(a)(4); and one lot each of club soda and grapefruit soda contained mold—402(a)(3).
DISPOSITION: Consent—authorized release to the dealer for bringing into compliance (i.e., bottles salvaged by emptying and destroying contents). (F.D.C. No. 65444; S. No. 88-543-348 et al.; S.J. No. I)

PRODUCT: Mung beans, dried bean curd sticks, and other Oriental food stocks, at San Francisco, N. Dist. Calif.; Civil No. 88-2778 TEH.
CHARGED 7-14-88: While held by Tien Chong Trading Co., San Francisco, Calif, all of the articles had been held under insanitary conditions—402(a)(4); and two lots of the articles contained rodent filth—402(a)(3).
DISPOSITION: A consent decree authorized release of the articles to the dealer for salvaging. Before the articles had been reconditioned, the claimant reported an armed robbery of cash ($300), cigarettes ($500), and food stamps ($100) from the firm’s retail grocery store. The next day, a follow-up report claimed $44,000 of wholesale foodstuffs had also been taken from the firm’s warehouse by the robbers.

The government contended that there was sufficient evidence to institute a contempt proceeding for improper removal of goods under court seizure. In a consent decree in place of proposed contempt proceedings, the claimant firm and its owners (Tien Chong Wong and Donna Leed) stipulated that if at any time during the next five years FDA had reason to believe that the claimant or its owners had improperly removed goods under an FDA seizure, FDA notice of sampling, notice of detention, notice of refusal, or automatic detention, FDA might institute a show cause order; and, if the court determined that the allegations of the show cause order were correct, the following sanctions should be imposed: Each person in contempt should be prohibited from engaging in the sale, importation or distribution of foodstuffs for 180 days. The
consent decree also ordered the claimant to pay FDA the sum of $1,000. (F.D.C. No. 65507; S. No. 88-540-272 et al.; S.J. No. 3)

PRODUCT: Oregano leaves, and other food stocks, at Chicago, N. Dist. III.; Civil No. 89 C 4340.
CHARGED 5-26-89: While held by John’s Import Foods, Inc., Chicago, Ill., the oregano leaves contained rodent filth, and all of the articles had been held under insanitary conditions—402(a)(3), 402(a)(4).
DISPOSITION: Consent—authorized release to dealer for salvaging. (F.D.C. No. 65677; S. No. 89-576-591 et al.; S.J. No. 4)

PRODUCT: Rice, and other food stocks, at Chicago, N. Dist. III.; Civil No. 89 C 4340.
CHARGED 5-26-89: While held by John’s Import Foods, Inc., Chicago, Ill., the oregano leaves contained rodent filth, and all of the articles had been held under insanitary conditions—402(a)(3), 402(a)(4).
DISPOSITION: Consent—authorized release to dealer for salvaging. (F.D.C. No. 65677; S. No. 89-576-591 et al.; S.J. No. 4)

PRODUCT: Rice, and other food stocks, at Norfolk, E. Dist. Va.; Civil No. 87-462-N.
CHARGED 7-23-87: While held by Sun Shine Trading, Inc., Norfolk, Va., the articles had been held under insanitary conditions—402(a)(4).
DISPOSITION: Consent—authorized release to dealer for salvaging. (F.D.C. No. 65233; S. No. 87-516-146 et al.; S.J. No. 5)

PRODUCT: Rice, and other food stocks, at Seattle, Dist. Wash.; Civil No. C 88-946-D.
CHARGED 7-20-88: While held by Sun Food Trading Co., Inc., Seattle, Wash., all of the articles had been held under insanitary conditions—402(a)(4); and two lots of rice contained insect filth—402(a)(3).
DISPOSITION: Consent—authorized release to dealer for salvaging. (F.D.C. No. 65506; S. No. 88-502-281 et al.; S.J. No. 6)

PRODUCT: Shrimp, frozen, at Fort Lauderdale, S. Dist. Fla.; Civil No. 89-6097.
CHARGED 2-7-89: When shipped by Shore Lobster & Shrimp Co., Perth Amboy, N.J., the article, labeled “White Gold Processed & Exported By: Mekran Fisheries Limited Fish Harbour, ... Karachi ... Pakistan ... Frozen Shrimp,” contained insect and rodent filth—402(a)(3).
DISPOSITION: Consent—authorized release to dealer for salvaging. (F.D.C. No. 65562; S. No. 88-515-866; S.J. No. 7)

PRODUCT: Fish product, artificially crab-flavored, in labeled and unlabeled packages, at Los Angeles, Calif.; Civil No. 88-02259 PAR (Kx).
CHARGED 4-22-88: While held by Ono Fish Cake Co., Inc., Los Angeles, Calif., who manufactured the article using interstate fish, the article (some of which was labeled “COPY CRAB Imitation Crab Meat ... Ono Fish Cake Co., Inc. Los Angeles CA,”) contained the nonconforming food additive glycine—402(a)(2)(C); the article lacked complete nutritional labeling in the prescribed format—403(a)(1); the label statement that the product contained natural color was false—403(a)(1); required nutritional information failed to appear prominently and conspicuously since it appeared in letters and numerals less than 1/16 inch high—403(f); the label lacked the common or usual name of the article—403(i)(1); the label of the article lacked the common or usual name of each ingredient—403(i)(2); the article contained a chemical preservative and lacked labeling stating that fact as specified—403(k); and the article was in violation of the Fair Packaging & Labeling Act, since the quantity of contents declaration was not declared in the specified manner (ounces and parenthetically in pounds) or type size (at least 3/16 inch high)—15 U.S.C. 1453(a)(3)(A)(i) & 1453(a)(3)(C).
DISPOSITION: Consent—ordered destroyed. (F.D.C. No. 65383; S. No. 88-480-425; S.J. No. 8)

Food Additives

PRODUCT: Animal feed pellets of rye grass seed screenings, in bulk, at Toppenish, E. Dist. Wash.; Civil No. C 89-002-AAM.
DISPOSITION: The article was claimed by A.R. Smith & Co., Inc., Bellevue, Wash. Subsequently, the U.S. Environmental Protection Agency promulgated a tolerance of 10 parts per million (ppm) for propiconazole in rye grass seed screening pellets, and analysis revealed levels of propiconazole in the article that ranged from 1 to 2 ppm. Thereafter, a consent decree of condemnation authorized release of the article to the claimant for use as animal feed. (F.D.C. No. 65575; S. No. 89-313-286; S.J. No. 9)

Drugs/Human Use

PRODUCT: Cantrol-brand and Nupro-brand kits of capsules for Candida albicans infection, at Springville, Dist. Utah; Civil No. 89-C-128-G.
CHARGED 2-9-89 and amended 3-8-89: While held by Health Products International, Nature’s Way Products, Inc., and/or Nutrition Professionals, Inc., Springville, Utah, the labeling of the kits—which kits were assembled by Health Products International for distribution by Nature’s Way Products (Cantrol-brand kits) and Nutrition Professionals (Nupro-brand kits) using capsules of caprylic acid, acidophilus, vitamin E, vitamin-mineral combination, linseed oil, and Pau d’Arco—failed to bear adequate directions for use and the kits were not exempt from such requirement due to the kits’ new drug status—502(f)(1); and the kits were new drugs without effective approved New Drug Applications—505(a).
DISPOSITION: Default—ordered destroyed. (F.D.C. No. 65562; S. No. 88-515-866; S.J. No. 7)

PRODUCTS: Herbal tea mixes, in bulk and in retail boxes and envelopes, at Newark, Dist. N.J.; Civil No. 88-1141.
CHARGED 3-11-88: While held by Costa Innovations, Inc. (Casa Costa), Newark, N.J., the articles, consisting of tea mixes Nos. 1-45, bore varying labeling (e.g., “Pau D’Arco . . . No. 38 para
tratamento de úlceras gastrícas e duodenais, reumatismo, diabetes ... anti canceroso e preventivo de leucemia ... Casa Costa ... Newark, N.J.)" and were accompanied by the dealer's booklet entitled "Sande e Natureza," which contained medical claims for the articles; the articles were new drugs without effective approved New Drug Applications—505(a); the articles' labeling lacked adequate directions for use—502(f)(1); and the articles' labeling failed to appear in the English language—502(c).

DISPOSITION: A consent decree authorized release of the articles to the dealer for the destruction of labeling of all of the articles, for the destruction of all of the articles in boxes and envelopes, and for bringing the bulk articles into compliance with the law. In addition, the claimant was permanently enjoined from importing, processing, packing, labeling, or distributing noncomplying teas, including teas labeled by a number reference or labeled with medical claims. (F.D.C. No. 65385; S. No. 88-438-387 et al.; S.J. No. 11)

PRODUCT: Hormone Helpers capsules, at Cheyenne, Dist. Wyo.; Civil No. C 88-0023-B.
CHARGED 1-15-88: While held by D & C Distributors, Cheyenne, Wyo., the article (labeled "Hormone Helpers . . . Capsules . . . Wild Yam Root, Evening Primrose, . . . Sandíce, . . . D & C Distributors . . . Cheyenne, Wyo."") was accompanied by promotional leaflets reading "Women! Have Health Problems? Overweight? Lumps, Tumors, . . . Hormone Helpers . . . D & C Distributors," and "A few years ago, . . . Cynthia D. O'Hare . . . Cheyenne, Wyoming"; and the article's labeling lacked adequate directions for use, since conditions for which the article was offered were not amenable to self diagnosis and treatment by the laity and, therefore, adequate directions for lay use could not be written for such intended purposes—502(f)(1); and the article was a new drug without an effective approved New Drug Application—505(a).

DISPOSITION: Default—ordered destroyed. (F.D.C. No. 65300; S. No. 87-448-927; S.J. No. 11)

PRODUCT: Povidone-iodine topical creams (flavored and unflavored), at Goldsboro, E. Dist. N.C.; Civil No. 87-448-927; S.J. No. 12)
CHARGED 10-27-88 and amended 11-15-88: When shipped by Redi Products Division, General Medical, Prichard, W. Va., the articles (which were labeled "Viradyne PVP-1 Cream [or "Viraldehyde Flavored PVP-1 Cream"] . . . Antiseptic - Microbicide - Viricide . . . For the relief of pain in genital lesions [or "For relief of fever blisters and cold sores"] . . . Mfg for G & S Medical, Ltd. . . . Goldsboro, N.C.") and which were accompanied by G & S Medical labeling bearing claims for fever blisters and cold sores, inactivation of HSV-1 and HSV-2, and relief of pain in genital lesions) were new drugs without effective approved New Drug Applications—505(a); and the labeling of the articles lacked adequate directions for use—502(f)(1).

DISPOSITION: The articles were claimed by G & S Medical, Ltd., Goldsboro, N.C., who denied the charges and asserted a number of affirmative defenses. The government served written interrogatories on the claimant. Subsequently, however, the claimant's claim and answer were withdrawn, and a default decree ordered the articles destroyed. (F.D.C. No. 65540; S. No. 88-537-401 et al.; S.J. No. 13)

Drugs/Veterinary

PRODUCT: Fresh Charger vitamin & mineral boluses, and aloe-vera udder cream, at Manchester, M. Dist. Pa.; Civil No. 89-0181.
CHARGED 2-3-89: While held by Animal Medic, Inc., Manchester, Pa., who made therapeutic claims for the articles in the firm's catalog, the articles' labeling lacked adequate directions for the uses for which they were intended—502(f)(1).

DISPOSITION: Default—ordered destroyed. (F.D.C. No. 65593; S. Nos. 89-570-404/5; S.J. No. 14)

PRODUCT: Medicated feed premixes, and medicated feeds, at Jamestown, M. Dist. Tenn.; Civil No. 2-89-0033.
CHARGED 4-28-89: While held by Burnett Poultry Co., Jamestown, Tenn., the articles, which contained interstate components, had been manufactured, processed or held under circumstances lacking current good manufacturing practice—501(a)(2)(B).

DISPOSITION: Consent—authorized release to the dealer for bringing into compliance. (F.D.C. No. 65602; S. No. 89-536-279 et al.; S.J. No. 15)

Medical Devices

PRODUCT: Gloves, latex, for patient examination, at Indianapolis, S. Dist. Ind.; Civil No. IP89-852C.
CHARGED 8-3-89: The article, which was labeled "Latex Exam Gloves . . . Made in Indonesia for Cypress Corporation Cleveland, Ohio," contained excessive holes, and the article's quality fell below its purported quality—501(c); and the article's case label contained the Food and Drug Administration acronym "FDA," which misleadingly created the impression of official FDA approval—502(a).

DISPOSITION: Default—ordered destroyed. (F.D.C. No. 65699; S. No. 89-455-595; S.J. No. 16)

CRIMINAL ACTIONS

DEFENDANTS: Colorado Plasma Co., Colorado Springs, Dist. Colorado; Civil No. 87-CR-245; and Brenda Lynn Asbury and Matthew William Melvin, plasma company employees, Colorado Springs, Dist. Colorado; Criminal No. 87-CR-153 and, upon transfer to N. Dist. Calif., CR87-20084-MAG.

CHARGED on or about 9-1-87 against the company: That the company shipped plasma labeled "Source Plasma (Human)" and "Caution: For Manufacturing Use Only," which labeling represented the plasma as suitable for further manufacture into injectable products, but which was false and misleading since the
company accepted plasma donors whose required donor-suitability determination had not been performed—301(f); and the company refused to permit entry and inspection and impeded FDA inspection, since Donor Record File entries were made concealing that donor-suitability determinations had not been performed and since Whole Blood Log entries were made concealing that whole blood had been drawn from donors in excess of permitted amounts—301(f).

CHARGED 5-18-87 against the individuals: That the individuals refused to permit entry and inspection and impeded FDA inspection, in that they made Donor Record File entries which concealed that required donor-suitability determinations had not been performed—301(f); and that the individuals also refused to permit entry and inspection and impeded FDA inspection, in that they made Whole Blood Log entries which concealed that whole blood had been drawn from donors in excess of permitted amounts—301(f).

DISPOSITION: Pursuant to plea agreements, the defendants pleaded guilty. The company was fined $2,000 and was also to pay $200 into the Crime Victim's Fund. The individuals had their case transferred to the Northern District of California; imposition of sentence was suspended; Asbury was placed on probation for three years with the condition that she complete 120 hours of community service and pay a $25 penalty assessment as to each of the two counts; and Melvin was placed on probation for three years with the condition that he complete 120 hours of community service and pay a $25 penalty assessment as to each of the two counts. (Misc. No. 789; S. No. 85-379-061 et al.; S.J. No. 17)


CHARGED 6-2-87 against corporation: That the defendant corporation, through its employees, in a matter within FDA's jurisdiction, knowingly and willfully made material false statements on Dec. 3, 1983, that bulk \(B_{15}\) was last received on June 8, 1983, that the remaining stock on hand of 723 50-tablet bottles of \(B_{15}\) was voluntarily destroyed, and that the corporation no longer would repack or distribute \(B_{15}\) in interstate commerce—18 U.S.C. 371.

DISPOSITION: Guilty plea by corporation—$10,000 fine, plus $90,000 reimbursement to the government for costs of investigation. Guilty plea by individual—$1,000 fine. (F.D.C. No. 64240; S. No. 84-357-004; S.J. No. 18)


CHARGED 4-12-88: While held for sale, chili pods and pickling spice were held in a building accessible to insects and were contaminated with insect filth—402(a)(3), 402(a)(4).

DISPOSITION: Guilty plea—$2,500 fine on each of two counts and a $50 special assessment. (F.D.C. No. 65020; S. No. 86-385-083 et al.; S.J. No. 19)

INJUNCTION ACTIONS

DEFENDANTS: Produce Supply Co. (a/k/a P.S.C. Foodservice, Inc.), and Harry R. Cooper, board chairman, and John R. Cooper, president, Spokane, E. Dist. Wash.; Civil No. C-89-489-JLQ.

CHARGED 7-17-89 in a complaint for injunction: That the defendants operated a food preparation facility at Spokane, Wash., processing potatoes into boiler, French fried, and hash-brown potatoes for distribution in interstate commerce, and processing interstate lettuce, cabbage, carrots, and other vegetables into salad mix for intra- and interstate sale; that such foods were prepared, packed and held under insanitary conditions; that the potato products were contaminated with filth; that FDA inspections had revealed a number of specified insanitary conditions, and established a history of sanitation control problems relating to the construction and maintenance of the defendants' facility; and that, unless enjoined, the defendants would continue such violations—402(a)(3), 402(a)(4).

DISPOSITION: A consent decree of permanent injunction enjoined the surviving defendants—the board chairman having died. The decree enjoined the defendants' operations at their facility involving interstate foods unless and until a number of specified conditions had been met, including: 1) eliminating all insects and the vermin from the facility; 2) cleaning and renovating the facility and its equipment; and 3) establishing a sanitation control program. In addition, a qualified expert was to certify compliance; and all foods were to be examined, analyzed when necessary, and—when shown to be contaminated—destroyed or otherwise brought into compliance. (Inj. No. 1218; S. No. 89-420-396 et al.; S.J. No. 20)
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