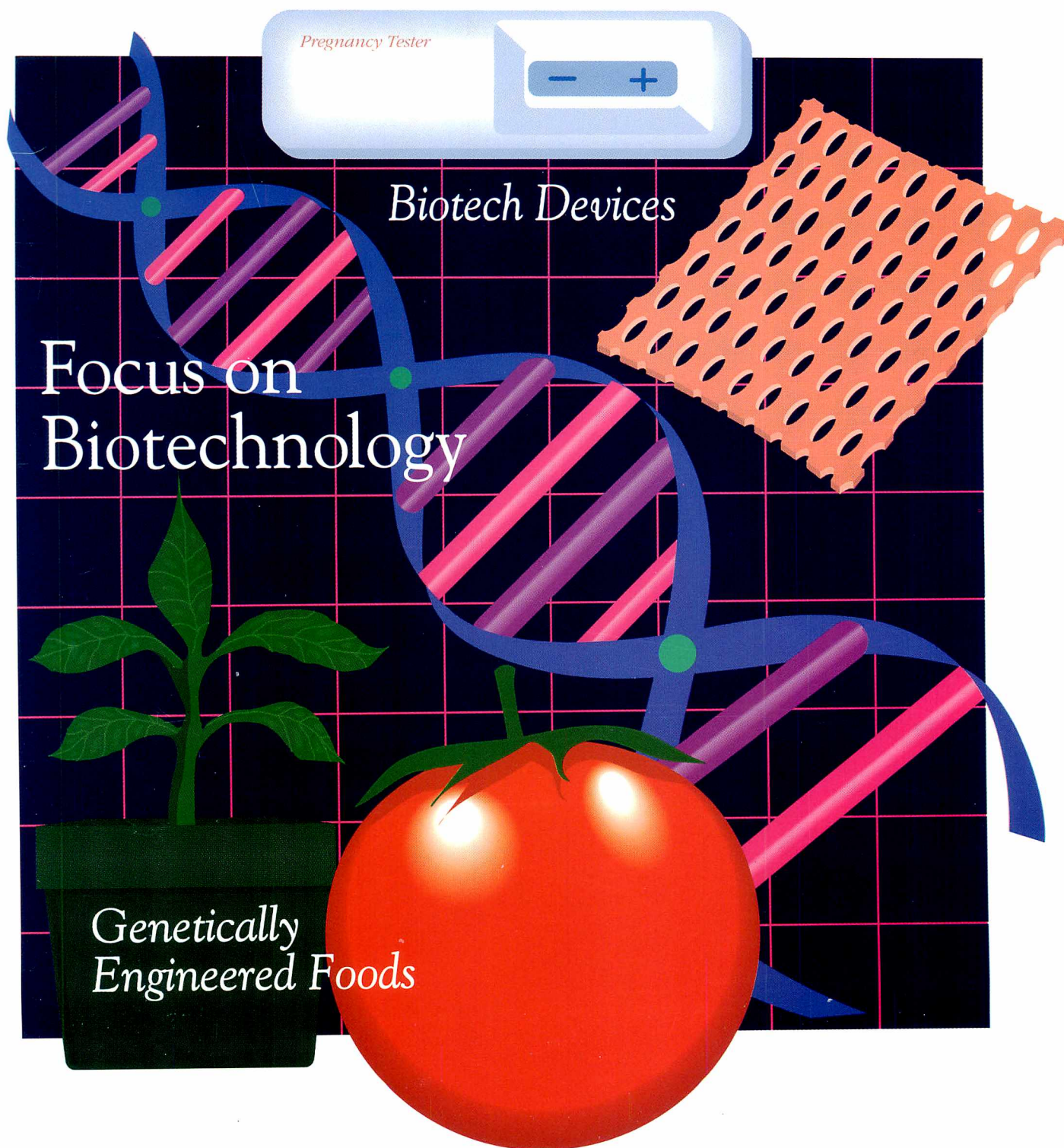


FDA CONSUMER

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

• VOL. 27 NO. 1

JANUARY–FEBRUARY 1993 •





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FDA Consumer (ISSN 00362-1332) is published by the Food and Drug Administration (HFI-40), 5600 Fishers Lane, Rockville, MD 20857, U.S. Public Health Service, Department of Health and Human Services. It is published monthly, except for combined issues for July-August and January-February. Use of funds for printing *FDA Consumer* has been approved by the Office of Management and Budget.

Editorial Matters

Address for editorial matters is *FDA Consumer*, Food and Drug Administration (HFI-40), 5600 Fishers Lane, Rockville, MD 20857. Articles in *FDA Consumer* may be republished without permission. Credit to *FDA Consumer* as the source is appreciated. *FDA Consumer* is indexed in the *Reader's Guide to Periodical Literature*. To obtain a copy of the current *FDA Consumer Index*, write to: FDA, HFE-88, 5600 Fishers Lane, Rockville, MD 20857.

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On the Teen Scene: Endometriosis Painful, but Treatable 24
About 5 million American women—some as young as 11—have this painful condition, which occurs when fragments of the uterus (womb) become embedded elsewhere in the body. Many report having symptoms as teenagers.

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Brandy is dandy, but does it contain a hidden substance that might be harmful? See page 19.



FDA Approves Injectable Contraceptive

Depo Provera, an injectable contraceptive drug, was approved by FDA last Oct. 29. It is more than 99 percent effective.

"This drug presents another long-term, effective option for women to prevent pregnancy," said FDA Commissioner David A. Kessler, M.D. "As an injectable, given once every three months, Depo Provera eliminates problems related to missing a daily dose."

The drug contains a synthetic hormone similar to the natural hormone progesterone. When injected into the muscle of the arm or buttock, the hormone is released into the bloodstream to prevent pregnancy. It must be given on a regular basis to effectively prevent pregnancy; women who decide to become pregnant can discontinue the injections.

FDA advises women interested in using Depo Provera to discuss the benefits and risks with their doctors. The most common side effects are menstrual irregularities and weight gain. Some women may experience headache, nervousness, abdominal pain, dizziness, weakness, or fatigue. The drug should not be used by women who have acute liver disease, unexplained vaginal bleeding, breast cancer, or blood clots in the legs, lungs or eyes.

Doctors are advised to rule out the possibility of an existing pregnancy in women requesting Depo Provera because of concerns about low birth weight in babies exposed to the drug. Recent data demon-

strated that long-term use may contribute to a woman's risk of developing osteoporosis.

Depo Provera was developed in the 1960s and has been approved for contraception in many other countries. The UpJohn Company of Kalamazoo, Mich., which will market the drug under the name Depo Provera Contraceptive Injection, first submitted it for approval in the United States in the 1970s. At that time, animal studies raised questions about its potential to cause breast cancer. Studies since then, both here and abroad, have found that the overall risk of cancer, including breast cancer in humans, is minimal, if it exists at all.

Hismanal Should Not Be Taken With Certain Other Drugs

People who take the non-sedating prescription antihistamine Hismanal (astemizole) should not take certain anti-

fungal or antibiotic drugs at the same time because of the risk of life-threatening cardiac arrhythmias, commonly known as abnormal heart rhythms. This is the second non-sedating prescription antihistamine found to have this potential drug interaction problem.

Hismanal is prescribed to treat seasonal allergies and hives.

Last October, FDA asked Janssen Pharmaceutica, manufacturer of Hismanal, to warn physicians and other health professionals not to prescribe the antibiotic erythromycin or the anti-fungals Nizoral (ketoconazole) or Sporanox (itraconazole) for people taking Hismanal. FDA took this step after receiving reports of serious arrhythmias in two patients who took Hismanal with erythromycin, or erythromycin plus Nizoral. Subsequently, Janssen submitted preliminary information indicating greatly increased blood levels of Hismanal in patients taking Nizoral.

Although no problems were reported with Sporanox, FDA included it in the warning because it is chemically and pharmacologically similar to Nizoral.

Last July, FDA warned that exceeding Hismanal's recommended dose of 10 milligrams (one tablet) per day also increased the risk of arrhythmias.

In addition, FDA warned, people with liver disease are at increased risk because they cannot properly metabolize (process) Hismanal. This leads to an accumulation of the drug in the body that can result in arrhythmias and other cardiovascular problems, including cardiac arrest and death.



Last July, FDA also asked Marion Merrell Dow, Inc., to issue a similar warning for its non-sedating prescription anti-histamine Seldane (terfenadine).

New Drug for Arrhythmias

Patients who experience periods of life-threatening irregular heartbeats called arrhythmias may now be treated with a drug approved by FDA on Nov. 5, 1992.

Betapace (sotalol hydrochloride) decreases the effects of nerve impulses that excite the heart tissues, and alters the way the heart conducts electrical signals that generate arrhythmias.

Like other anti-arrhythmic drugs, Betapace is not recommended for use in less severe circumstances because the drug itself can induce serious arrhythmias. In patients with life-threatening arrhythmias, however, the drug's benefits outweigh the risks.

FDA's approval was based on the results of safety studies involving more than 3,000 patients, during which Betapace was compared with other anti-arrhythmic drugs.

Studies of the drug's efficacy involved approximately 1,300 patients who had life-threatening arrhythmias. In a small comparison study, Betapace proved about 30 percent effective in preventing arrhythmias, somewhat better than procainamide, a widely used anti-arrhythmic drug. A larger study by the National Institutes of Health found Betapace to be more effective in preventing recurrent arrhythmias than a group of six other drugs, even over the long term.

Studies also found that a life-threatening arrhythmia called torsades de pointes occurred in 4 percent of patients treated with Betapace for life-threatening arrhythmias, and in 1 percent of those treated for less serious arrhythmias.

Other adverse effects include breathing difficulty, worsening of existing congestive heart failure, fatigue, and excessive slowing of the heart rate.

Patients taking Betapace must be carefully monitored to ensure the drug is having the desired effect, but not the undesired ones.

Betapace is marketed by Berlex Laboratories of Wayne, N.J.

Dietary Supplements and NLEA

Vitamin tablets, mineral pills, herbs, and other "dietary supplements" need not comply with FDA's new food labeling regulations until at least December 1993, according to a law passed by Congress and signed by President Bush last October.

The Dietary Supplement Act of 1992 placed a one-year moratorium on implementing the Nutrition Labeling and Education Act (NLEA) of 1990 with regard to such supplements. However, FDA is allowed to approve for use on supplement labels health claims about the relationship of certain nutrients to specific diseases or health conditions.

In November 1991, FDA issued proposed regulations to implement the NLEA. A special provision of the NLEA stated that final regulations were to be issued by Nov. 8, 1992, or else the proposals would automatically become final. Since FDA did not issue its planned final regulations by that date, the proposals,

which included four approved health claims, did become final regulations, with an effective date of May 8, 1993.

It is those regulations from which the Dietary Supplement Act is exempting supplements.

The new law also calls for reports and studies about dietary supplements: FDA must report to Congress on its enforcement priorities and practices concerning supplements; the General Accounting Office, an arm of Congress, will study FDA's management activities; and the Office of Technology Assessment, also run by Congress, will study the relationship between regulation of supplements and "health outcomes" in the United States and other countries.

The new law also prohibits until November 1993 any regulations that use recommended daily intakes for vitamins and minerals other than the Recommended Dietary Allowances set by the National Academy of Sciences in 1968. FDA had proposed issuing new recommended intakes based on more recent data.

FDA will continue to ensure the safety of dietary supplements, taking action against products that are dangerous or whose claims are misleading.

Poultry Dip Reduces Bacteria

Poultry processors can now use a trisodium phosphate (TSP) dip to reduce the levels of *Salmonella* and other bacteria that could be present in the raw meat, the U.S. Department of Agriculture announced last Oct. 13.

FDA lists TSP as a multiple-purpose food substance on the agency's generally recognized as safe (GRAS) list. FDA has determined that TSP is not a food additive and that no new compounds are formed during the processing of chicken with TSP.

Data from tests in Arkansas and Puerto Rico, conducted by USDA's Food Safety and Inspection Service (FSIS) and TSP manufacturer Rhône-Poulenc, Inc., show that TSP effectively reduces food-borne pathogens found on raw poultry. The data support the safe and immediate use of TSP, FSIS administrator H. Russell Cross, Ph.D., said.

The process, in which poultry goes through a TSP solution near the end of processing operations, can be adapted to existing equipment in poultry plants.

Some Germicides Associated With More Dialysis Deaths

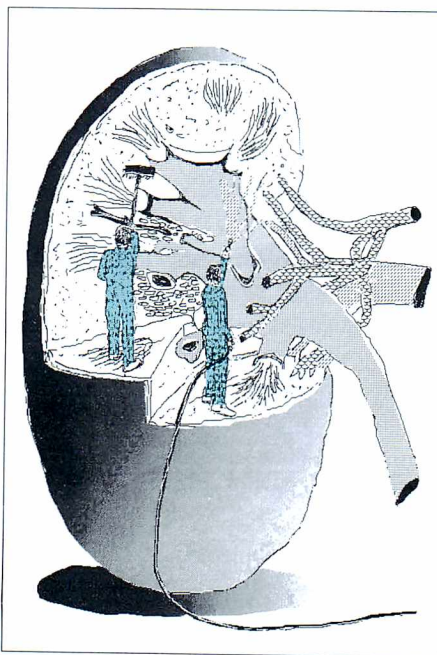
Last Oct. 23, FDA alerted kidney dialysis centers and dialysis patients of an association of higher death rates with certain germicides used in reprocessing dialyzers. Dialyzers are devices that perform the function of failed kidneys by filtering impurities from the blood.

The agency also took steps to resolve questions about the association and to make sure dialysis centers use the germicides correctly.

The actions came as the result of a review of preliminary data from two studies. One study, by the Urban Institute with support from the Health Care Financing Administration, showed more deaths, on average, in facilities where dialyzers were

disinfected with Renalin (peracetic acid-hydrogen peroxide solution) or glutaraldehyde, two commonly used germicidal solutions.

The other study, by the National Institutes of Health, showed higher mortality only among patients whose dialysis machine filters were disinfected by hand with Renalin, but not those disinfected with au-



tomated cleansing systems or those using glutaraldehyde.

Neither study showed increased mortality associated with formaldehyde, a third disinfectant.

The studies *did not find* that reusing dialyzers was less safe than using them only once.

Also, the studies did not determine whether the problem was the germicides themselves or the way they were used, or whether other factors, such as other medical problems or insufficient dialysis time,

might be responsible for the increased deaths.

In response to the findings, FDA:

- asked Renalin's manufacturer to notify dialysis facilities about the study results and provide technical assistance on proper use of the germicide
- notified medical organizations and dialysis facilities about the studies
- is working with manufacturers of dialyzers to include instructions in their labeling for proper reprocessing of their dialyzers.

Other Public Health Service agencies are continuing to conduct research to explain the higher mortality rates.

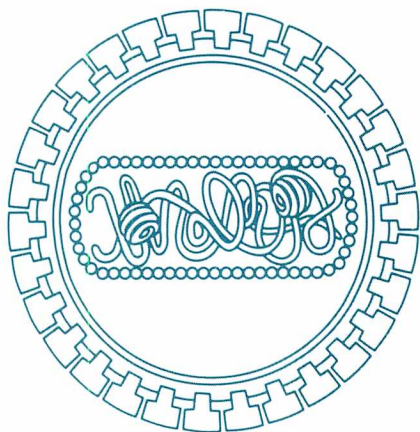
New Reprints

Free reprints of four *FDA Consumer* articles have recently become available:

- Hope or Hoax? Unproven Cancer Treatments (FDA93-1198)
- Vegetarian Diets: The Pluses and the Pitfalls (FDA93-2258)
- Silicone Breast Implants: Available Under Tight Controls (FDA93-4253)
- Cosmetic Ingredients: Understanding the Puffery (FDA93-5013)

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



Recurring 'Yeast' Infection May Be Early HIV Sign

An addition to the labeling of over-the-counter remedies for vaginal yeast infections warns that women who may have been exposed to HIV and who have recurring or persistent vaginal fungal infections should immediately seek professional medical attention. These infections are technically known as candidiasis and commonly called "yeast."

Although pregnancy, diabetes, contraceptive pills, and antibiotics are the more common causes of candidiasis, women at risk for HIV should be aware that repeated or extended vaginal fungal infections can sometimes be an early warning sign of HIV infection.

FDA requested the new label warning last October after reviewing several studies, including one showing that 38 percent of women diagnosed with HIV-caused suppressed immunity had recurring or persistent vaginal candidiasis as their first symptom.

The labeling of these drugs, which are miconazole nitrate (Monistat-7) and

clotrimazole (Gyne-Lotrimin, Mycelex-7, and FemCare), already stated that such recurrent infections may result from hormonal changes, oral contraceptives, or antibiotics.

The additional warning states: "In someone with frequently recurrent vaginal yeast infections, especially infections that don't clear up easily with proper treatment, the vaginal yeast infection may also be the result of serious medical conditions, including infection with HIV, that can damage the body's normal defenses against infection."

Women who need further information on risk factors or testing for HIV infection should contact their doctors or the Centers for Disease Control's and Prevention National AIDS Hotline at (1-800) 342-AIDS. (Spanish-speaking persons can call 1-800-344-7432; the number for the hearing impaired is TDD 1-800-243-7889.)

Publicly Funded HIV Services Increase Dramatically

Publicly funded HIV counseling and testing services have dramatically increased, according to the national Centers for Disease Control and Prevention.

More than 2 million HIV-antibody tests were performed in 1991, compared to about 79,000 in 1985, CDC reported in the Aug. 28, 1992, *Morbidity and Mortality Weekly Report*. More than 1 million of these tests were requested by persons who reported neither they nor their partners had engaged in high-risk behavior, or by persons for whom risk information was not specified.

HIV counseling and testing services:

- reinforce perception of risk by those who are unaware or uninformed
- help uninfected persons change their be-

havior to reduce their risk of becoming infected

- identify HIV-infected persons who can be referred for early medical care and counseled to practice safer behaviors.

These services are currently provided by 65 HIV-prevention programs in all 50 states and major cities with separate CDC-funded programs, including Chicago, Houston, Los Angeles, New York City, Philadelphia, San Francisco, and Washington, D.C. Programs are also located in eight U.S. territories: American Samoa, Federated States of Micronesia, Guam, the Marshall Islands, the Northern Mariana Islands, Palau, Puerto Rico, and the Virgin Islands.

Some of the programs are located in freestanding sites, while others are parts of clinics, drug abuse treatment centers, and prisons. Each program reports quarterly to CDC the number of pretest counseling sessions, HIV-antibody tests (including positive results), and follow-up counseling sessions.

Of the more than 2 million HIV-antibody tests performed during 1991, just under 58,000 were positive.

Of the nearly 2 million HIV tests for which self-reported risk information was available, the highest percentage of positive test results, 17.4 percent, was among homosexual and bisexual men who were intravenous (IV) drug users. Of the homosexual and bisexual men who were not IV drug users, 11.8 percent tested positive, and of the heterosexual IV drug users, 8.3 percent tested positive.

Nutrition Info Available For Raw Fruits, Vegetables, Fish

by Paula Kurtzweil

Customers of D'Agostino Supermarkets in New York have taken to reading the writing on the wall—and at the counter, in the aisles, and just about everywhere else that store managers have posted nutrition information on raw produce and fish.

They're reading about the amounts of sodium, vitamins A and C, calcium and iron, and other nutrients in their favorite fruits and vegetables and fish. And, thanks to accompanying take-away brochures, they're learning how those foods can help them follow the Dietary Guidelines for Americans.

"Customers are interested," acknowledges Mary Moore, director of public affairs for the company. "They're picking up the brochures; they're taking them home. And our managers tell us they see people reading the charts all the time."

They're not alone. Food shoppers across the country are helping themselves to the same type of information. It's all part of FDA's voluntary point-of-purchase nutrition information program for raw fruits, vegetables and fish, and D'Agostino Supermarket Inc. is one of many grocers participating.

It's well that these grocers are participating because under FDA guidelines, at least 60 percent of a nationwide sample of grocery stores surveyed in late 1992 must have been in compliance at that time. If they're not, FDA is required by law to make the program mandatory.

Grocers have some flexibility: They can choose from a variety of ways in which to convey nutrition information—poster, brochure, leaflet, notebook, or individual stickers—as long as those materials are available in the appropriate food department.

They're required to provide nutrition information only for the 20 most frequently eaten raw fruits, vegetables and fish. (See accompanying lists). And, they have to provide information only on calories and eight nutrients.

Setting Standards

FDA established the current guidelines for voluntary nutrition information in November 1991, in accordance with the Nutrition Labeling and Education Act of 1990. Although the law mandates nutrition labeling for almost all processed foods, it allows voluntary point-of-purchase nutrition information for raw fruits, vegetables and fish—as long as a sufficient number of retailers participate.

According to Jean Pennington, Ph.D., a registered dietitian and associate director of dietary surveillance in FDA's Center for Food Safety and Applied Nutrition, the program is intended to give retailers flexibility while ensuring that as many consumers as possible have access to consistent, reliable information.

Offering in-store nutrition information on these types of foods isn't new, she noted. Many grocers have been doing it on their own for years.

For example, almost 10 years ago, Schnuck Markets Inc., a 60-store grocery chain headquartered in St. Louis, began offering customers its *Nutri Guide* booklet—which lists calorie, fat, cholesterol, sodium, and fiber content of nearly 2,500 in-store foods, including perishable items.

And Giant Foods Inc., a Washington,



Lucille O'Connell, of metropolitan St. Louis, checks the nutritional content of her favorite fish at her local supermarket. Many grocers are offering such information under FDA's new voluntary point-of-purchase nutrition information program for raw foods. This photo and the one on page 8 were taken in Schnuck's Kirkwood, Mo., store.



A large poster with nutrition information about the 20 most popular raw vegetables is prominently placed in the produce section. It is one of several options grocers may use to present nutrition information for raw produce and fish.

D.C., area retail chain headquartered in Landover, Md., has been selling its *Eat for Health Food Guide* since the 1980s. This guide, too, provides nutrition information on thousands of store products, including fresh fruits and vegetables and raw fish.

What is new is that, for the first time, consumers at grocery stores across the country will have access to the same basic nutrition information. "We're aiming for consistency here," Pennington said. "From store to store and from state to state."

What Shoppers Will See

That's why the program, although voluntary, carries some mandatory components. Chief among them is the information that must be provided.

To meet the FDA guidelines, point-of-purchase nutrition information for raw fruits, vegetables and fish must include the following:

- name of the fruit, vegetable or fish that has been identified by FDA as being one of the 20 most commonly eaten in the United States
- serving size

- calories per serving
- amount of protein, total carbohydrates, total fat, and sodium per serving
- percent of the U.S. Recommended Daily Allowances for iron, calcium, and vitamins A and C per serving.

This information is required because FDA believes it's important for consumers to know which foods will increase one's intake of nutrients and which foods will not.

Declaring the percent of U.S. RDAs for thiamin, riboflavin, niacin, and protein, and the amounts of complex carbohydrates, sugars, dietary fiber, saturated fat, and cholesterol is optional.

The serving size, determined by FDA, is defined as that portion of food "customarily consumed per eating occasion."

For raw produce, the serving size is often an individual unit (for example, one medium orange or two stalks of celery), or a fraction of a unit (for example, one-sixth of a medium head of lettuce or one-eighth of a medium watermelon)—which ever is most appropriate for a particular product.

For fish, the serving size is a 3-ounce, or 85-gram, *cooked* weight—without added fat or seasoning.

According to Pennington, using a cooked weight is a departure from usual FDA practice, which is to require food labels to state a serving size based on a measurement of the food as purchased. In the case of raw fish, however, FDA officials feared that the word "raw" on the label might lead some consumers to conclude that eating raw fish is OK, when in fact it generally is not.

"We certainly don't want to suggest that eating raw fish is a safe thing to do," she said.

While some types of shellfish have been customarily eaten raw, and sushi and sushimi are considered by some to be raw fish delicacies, there are dangers of food-borne illness from eating raw fish. In particular, people with liver diseases, certain gastrointestinal disorders, diabetes mellitus, or weakened immune systems are advised not to eat raw molluscan shellfish, such as oysters, clams, mussels, and scallops. And sushi and sushimi must be commercially frozen to kill any parasites.

Presenting Nutrition Information

Equally important as the type of information provided is the manner in which it is conveyed. Unlike processed, prepackaged food, raw produce and fish do not lend themselves well to individual labeling.

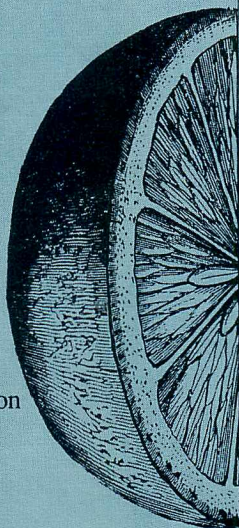
So FDA is allowing retailers to display nutrition information on large placards or to list it in consumer pamphlets or brochures—provided the information is in the appropriate food department for easy consumer access. If they want, retailers may place nutrition information on individual food wrappers or, when appropriate, on stickers affixed to the outside of a food (for example, bananas).

One trade organization, the Food Marketing Institute, is making the job easier for retailers. It offers brochures, charts and posters that contain all the necessary information. The materials were developed as part of the Nutri-Facts Program, a point-of-purchase nutrition information project begun in 1985 and now sponsored by FMI

Most Common Fruits, Vegetables and Fish Sold Raw

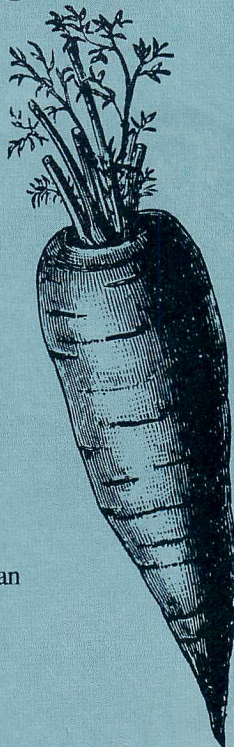
Top 20 Fruits

- banana
- apple
- watermelon
- orange
- cantaloupe
- grape
- grapefruit
- strawberry
- peach
- pear
- nectarine
- honeydew melon
- plum
- avocado
- lemon
- pineapple
- tangerine
- sweet cherry
- kiwi fruit
- lime



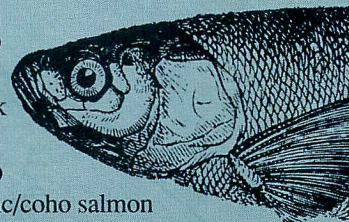
Top 20 Vegetables

- potato
- iceberg lettuce
- tomato
- onion
- carrot
- celery
- sweet corn
- broccoli
- green cabbage
- cucumber
- bell pepper
- cauliflower
- leaf lettuce
- sweet potato
- mushroom
- green onion
- green (snap) bean
- radish
- summer squash
- asparagus



Top 20 Fish

- shrimp
- cod
- pollock
- catfish
- scallop
- Atlantic/coho salmon
- flounder
- sole
- oyster
- orange roughy
- Atlantic/Pacific and jack mackerel
- ocean perch
- rockfish
- whiting
- clam
- haddock
- blue crab
- rainbow trout
- halibut
- lobster



and nine other industry trade groups. (See inside back covers of the May 1992 through November 1992 *FDA Consumer*.)

Live demonstrations, and videotapes and other electronic means also may be used to convey nutrition information, but only as adjuncts to the print pieces. In FDA's view, non-print media are less likely than print media to be dependably available. Breakdown of videotape players, for example, may make the information unavailable for any length of time.

Other means of conveying nutrition information for these foods may exist, and, according to Pennington, FDA would like to see retailers and others identify them.

"We encourage retailers to experiment in finding ways that best convey nutrition information to consumers," she said. "And we hope that they share their findings with us."

Checking for Compliance

FDA plans to keep tabs on how well food retailers comply with the voluntary

guidelines. Under the Nutrition Labeling and Education Act, the program can remain voluntary only as long as there is "substantial compliance."

FDA defines "substantial" as at least 60 percent of a nationwide representative sample of grocery stores. Grocers are considered in compliance if at least 90 percent of the 20 most commonly eaten raw fish and at least 90 percent of the 40 most commonly eaten types of raw produce sold in their stores are properly labeled. Thus, retailers have to provide nutrition information for only those most commonly eaten fruits, vegetables and fish that they sell in their stores.

FDA will check compliance by surveying every two years a sample of 2,000 U.S. food stores that sell produce or raw fish. Results of the first survey, which began in late 1992, will be issued in an FDA report due to Congress in May 1993.

If substantial compliance is found, the program will continue on a voluntary basis. But if FDA determines that compli-

ance is not substantial, it will issue new regulations *mandating* point-of-purchase nutrition information for raw fruits, vegetables and fish.

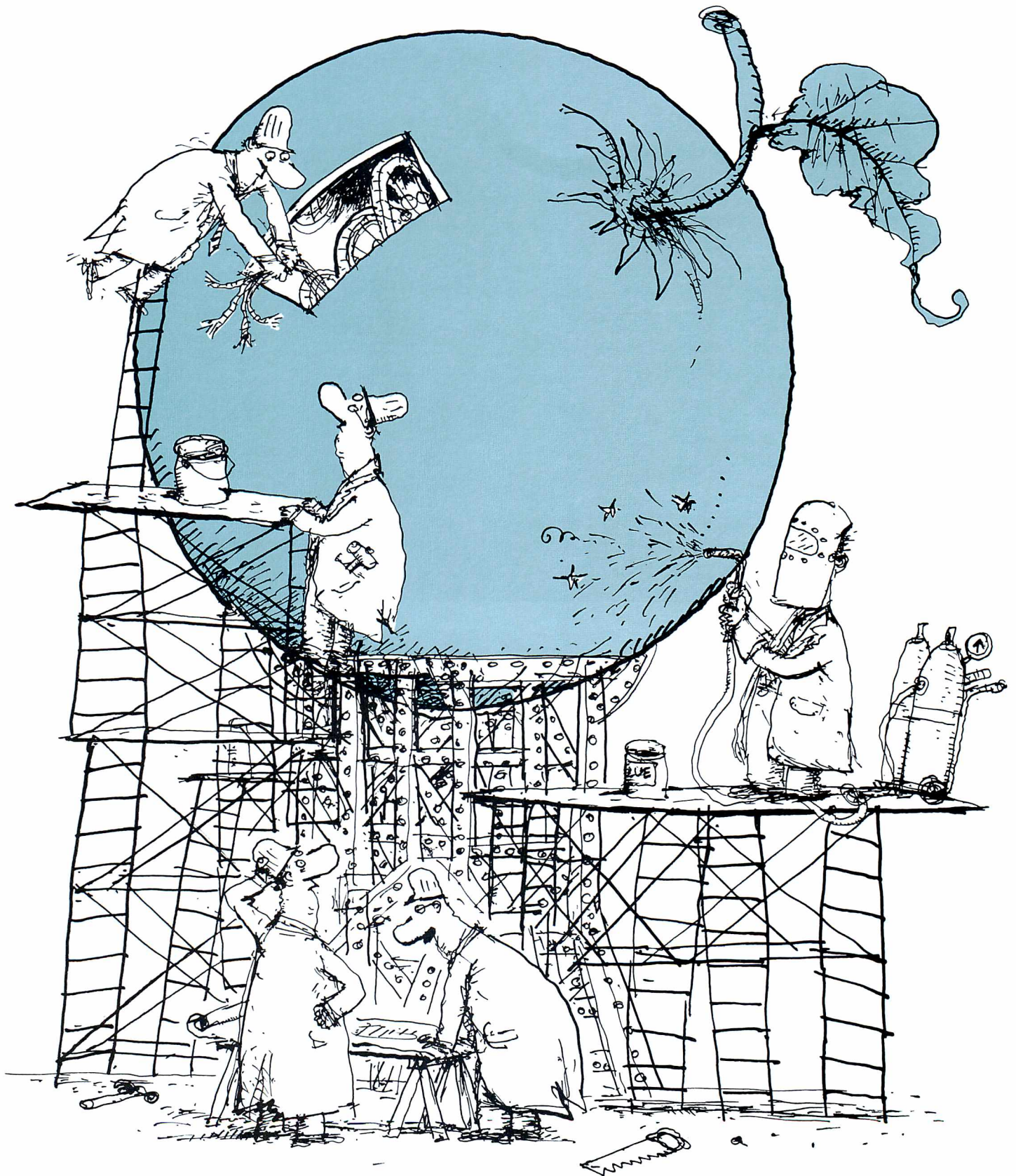
In addition, at least every two years, FDA will revise and publish in the *Federal Register* nutrition labeling data for the 20 most frequently eaten raw fruits, vegetables and fish.

At the same time, it will conduct a survey of food retailers and issue a report to Congress on the status of the voluntary program.

At least one food retailer hopes to be part of those proceedings—D'Agostino Supermarkets, where, according to spokeswoman Moore, voluntary in-store nutrition information programs are in place in all 25 of its chain stores.

"I certainly hope [FDA comes] to D'Agostino," she said. "Because we're more than ready." ■

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



Genetically Engineered Foods

Fears & Facts

An Interview with FDA's Jim Maryanski

Genetic engineering of fruits and vegetables and FDA's policy concerning these foods have been the subject of many consumer questions recently. To help answer the questions, FDA Consumer writer Mary Alice Sudduth talked to James Maryanski, biotechnology coordinator in FDA's Center for Food Safety and Applied Nutrition.



Q: What is “new biotechnology” in reference to food plants, and how does it differ from old biotechnology?

A: All plant breeding involves genetic manipulation of plants. There are hundreds of new plant varieties introduced every year in the United States, and all have been genetically modified through traditional plant breeding techniques—such as cross-fertilization of selected plants—to produce desired traits. This is “old biotechnology.”

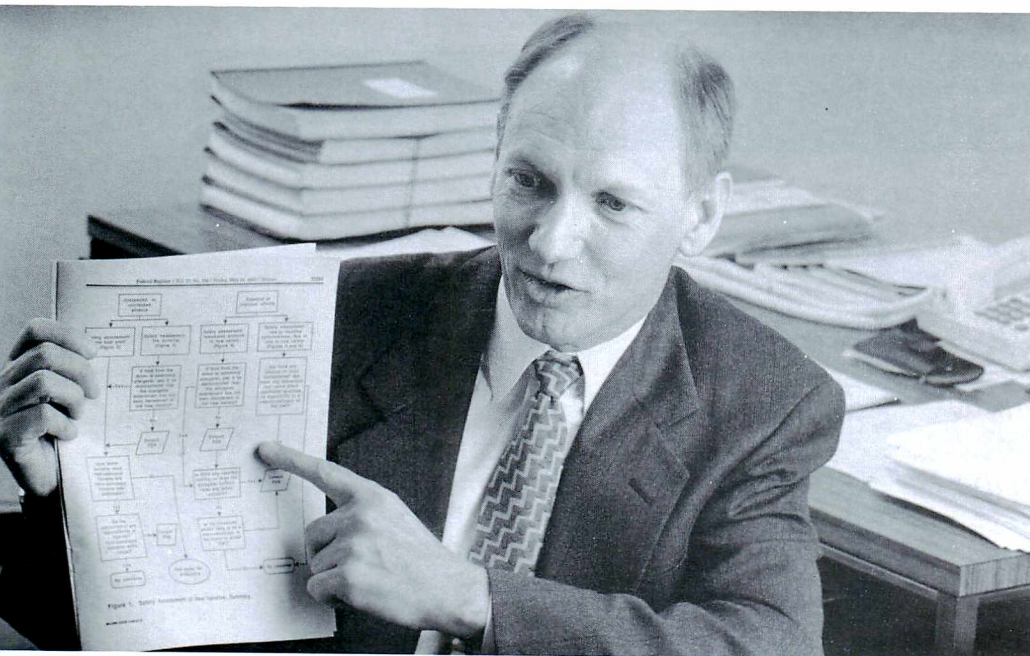
The new biotechnology—known variously as gene splicing, recombinant DNA, or genetic engineering—is actually an extension of traditional plant breeding. It involves direct modification of DNA, a living thing’s genetic material. This new technique is more precise, making it possible to direct and predict changes without introducing extraneous,

of potentially useful traits. These may include size, solids content, or resistance to certain viruses or fungi.

Q: Under what circumstances will FDA require labeling of genetically engineered foods?

A: One important area is that of potential allergens. If a gene from a food that commonly causes allergic reactions, like fish or peanuts, is inserted into tomatoes or corn, where people would not expect to find allergens, then the vegetables would have to be labeled to alert sensitive consumers. If companies can demonstrate scientifically that the allergenic component was not transferred to the vegetable, no special label will be required. FDA’s policy states that proteins taken from commonly allergenic foods are presumed to be allergens unless demonstrated otherwise.

People have this perception that all these things are just coming out of the sky and landing in the grocery stores next week, and that’s just not true.



undesirable traits. The new technique also will allow scientists to introduce genes from essentially any organism into a plant.

Q: Why do we need these plants and the foods they produce?

A: Plant breeders have a limited pool of genes—and, therefore, traits—available for use in improving plants. By looking at bacteria and animals, scientists can find other traits that may expand the number

Labeling also could be required if the nutritional content of the food is changed. Tomatoes are a major source of vitamin C, and if someone develops a tomato that no longer contains vitamin C, then that will have to be disclosed. So we envision a number of circumstances where labeling will be necessary, and we’ll use the same labeling regulations we’ve always used under the FD&C Act. We’ve invited public comment on this issue, because we anticipate consumers will have diverse opinions about genetic engineering and about what information should appear on labels.

Q: FDA has emphasized the importance of proper labeling of foods and has initiated legal action against certain products—Citrus Hill “fresh” orange juice, for example—because of misleading labeling. How does this differ from labeling biotechnology-derived foods? Isn’t the fundamental issue the same—full disclosure?

A: The law says labeling for foods must disclose information that’s material, as well as avoid false or misleading statements.

It’s our view that the method by which a plant is developed by a plant breeder is not material information in the sense of the law. For example, we do not require sweet corn to be labeled “hybrid sweet corn” because it was developed through cross-hybridization. And plant breeders have many other traditional techniques through which they coax nature to change genes that would not occur otherwise. A process called somoclonal variation allows breeders to take advantage of natural mutations in plant cells that produce desired traits. Through embryo rescue, breeders nurture embryos produced by crossing two plant varieties that would not breed naturally, producing potentially useful plants that would not have survived on their own. Historically, we have not required this information to be on labels. It would not be practical.

If genetic engineering or any other technique changes the composition of a tomato

Splicing to the Nitty Gritty

FDA's policy for genetically engineered foods covers all foods produced from new plant varieties developed by any method of plant breeding. The policy is based on the Food, Drug, and Cosmetic Act's requirements of post-market surveillance of foods and pre-market approval of new substances. This system has ensured the safety of foods and food additives for many years.

Under the FD&C Act, GRAS substances (those "generally recognized as safe") are excluded from the requirement for pre-market approval. But a new substance introduced via breeding for which safety has not been established must be approved as a food additive before marketing. Genetically engineered food crops that do not contain substances significantly different from substances already in the diet will not require approval as food additives. A substance that is significantly different from those already in consumers' diets will have to be approved by FDA.

All foods are subject to FDA's post-market authority under the "adulteration" provisions of the act, and producers have a legal duty to ensure that the foods they place on the market meet the safety standards of these provisions. Adulterated foods are subject to seizure; producers and distributors who fail to meet their statutory duties are subject to injunction or criminal prosecution. These provisions have been FDA's primary tools for ensuring the safety of new varieties of fruits, vegetables and grains.

New plant varieties routinely go through many years of testing and evaluation before marketing, and foods from these plants are tasted and tested.

Plants developed by genetic engineering are being subjected to the usual tests for quality (Is the fruit firm? Does it look good?) and agronomic traits, such as improved processing and pest resistance. In addition, companies are using new tools of molecular biology and genetics to look at

the very nature of these genetic changes. Biotechnology not only allows scientists to make new products, it also provides better tools to assess safety.

In addition, companies are testing for known plant toxins, comparing levels in new varieties with levels in parent varieties. For example, tomatine is a natural toxin in tomatoes, but when using traditional breeding techniques, scientists don't usually look for it. However, the developer of a tomato that is genetically engineered to stay fresh longer is evaluating tomatine levels in that tomato.

FDA has told companies that they will need to do more tests on the first foods developed using new biotechnology, to ensure that these foods are safe. But as developers gain more experience with these techniques, they will not need to do as many tests. ■

—M.A.S.

in a way that it's really not the same tomato anymore, then it would have to be called something different. It would have to have a different varietal name, or, if it was a significant difference, it may not even be called a tomato.

We are reviewing the comments from the public on this issue to see if there is a basis for modifying our policy. However, if we were to require labeling of all genetically engineered fruits and vegetables, it would not be merely a matter of putting a sticker on a tomato or a banana. Producers would have to segregate the genetically engineered foods from other varieties, whereas normally those are all just lumped into a barrel. And then what happens when you make tomato paste, and that tomato paste is used to make pizzas? Does the label have to follow along through the food processing chain? It would increase the cost of these foods to consumers and would disrupt our complex food distribution system.

Q: *Are there environmental risks involved in producing genetically altered foods?*

A: Potential environmental risks from these crops are the same as those that occur in plants developed by traditional methods. There are many complex issues—such as potential transfer of traits to other plants and potential adverse effects on other organisms, particularly endangered species—that need to be taken into account. For example, if a plant has many wild relatives, it could pass a gene to one of those, resulting in an outcross plant species with some undesirable traits. The wild plants could develop into a fast-growing weed species, for instance. For some crops, like tomatoes, this really isn't a risk in the United States because there are few, if any, wild relatives of tomatoes that could be bred accidentally. But there are other plants, such as soybeans and squash, where there will be potential for an outcross species. Whether outcrossing is a problem depends on the trait that's introduced, as well.

Environmental risks are looked at during the research and development phase. Right now, crops developed using recombinant DNA methods are reviewed by the U.S. Department of Agriculture's Animal and Plant Health Inspection Service. If FDA acts on a food additive petition or GRAS [generally recognized as safe] petition for a new ingredient, we will do an environmental assessment. We will look at what the other agencies have done, and, to the extent possible, we will rely on their information. If there are other issues, they will have to be considered.

Q: *How can consumers be sure companies producing these foods will test them adequately and take all necessary measures to ensure they are safe for consumption and will not harm the environment?*

A: All the companies that we've talked to are doing the kinds of tests that we would think need to be done. In May, FDA published a notice in the *Federal*

A breeder does not actually take something from the animal and introduce it into the plant. . . . So you don't really have pieces of animals in vegetables.

Register providing a guide for companies that establishes a standard of care. What's happening now is that companies are coming to us and telling us the kinds of tests they're proposing based on the guidance in our *Federal Register* notice. And they're asking for our advice.

Q: *How long will it be before most of the foods now being developed through new biotechnology are available to consumers?*

A: That's a good question. People have this perception that all these things are just coming out of the sky and landing in the grocery stores next week, and that's just not true. There are products, like the Flavr Savr tomato, that are nearing commercialization. Assuming all the safety questions are answered, it probably will be introduced within the next year. USDA has received a request to rule on whether a variety of virus-resistant squash may be grown without USDA oversight, so one would assume it's close to commercialization. But most of the products—such as insect-resistant produce, vegetables with increased amino acids, and low-caffeine coffee—are two to five years away. We're going to see a gradual introduction of these products over the next several years, not an avalanche.

Q: *What about the possibility of plants containing animal genes?*

A: Several experimental plants have been developed that have copies of genes found in animals, such as the "antifreeze protein" gene from the Arctic flounder that may make tomato paste freeze and thaw better.

However, there really aren't any plants with animal genes, that we know of, that are going to be marketed foods in the near future. So we have a good deal of time to think about the issue of animal genes. We believe the safety of the proteins produced by these genes should be evaluated based on their characteristics. If, for example, the flounder antifreeze protein is a component of fish fillet, it likely would be safe to eat as a component of tomato paste. But proteins derived from animals that have not been consumed safely will be treated as new food additives.

Q: *Has FDA considered the ethical or religious implications of injecting animal genes into plants? How will this affect vegetarians?*

A: FDA is considering these issues. There are thousands of genes in a plant. When a scientist adds new genes from an animal, it gives that plant several new proteins. But these proteins would not seem to give animal characteristics to the vegetable.

A breeder does not actually take something from the animal and introduce it into the plant. For example, a scientist copies the fish "antifreeze protein" and modifies the gene. We know the characteristic of the fish gene, and we can tinker with it to make a different version. The copy is what is introduced into the plant, and the new gene works just like any other plant gene. So you don't really have pieces of animals in vegetables. You have pieces of plant DNA that are the same as, or nearly the same as, pieces of animal DNA.

One of the things people probably don't realize is that there are genes in humans and animals that are in plants. There is a gene that occurs in rice that also occurs in the human brain. Vegetarians would not avoid rice because of that.

Our current view is that these modifications will not result in foods that violate any ethical or religious considerations. However, we recognize people will have different views, and we specifically invited comment on this issue. We're also

trying to get comments from various religious and other authoritative leaders so that we can get some sort of official opinion.

Q: *What values will these genetically engineered plants have—more nutrients, better taste?*

A: Both of those, and many agronomic values: better processing, freeze resistance. That's what using a flounder gene is all about—making a tomato freeze and thaw better. That protein also is being used as a model for developing a food additive to use in ice cream so ice crystals don't form.

In addition, scientists actually will be able to make food safer. They'll be able to reduce the natural toxins. We're already looking at ways to identify the allergenic proteins in foods like milk. But those things are many years in the future.

Right now, it's more a matter of giving fruits and vegetables better shelf life and shipping properties. Most of the traits will have economic values for farmers and processors.

Q: *Surveys of consumer attitudes have shown that most people will eat genetically engineered foods, but that a considerable portion will not. Is it FDA's role to ensure public acceptance of these foods?*

A: No, it is not. Our role is to tell the public how we ensure the safety of foods under the FD&C Act. We tell people about the important scientific questions that need to be answered and about the kinds of tests that should be done. But we can't be proponents of the products. We can't say genetically engineered food is something consumers should buy. However, we can explain to the public how these foods are the same and how they are different from other varieties.

The U.S. government has a policy to foster biotechnology, and FDA recognizes that there are immense potential benefits to be derived from this science. It's not our responsibility to promote individual products, but we see that this technology does have beneficial applications. We are encouraging industry by working with them to ensure that safety questions are resolved. We're expecting rigorous testing and will not accept unsafe products. ■

BIOTECH DEVICES

Replacing Test Animals, Improving Diagnoses

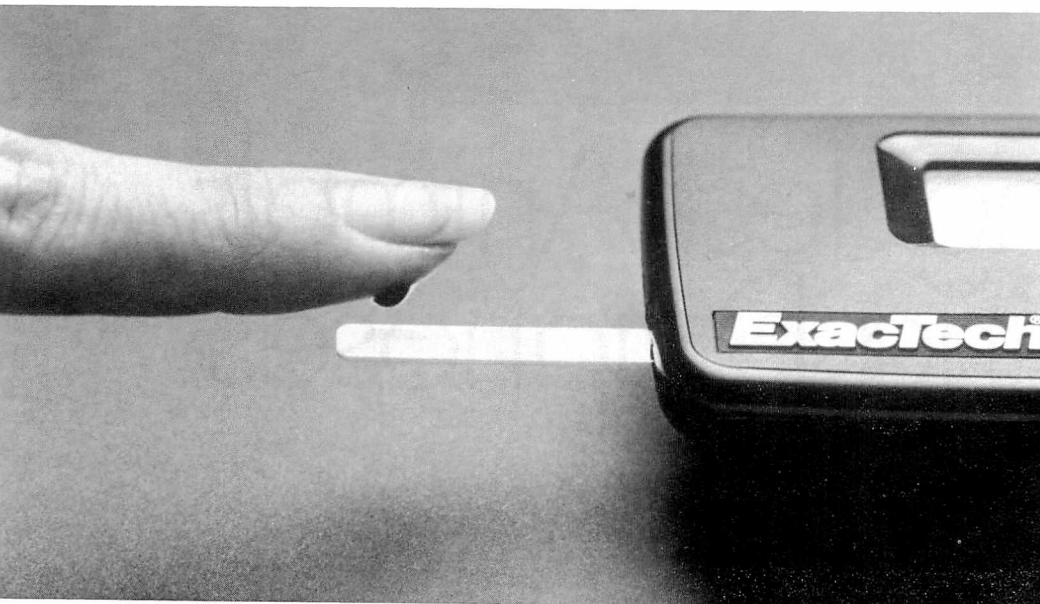
by Ricki Lewis, Ph.D.

This is the first of two articles on biotechnology and medical devices.

The young woman hadn't been feeling well. She tired easily, and her breasts were sore. When her menstrual period was a week overdue, she bought a home pregnancy test kit. The next morning, she placed a few drops of her urine onto an applicator stick, then spent five very nervous minutes pacing. Finally, a blue spot appeared on the applicator. She broke into a broad grin—she was pregnant!

A generation ago, when the young woman's mother suspected she was pregnant, confirming her suspicions wasn't as easy.





People with diabetes can use an over-the-counter glucose meter that is a sophisticated biosensor device. The person places a drop of blood on a disposable test strip and inserts the strip into the device. An enzyme binds to the blood glucose, producing a reaction that stimulates electrodes and, within seconds, the blood sugar level flashes on a digital display. (Photo courtesy Medisense)

After two missed menstrual periods, the doctor sent a sample of her urine to a lab, where it was injected into a female rabbit. The rabbit was killed, and its ovaries examined. If they were swollen, it meant the urine contained human chorionic gonadotropin (HCG)—the very same hormone indicating pregnancy that today is detected in minutes, and weeks earlier, with a home pregnancy test kit.

A pregnancy test kit is one of the most familiar medical devices made possible by biotechnology—the use of biochemicals, cells, or other components of living organisms to make or modify products. Not only has biotechnology replaced the use of animals in some medical tests, but it now routinely diagnoses a variety of illnesses faster and more accurately than standard laboratory procedures.

In a home pregnancy test kit, a protein called a monoclonal antibody (MAb) binds to HCG, causing a color change. HCG is present in a woman's urine only during pregnancy. MAb test kits are the most common type of biotech device regulated by FDA. The agency has cleared for marketing more than 635 biotech de-

vices, a growing subdivision of the broader area of medical devices.

"A medical device is any health-care product that does not achieve its primary purpose by chemical action in or on the body or by being metabolized [altered to a different chemical]," says Kiki Hellman, Ph.D., senior scientist and manager of the biotechnology program at the Center for Devices and Radiological Health. MAb-based devices are used *in vitro* (in laboratory glassware) to detect infections, hormone levels, drug levels (therapeutic and "recreational"), and cancer cells.

A second major type of biotech device uses a DNA probe, which diagnoses infectious or genetic diseases by detecting specific sequences of DNA (deoxyribonucleic acid), the biochemical components of genes. Other biotech devices include new drug delivery systems, replacement cells and tissues that combine natural and synthetic components, and biosensors (devices that detect a biochemical reaction and convert it into an electronic signal). Biotech devices are used in hospital and private labs, physicians' offices, and in consumers' homes.

Biotech-based diagnostic devices are often more direct than their conventional counterparts. Monoclonal antibodies and DNA probes rapidly recognize proteins or genes distinct to a particular disease-causing microbe or virus. These techniques are also able to spot an errant biochemical that makes up a very small part of a specimen (such as blood or urine).

"Biotechnology has provided significant improvement in the specificity and reproducibility of diagnostic tests," says Hellman.

Biotechnology offers different approaches to a single problem. Consider detecting the human immunodeficiency virus (HIV). The most widely used test detects antibodies that a person's immune system manufactures in response to encountering HIV. If that test (using a technique called enzyme-linked immunosorbent assay, or ELISA) is positive, the result is confirmed with a Western blot test, which detects a protein unique to HIV.

Still other HIV tests using biotechnology are experimental. These include growing the virus; finding other HIV-specific

proteins; and using various gene amplification techniques to make enough copies of HIV's genetic material in a body fluid sample to detect it. And a biosensor HIV test is being developed that couples binding of a person's antibodies against HIV to a change in capacitance (the ability to store charge) of an electrical system.

The aim of these experimental HIV tests is to be more precise and to do this by directly detecting part of HIV. (In contrast, antibody-based tests detect the body's response to HIV, which can appear six weeks to a year after infection.)

Four areas where biotech devices are having an exciting impact are biomaterials, biosensors, monoclonal antibodies, and DNA probes.

New Materials

Developing replacement body parts has long been a goal of medicine, but one surrounded by steep obstacles. Donor organs and tissues are exceedingly scarce, and even when they are available and transplanted, the recipient must take immunosuppressant drugs such as cyclosporin for life. Yet a synthetic implant can be toxic or walled off by scar tissue.

"Many of the synthetic materials now used pose all sorts of problems, such as toxicity and bioincompatibility, so there is a push to use more natural derivatives or

biotech-derived materials," says Hellman.

For example, elastin is a naturally occurring connective tissue protein that is useful in surgery. When applied as a foam, powder or sheet, the biocompatible protein prevents scar tissue adhesions from forming at the sites of surgery.

Where does elastin come from? Synthesizing it chemically is time-consuming and costly, yet obtaining elastin, or any biomolecule, from cadavers introduces the risk of infection. Enter recombinant DNA technology. Bacteria given human genes encoding elastin produce pure, plentiful amounts of the valuable protein.

New products resulting from recombinant DNA technology are proteins or peptides (pieces of proteins), because these are the types of molecules that genes instruct a cell to manufacture. These drugs and biologics include insulin (to control diabetes), human growth hormone (to treat some forms of dwarfism), the immune system biochemicals interferon and interleukin (used to treat some cancers), and erythropoietin (to treat severe anemia

are developing biomaterials to surround these drugs so that they can reach their sites of action.

Bioengineered Tissue

Recombinant DNA-derived proteins combined with synthetic materials can function as implants. Two companies, Advanced Tissue Sciences in La Jolla, Calif., and Organogenesis, in Canton, Mass., have a variety of such bioengineered tissues in development, with a few in FDA-sanctioned clinical trials.

The basic recipe for a bioengineered tissue is to sculpt a scaffold from a synthetic material that is accepted in the body, and place cells in or on it. These cells secrete substances as they normally would, or they may be genetically altered to overproduce their natural proteins or manufacture entirely different ones, such as growth factors that might help make the implant more acceptable to the body.

"The primary goal of our tissue engineering research is to grow these tissues as replacements for damaged or failing or-

in kidney transplant recipients).

Protein products require special delivery systems to enable them to circumvent biochemicals that dismantle them along the digestive tract, such as stomach acid and protein-digesting enzymes in the small intestine. Several biotechnology companies

A pregnancy test kit is one of the most familiar medical devices made possible by biotechnology.

The agency has cleared for marketing more than 635 biotech devices.

gans. The benefits of this research could positively impact the lives of patients requiring organ transplants as well as those who suffer from diseases or injuries," says Gail K. Naughton, Ph.D., executive vice president at Advanced Tissue Sciences.

Advanced Tissue Sciences' artificial skin, called Dermagraft, has helped more than 70 burn patients so far in clinical trials. A similar product from Organogenesis, called Graftskin, is being tested to replace skin lost during surgery to remove cancers, moles and tattoos.

"Rather than create a new wound by removing skin from another location on the body, surgeons could use biologically equivalent skin that won't be rejected and will promote natural healing," says David J. Leffell, M.D., chief of surgery at Yale University School of Medicine (New Haven, Conn.), where Graftskin is being tested.

Other tissues on the drawing board at these and other companies include liver, connective tissue, bone marrow, and blood vessels. Some bioengineered tissues are already commercially available for use in toxicity testing, in place of animals.

A scaled-down version of an engineered tissue, a cell implant, is a new route to drug delivery, placing cells that naturally manufacture needed substances precisely where they are needed.

The key advantage of a cell implant is that it is "immunoisolated"; its packaging enables the cells to secrete without being detected by the immune system and destroyed. This is done by surrounding cells with a polymer membrane with holes small enough to allow nutrients in and the

therapeutic protein out, while excluding the large molecules and cells responsible for immune rejection, according to Seth A. Rudnick, M.D., president of CytoTherapeutics, Inc. in Providence, R.I.

Prime targets of cell engineers are the beta cells of the pancreas. These cells secrete insulin, a peptide hormone that enables glucose (blood sugar) to enter cells, where it is a source of energy. A cell implant would far better mimic the body's continual secretion of insulin than once or twice daily injections and might prevent some of the damage associated with diabetes caused by the on-again off-again delivery of insulin.

The beta cells lie in a portion of the pancreas called the islets of Langerhans. Researchers have been trying to transplant "naked" islet tissue—just cells—for 20 years, with little success, because the immune system attacks them. Throughout the 1970s and 1980s, various biotechnology companies "played with the idea of encapsulating cells to hide from the immune system. But in two to three months, the capsules broke down," says Rudnick.

Several companies, including CytoTherapeutics and BioHybrid Technologies in Shrewsbury, Mass., are working on finding the right mix of casings and cells to engineer the long-awaited "artificial pancreas." Both companies' products are in the animal testing stage, and both say they will apply to FDA for permission to begin clinical trials by 1994. The same companies are exploring using cell implants in the brain to treat Parkinson's disease and in the spinal cord to relieve chronic pain.

Biosensors

Biosensors wed nature to electronics. A biosensor consists of a biological structure that recognizes another biological structure (such as an enzyme, antibody or receptor), plus a mechanism to transduce, or convert, the reaction of biological recognition into an observable signal, such as a voltage change, light emission, or sound.

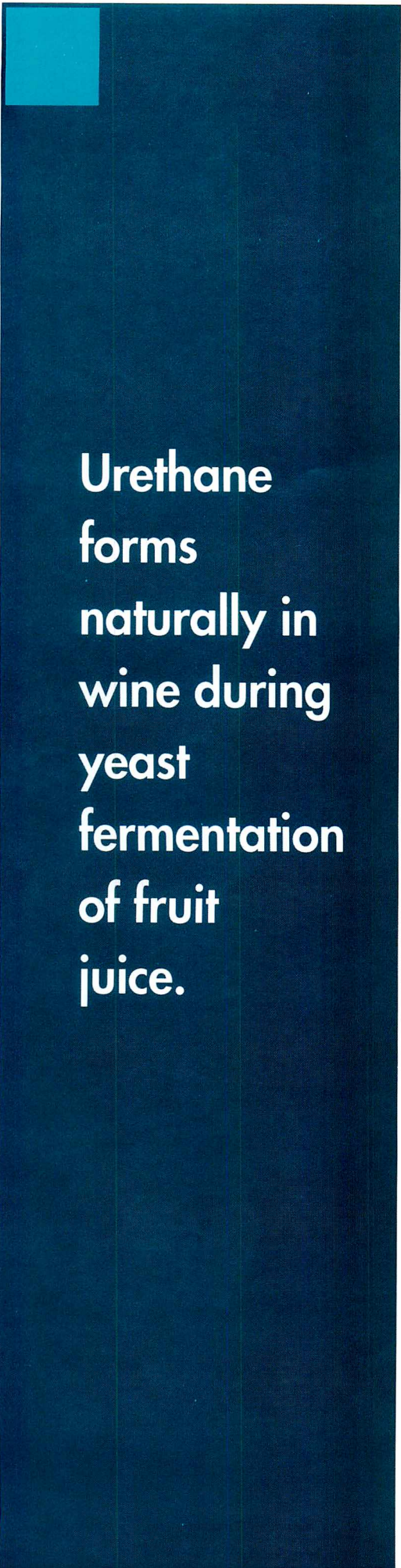
Many people who have diabetes use a biosensor to monitor their blood glucose (sugar) levels, information needed several times a day to determine the timing of insulin doses. The device, called a glucose meter, resembles a pen and has been on the market since 1988.

The biological component is the enzyme glucose oxidase. A person drips blood onto a disposable test strip, and inserts the strip into the pen. The enzyme binds to glucose in the blood, producing an electrochemical reaction that stimulates electrodes attached to a meter in the pen device. The meter measures the signal, and in 30 seconds, the blood sugar level flashes on a digital display.

In the future, people with diabetes may be treated from within, thanks to combinations of biotechnology devices. Recombinant DNA-derived insulin, or perhaps transplanted beta cells, may be implanted along with a glucose biosensor that controls rate of insulin delivery. ■

(Next: Monoclonal antibodies and DNA probes)

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



Urethane forms naturally in wine during yeast fermentation of fruit juice.

Until all scientific research is completed and evaluated, and regulations established, FDA is working with industry to reduce any potential risk to humans from urethane and is participating in tests to find out if the small amounts of urethane present in alcoholic beverages might be harmful.

Industry has voluntarily agreed to develop and use manufacturing techniques to reduce urethane's levels as much as possible. The Distilled Spirits Council of the United States (DISCUS), the American Association of Vintners, and the Wine Institute have told FDA they are studying how urethane forms during fermentation and are changing manufacturing processes to control its formation in alcoholic beverages.

FDA and the Bureau of Alcohol, Tobacco and Firearms (ATF) have done limited surveys of the urethane content in alcoholic beverages, and FDA has evaluated existing urethane toxicity data. In addition, at FDA's request, the National Toxicology Program, a federally funded research group, has done an initial study in animals to help FDA determine if urethane in alcohol poses a significant risk to humans.

Follow-up studies are not complete, and for now, according to the Cancer Assessment Committee of FDA's Center for Food Safety and Applied Nutrition, there is not yet enough information to assess the risk.

Urethane by Nature

Urethane formation is not a new phenomenon produced by high-tech processing. The chemical forms naturally in wine during yeast fermentation of fruit juice.

Fermentation also produces urea from the yeast metabolism of arginine, an amino acid in grapes. Recent studies show that when urea reacts with ethyl alcohol after fermentation, ethyl carbamate, another name for urethane, results.

Alcoholic beverages other than wine present variations on this process, which complicates studies. Levels of urethane differ with each type of alcoholic beverage, explains Benjamin J. Canas, of FDA's division of food chemistry and technology. For example, heat seems to accelerate the production of urethane. Some sherries are baked to provide a rich taste, and bourbons are distilled at high temperatures. Both processes may raise urethane levels. Also, levels can differ significantly, even among different bottles of the same variety or brand, Canas says. (See "Too Many Drinks Spiked with Urethane" in the April 1988 *FDA Consumer*.)

In 1985, work done by Health and Welfare Canada, FDA's Canadian counterpart, brought international attention to the issue of urethane in alcoholic beverages. Canadian authorities had detected the chemical in certain wines and distilled spirits, and had set levels for regulatory action.

FDA and ATF sampled the market and found that imported fruit brandies contained the highest levels of urethane—averaging a little less than 1,200 parts per billion (ppb). Sake followed with about 300 ppb, and then bourbon with levels averaging 150 ppb.

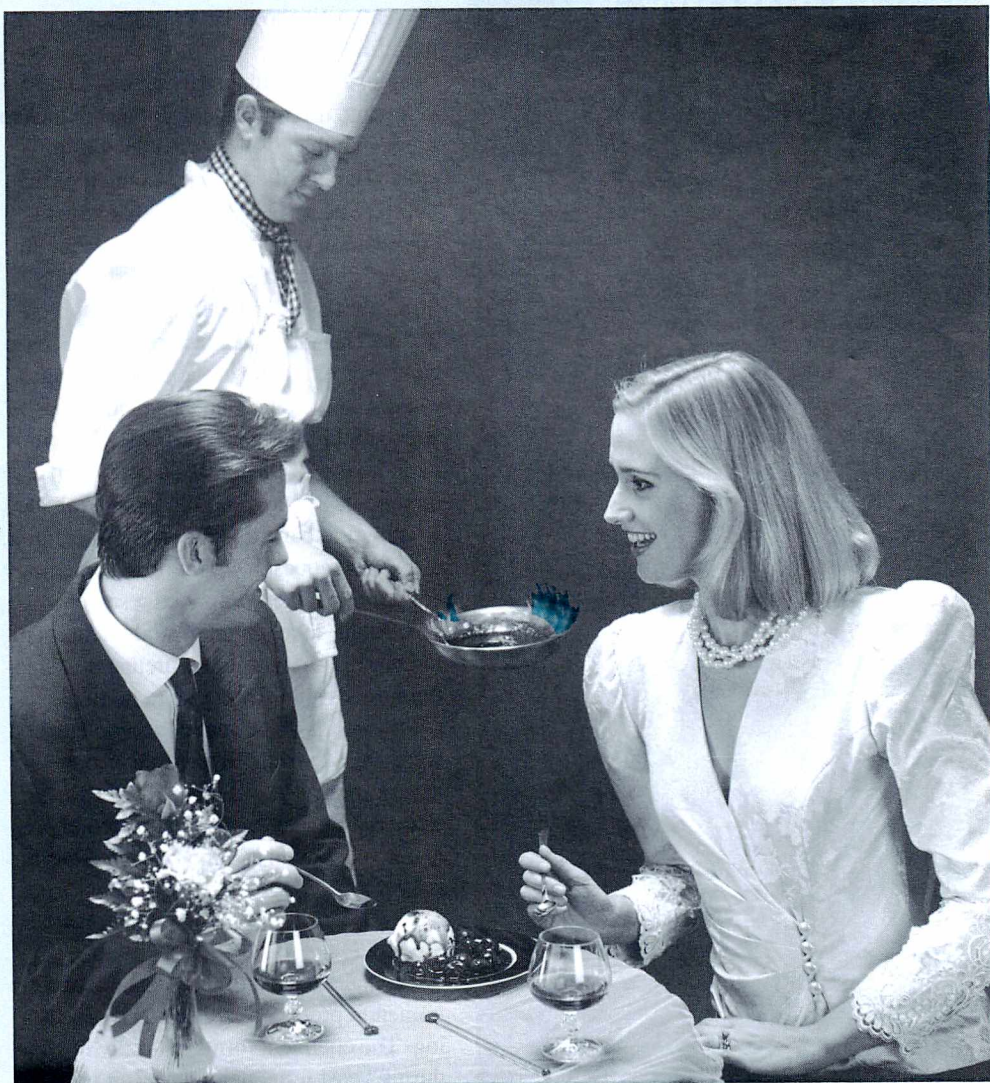
Grape table wines had urethane levels averaging 13 ppb, but dessert wines, such as sherries and liqueurs, averaged about 115 ppb.

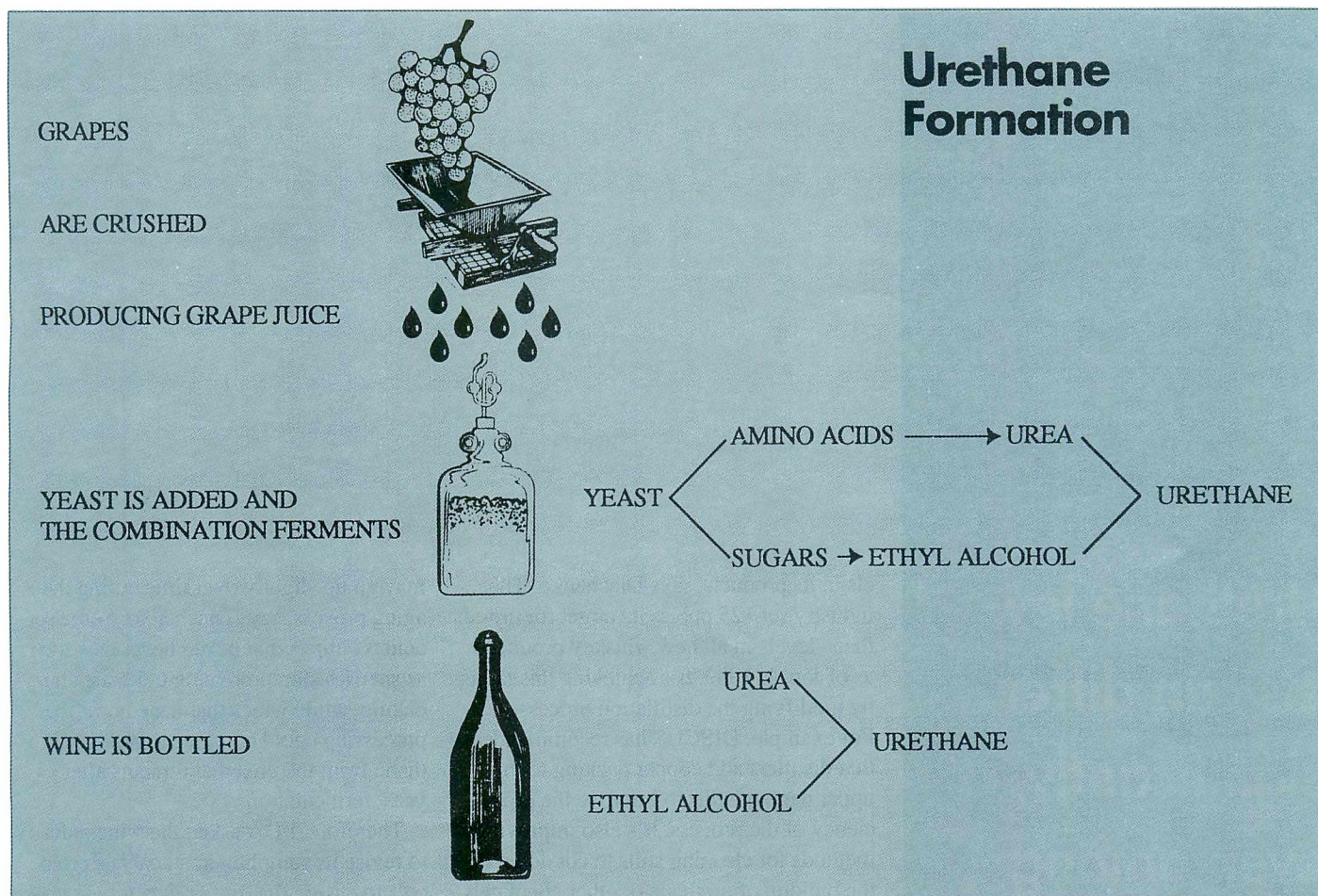
Urethane In Alcoholic Beverages Under Investigation

by Judith E. Foulke

The Food and Drug Administration is carefully evaluating studies to determine if there could be a long-term health risk to consumers from urethane in alcoholic beverages.

Urethane is a chemical substance that forms naturally during the fermentation process. It causes cancer in animals, but it is not known if it poses any significant health risk to humans. Based on data currently available, FDA does not believe that urethane levels in alcoholic beverages currently on the market are an immediate short-term health risk.





While grape juice ferments into wine, the yeast reacts with amino acids to produce urea and with sugars to produce ethyl alcohol. The urea and ethyl alcohol then react together to produce very low levels of urethane (also called ethyl carbamate). After the wine is bottled, the urea continues to react with ethyl alcohol, and more urethane is produced.

Industry Efforts

The wine and distilled spirits industries have invested in basic research, plant modifications, and analytical testing to achieve the reductions in urethane levels they've made so far, says Gregory W. Diachenko, Ph.D., chief of FDA's food formulation branch.

The Wine Institute, for example, is encouraging several changes in grape growing and wine production that can lower urethane levels. For example, it is encouraging grape growers to minimize fertilization. Heavily fertilized vineyards tend to produce grapes that contain high levels of arginine, thus leading to higher urea and urethane levels.

The institute also recommends using a type of yeast, known by the French name

prise de mousse, for the fermentation process. This yeast produces wine with lower levels of urea. And the institute is asking the industry to fortify (add alcohol to) desert wines at a specific time during the fermentation process when the urea levels are the lowest. (Fortified wines contain more than 14 percent alcohol and have the most urethane of all wines.)


The wine industry has a monitoring program involving 20 of the largest-volume U.S. wineries and about 60 other wineries. Under this program, the companies annually sample a cross-section of their bottled wines for urethane levels. The wine industry has given FDA yearly summaries of sampling surveys since 1989.

Urethane levels in wines are getting lower, according to FDA supervisory re-

search chemist Frank L. Joe, Ph.D., who has assembled statistics from the summaries. In 1987, a sampling showed table wines averaged 13 ppb, and retail bourbons averaged 150 ppb. In 1991, those numbers had dropped to 10 ppb for domestic table wines and 70 ppb for bourbons (see accompanying article).

The Wine Institute and the American Association of Vintners, representing the U.S. wine industry, voluntarily set a target of 15 ppb for table wines from the 1988 harvest, and 60 ppb for fortified wines from the 1989 harvest. FDA has asked the industry to consider reducing its target levels based on the encouraging results of its urethane-lowering efforts.

The distilled spirits industry is also working toward lowering the urethane lev-



Urethane levels can differ significantly, even among different bottles of the same variety or brand.

els in its products, says Diachenko. The industry set 125 ppb as its target for urethane levels in all new whiskey produced as of Jan. 1, 1989. It's achieving this target by modifying the distillation processes. For example, DISCUS has recommended that distillers add copper packing to the upper parts of stills to improve the efficiency of the process. It's also improving methods for cleaning stills to cut down on the buildup of urethane or other chemicals that might form, and it's monitoring the operation of the stills so that urethane is not carried by distilled vapors into new batches.

Like the wine industry, DISCUS is monitoring production of all its 17-member bourbon distillers in the United States. Distillers sample daily for urethane in fresh distillate.

DISCUS provides FDA with quarterly reports of weekly averages of urethane levels, with the highest and lowest levels on any day for each week of the quarter. The weekly averages for all distillers have been below their target levels.

The highest average level in the first quarter of 1992 was 109 ppb, Joe reports. Many distillers have achieved weekly averages below 30 to 40 ppb.

ATF does its own sampling as a backup to the data FDA receives from industry. Although industry has been sampling products since 1987, the lower urethane levels may not show up this year in some brands of distilled spirits because distillates are usually aged four to eight years before marketing, says Canas.

Some companies have found that urethane levels in certain bourbon batches

may go up slightly over time during the aging process, says Diachenko. Some scientists believe that baked beverages such as sherries stop producing urethane after baking, while wines that have no further processing could continue to produce urethane from the urea that remains after yeast fermentation.

Therefore, FDA asked the wine industry to revise its sampling and analysis protocols to ensure that future data reflect urethane levels found in bottled products purchased by consumers. DISCUS has also asked its members to investigate ways to identify and eliminate any other substances that could be causing the increases in aged products.

Industry studies suggest that if urease, an enzyme capable of reducing urea levels in fermented drinks, is added to products such as dessert wines, which contain high levels of urea, the urethane content could be reduced, Diachenko says. FDA is currently evaluating a petition from industry to permit the use of urease in wine production.

Foreign Exporters

FDA has alerted all countries that export alcoholic beverages to the United States that they need to develop programs to meet the voluntary urethane target levels established by the U.S. industry. Research published in Britain, France, Germany, and Switzerland suggests that these countries are making some progress and that the levels in most imported alcoholic products have come down considerably (see accompanying article).

H. Tanner, Ph.D., from the Swiss Fed-

Wine and Whiskey Sampling

FDA and the U.S. Bureau of Alcohol, Tobacco and Firearms has sampled wines and whiskeys from domestic and foreign producers to determine urethane levels.

The following are the results of two samplings measuring average urethane levels in parts per billion (ppb). The 1987 figures represent the FDA-ATF initial survey of domestic and imported alcoholic beverages, collected from January 1986 through August 1987. This compares with an ATF sampling done in 1991 that shows urethane levels decreasing in most instances.

Product	Average Urethane Level (ppb)		
	1987	1991	
		Domestic	Imported
brandy (grape)	40	10	45
brandy (fruit)	1,200	5	255
bourbon (retail)	150	70	55
rum	20	2	5
liqueur	100	10	25
scotch	50	*	55
sherry	130	10	40
port	60	23	26
grape wine	13	10	15
sake	300	55	60

* Scotch is not manufactured domestically.

eral Research Institute, recommends that fruit pits, such as cherry and apricot, not be used in the manufacture of fruit brandies. His study shows that when pits are crushed and used in the beverage, reactions involving chemicals naturally in the pits cause more urethane to form.

Diachenko says that FDA presently has little data to confirm how effective this and recommendations of other European countries have been in reducing urethane levels in fruit brandy.

FDA will continue to be involved in urethane-related activities with industry, the National Toxicology Program, and ATF. The agency is continually reevaluating its urethane policy as new information becomes available.

Should consumers be worried about urethane in alcoholic beverages? Keeping in mind the recommendation to consume alcohol in moderate amounts, the answer is "no." However, a prudent choice might be to limit consumption of products, such as fruit brandies, that show consistently higher levels of urethane. ■

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



On The Teen Scene

"The pain was so sharp I thought I'd ruptured my appendix, but the doctor said, no, it wasn't that. It was between my periods, so I didn't connect it with menstruation. I was 16.

"Over the next 10 years, I had more and more of these 'pain attacks,' and my periods gradually became heavier and more painful.

"When I was pregnant with my first child, I was virtually pain-free. But shortly after he was born, each month around ovulation, I went to bed in tears from horrible pain. And I bled so much during menstruation I didn't dare leave the house. I went back to the doctor. It was endometriosis."

—A woman from Des Moines, Iowa

ENDOMETRIOSIS

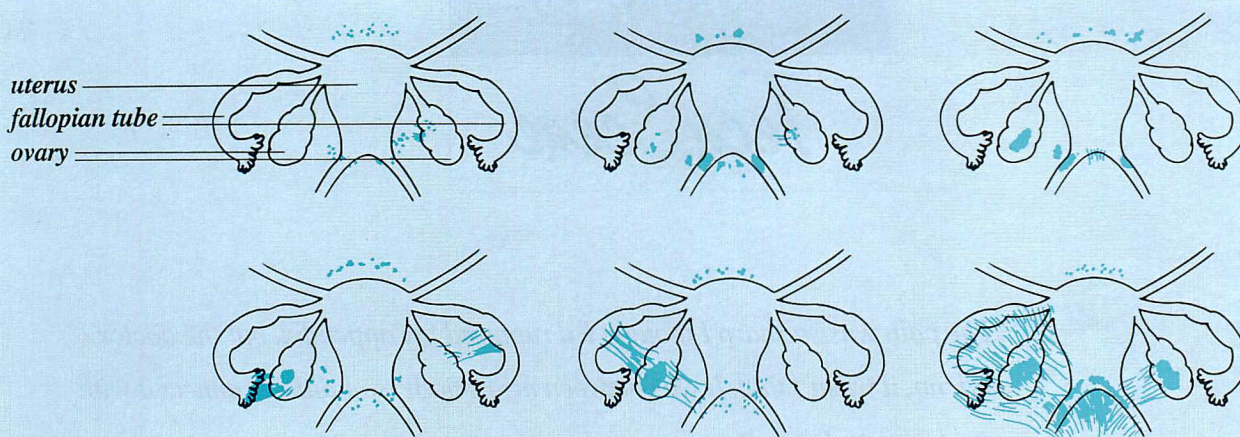
Painful, but TREATABLE

by **Dixie Farley**

Endometriosis is a mysterious, often painful, and disabling condition in which fragments of the lining of the uterus (womb) become embedded, or implanted, elsewhere in the body.

Of the more than 3,000 patients registered with the research program of the international Endometriosis Association in Milwaukee, 41 percent report having symptoms as teenagers. About 5 million American women and girls, some as young as 11, have endometriosis, according to the association.

"These girls have terrible pain," says Lyle Breitkopf, M.D., a gynecologist in New York City. "Typically, they come to the school nurse month after month—maybe six to eight of their 12 menstrual cycles—needing something for pain or being sent home vomiting, writhing on the floor."



Endometriosis is depicted here in stages from very little disease (upper left) to severe (lower right), but not necessarily as it would progress in an individual patient.

In the upper middle sketch, endometriosis is deep in the abdomen behind the uterus. In the upper right, endometriosis affects one ovary and partially covers the area between the uterus and rectum. On the lower left, diseased tissue fixes the left ovary to a fallopian tube. In the lower middle, deep endometriosis attaches the left ovary to a tube and a band of tissue holding the uterus in place. In the lower right, the disease affixes both ovaries and the left tube to other tissue.

(Drawings were made from the Revised American Fertility Society Classification of Endometriosis, 1985)

For the woman from Des Moines, 25 years with endometriosis led to removal of her uterus, fallopian tubes, and ovaries a number of years ago. For many women today, new medicine and less drastic surgery reduce endometriosis symptoms and preserve reproductive organs. FDA has approved several drugs to treat endometriosis and regulates medical devices, such as lasers, used in surgical treatment.

A teen who thinks she may have endometriosis should be examined by a gynecologist. The sooner treatment begins, the better it is for the patients, says Breitkopf. "When we find them at an early stage, we can arrest the condition more easily and keep after it so it doesn't progress as far."

Doctors don't know why endometriosis only strikes certain women.

Some probably inherit it, says Breitkopf. "I've seen it in sisters, including identical twins, and in grandmother-mother-daughter situations."

According to Robert Badwey, M.D., a gynecologist in suburban Washington, D.C., "For whatever reason—greater incidence, better diagnostic techniques, or both—we're much more aware of endometriosis now than even a few years ago."

What's Happening in the Body?

Normally, an increased level of hormones each month triggers the release of

an egg from the ovary. Finger-like tissues on one of the fallopian tubes grasp the egg, and tiny hair-like "cilia" inside the tube transport it toward the uterus. The egg is not fertilized, so the uterine lining breaks down and is shed during menstruation.

Though not in the uterus, the abnormal implants of endometriosis also respond to hormonal changes controlling menstruation. Like the lining, these fragments build tissue each month, then break down and bleed. Unlike blood from the lining, however, blood from implants outside the uterus has no way to leave the body. Instead, it is absorbed by surrounding tissue, which can be painful.

As the cycle recurs month after month, the implants may get bigger. They may seed new implants and form scar tissue and adhesions (scarring that connects one organ to another). Sometimes, a collection of blood called a sac or cyst forms. If a cyst ruptures, it often causes excruciating pain.

Symptoms vary from patient to patient. Severity of symptoms frequently has little to do with the extent of the implants. For instance, some women with just a few implants have severe pain, while some with many implants have little or no pain.

For some, pain starts before or during menstruation and gets worse as the period progresses. Others report pain at a variety of times during the month. There may be a

sharp pain at ovulation when the egg, trying to move into the fallopian tube, causes a cyst on the ovary to burst. (Many women normally feel a twinge of pain at ovulation. Pain caused by a ruptured endometriosis cyst is severe.)

Patients whose implants affect the bladder or intestines often report painful urination or bowel movements and, sometimes, blood in the urine or stool.

Endometriosis sometimes causes premenstrual staining and, as the period progresses, heavy menstrual flow.

Often, endometriosis remains hidden a long time. A symptom such as pain at menstruation may not be seen as unusual, explains Mary Lou Ballweg, executive director of the Endometriosis Association.

"Perhaps a young woman is told by Mom, who had the same problems, that menstrual pain is normal," Ballweg says. "So she just lives with it and doesn't see a doctor until the symptoms become unbearable. Some young women with endometriosis have apparently normal menstrual periods for years before having discomfort and pain. Others report they've nearly always had difficult periods."

As many as 30 percent of women who report infertility problems have endometriosis.

Severe endometriosis can lead to infertility in different ways. In the ovaries, it can produce cysts that prevent the egg's release. In the fallopian tubes, implants

DOCTOR Talk

- **Endometriosis**—a disorder in which fragments of the uterine lining (called the endometrium) implant elsewhere in the body, where they bleed—similar to menstruation, only the blood is absorbed by the body. The name is a combination of three Greek terms: *endo* = within, *metri* = uterus (womb), and *osis* = condition.
- **Gynecologist**—a doctor who specializes in disorders of women's reproductive organs.
- **Infertility**—the inability to conceive a baby.
- **Laparoscope**—a lighted, flexible, telescope-like device inserted into the body through a tiny incision to allow the doctor a close look at tissue.
- **Laser**—its letters stand for **l**ight **a**mplification by **s**timulated **e**mission of **r**adiation. Radiation here means electromagnetic energy, which includes light. Doctors use lasers with laparoscopes to remove endometriosis implants.
- **Ovulation**—the discharge of an egg from an ovary.
- **Uterus**—the technical term for “womb,” where a fertilized egg attaches to the lining to grow. If the egg is not fertilized, the lining is shed as menstruation. ■

can block the passage of the egg. Also, adhesions can fix ovaries and tubes in place so that projections on the tubes can't grasp the egg and move it into the tube. The effect of mild endometriosis on infertility is less clear.

Women with endometriosis may have a higher rate of “ectopic” pregnancy, a potentially life-threatening condition in which the fertilized egg begins to develop outside the womb.

The only way a doctor can be sure a woman has endometriosis is by surgical examination using laparoscopy, a fairly simple procedure usually done without an overnight hospital stay. The doctor makes a tiny incision and inserts a lighted, flexible, telescope-like device called a laparoscope that allows a close look at the tissue.

New Drugs

Among the drugs approved to treat endometriosis is a synthetic hormone called Danocrine (danazol), used to shrink the abnormal implants. A study at Harvard Medical School in Boston showed Danocrine improved symptoms in 89 per-

cent of the patients and reduced the size or number of implants in 94 percent. In a third of the patients, the condition recurred within five years. Most patients complained of side effects such as weight gain, decreased breast size, and deepened voice, but only one patient stopped the treatment because of the effects.

In 1990, FDA approved a nasal spray called Synarel (nafarelin acetate) to relieve symptoms and shrink the implants or stop them from growing. Of 247 women treated with Synarel for six months, 85 percent had their implants shrink or disappear and their symptoms relieved. Six months after treatment stopped, symptoms reappeared in half of those who had been helped. The side effects are mainly those of menopause, such as hot flashes, vaginal dryness, and lighter, less frequent, or no menstruation. Other effects include headaches and nasal irritation.

Last year, FDA approved an injectable drug named Lupron Depot (leuprolide acetate) for treatment of endometriosis. It is similar to Synarel. Patients get injections once a month for six months. In clinical studies, Lupron's effectiveness

was about the same as Danocrine's, the manufacturer reported. Side effects were similar to those with Synarel.

People taking endometriosis drugs need to watch for problems such as difficulty breathing or chest or leg pain, which may indicate a blood clot and should be reported to the doctor immediately. Frequent checkups are needed to monitor effects such as possible thinning of the bones. A patient should immediately report any new or worsened symptoms to the doctor. However, it's *normal* for endometriosis symptoms to temporarily worsen when a woman begins taking medicine.

Surgery

Sometimes medicine is not enough. Surgery may be needed to remove diseased tissue or to correct misaligned organs.

One method to remove diseased tissue combines laparoscopy with laser surgery. The laser is connected to the laparoscope and positioned so that its intense light beam is directed through the laparoscope onto the tissue to destroy it. The procedure usually is done without an overnight hospital stay and requires only about a week's recovery time at home.

“You're always reluctant to perform surgery or use medication on teenage patients,” says Breitkopf. “But these young women are in terrible pain, and they can be helped. They really need to see a gynecologist so the endometriosis can be stemmed at the lowest possible stage of development.”

Recurrence rates after treatment need further study, Ballweg says.

The monthly pain and heavy menstrual periods of chronic endometriosis can be frustrating, especially during the teenage years, when social and school activities are so important. Today, with diagnosis and treatment, a young woman's life can often return to normal. ■

Dixie Farley is a staff writer for FDA Consumer.

For more information, contact:

The Endometriosis Association
8585 N. 76th Place
Milwaukee, WI 53223
(1-800) 992-3636



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.

■ **A "lite" eggnog** received the green light from FDA for test-marketing in several states for 15 months. The manufacturer, Sani-Dairy, of Johnstown, Pa., has reduced fat in the eggnog from 6 percent milk fat to 1 percent and reduced calories by using aspartame sweetener. (FR Oct. 21)

■ **Chaparral nutrition supplements** caused acute toxic hepatitis in two people in July 1992, according to the national Centers for Disease Control and Prevention. Both patients recovered after they stopped taking the product. Chaparral is made from ground leaves of the creosote bush. It is promoted for use as a tea, capsules or tablets. Unproven claims assert chaparral is an "antioxidant" or "free radical scavenger." (*Morbidity and Mortality Weekly Report*, Oct. 30)

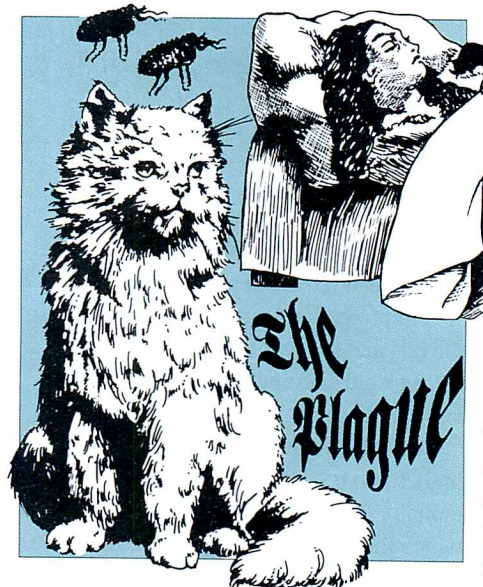
■ **New standards for pediatric immunization practices** have been recommended by the National Vaccine Advisory Committee. The publication's 18 standards offer guidance on overcoming barriers to immunization access, delivery, documentation, and education. Studies show that as many as 4 million preschool children in the United States are not receiving all their recommended immunizations on schedule. Single copies are available from the Information Services Office, National Center for Prevention Services, Centers for Disease Control and Prevention, at (404) 639-1838.

■ **This year's flu vaccine** is recommended by CDC for: healthy people 65 and older; adults and children with long-term heart or lung problems; nursing home residents; kidney disease, cystic fibrosis, diabetes, anemia, or severe asthma patients; people who have cancer or other immunological disorders; and children and teenagers on long-term treatment with aspirin who, if they catch the flu, may be at risk of getting Reye syndrome. (*MMWR* Oct. 30)

■ **Fiber and fat intakes** do not affect a woman's risk for breast cancer, according to a study by Walter C. Willett, M.D., and colleagues at Brigham and Women's Hospital, Boston. The researchers reported on 89,494 women who are part of the Nurses' Health Study. They found 1,439 cases of breast cancer, but no evidence that dietary fiber protected against breast cancer or that fat increased the risk. (*Journal of the American Medical Association*, Oct. 20)

■ **Thirty-two health-care workers** have been infected with the human immunodeficiency virus (HIV) on the job throughout the United States through September 1992, according to CDC. The workers contracted the disease after coming into contact with HIV-positive blood, body fluids, or laboratory specimens. Another 69 health-care workers are suspected of having been infected while on the job. (*MMWR* Oct. 30)

■ **Eleven human plague cases** occurred in the western United States between Jan. 1, 1992, and Oct. 15, according to CDC. Ten patients with bubonic plague recovered with antibiotic treatment. One patient with pneumonic plague died. Fleas caused the infection in seven cases, domestic cats in two, a wild rodent carcass in one, and the source of one case was undetermined. (*MMWR* Oct. 23)



■ **Entries** for the 11th annual Secretary's Award for Innovations in Health Promotion and Disease Prevention are being accepted from undergraduate and graduate students of the health professions. Entries are to consist of a 2,500-word proposal for an innovative project and are due by April 15. First prize is \$5,000. For more information, contact the dean or head of the program of the participating academic institution. (*Public Health Reports*, September–October 1992)



FDA Seizes Substandard Peaches

The Food and Drug Administration's New York district office and a New York importer of Greek peaches signed a consent decree Nov. 6, 1992, requiring the company to relabel or destroy contaminated peaches.

The U.S. District Court of New Jersey approved the decree Nov. 10.

FDA first noted a problem with the peaches imported by Alcona, Inc. of Syosset, N.Y., during an inspection of the firm July 9, 1991. New York district inspector Brian Brody sampled two lots of the peaches at Pittston warehouse in New Jersey, where Alcona had them delivered for storage pending release by FDA for distribution in the United States.

Brody opened 192 of the 2,000 cartons in the shipment, checking the 6-pound cans for any defects and collecting samples for analysis. He noticed several inconsistencies that made him suspicious:

First, the peaches were being imported through Canada. "Usually, Greek peaches come straight here to the Port of New York [from Greece]," Brody said.

Second, there were no labels on any of the cans or cartons in either of the two lots. Brody suspected the labels had been torn off before arrival in New York because glue marks remained where the labels had been, he said.

And third, Brody noticed the date and initials "FDA 2/26/91 AMK" on one of the cartons, indicating the peaches had been previously inspected by FDA.

The New York district office's import operations branch conducted a computer search of all agency offices that had detained canned peaches since Feb. 26.

On July 22, after calling several offices on the list, Brody learned the peaches had first been shipped to Baltimore by World Pride Enterprises, N.Y., and inspected and detained there after laboratory analysis

found mold in the peaches.

Deciding to reexport the peaches rather than destroy them, World Pride shipped them to Canada, where Alcona purchased them.

Arnon Ziv, Alcona's owner, removed the labels and tried to import the peaches into the United States through Buffalo on July 5. But when the Buffalo district office decided to sample them, he shipped the peaches to New York City instead.

This practice, in which a shipper or importer goes from port to port in an effort to evade import regulations and bring in violative products, is known as "port shopping." (See "New Initiatives for Import Safety" in the October 1992 *FDA Consumer*.)

Upon arrival in New York, the peaches were stored at Pittston warehouse until Brody inspected them July 9.

Based on the inspection findings and the laboratory results of samples collected, which showed the peaches contained *Geotrichum* mold, the New York district

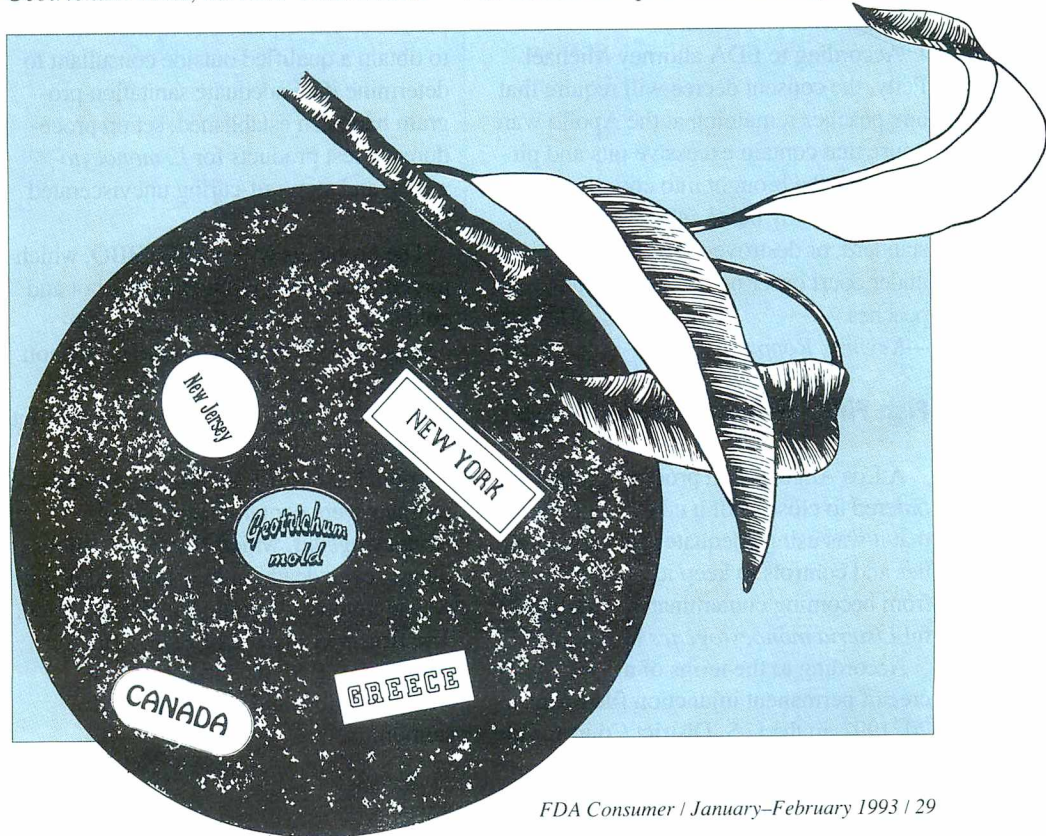
office asked the New Jersey officials to embargo the peaches. When Brody returned to the warehouse on July 25 with an official from the New Jersey Department of Health, however, the peaches were gone.

Brody learned from a warehouse executive that Ziv sold the peaches to Port Royal Sales, Great Neck, N.Y., and they were shipped out July 11 and 12. Port Royal then sold the peaches to H. Maramount, a Philadelphia manufacturer with offices in Brooklyn, N.Y.

When confronted with the violation July 25, Ziv agreed to get the peaches back, but he could not trace their location.

On July 17, Alcona had again tried to import Greek peaches into the United States through Canada. The New York district office issued a Notice of Sampling requesting the location of the peaches, but Ziv failed to respond.

Then, on Sept. 3, during a routine inspection, FDA inspectors sampled one lot of Nifda Chef-pac brand Greek peaches



Alcona had stored at the Apollo warehouse in Newark, N.J., and sent the samples to the New York Regional Laboratory for analysis. Test results indicated the peaches contained excessive pits and pit fragments, as well as mold.

When FDA officials returned to the warehouse, they found that Alcona had distributed some of the peaches before receiving FDA approval.

At FDA's request, New Jersey officials embargoed the remaining peaches on Sept. 17, 1991. On Oct. 17, FDA issued Alcona a warning letter for twice shipping peaches before FDA had released them for sale and for failing to make a shipment available for inspection.

The warning letter required Alcona to outline steps the firm was taking to prevent future violations.

On May 19, 1992, at FDA's request, U.S. marshals seized the more than 1,000 cases of Greek peaches belonging to Alcona because they contained excessive pit fragments and mold.

According to FDA attorney Michael Petty, the consent decree will require that any peaches remaining at the Apollo warehouse that contain excessive pits and pit fragments be brought into compliance with the law by being relabeled as below standard, or destroyed. The company is under court order not to remove the peaches.

—Kevin L. Ropp

Fish Firm Ordered to Clean Up

A Los Angeles fish processing firm was ordered to close until it could assure FDA that it was using adequate methods, facilities and controls to keep its fish products from becoming contaminated with harmful *Listeria monocytogenes* bacteria.

According to the terms of a consent decree of permanent injunction filed Aug. 20, 1992, in the U.S. District Court for the

Central District of California, Smoky BBQ Fish Company owners Suk Eun Cho and Danny Cho agreed to destroy or recondition all of the firm's adulterated fish products. The injunction required the firm to obtain a qualified outside consultant to determine if an adequate sanitation program had been established, set up procedures to test products for *L. monocytogenes*, and stop salt-curing uneviscerated fish.

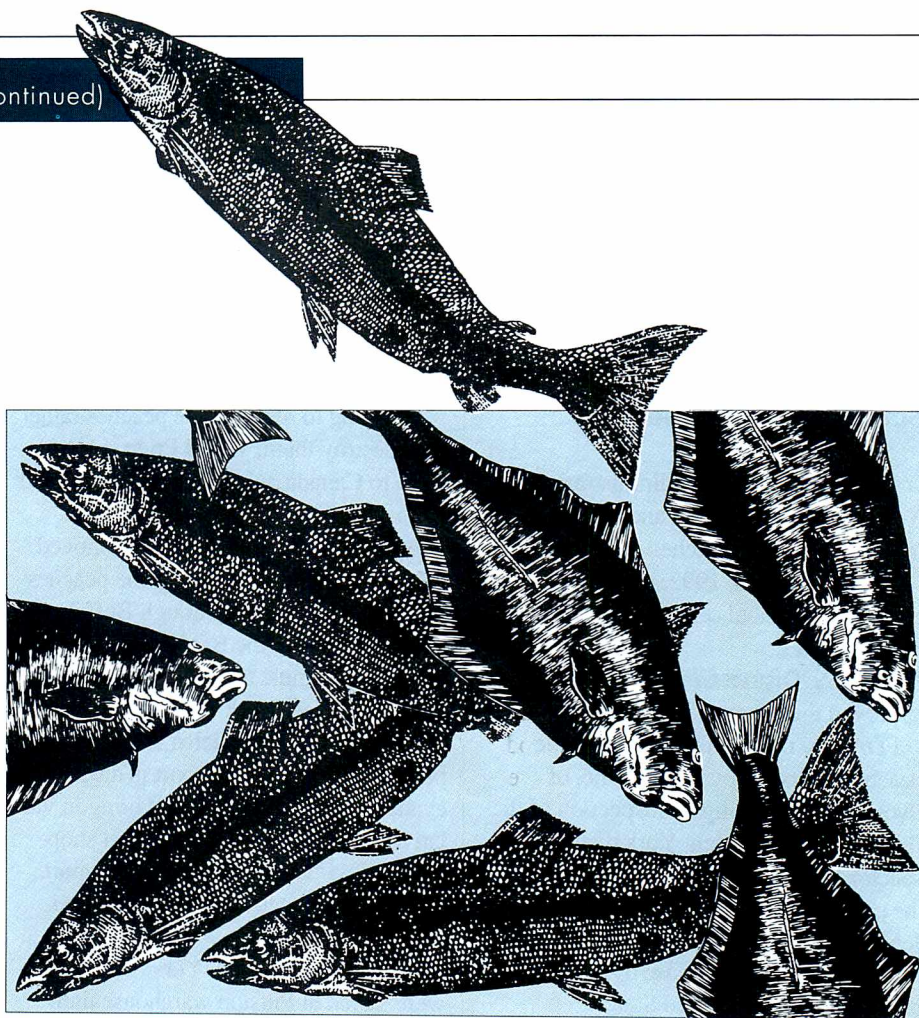
The problems with Smoky BBQ, which manufactures fish products using hot and cold smoking and dry salt-curing processes, started during a routine inspection of the firm April 30, 1990. FDA investigators from the Los Angeles district office collected samples of halibut and salmon. Laboratory analyses showed the samples were contaminated with *L. monocytogenes*, which can cause serious illness, even death, in the elderly or people whose immune systems are compromised. The firm was advised of FDA's findings, and in May 1990 recalled one lot of smoked halibut and one of smoked salmon.

An FDA inspection from May 31 until June 11 revealed numerous insanitary conditions, including failure of the employees to clean and sanitize their hands and equipment in the processing area. During another inspection in December 1990, investigators found more sanitation violations, including a hose without backflow protection being moved from the floor to the fillet table, where it dripped on the raw fish and production tools.

On May 9, 1991, FDA sent Cho a letter notifying him of the adverse findings. He promised to correct the problems, but another inspection from May 2 through June 9, 1992, showed *L. monocytogenes* contamination in samples of smoked halibut, in water from a bucket of cleaning solution, and in standing water from a floor crack. The bacteria had also contaminated handles of the fillet knives and the knife sharpener.

On June 25, FDA investigators visited the firm to inform the owners of the *L. monocytogenes* findings. The firm recalled the smoked halibut.

FDA recommended to the federal court



that the firm be enjoined. While the recommendation was being considered, FDA inspected once more, from July 7 to 9, 1992, to investigate the firm's practice of using unviscerated fish in its salt-cure process. Applying the salt-cure process to unviscerated fish is a health hazard because the viscera of fish sometimes harbor the spores of the bacteria that cause botulism, creating a potential for contamination. FDA informed the California Food and Drug Branch of this hazard, and the state immediately embargoed the unviscerated salt-cured fish at the firm, and ordered its destruction.

In addition, the investigators found that previously cited insanitary conditions had not been corrected, including the continuing use of the same wooden-handled knives previously found to be contaminated with *L. monocytogenes*.

FDA forwarded a complaint for injunction with a temporary restraining order to the U.S. attorney's office in Los Angeles in August 1992. The firm signed the document Aug. 14.

—Judith E. Foulke

Devices for Newborns Found Faulty

A Salt Lake City, Utah, firm that manufactures devices used to treat newborns with respiratory distress syndrome was ordered to stop distributing them after FDA discovered that the devices could cause serious injury or death.

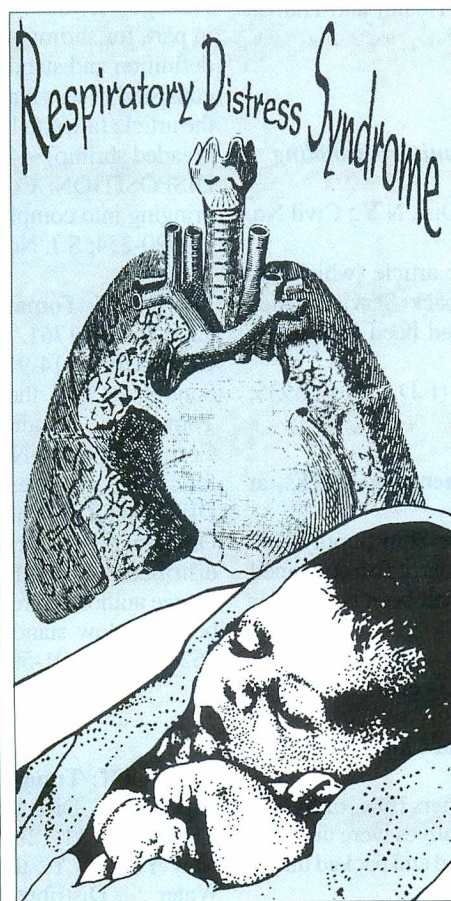
Bunnell, Inc.'s Life Pulse High Frequency Jet Ventilators emit rapid bursts of air that help premature infants with this syndrome to breathe normally until their lungs develop fully. Their lungs fail to produce surfactant—a foamy substance that coats the inside of the lungs and keeps them from collapsing during exhalation.

On Sept. 19, 1991, FDA's Denver district office was notified by a former

Bunnell employee about an alleged death attributed to one of the devices. (This was never proved.)

During inspections of Bunnell conducted between Sept. 30 and Dec. 16, FDA investigators learned from company records that the firm had received hundreds of complaints from hospitals about mechanical problems with its Jet Ventilators, but did not adequately investigate or report them, as required, to FDA.

Investigators also learned that Bunnell was promoting the devices for other than approved purposes, and that it did not follow critical good manufacturing practices, adhere to its own standard operating procedures and engineering changes, or keep adequate records.



At the end of the inspection, FDA investigators presented the firm with the list of violations they had uncovered.

On Feb. 7, 1992, Bunnell submitted a plan to FDA for correcting the violations. The plan included installing new parts in existing ventilators, but it failed to demonstrate that the new parts would keep the devices from malfunctioning.

As a result, FDA, on April 14, issued the firm a letter warning that its plan was unacceptable and restating that the devices posed a high risk of serious injury or death.

On July 30, FDA ordered Bunnell to stop distributing Jet Ventilators and to notify health professionals of the potential risks associated with their use.

At Bunnell's request, FDA met with the firm Aug. 12 and 13 to provide Bunnell an opportunity to express its objections to FDA's order. The agency remained unconvinced that the devices were safe.

On Sept. 8, FDA issued a new order, which Bunnell signed, allowing the firm to ship Jet Ventilators in emergency situations. An emergency form would have to be signed by the hospital administrator and attending physician, stating that the health provider understood the risks involved with using the device.

The order also requires Bunnell to recall or put new parts in devices already distributed and perform studies to ensure the changes are appropriate.

FDA will reinspect Bunnell after an independent consultant certifies that the firm has met all medical device reporting requirements, pre-market approval supplementary requirements, and good manufacturing practice requirements.

The recall began on Oct. 8. The order will expire one year after the recall is completed if FDA has certified that the firm is in compliance with all the appropriate regulations.

—Victor Lambert

SUMMARIES OF COURT ACTIONS



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

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

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

SEIZURE ACTIONS

Food/Contamination, Decomposition, Insanitary Handling

PRODUCT: Curry powder, at Brooklyn, E. Dist. N.Y.; Civil No. 90-3392.

CHARGED 10-1-90: While held for sale, the article (which had been previously stored at New York Piggyback Services, Inc., Brooklyn, N.Y.) contained rodent hair and had been held under insanitary conditions—402(a)(3), 402(a)(4).

DISPOSITION: Consent—ordered destroyed. (F.D.C. No. 65935; S. No. 90-626-628; S.J. No. 1)

PRODUCT: Flour, salt-cured fish, and other food stocks, at Philadelphia, E. Dist. Pa.; Civil No. 88-3039.

CHARGED 4-11-88: While held by Delaware Ship Supply Co., Inc., Philadelphia, Pa., one lot of flour and two lots of fish contained rodent filth—402(a)(3); and all of the articles had been held under insanitary conditions—402(a)(4).

DISPOSITION: Consent—authorized release to the dealer for salvaging. (F.D.C. No. 65410; S. No. 88-334-834 et al.; S.J. No. 2)

PRODUCT: Olives in brine, and pita bread, at Chicago, N. Dist. Ill.; Civil No. 91 C 3441.

CHARGED 6-4-91: While held by Ziyad Brothers (Div. of Syrian Baking & Grocery Co., Inc.), Chicago, Ill., the olives were unfit for food—402(a)(3); and the pita bread was prepared and packed under insanitary conditions—402(a)(4).

DISPOSITION: The articles were claimed by the dealer, who denied the charges. A consent decree authorized release of the olives to the dealer for salvaging. However, FDA rejected the dealer's reconditioning plan as being insufficient, and the dealer sought to withdraw its claim. Ultimately, upon the agreement of the parties, the articles were destroyed by the claimant under supervision by FDA. (F.D.C. Nos. 66157 & 66164; S. No. 91-610-425 et al.; S.J. No. 3)

Food/Economic and Labeling Violations

PRODUCT: Shrimp, breaded, frozen, Grand Bay, at Mobile, S. Dist. Ala.; Civil No. 91-0111-BH-S.

CHARGED 2-8-91: When shipped by Gulf City Seafoods, Inc., Pascagoula, Miss., the article had had breeding material substituted, in part, for shrimp—402(b)(2); the article failed to conform to the definition and standard for frozen raw breaded shrimp, because it consisted of less than 50 percent shrimp material—403(g)(1); and the article failed to bear the specified name of the food (frozen raw breaded shrimp)—403(g)(2).

DISPOSITION: Consent—authorized release to the shipper for bringing into compliance with the law. (F.D.C. No. 66027; S. No. 91-520-254; S.J. No. 4)

PRODUCT: Tomatoes, peeled, canned, at Miami, S. Dist. Fla.; Civil No. 91-1761.

CHARGED 8-14-91: When shipped by Agroindustrial Surfut Ltd., Santiago, Chile, the article labeled "Ciccio . . . Imported Peeled Tomatoes . . . Product of Chile . . . Distributed By: Orlando Foods Corp., Maywood, N.J." failed to conform to the standard of quality for canned tomatoes due to excessive peel—403(h)(1).

DISPOSITION: The food was jointly claimed by the food's owner, Orlando Food Corp., Maywood, N.J., and the food's intended distributor, Truscello & Sons, Miami, Fla. Subsequently, a consent decree authorized release of the food to the owner for relabeling as being "below standard in quality—excessive peel." (F.D.C. No. 66247; S. No. 91-595-103; S.J. No. 5)

Animal Feed

PRODUCT: Tuna chunks, in water, canned, at La Crosse and Superior, W. Dist. Wis.; Civil No. 91-C-960-S.

CHARGED 11-12-91: When shipped by Ocean King Foods, Inc., New York, N.Y., the article labeled "IGA Chunk Light Tuna In Water . . . Distributed by IGA, Inc., Chicago, Ill.," was pet food

reabeled as human food, thus concealing its inferiority—402(b)(3); the article contained decomposed tuna fish—402(a)(3); and the article was offered for sale under the name of another food—403(b). **DISPOSITION:** Default—ordered destroyed. (F.D.C. No. 66297; S. No. 91-563-861 et al.; S.J. No. 6)

Drugs/Human Use

PRODUCT: Damason-P hydrocodone bitartrate, aspirin and caffeine combination tablets, three seizure actions, at Irvine, Sylmar and Anaheim, C. Dist. Calif.; Civil Nos. 90-4023 AAH(JRx), 90-4669 WDK(JRx), and 90-4656 AWT(GHKx).

CHARGED 7-31-90, 8-29-90, and 8-29-90: While held for sale, the articles (which were labeled “Damason-P . . . Tablet Contains: Hydrocodone Bitartrate . . . Aspirin . . . Caffeine . . . Mason Pharmaceuticals, Inc., Newport Beach, CA,” which had been manufactured in California and which contained interstate hydrocodone bitartrate) were new drugs without effective approved New Drug Applications—505(a); and the articles’ labeling lacked adequate directions for use, due to the articles’ new drug status—502(f)(1). **DISPOSITION:** The articles were claimed by Mason Pharmaceuticals, Inc., Newport Beach, Calif. Following the claimant’s entry into a settlement agreement and the withdrawal of an appeal in a similar earlier seizure action, a consent decree of condemnation and permanent injunction was entered, and the articles were destroyed. (F.D.C. Nos. 65891 and 65911/2; S. Nos. 90-566-643, 90-566-632, & 90-566-643; S.J. No. 7)

PRODUCT: Oxygen in cylinders, at Detroit, E. Dist. Mich.; Civil No. 91 CV 70904 DT.

CHARGED 2-28-92: While held by Homedic, Inc., Detroit, Mich.; the circumstances used for the article’s manufacture, processing, packaging and holding failed to conform with current good manufacturing practice—501(a)(2)(B); and the article was manufactured in an unregistered establishment—502(o).

DISPOSITION: A consent decree authorized release to the dealer for salvaging. Following a motion for withdrawal of the consent decree, the court ordered the article forfeited and disposed of by the U.S. marshal. (F.D.C. No. 66029; S. No. 91-554-466; S.J. No. 8)

Medical Devices

PRODUCT: Collagen implants and collagen implant-screening-test intradermal injection, at Fremont, N. Dist. Calif.; Civil No. C91-2637 FMS.

CHARGED 8-15-91: The articles’ labeling was false and misleading in various particulars—502(a)(1); and the articles’ labeling lacked adequate warnings against possibly dangerous/unsafe use—502(f)(2).

DISPOSITION: The articles were claimed by Collagen Corp., Palo Alto, Calif. Subsequently, a consent decree authorized release of the article to the claimant for bringing the articles into compliance. (F.D.C. No. 66231; S.J. No. 91-625-321 et al.; S.J. No. 9)

PRODUCT: “Finally Free” hair removal electronic tweezer appliance for home use, at Dresher, E. Dist. Pa.; Civil No. 90-6106.

CHARGED 9-21-90: The article, which had been manufactured in Florida and was labeled “Model F-125 Finally Free . . . Hair Removal Appliance . . . Selvac Corp. . . Dresher, PA,” failed to bear adequate directions for the article’s intended purpose—502(f)(1); the article’s labeling contained false and misleading claims for imparting radio frequency energy to the body through tweezers for the purpose of hair removal and root destruction—502(a); and the article, which was a class III device, did not have in effect an approved application for pre-market approval—501(f)(1)(B).

DISPOSITION: The article was claimed by Selvac Corp., Dresher, Pa. Pursuant to stipulation of the parties, the action was stayed for 30 days. Subsequently, the claimant moved to stay the proceedings pending completion of FDA review of the claimant’s hair removal appliance for professional use because FDA had advised that it might reconsider its denial of marketing clearance based on an evaluation of additional information to be submitted. The government opposed such motion because there was no proceeding pending before FDA involving the seized device and because, even if there were such a proceeding, it would not bar this seizure action. The court ruled for the government and denied the claimant’s motion for a stay. Ultimately, a consent decree of condemnation authorized release of the article to the claimant for bringing into compliance. The decree also contained injunctive provisions ordering that the claimant not manufacture, process, pack, label, promote, advertise, distribute, or sell the Finally Free Hair Removal Appliance, except for export, unless and until it received a specified FDA determination for approval. (F.D.C. No. 65905; S. No. 90-569-465; S.J. No. 10)

PRODUCT: Gloves for medical exams, latex, at McHenry, N. Dist. Ill.; Civil No. 91 C 20285.

CHARGED 9-30-91: The quality of the article, which was labeled “latex exam gloves . . . Manufactured by Yung Mao Corp. Taipei, Taiwan,” fell below the article’s purported quality, due to excessive

defects—501(c).

DISPOSITION: Default—ordered destruction. (F.D.C. No. 66272; S. No. 91-612-933; S.J. No. 11)

PRODUCT: **Lintro-Scan breast transillumination device**, at Marietta, N. Dist. Ga.; Civil No. 1:91-CV-885-JTC.

CHARGED 4-17-91: The labeling of the article (which was labeled “Lintro-Scan Lintronics . . . Lintronics Industries, Inc. . . . Ft. Lauderdale FL.” and which was accompanied by brochures reading “a safe, new effective procedure for the early detection of breast diseases . . . Lintronics International Limited Inc. . . . Plantation, FL.” and “Interpretation of the Lintro-Scan Examination . . . b. Benign Breast Disease . . . c. Fibroadenoma . . . e. Papilloma . . . k. Carcinoma”) failed to bear adequate directions for the article’s intended use—502(f)(1); and the article’s labeling contained false and misleading claims for the early detection of breast cancer, as an alternative to x-ray mammography, for the detection of breast cancer and differentiating benign conditions from breast cancer—502(a). DISPOSITION: Default—ordered destroyed. (F.D.C. No. 66053; S. No. 91-538-729; S.J. No. 12)

PRODUCT: **Sensor pad for breast self-examination**, at Chicago Heights, N. Dist. Ill.; Civil No. 92 C 0281.

CHARGED 1-13-92: The article, which was distributed by Inventive Products, Inc., Decatur, Ill., was a class III device and it did not have an approved pre-market approval application in effect—501(f)(1)(B).

DISPOSITION: Default—ordered destroyed. (F.D.C. No. 66339; S. No. 92-503-638; S.J. No. 13)

PRODUCT: **Tanning booths, beds, and ultraviolet lamps**, two seizure actions, at Anchorage, Dist. Alaska; Civil Nos. A87-625 and 89-134.

CHARGED 12-28-87 (articles at Sunburst Sun Spa) and 4-17-89 (articles at The Perfect Tan): The labeling of the locally constructed booths, the commercially manufactured beds, and the interstate ultraviolet lamps lacked adequate warnings against unsafe uses—502(f)(2); and the labeling of a Klufurn Saturn suntanning bed and other specified articles lacked adequate directions for use—502(f)(1).

DISPOSITION: *Articles at Sunburst Sun Spa*—the articles were claimed by Ms. Whadan K. McKay (McKay Enterprises), Anchorage, Alaska. After the government served written interrogatories on the claimant, the government moved for summary judgment. Meanwhile, similar articles seized in another seizure at Sunburst Sun Spa

were forfeited to the government pursuant to a default decree (see *FDA Consumer*, December 1992, S.J. No. 15). The court granted the government’s motion for summary judgment and also ordered the articles forfeited. Pursuant to an order of destruction, the articles were dismantled and destroyed.

Articles at The Perfect Tan—The articles were claimed by Ms. Chin S. Hilbers. However, no answer to the complaint was filed, the claimant made no further contact concerning the articles, attempts to reach the claimant were unsuccessful, and the premises of The Perfect Tan were vacated except for the seized articles. The government moved for the removal of the articles by disassembly and moved for a default decree. Ultimately, the articles were disassembled and destroyed. (F.D.C. Nos. 65390 & 65641; S. Nos. 87-463-302 et al. and 89-463-512 et al.; S.J. No. 14)

CRIMINAL ACTIONS

DEFENDANT: **James D. Irving (t/a World Health Imports)**, Palm Desert, C. Dist. Calif.; Criminal No. SA CR 19-19(A)-AHS. CHARGED on or about 6-4-91: That the defendant conspired to traffic in various drugs illegally acquired or illegally imported from Europe and Mexico; that various of such drugs were counterfeit drugs, unapproved New Drugs, drugs with labeling and directions in a foreign language, and drugs lacking a prescription from a licensed physician; that, in pursuance of the conspiracy, various overt acts were committed, including: advertising the sale of Gerovital H-3 (GC-3), Retin A, and Mexican Premarin; renting and storing drugs at several Public Storage Rental facilities; and shipping various of the above and other drugs—18 U.S.C. 371.

DISPOSITION: Guilty plea—\$2,000 fine, and supervised release for a term of three years with conditions that included home detention for four months. (IG-52; S.J. No. 15)

DEFENDANT: **Alfred G. Maroun**, corporate officer of a food storage facility, Lawrence, Dist. Mass.; Criminal No. 90-10027-T. CHARGED 2-12-90 by grand jury: While held for sale, flour, corn flour mix, and macaroni contained rodent or insect filth and had been held under insanitary conditions—402(a)(3).

DISPOSITION: Guilty plea; \$5,000 fine, probation for three years with special conditions. (F.D.C. No. 65707; S. No. 89-568-124 et al.; S.J. No. 16)

DEFENDANTS: **Rophae Lens Co., Inc.**, St. Petersburg, M. Dist. Fla.; Civil No. 92-507-CIV-T-15-C.

CHARGED on or about 4-17-92: That the defendant manufactured,

shipped, and held for sale interstate intraocular lenses (IOLs); that during a specified period some of such IOLs were adulterated, some of such IOLs failed to comply with the requirements of their approved exemption for investigational use, and some of such IOLs failed to meet the minimum specifications for lens resolution and refractive power—301(q); and that, unless restrained by the court, the defendant might again continue to violate the law.

DISPOSITION: A consent decree of permanent injunction enjoined the doing of a number of specified acts with respect to the defendant's IOLs unless and until there was in effect an approved exemption for investigational use, as follows: (A) shipping any such IOL in interstate commerce; (B) receiving any such IOL in interstate commerce and delivering it to another person; (C) holding any such IOL for sale or use in any medical, surgical or other procedure, after interstate shipment of the IOL or its components; (D) promoting, counseling, or demonstrating to any person the use of any such IOL in any medical, surgical or other procedure; (E) sponsoring the use of any such IOL in any medical, surgical or other procedure; (F) failing to comply with any 21 U.S.C. 360j(g) requirement; and (G) after approval of such an application or exemption, shipping or holding for sale any adulterated or misbranded IOL. In addition, the defendant was ordered to pay a mutually agreed upon sum for investigational fees and costs (F.D.C. No. 65711; S.J. No. 88-459-747 et al.; S.J. No. 17)

INJUNCTION ACTIONS

DEFENDANT: Janet V. Hopper, Greensboro, M. Dist. N.C.; Civil No. 2:90CV00525.

CHARGED 10-15-90 in a complaint for injunction: That, until recently, the defendant had been president and sole shareholder of AMT Research, Inc., Greensboro, N.C., and had been engaged in taking orders for and shipping the cosmetic products "BronzTan" tablets and "BronzGlo" tablets; that the cosmetic product "BronzTan" tablets contained the nonconforming color additive canthaxanthin—601(e); that the labeling of BronzTan tablets was false and misleading in a number of respects (i.e., false claims of governmental approval for tanning purposes and of wide usage in Canada and Europe, and false claims of no known harmful side effects when the formation of deposits on the retina of the human eye and vision problems had been reported in medical literature—602(a)); that, despite repeated warnings, the defendant had continued to sell BronzTan tablets; and that the government believed that, unless enjoined, the defendant would continue such violations.

DISPOSITION: A consent decree of permanent injunction enjoined

the interstate shipment of BronzTan, BronzGlo, or any other cosmetic containing canthaxanthin or any other unapproved color additive. The decree included other provisions, including the government's reliance upon representations concerning the dissolution of AMT Research, Inc., the defendant's giving of notice before involvement in any business involving the distribution of foods, drugs, devices or cosmetics, and the parties' acknowledgment that the decree represented a compromise settlement for the purpose of settling the action. (Inj. No. 1222; S. No. 90-606-394 et al.; S.J. No. 18)

MISCELLANEOUS ACTIONS

SUBJECT: Processing of shrimp with sodium hydroxide which was not disclosed on product labels and the termination of inspection service, Washington, Dist. Columbia; Civil No. 87-3229.

PETITIONED 11-30-87 by Sea Snack Foods, Inc., Los Angeles, Calif., against the United States, the National Oceanic and Atmospheric Administration, the National Marine Fisheries Service (NMFS), the National Seafood Inspection Laboratory, the U.S. Department of Commerce, FDA, other federal agencies and agency officials, and a Los Angeles, California, corporation and individual, in a suit in the nature of mandamus to compel continued NMFS inspection services: that Sea Snack processed shrimp with a Department of Commerce inspector in its plant to certify the shrimp as "Grade A" or "Packed Under Federal Inspection" on the label of the finished product; that, with the inspector's knowledge, Sea Snack used sodium hydroxide as a "processing aid" to facilitate the removal of shell and antennae; and that Sea Snack had been notified that the NMFS inspection services would be terminated within 20 days for all products that did not have sodium hydroxide declared on their labels.

However, Sea Snack asserted that, as used by Sea Snack, sodium hydroxide was considered an incidental food additive and therefore it did not need to be declared on the label; that Sea Snack had discussed with FDA the necessity of labeling declaring sodium hydroxide and FDA had refrained from making an advisory opinion because FDA believed more data was necessary; that, upon Sea Snack's request, the National Seafood Inspection laboratory had tested Sea Snack's spice blend that included sodium hydroxide but had informed Sea Snack that the test results were inconclusive and that in-plant studies would be necessary; that a private laboratory was contracted by Sea Snack to perform various analyses and had determined that sodium hydroxide was a processing agent and no

labeling was required.

Nevertheless, the NMFS advised Sea Snack that the private laboratory's analysis failed to substantiate Sea Snack's claims, and that Sea Snack should list sodium hydroxide on the ingredient label or discontinue its use, in order to continue the Department of Commerce's certification. FDA advised Sea Snack's laboratory consultants that the burden was on Sea Snack to prove that sodium hydroxide was an incidental additive. Among the six asserted causes of action, Sea Snack charged that the NMFS's action in terminating inspection services was illegal and a breach of contract, that the NMFS violated Sea Snack's right to due process, and that there was a conspiracy to terminate Sea Snack's right to inspection services. **DISPOSITION:** The court issued a temporary restraining order against discontinuance of the inspection service. Subsequently, after a hearing, the court found that there was no basis for a preliminary injunction and that no material factual questions remained unresolved. The court concluded that the case must be decided on the merits in the defendants' favor. In the court's memorandum opinion, the court found that, absent clear statutory or regulatory language to the contrary, the party claiming the benefits of an exemption had the burden of showing that it qualified for that exemption (and that this was particularly true in this instance where the petitioner was placing an item into commerce and requesting the benefits of a voluntary government certification).

The court noted that Sea Snack's use of sodium hydroxide was not a mere technical matter. FDA had reviewed the study submitted by Sea Snack's independent laboratory and had determined not only that a flawed testing methodology had been used but also that the study indicated that the use of sodium hydroxide caused water retention, thereby altering the weight of the shrimp and suggesting that consumers purchasing the product paid for shrimp but received water.

As to Sea Snack's complaint that, in refusing to certify its shrimp, the NMFS had violated its own regulations regarding debarment, the NMFS was only refusing to certify shrimp that did not meet the standards of the certification program. As to the conspiracy allegation, Sea Snack's counsel was unable to do more than to express speculative hope that the charge would be substantiated, and since the NMFS provided inspectional services pursuant to contract, Sea Snack had no right to inspection services that could be terminated. For such reasons, Sea Snack's motion for a preliminary injunction was denied, and the complaint was dismissed. (Misc. No. 855; S.J. No. 19)

Statement of Ownership, Management, and Circulation

(Required by 39 U.S.C. 3685)

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

Date of filing: Oct. 1, 1992, issued 10 times annually (monthly, with combined issues July–August and January–February); annual subscription price \$12 (\$15 foreign).

Extent and Nature of Circulation:

	Average No. Copies Each Issue During Preceding 12 Months	Actual No. Copies of Single Issue Published Nearest to Filing Date
A. Total number of copies printed (net press run)	29,011	29,051
B. Paid circulation		
1. Sales through dealers and carriers, street vendors, and counter sales	0	0
2. Mail subscriptions	26,000	26,000
C. Total paid circulation (sum of B1 and B2)	26,000	26,000
D. Free distribution by mail, carrier, or other means, samples, complimentary, and other free copies	2,811	2,851
E. Total distribution (sum of C and D)	28,811	28,851
F. Copies not distributed		
1. Office use, left over, unaccounted, spoiled after printing	200	200
2. Returns from news agents	0	0
G. Total (sum of E, F1, and F2—should equal net press run shown in A)	29,011	29,051

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