DANGER

HERBS

Often More Toxic Than Magical
Herbs Are Often More Toxic Than Magical

"Better to be safe than sorry" is a good maxim when using many exotic herbs.

Drugs For Those Other Animals

Minor species have generally been neglected by drug researchers and developers. But things may be changing.

Using Drugs To Lift That Dark Veil Of Depression

For reasons not fully known, millions suffer from depression. However, sometimes drugs can alleviate the dismal hours.

On Treating Warts With Spunk Water And Other Things

Huck Finn and Tom Sawyer liked to play with frogs. They swore by spunk water to get rid of the resulting warts. Today we know warts come from a virus and disappear with time or proper treatment.

Would Rx Ads Make People Learn Or Yearn?

Direct-to-consumer advertising of prescription drugs is a subject of great debate these days. A decision awaits more research.

Kidney Stones = Mighty Hurtful Mites

There are ways to treat kidney stones and also ways to avoid them. This article tells about both.

No More False Hopes From Bust Developer

The Mark Eden bust developer was sold by the millions. But no more. Facing a trial, its promoters agreed to cease selling the worthless device.

Updates

Investigators’ Reports

Consumer Forum

Summaries of Court Actions

The Notebook

The Mark II bust developer, which this woman is demonstrating, will be manufactured no more without FDA certification. The production halt was part of a pretrial settlement in a mail fraud case. The Mark II had been sold over the years to thousands of women. The story of the end of the device, and how it was proved ineffective, is told in No More False Hopes From Bust Developer beginning on page 31.
Reprints Available

Reprints are available of three articles that appear in the July-August 1983 issue of FDA Consumer: "Doctors, Patients Don't Communicate," "Cook's Questions Answered Here," and "Tracking Trace Minerals." Single copies of these reprints can be obtained from the Food and Drug Administration, HFE-88, 5600 Fishers Lane, Rockville, Md. 20857. Multiple copies are available from FDA, HFW-40, at the Rockville address. Copies of reprints are also available from FDA's consumer affairs officers, who are located in 30 cities around the country.

How Pharmacists Help

Use of auxiliary sticker labels is the most common method by which pharmacists supply information about prescription drugs to consumers, according to a recent survey conducted by FDA field personnel. Auxiliary labels are small stickers pasted on prescription drug containers to remind the consumer to shake the bottle well, take the medication at a certain time before or after meals, etc.

FDA employees, visiting 241 stores in 23 cities selected at random around the United States and Puerto Rico, interviewed pharmacists and asked about their use of various drug information materials. The study was made as part of the agency's patient education program.

Nearly all the pharmacists (97 percent) said they use auxiliary labels on prescription drugs. A total of 37 percent said they also provide product leaflets of some sort. Two-thirds of these leaflets were professional package inserts (material the manufacturer prepares for doctors and other health professionals); 14 percent were supplied by state pharmacy associations, and 13 percent were "homemade" leaflets supplied by pharmacy chain stores. The remaining leaflets were a variety of commercially available materials (6 percent) or leaflets prepared by nonprofit organizations (2 percent).

More than a third of the pharmacists said they are active in helping to educate patients, most often by answering patient questions and providing consultation (56 percent of the activities mentioned).

Of the stores surveyed, 29 percent had some sort of free pamphlets available for customers about prescription drugs. About 22 percent offered books for sale with information about prescription drugs. And 44 percent made reference materials available such as the Physicians' Desk Reference, Facts and Comparisons, and the USP Dispensing Information book.

Report On Wound Cleansers

Contrary to the recommendations of an expert advisory committee, sodium perborate monohydrate is safe and effective as an oral wound cleanser and OTC drug products containing it can be used for the temporary cleansing of canker sores. So FDA said in a tentative final monograph (proposed standard) for OTC oral mucosal injury drug products. These are drug products that relieve oral soft tissue injury by cleansing or promoting healing of minor oral wounds or irritations.

FDA's proposed monograph is based on an evaluation of recommendations of the Advisory Review Panel on OTC Dentifrice and Dental Care Drug Products and of public comments on the panel's report. The advisory panel was one of 17 groups set up by the agency to evaluate the ingredients in all OTC drugs.

Other FDA changes include: revising the indications section in product labels to read "For temporary use in cleansing minor wounds or minor gum inflammation ..."; moving references to the use of carbamide peroxide and hydrogen peroxide in teething from the product label to a new professional labeling section in the monograph; and reconsidering allowing use of the terms "soothing" and "for relief of oral discomfort" if adequate data are submitted to substantiate claims that an ingredient's action has such effects.

Eye Medicines Assessed

All currently marketed OTC ocular anti-infectives should be classed as not safe and effective, FDA said in a "tentative final monograph" (proposed standard) for OTC ophthalmic drug products. This means that these ingredients will have to be taken off the market within six months after the final standards for this class of nonprescription drug products are published.

A panel of experts reviewing the safety and effectiveness of OTC ophthalmic product ingredients had recommended further testing of most of the anti-infective ingredients to determine whether they could be used in OTC eye-care products. One was declared not safe and effective by the panel.

The agency also added three ingredients not reviewed by the advisory panel to the ingredient lineup. Polyethylene glycol 6000 was recommended as an ophthalmic demulcent (eye lubricant) if further tests show it is safe and effective. Petroleum jelly and yellow wax are acceptable as ophthalmic emollients.
agents applied to the eyelids to soften the tissues and prevent drying).

These additions bring to 31 the number of active ingredients FDA considers safe and effective as OTC ophthalmic astringents, demulcents, emollients, hypertonicity agents, or vasoconstrictors. There are no therapeutically active ingredients in eyewashes, but the agency is proposing to require that all ingredients be listed in the statement of identity for this class of eye-care product.

FDA is calling for terminology that is more understandable to consumers. For instance, “eye lubricant” will replace “ophthalmic demulcent” and “eye redness reliever” will be used instead of “ophthalmic vasoconstrictor” in product labels. Label warnings for products in which mercury is used as a preservative should include the specific name of mercury-containing compounds and not just the word “mercury.”

The panel recommended that the term “tired eyes” be dropped from ophthalmic vasoconstrictor product labeling. However, FDA said the phrase would be acceptable in the final monograph if adequate data are presented to show that consumers equate “tired eyes” with symptoms of minor irritation and redness in the eyes.

The Advisory Review Panel on OTC Ophthalmic Drug Products was one of 17 groups assisting FDA in an evaluation of all over-the-counter drugs. The panel’s recommendations were the subject of “To Treat Eyes Right, Treat Them Seldom” (July-August 1980 FDA Consumer). FDA’s tentative final monograph, based on a review of the panel’s report and public comments on it, was published in the June 28 Federal Register. After an evaluation of comments on the proposed monograph, final standards will be issued for OTC ophthalmic drug products.

**Machine Use Discontinued**

The Puritan-Bennett Corp., Kansas City, Mo., has sent a letter to 5,200 U.S. hospitals urging them to discontinue use of its Foregger Model 705 and 710 anesthesia machines. The action followed two deaths at the Rose Medical Center in Denver. Similar information was sent to the company’s international distributors.

The patients who died were being anesthetized with the Foregger Model 705 machines on which a control valve malfunctioned for reasons that were not clear. The malfunction may have resulted in an anesthetic overdose. Model 710 is equipped with the same unique valve system. It is not used on other Foregger anesthesia machines. FDA is investigating the deaths and the anesthesia machines affected.

It is estimated that fewer than 800 of these machines are in use in American hospitals. Both models have been discontinued. In most hospitals there are other types of machines available. However, if an emergency situation exists in which one of the Foregger models must be used, hospitals are urged to contact Puritan-Bennett for instructions on how to do so safely.

### Consumer Forum

‘A Real Winner’

For the past couple of years I have been receiving from the Food and Drug Administration those publications that are designed for consumers, and have been most appreciative to be included in the FDA mailings. I want to express my strong, positive appreciation for the content of the magazine “The FDA Consumer.” It is a real winner.

The last 3 issues have contained a variety of articles that are well written and on target. The articles have dealt with current issues in a very readable manner. The explanations are logical and easily understood. The most recent August issue is especially good with its discussion of Doctor/Patient Communications, Cook’s Questions, Spices, Trace Minerals and the article “You Can’t Tell a Nutritionist by the Diploma.”

I wanted you to know how much we in Home Economics in the Ohio Cooperative Extension Service appreciate the “FDA Consumer” as a resource and how fortunate we consider ourselves to be able to work so cooperatively with Ruth Weisheit and Theresa Hoog. We maintain close contact and exchange program progress on a somewhat periodic basis. We find them both extremely competent professionals and look forward to our continuing program cooperation.

Naurine R. McCormick
Assistant Director
Home Economics
Cooperative Extension Service
Ohio State University
Columbus, Ohio

Ms. Weisheit and Ms. Hoog are FDA consumer affairs officers in Cleveland and Cincinnati, respectively.
ARNICA • WOLF'S-BANE • BELLADONNA • DEADLY NIGHTSHADE • BITTERSWEET • BLOODROOT • IRISH BROOM • HORSE CHESTNUT • SWEET FLAG • HELIOTROPE • POISON HEMLOCK • SPOTTED COWBANE • HENbane • JALAP ROOT • JIMSON WEED • LILY OF THE VALLEY • LOBELIA • MAN- DRAKE • MAY APPLE • MISTLETOE • MORNING GLORY • PERIWINKLE • ST. JOHN'S WORT • SPINDLE-TREE • TONKA • WAHOO BARK • WHITESNAKE ROOT • WORMWOOD
Some words are brimful of magic: gold, silver, nectar, paradise, jewel, check enclosed. Certainly qualified for admission into this company is another glittering word: herb. Indeed, “herb” may actually outshine precious metals and gems in its power to evoke magical connotations. After all, gold, silver and precious stones merely enrich or beautify; nectar only titillates the taste buds; and paradise still eludes us. But herbs not only sprinkle magic upon otherwise insipid food; they were, for centuries, the physician’s primary source of help for the sick. Perhaps that is why herbs outnumbered gold two to one among the gifts bestowed by the Three Wise Men.

Attesting to the importance of herbs to people throughout history is the fact that among the writings remaining to us from the ancient civilizations of Sumer, Assyria, Egypt, Greece, China and Rome are “herbals”: manuals that help identify plants believed to possess medicinal qualities. These herbals show clearly that thousands of plants, from absinthe (Artemisia absinthium—wormwood) to yarrow (Achillea millefolium—milfoil), have, from the dawn of history, been considered medicines with the power to cure or alleviate a host of afflictions. The famous “Ebers Papyrus,” written some 35 centuries ago, contains the herbal remedies used by an unknown Egyptian physician. Dioscorides, a surgeon in the army of the Roman Emperor Nero, made the first comprehensive list, or materia medica, of all known medicinal herbs. This list was modified and expanded through the centuries, with many entries finding their way into official lists of drug formulas such as the U.S. Pharmacopoeia. In the early years of the 20th century the more scientific approach eliminated most of these herbal compounds as ineffective. Others, such as quinine from the bark of the cinchona plant (Cinchona calisaya), have been replaced gradually by synthetic compounds that do the job more effectively.

Since the role of herbs in modern medicine has been reduced almost to the vanishing point, it would seem logical to conclude that their magic also would disappear. But, like so many conclusions that seem called for by logic, it hasn’t happened, for several reasons:

- First, medicinal reputations of herbs have been kept alive by knowledge that herbs were the original source of many important medicines, such as the heart medicine digitalis derived from the foxglove plant (Digitalis purpurea). Also, scientific research on the therapeutic properties of botanicals continues to yield new and useful compounds, such as chymopapain (Chymodiactin), a derivative of the papaya plant, approved in 1982 by FDA for treating certain types of herniated lower back disks. Thus the word “herbs” still wears a kind of halo.

- Second, there are a wide variety of publications—such as “natural” or wild food guides, books on American Indian lore, and modern herb manuals—extolling the virtues of the “healthful herbs.”

- Third, there is the attraction that “natural” foods currently hold for those who want their food and drink farther from the test tube and closer to nature.

- And fourth, there has been the search for beverages less burdened with calories or caffeine.

The soaring figures on sales indicate that a great many persons are reaching out to embrace the magic of herbs. They simultaneously satisfy their desire for natural products and for low-calorie, caffeine-free drinks by consuming herbal teas—mint, chamomile, and some 400 other now commercially available combinations of herbs and spices. Given this new trend, it’s well to ask, “Are these teas safe?” The Herb Trade Association, which represents over 200 herb growers, believes they are. As Mark Blumenthal, founder of the association, notes, “Many of these teas have been used in cultures around the world with impunity from toxic reactions for thousands of years.” And he adds, “I have no question in my experience personally and in my business that the vast majority of herbs are safe in normal amounts.”

While many peppermint, rose hip, orange, and others of the more usual herbal teas do offer delicious alternatives to two traditional drinks that contain caffeine—coffee and common tea (Camellia sinensis)—we cannot conclude from these facts that all herbal teas are safe, nor that it’s safe to consume large amounts of any herbal tea over extended periods. In weighing the safety of this practice, it’s very impo-
tant to note a number of cautions.

Caution Number One: Some herbs contain the wrong kind of magic. Found among the herbs are nature's most potent poisons. Socrates died from being administered an herbal drink, hemlock (not from the evergreen tree but from the plant Conium maculatum). South American Indians poisoned the tips of their arrows with the herbal extract cupre. And no self-respecting witch would be found without a handy supply of deadly nightshade (Atropa belladonna). No one would knowingly consume these poisonous herbs, of course. And no responsible herb company would even consider putting such poisons in its products. But the fact is that poisonous herbs have been found in medicines and diet aids. For example, FDA recently took action against an herbal product, Herbalife Slim and Trim Formula. Advertisements for this product claim that it offers a "safe, sensible, all natural Health and Nutrition Program that gets us back to the Natural way of being Slim and Healthy using herbs."

Among the herbs listed for one of the diet formulas are mandrake and pokeroott. Mandrake, whether the American (Podophyllum peltatum—May apple) or European (Mandragora officinarum) variety, is highly toxic, as is pokeroott (Phytolacca americana). Indeed, mandrake was once used by American Indians as a suicide drug. This diet aid claims that it will "keep the weight off indefinitely," which may well prove all too true for those unfortunate enough to consume too much of it.

Caution Number Two: We don't know enough about herbal teas to conclude that they are safe. The miniature chemical factory that is an herb produces a wide variety of compounds that can affect the human body. The principal types are acids, tannins and essential oils, and the most potent are alkaloids (morphine and nicotine are examples) and glycosides (digitalis, amygdalin, etc.). Those chemicals soluble in hot water will appear in teas brewed from herbs. Since some alkaloids and glycosides build up in body tissue, it's possible for even small amounts to add up eventually to significant exposure. Also, from time to time new evidence comes to light that causes a long-accepted herbal product to be dropped from the list of those approved or generally recognized as safe products. Thus, only a few years ago substances derived from the plants calamus, sassafras and the tonka bean (see accompanying article) were considered perfectly safe. When subsequent research determined that these substances were either toxic or caused cancer, they were banned from the food supply. Manufacturers of herbal teas have not submitted their products to FDA nor made the required animal studies for a determination of safety based on the kinds of exposure that drinking tea represents. Thus, ironically, people who drink herbal tea to avoid the known effects of caffeine are exposing themselves to thousands of chemicals about which far less is known.

As Dr. James Duke, chief of the economic botany laboratory at the Department of Agriculture's Beltsville, Md., laboratory, put it: "Each plant has thousands of chemicals in microquantities. All things contain poisons if you look hard enough. Just knowing a toxin is in a plant, you still don't know how it affects humans until you've tested it in them."

And then he added, "Nobody has tested these herbs, at least under laboratory conditions, recently. There's almost no clinical research work done."

While there is a dearth of clinical research on the chronic or long-term effects of consuming herbal teas, there is ample clinical evidence of the acute, short-term impact of some herbal teas. Nutmeg does add spice to the Christmas egg-nog, and jimson weed is an important source of certain drugs, but when brewed into tea they can be and have been deadly. Peony root is recommended in various modern herbs for its antispasmodic qualities, but when brewed into tea it can be and has been deadly. This list of fatal encounters involving herbal teas could be extended for many pages.

Caution Number Three: Doctoring yourself with herbs can be very dangerous. Before the era of modern medicine (and even today among various cultures), herbs were widely used to treat sickness. Some herbal treatments succeeded. Thus, 2,300 years ago when Hippocrates recommended chewing willow bark to counter fever and pain, the advice worked because, as we now know, willow bark contains salicylates, the chemical basis of aspirin. Other herbal medicines may have appeared to work because most illnesses are self-limiting or because of the placebo effect (some treatments succeed if the patient believes they will succeed). Further, when the Zuni Indians used yarrow root as an antiseptic, or the Menominees used wild lettuce (Lactuca spp.) as a sedative, when the Apaches and Mescaleros used pen-nnyroyal (Hedeoma pulegioides) to relieve headaches—that's all they had. Nothing else was available.

Given the availability of modern medicines with proven effectiveness and safety when used as directed, treating ailments with herbs is both unnecessary and risky. A recent medical journal article shows just how risky. A young woman complained of excessive menstrual bleeding, the cause of which could not be detected by examination and tests. It was subsequently found that she was devoted to eating only "natural" foods and had been drinking three to five pots of an herbal tea at each change of season as a "tonic," and had lately consumed 20 pots in a two-week period. Her recipe for this tea was found to contain three sources of natural coumarins—tonka beans, meillot, and sweet woodruff. Coumarins reduce the ability of the blood to clot, and thus this homemade "tonic" could have cost this young woman her life.

This caution against self-treatment covers advice found in promotional literature, herbal books and similar material. Such advice is rarely based on the results of scientific studies, usually fails to include necessary warnings, and is often
totally incorrect and outdated.

Caution Number Four: Ne quid nimis—moderation in all things. A study by the National Academy of Sciences (Toxics in Foods) amply documents that even ordinary foods consumed by millions every day can, if consumed to excess, lead to serious health problems. We all know from Popeye cartoons how healthy we can be if we eat spinach. But few know that, due to the large amount of oxalic acid in spinach, excessive consumption—particularly among persons with a kidney disorder—can be decidedly unhealthful. As another example, chamomile contains goitrogens, substances that block the body’s ability to absorb adequate amounts of iodine. Excessive consumption of cabbage (particularly in parts of the world where the iodine content of the diet is low) can produce a greatly enlarged thyroid gland (goiter). Even some nutrients vital to health can, if taken in excess, prove damaging, notably vitamins A and D.

Most Americans are not harmed by the toxic substances in foods because they eat a balanced diet—by definition, one in which nothing is in excess. Although many of the same herbs found in commercially available herbal teas are approved by FDA on the basis of occasional use as seasonings, this does not signify that we know enough about herbs to say with certainty what is an excessive amount that transforms a pleasant beverage into a toxic one. We do know, however, that some herbs contain active principles (chemical compounds) that can exert powerful pharmacologic (drug) or toxic effects if consumed in sufficient quantities.

Caution Number Five: Not all men are created equal, nor women either. Drugs approved by the Food and Drug Administration only after long and painstaking tests involving human subjects quite often produce wholly unanticipated side effects, sometimes serious ones, after they are put on the market. This does not show that the tests were improperly conducted. But it is evidence that the human population, unlike the pure-bred rats so often used to test chemicals, represents an enormous amount of genetic variability. A drug tested among a human population of 2,000 will naturally encounter far more genetic diversity when consumed by 2 million persons. This merely proves that one man’s remedy can be another man’s allergen.

If allergic (or at least nontypical) reactions can occur regarding medicines tested under the strictest safeguards known to modern science, it seems likely that herbal substances that have not been subjected to such tests, and which are consumed in large amounts, may also produce allergic reactions. And medical reports substantiate this conclusion. For example, a 35-year-old woman allergic to ragweed suffered a serious reaction after having a few sips of one of the more popular teas, chamomile. Following emergency treatment, she showed a positive reaction in an allergy test to chamomile, as did 5 of 15 other ragweed patients who were tested, an outcome that would not surprise those who know that chamomile is a member of a plant family that includes ragweed, asters and chrysanthemums.

Caution Number Six: Remember the old, bold mushroom hunter. Among those who gather wild mushrooms there is a cautionary proverb: “There are old mushroom hunters. And there are bold mushroom hunters. But there are no old, bold mushroom hunters.” Thus, if you gather your own herbs to brew a cup of tea be absolutely 100 percent certain that the herb you pick is the herb you seek. Boldness here, as with wild mushrooms, is not compatible with longevity. There are a half million known plant species. Less than 1 percent are poisonous. The odds against ingesting a deadly plant thus seem large, but it takes only one error. And the stakes are a life against a cup of tea. This was tragically illustrated in 1977 when an elderly couple in Washington state died within 24 hours of drinking tea brewed from foxglove that they had mistaken for comfrey leaf (Symphytum officinale—knitbone or healing herb). Such errors are easy to make, as pointed out in a discussion of the water hemlock (Cicuta maculata and C. bulbifera) in a wild food trail guide. After stating that a single bite of the root of this plant is sufficient to kill, the guide points out that, “As a member of the Parsley family, it is a close relative of many of our food plants including parsley, chervil, coriander, caraway, dill, fennel, parsnip, and carrot, and, unfortunately, it resembles many of these plants.”

FDA has authority over the use of herbs in food, drugs and cosmetics, but there are practical limits to the agency’s ability to protect the consumer. FDA’s ability to protect against ingestion of a harmful herb is limited because a product may be so new or sales so limited that the agency may not actually know about the product unless or until it injures someone or unless an alert consumer informs a public health agency or the local or national office of the FDA. Consumer cooperation in reporting reactions, even minor ones, that result from drinking herbal teas—or from any product—is important in protecting the public health.

As Dr. Sanford Miller, director of FDA’s Bureau of Foods, puts it, “You have to be careful. People feel that because there are no reports of toxicity, that makes an herb safe. But just because there are no reports doesn’t mean there weren’t reactions. Most are not life-threatening. Most people don’t go to doctors with them.” So, if you, as a consumer, know of or experience an adverse reaction to an herbal tea or other herbal product, by all means report it. Such information is not only important to FDA’s efforts to protect the public health but also to herbal tea companies which are anxious to sell only products that are safe and wholesome.

Tim Larkin is a freelance writer.
### Unsafe Herbs
Following is a list compiled by FDA of some herbs that should not be used in foods, beverages or drugs.

<table>
<thead>
<tr>
<th>Botanical Name of Plant Source</th>
<th>Common Names</th>
<th>Remarks</th>
</tr>
</thead>
<tbody>
<tr>
<td>Arnica montana L.</td>
<td>Arnica. Arnica Flowers. Wolf's-bane. Leopard's Bane. Mountain Tobacco. Flores Arnicae.</td>
<td>Aqueous and alcoholic extracts of the plant contain choline, plus two unidentified substances that affect the heart and vascular systems. Arnica, an active irritant, can produce violent toxic gastroenteritis, nervous disturbances, change in pulse rate, intense muscular weakness, collapse and death.</td>
</tr>
<tr>
<td>Atropa belladonna L.</td>
<td>Belladonna. Deadly Nightshade.</td>
<td>Poisonous plant that contains the toxic solanaceous alkaloids hyoscyamine, atropine and hyoscine.</td>
</tr>
<tr>
<td>Acorus calamus L.</td>
<td>Calamus. Sweet Flag. Sweet Root. Sweet Cane. Sweet Cinnamon.</td>
<td>Oil of calamus, Jammu variety, is a carcinogen (causes cancer). FDA regulations prohibit marketing of calamus as a food or food additive.</td>
</tr>
<tr>
<td>Heliotropium europaeum L.</td>
<td>Heliotrope.</td>
<td>A poisonous plant. It contains alkaloids that produce liver damage. Not to be confused with garden heliotrope (Valeriana officinalis L.).</td>
</tr>
<tr>
<td>Botanical Name of Plant Source</td>
<td>Common Names</td>
<td>Remarks</td>
</tr>
<tr>
<td>-------------------------------</td>
<td>--------------</td>
<td>---------</td>
</tr>
<tr>
<td><strong>Convallaria majalis L.</strong></td>
<td>Lily of the Valley. Convallaria. May Lily.</td>
<td>Contains the toxic cardiac glycosides convallatoxin, convallarin and convallamarin. Poisonous plant.</td>
</tr>
<tr>
<td><strong>Lobelia inflata L.</strong></td>
<td>Lobelia. Indian Tobacco. Wild Tobacco. Asthma Weed. Emetic Weed.</td>
<td>A poisonous plant that contains the alcaloid lobeline plus a number of other pyridine alkaloids. Overdoses of the plant or extracts of the leaves or fruits produce vomiting, sweating, pain, paralysis, depressed temperatures, rapid but feeble pulse, collapse, coma and death.</td>
</tr>
<tr>
<td><strong>Mandragora officinarum L.</strong></td>
<td>Mandrake. Mandragora. European Mandrake.</td>
<td>The plant is a poisonous narcotic similar in its properties to belladonna. Contains the alkaloids hyoscyamine, scopolamine and mandragorine.</td>
</tr>
<tr>
<td><strong>Phoradendron juniperinum Engelm.</strong></td>
<td>Mistletoe. Viscum. Juniper Mistletoe.</td>
<td>May be poisonous. Little is known about its properties.</td>
</tr>
</tbody>
</table>

(continued on next page)
<table>
<thead>
<tr>
<th>Botanical Name of Plant Source</th>
<th>Common Names</th>
<th>Remarks</th>
</tr>
</thead>
<tbody>
<tr>
<td><em>Ipomoea purpurea</em> (L) Roth</td>
<td>Morning Glory.</td>
<td>Contains a purgative resin. In addition, morning glory seeds contain amides of lysergic acid but with a potency much less than that of LSD.</td>
</tr>
<tr>
<td><em>Vinca major</em> L. and <em>Vinca minor</em> L.</td>
<td>Periwinkle. Vinca. Greater Periwinkle. Lesser Periwinkle.</td>
<td>Contains pharmacologically active, toxic alkaloids such as vinblastine and vincristine that have cytotoxic and neurological actions and can injure the liver and kidneys.</td>
</tr>
<tr>
<td><em>Eupatorium rugosum</em> Houtt. <em>E. ogeratoides</em> L.f. and <em>E. urticaefolium</em></td>
<td>White Snakeroot. (Also called Snake-root, Richweed.)</td>
<td>Poisonous plant. Contains a toxic, unsaturated alcohol called tremetol combined with a resin acid. Causes &quot;trembles&quot; in cattle and other livestock. Milk sickness is produced in humans by ingestion of milk, butter, and possibly meat from animals poisoned by this plant.</td>
</tr>
<tr>
<td><em>Corynanthe yohimbi</em> Schum. <em>Pausinystalia yohimbe</em> (Schum.) Pierre</td>
<td>Yohimbe. Yohimbi.</td>
<td>Contains the toxic alkaloid yohimbine (quebrachine) and other alkaloids.</td>
</tr>
</tbody>
</table>
Tourists heading for Mexico to swap their U.S. dollars for drastically devaluated Mexican pesos may find some bargains to offset the high costs of inflation in our own country. But one "bargain" that isn’t is coumarin extract, passed off as genuine vanilla extract or put into real or artificial vanilla flavoring to give it more zing.

Many tourists from the United States fall for this South of the Border offering because it looks like a bonanza. It isn’t. Coumarin, or tonka bean extract, may be displayed on a store shelf or at a roadside stand for as little as $1.50 for a quart. When you sniff it, the stuff smells like real vanilla. It isn’t. What’s more, it could be damaging to health.

The genuine vanilla bean, *Vanilla fragrans*, is a native of Mexico, but it doesn’t come cheap, even where it’s grown. The vanilla plant is an orchid in a vine form that ascends into trees in the subtropical areas of southeast Mexico and nearby countries.

South America is the home of the tonka bean, *Dipteryx odorata*, an entirely different plant, a tree up to 150 feet tall, that belongs to the pea family. The tonka bean will grow in Mexico too. It smells enough like vanilla to satisfy all but the experts. But look out! Coumarin, the impostor, has been prohibited by FDA as a food or food additive in the United States since 1954 and also is outlawed in many other countries for these uses.

It has been prohibited for these uses for a very good reason. FDA in 1954 determined that it’s a poisonous and deleterious substance. A pharmacologist testified during a hearing that it caused damage to various organs of test animals, particularly the liver. FDA terminated its use, dating from 1940, as an optional ingredient in certain types of chocolate products. The agency also prohibited its use in any other way as a food or food additive. The logical inference is that coumarin is not one of the things you would want to have in your ice cream or piece of cake. In short, coumarin as a flavoring agent or as a food is no bargain at any price.

Strangely enough, the use of a derivative of coumarin in certain drugs is perfectly legitimate. This factor, dicumarol, is the active ingredient in certain blood-thinning medicines, anticoagulants. This factor, also known as warfarin, is used in rat poison as well, causing the rodent to die from hemorrhaging. But there has been no indication that coumarin itself produces this blood-thinning effect in humans.

The chances for deception in buying vanilla would be a lot less if the tourist bought the whole bean instead of some liquid product that allegedly contains the essence of the bean. Vanilla beans are long and thin, about 7 to 10 inches long and around a quarter of an inch wide. They turn dark brown to black when cured. Seeds are small and round. The entire pod is ground up and used as flavoring, or the flavoring extracted with a solution of ethyl alcohol and water. Tonka beans are oval in shape, about 5 inches long by 3 or so inches wide. Only the seeds are used as flavoring. These are about 3½ by 2 inches in size. The seedpod is not used at all.

FDA standards for vanilla extract specify that 13.35 to 15 ounces (depending on moisture content) of vanilla beans be used per gallon of extracting fluid, which consists of 35 percent ethyl alcohol and the rest water. There are other standards for vanilla flavoring, which is a more dilute solution; for mixtures with artificial vanilla (vanillin); and for concentrates and powders. Some additives, including sugar, are permitted. Verifying the presence of coumarin in such products is a fairly simple laboratory procedure, and FDA in testing some extracts or flavors from Mexico offered as vanilla or vanillin has found coumarin often, with wide inconsistency in amounts. This suggests that the U.S. tourist buying such a product has no way of knowing how much coumarin may be present. It follows that the person who takes a little gamble that the amount of coumarin in the bottle isn’t enough to be toxic is playing with loaded dice.

—Harold Hopkins
Drugs For Those Other Animals

by Carol Ballentine

On a hot summer evening in Kensington, Md., a young man walked into a veterinary clinic with a raccoon perched on his shoulder. Some of the other patients—three cats, a collie and a Great Dane puppy—showed signs of perturbation and their owners eyed the unusual pair with curiosity. But the raccoon and its owner seemed completely at ease.

The man smiled at the receptionist. "I'd like to get some worm medicine for her," he said, indicating the raccoon.

The receptionist seemed nonplused. "Well, I don't know," she said. "Just a minute." She disappeared into a back room and returned smiling. "The doctor says okay," she said. "Just have a seat."

The Maryland veterinarian would have had to do some educated guesswork to treat a raccoon because there are no drugs made specifically for this species. Most likely, the vet prescribed a drug meant for dogs or cats and adjusted the dosage according to the animal's body weight, perhaps with a warning to the young man that the drug might not be effective.

Although people's tastes in pets range from mice to ocelots, using educated guesswork in treating animals is a part of every veterinarian's job because there are many animal diseases for which there are no approved drugs.

Like drugs for people, most animal drugs—including medicated feeds—must be approved by the Food and Drug Administration as safe and effective for treating a particular disease or condition (although both physicians and veterinarians can and do use drugs to treat conditions other than those for which the drugs are approved; they also have the responsibility for any adverse consequences.) In the case of food-producing animals, such as cattle, the person seeking approval of a drug (applicant) must also provide data showing that any drug residues that may be in the meat or other products (milk, for instance) do not pose a hazard to humans.

When animal drugs are approved it must be for use only in particular species, and applicants must test a drug for safety and effectiveness in those species for which it is intended—and it is approved for use only in those species. Because placing a new animal drug on the market can be a costly and lengthy business, manufacturers tend to be most interested in producing drugs for animals raised and/or kept in large numbers. Thus, most approved animal drugs are for use in what FDA has defined as the "major species": cattle, horses, swine, turkeys, chickens, dogs and cats. For all other animals, the "minor species," the veterinarian has to more or less improvise.

The lack of approved drugs is a growing problem for producers of some of these species, particularly ducks, geese, game birds, goats, sheep, chinchillas, mink, rabbits, and for many fresh water and marine "crops" such as catfish, clams, salmon and crayfish.

There are, in fact, some common diseases in these species for which there are no approved drugs. Faced with a disease outbreak, animal producers frequently have little choice but to use a drug approved for some other species and hope that it will be effective and that it will not harm the animals. So goat producers treat respiratory disease in their herds with drugs approved for use in cattle, and sick ducks are treated with drugs tested on chickens. Some common diseases for which drugs are needed include coccidiosis (primarily an intestinal disease) of sheep and rabbits, liver flukes in goats, ICh (Ichthyophthiriasis, a protozoan disease) of food fish, and bacterial gill disease in trout and salmon.

Treating animals with drugs not tested and approved for that species can be risky. It's risky because the drugs could harm—or kill—the animals, or may not be effective. When food-producing animals are so treated it can also be hazardous for humans because of the possibility that harmful levels of drug residues may end up in the meat or other products.

However, the alternative—not treating animals for disease when there are no drugs approved for them—is also a problem. Animal producers often risk losing a large part of their stock to disease. In addition, some diseases can be transmitted from animals to people and when disease is left untreated, the risk of transmission increases. For example, Salmonella bacteria are widespread in domestic animals. People handling contaminated animals can become infected or can cause food to become contaminated. In animals for which there are no approved drugs to treat this disease, such as game birds, transmission of the bacteria is a particular problem. And even when diseases are not directly transmissible to humans, disease organisms can still render the meat of an animal unfit for human consumption.

Because there are so many "minor" species, there probably never will be drugs approved to treat every disease in every animal. FDA, however, has taken steps to make it easier to obtain approval for drugs intended for use in the lesser animals. In January 1983 FDA approved new regulations designed to reduce the costs of research and development of drugs for minor species. Basically the regulations change the data requirement for "minor use" drugs. (Minor use drugs are those intended for use in minor species or for use in any species to treat diseases that occur infrequently or are limited to small geographic areas of the country.)

One major provision of the regulations permits extrapolation of data between physiologically similar species, where appropriate, in New Animal
Drug Applications for minor species. For example, one company may own a drug that is approved for treating a particular respiratory disease in cattle. This means that this company ("the proprietary holder") has done extensive—and expensive—testing necessary to get the drug approved, which includes showing that the drug is safe and effective for treating this disease in cattle and that residues of the drug in the meat (or milk, etc.) of treated animals are not above safe levels. A producer of goats might want to obtain approval of the drug for treating respiratory disease in goats. Before the new regulations went into effect, this producer would have had to go through the same testing procedures as if the drug were not approved for any use. Now the goat producer, with the permission of the proprietary holder, can use the approved basic data, thus cutting time and costs in getting the drug approved. Of course, a drug can qualify for approval under the minor use regulations only if it is already approved in a major species.

The new regulations also will allow sponsors of minor use drugs to extrapolate or take this sort of "data shortcut" to show food safety—that is, to show that residues of the drug don't pose a human safety hazard when used in food-producing animals. Unless there is some specific question about a minor use drug, FDA will allow data extrapolation for all minor species except sheep. Because lamb and mutton can form a substantial part of the diet of some people, sponsors of drugs for sheep must provide the same kind of data on human safety as that required of drugs for use in major species. This includes information on (1) toxicity of the drug for humans; (2) residues—how the animal metabolizes the drug and the range of residues (or metabolites) that could end up in meat or other products intended for human consumption; and (3) analytical methodology—the methods that can be used to analyze for residues in the slaughtered animal.

The new regulations also alleviate some of the burden drug sponsors face in providing information on how the drug might affect the environment (including method of administration, metabolic transformations of the drug before it is excreted, and conditions under which the animals are reared). Animal drugs, much more than human drugs, are likely to escape into the environment in significant quantities because most domesticated animals are concentrated in a production area and also tend to be medicated en masse. Knowing how a drug is metabolized, and the amount of and form in which it will be excreted, is important since animal waste is frequently used as fertilizer or might be processed for use in animal feed. (In most states, recycling of animal waste is monitored by state feed control agencies. The waste is processed to free the product of disease-producing microorganisms but it is possible that drug residues might remain and thus occur in feed for other animals.)

Environmental impact information must be provided for all New Animal Drug Applications, even minor species, because even when animals are not reared in large numbers on a national basis, they are frequently concentrated in particular regions of the country. For example, catfish farming is largely located in the South, particularly in Mississippi, Arkansas and Alabama; and 99 percent of America's crayfish industry is in Louisiana. Fish in particular are raised in ecologically sensitive and valuable sites such as estuaries and rivers, and FDA is concerned about the potential for drug contamination of these areas. Collection of environmental data will be made easier for applicants for minor use drugs, however, since the new regulations allow use of data from approved "major use" applications.

The new regulations do not totally relieve animal drug applicants of testing requirements. FDA requires that some tests be made in the species for which the drug is intended because even physiologically similar species may metabolize drugs in different ways. There is substantial evidence, for instance, that chickens and turkeys can have quite different responses to the same drug—some drugs that are safe for chickens have proved toxic in turkeys, and some anticoccidials that are effective in chickens are ineffective against coccidiosis in turkeys.

The fact that FDA will permit extrapolation of data only between species that are physiologically similar—for example, from cows to goats—does create a problem in the case of minor species for which there is no similar or "model" major species. There is, for example, no model major species for any fish. Aquaculture "crops" include many species—salmon, catfish, oysters and clams, lobsters and crayfish, trout and shrimp. The aquaculture business has been booming, which means that the use of drugs for these aquatic species may also be expected to increase. (See "They're Growing Food Under Water" in the November 1981 FDA Consumer.) Unfortunately, many of the drugs used are not approved for the particular species. Approved drugs must be available if aquaculture is to continue to prosper and still not pose a hazard to humans consuming edible aquatic products.

Since no aquatic animal falls into the major species category, FDA has designated four species as representative of several families of fish: rainbow trout (representing salmon and trout); bluegill (representing sunfishes such as black basses and crappies); channel catfish (representing catfish); and fathead minnow (representing minnows). Data derived from these four species may be used for other fish in the same family.

FDA is also coordinating research into how various minor species handle drugs so that model species can be developed. With money allocated by the U.S. Department of Agriculture, this research is being conducted by the Interregional Research Project No. 4, located at the New Jersey State Agricultural Experiment Station at Rutgers University, which for many years has been working with the Environmental Protection Agency developing data to use in setting tolerances for pesticides used in minor species of vegetables and fruits. The research project staff will work with FDA to generate safety and efficacy data on minor species and minor use drugs in animals and to represent petitioners who want drugs approved for minor use in animals. The group has identified more than 50 drugs for which approval for minor species is urgently needed.

Even with the new regulations, there probably never will be a profitable market for drugs to use in some species—such as raccoons—which means veterinarians will continue to do their educated guesswork. But for producers of a lot of heretofore neglected species, the guessing may be coming to an end.

Carol Ballentine is a member of FDA's publications staff.
The Antibiotics Controversy

For nearly two decades the use of antibiotics in animal feed has been a concern for FDA and scientists. Medicated feeds with low levels of antibiotics are widely fed to meat-producing animals because they can control animal diseases and cause the animals to gain weight faster—with less feed. Proponents hold that without this use of antibiotics in feed, more feed and fattening time would be required and prices would rise substantially.

But there is evidence that bacteria in these animals are able to develop a resistance to antibiotics fed to the animals at such low, or subtherapeutic, levels. Knowledgeable scientists say that this resistance can be transferred to other bacteria, including those that are pathogenic to humans, and that this resistance can be genetically stamped upon entire strains of such pathogens, making the antibiotics ineffective in the treatment of humans infected by the bacteria. A task force appointed by FDA to study the issue recommended that low-dosage use of antibiotics in feed be discontinued unless it could be shown conclusively that no health hazard exists from the practice.

In May 1977 FDA published a Federal Register notice of proposed rulemaking that would withdraw permission for use of penicillin in animal feed and drastically limit the use of the antibiotics chlortetracycline and oxytetracycline in animal feeds. Manufacturers of the antibiotic drugs requested a hearing on the FDA proposals.

During congressional hearings on the FDA budget for the 1979 fiscal year, Congress reviewed the FDA proposals and requested that the National Academy of Sciences review published literature on the question and make recommendations on the issue. FDA was expected to postpone any action on the matter until March 1980, when the National Academy was to issue its study report.

At the conclusion of the study, the National Academy could neither confirm nor deny that the use of antibiotics in animal feed presented a health hazard to the public. Congress then directed FDA to undertake further research on this issue, research that will take several years to complete. In the meantime, a congressional committee urged that FDA not take final action to withdraw the use of antibiotics in animal feeds.

The Animal Drug Monitors

Since its creation on Nov. 7, 1965, FDA's Bureau of Veterinary Medicine has been the federal regulatory authority primarily responsible for animal drug products marketed in interstate commerce. Most animal drugs must be approved by the bureau as safe and effective before they can be marketed commercially. In the case of food-producing animals, the bureau also establishes the level of drug residues, if any, that may be permitted in meat and other edible animal products intended for human consumption before allowing the drug to be marketed in the United States.

Two other federal agencies also have a major hand in regulation of products used to treat animals.

The Environmental Protection Agency has jurisdiction over germicidal preparations and rodenticides, fungicides and insecticides. A number of products of this kind, when used on animals, fall under the jurisdiction of both EPA and FDA, but the agencies have signed an agreement which provides for one or the other to assume primary responsibility for specific classes of products. Flea and tick-collars, for example, are considered an EPA responsibility—they must be registered with EPA and do not need FDA approval unless medical claims are made.

The U.S. Department of Agriculture is responsible for monitoring livestock and poultry for illegal drug residues; however, if such residues are found, it is FDA's responsibility to take legal action to halt such drug misuse. USDA also is responsible for licensing animal biological products and the establishments for making such products. (Biologics include vaccines, such as for rabies and distemper.) USDA has had this authority since Congress passed the Virus, Serum, and Toxin Act in 1913. Biological products produced and distributed in full conformance with the provisions of this act are exempt from premarket approval by FDA. However, FDA can take legal action under the Food, Drug, and Cosmetic Act against illegal products or unlicensed producers.
One day, Abraham Lincoln sat down and wrote to his law partner, John Stuart: "I am now the most miserable man living. If what I feel were equally distributed to the whole human family, there would not be one cheerful face on earth. Whether I shall ever be better, I cannot tell; I awfully forebode I shall not. To remain as I am is impossible. I must die or be better..."

Lincoln suffered from a disorder that affects some 127 million people throughout the world and an estimated 9 to 11 million Americans at any given time. Depression—also known as clinical depression or depressive disorders—is the most prevalent mental illness in the United States.

As old as recorded civilization—ancient Egyptian manuscripts and the writings of Greek physicians refer to it as "melancholia" or madness—depression respects neither social class, race, sex nor ethnic group. Children as young as age 5 have been treated, although the peak years for depression are ages 25 to 44. Outbreaks usually taper off after age 60.

But depression can be treated. A variety of therapies—electroconvulsive therapy (ECT), psychotherapy and antidepressant drugs—lessen the oppressive load.

Antidepressant drugs provide one of the most widely used therapies. These drugs have been credited with miraculous results and also blamed for false hopes and debilitating side effects. Patients who have spent years trying alternatives and finally discover the right antidepressant swear by the results. Those who can't be helped by the drugs—a sizable minority—lament the wasted time. But the fault lies not so much in the imperfections of the various therapies as in the disorder itself. We still don't know much about depression. The brain does not give up its secrets easily and any talk about "cures" for depression is premature.

The word "depression" evokes numerous—and often erroneous—interpretations. Many people think that depression is the feeling of sadness engendered by the vicissitudes of everyday living. Losing a loved one or a job, or suffering any setback, often makes the world seem like a dreary place.

"But those feelings fall into a class of normal emotional reactions and not clinical depression," says Dr. William Potter, a psychopharmacologist at the National Institute of Mental Health (NIMH).

Although one may cry, lose weight, or complain of sleeplessness these symptoms soon pass.

"What determines clinical depression is the severity and duration of symptoms," says Dr. Frederick Goodwin, chief of research at NIMH.

Instead of lasting only a few days, the symptoms of severe depression last for weeks or months, perhaps years. They fall into several categories: mood disturbances (enduring feelings of sadness, guilt or hopelessness); disturbance of biological functioning (sleep disturbance, appetite change, weight gain or loss, loss of sexual drive, fatigue); and disturbances of thought (morbid preoccupations, delusions, hallucinations). Clinical depression may be precipitated by the same losses and stresses that trigger "normal" depressed feelings. It also may occur spontaneously or in response to events that seem quite minor.

"At its extreme," says Dr. Potter, "individuals won't
have a few good days or a few bad days. Depression's a long-lasting, bleak picture. Seriously depressed individuals lack the ability to take pleasure in anything—nothing cheers them up. They block, think slowly, and frequently can't answer questions directly."

Research shows that depression is a recurrent illness. Recent studies suggest that 70 to 90 percent of depressed individuals will experience more than one episode or have a chronic depression that is characterized by persistent symptoms and significant problems in social functioning.

Two serious complications frequently accompany depression: alcoholism and suicide. Dr. Kay Jamison, director of the Affective Disorders Clinic at the University of California at Los Angeles, reports that of those with a major depressive illness, 20 to 70 percent have drinking problems. And among those who are severely depressed, approximately one person out of every six will commit suicide. Although twice as many women as men attempt suicide, men more often succeed.

Since ancient times, healers have put their faith in medicines or drugs to cure mental illnesses. Potions, mineral baths, crushed herbs, vapors and bromides all have been tried.

The successful breakthrough in treating mental disorders with drugs came in the early 1950s with the development of antidepressants and tranquilizers. The discovery of antidepressants was by accident. One of the antidepressant drugs had been used experimentally at first for treating TB. Another drug was intended as an antihistamine.

A second important breakthrough came when scientists discovered the existence of a variety of chemicals in the brain—the ramifications of which they are just beginning to appreciate. Called neurotransmitters or neurojuices, these chemicals perform an endless number of functions, including the regulation of pain, learning and memory, and the desire to eat, drink and sleep. Neurotransmitters also affect moods, feelings and behavior.

Approximately 40 have been identified but according to Dr. Candace Pert of NIMH, co-discoverer of the endorphin neurotransmitters, "There might be 100 to 200 different kinds of neurojuices that help regulate emotions and other body processes."

Three neurotransmitters—dopamine, serotonin and norepinephrine—have been implicated as culprits in depressive illnesses. Too much of them, too little of them, or problems in regulating them as they journey through the brain may account for some types of depressive illnesses.

In fact, one clue as to why such a large number of depressed individuals commit suicide has been traced to lowered activity of the neurotransmitter serotonin. Significantly, low serotonin activity also has been linked to aggression and impulsiveness. Autopsies performed on the brains of suicide victims showed that those who committed violent suicide (gunshot and knife wounds) had lower levels of serotonin functioning than those who committed nonviolent suicide (such as an overdose of sleeping pills). Dr. Goodwin of NIMH hypothesizes that such suicides result from an interaction of depression with a biochemical predisposition to aggression and impulsiveness.

The biological basis for depression is demonstrated fur-

### Antidepressant Drugs

<table>
<thead>
<tr>
<th>Drug</th>
<th>Trade Name</th>
<th>Usual Dosage in Milligrams</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Tricyclics</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Amitriptyline</td>
<td>Elavil</td>
<td>150 to 300</td>
</tr>
<tr>
<td></td>
<td>Endep</td>
<td></td>
</tr>
<tr>
<td></td>
<td>SK-Amitriptyline</td>
<td></td>
</tr>
<tr>
<td>Amoxapine</td>
<td>Asendin</td>
<td>150 to 300</td>
</tr>
<tr>
<td>Desipramine</td>
<td>Norpramine</td>
<td>150 to 300</td>
</tr>
<tr>
<td></td>
<td>Pertofrane</td>
<td></td>
</tr>
<tr>
<td>Doxepin</td>
<td>Sinequan</td>
<td>150 to 300</td>
</tr>
<tr>
<td></td>
<td>Adapin</td>
<td></td>
</tr>
<tr>
<td>Imipramine</td>
<td>Tofranil</td>
<td>150 to 300</td>
</tr>
<tr>
<td></td>
<td>SK-Pramine</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Janimine</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Imavate</td>
<td></td>
</tr>
<tr>
<td>Nortriptyline</td>
<td>Aventyl</td>
<td>75 to 150</td>
</tr>
<tr>
<td></td>
<td>Pamelor</td>
<td></td>
</tr>
<tr>
<td>Protriptyline</td>
<td>Vivactil</td>
<td>10 to 60</td>
</tr>
<tr>
<td>Trimipramine</td>
<td>Surmontil</td>
<td>150 to 300</td>
</tr>
<tr>
<td><strong>Antimanic</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Lithium Carbonate</td>
<td>Eskalith</td>
<td>300 to 2,400*</td>
</tr>
<tr>
<td></td>
<td>Lithane</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Lithonate</td>
<td></td>
</tr>
<tr>
<td><strong>MAO Inhibitors</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Phenelzine</td>
<td>Nardil</td>
<td>45 to 90</td>
</tr>
<tr>
<td>Tranylcypromine</td>
<td>Parnate</td>
<td>20 to 60</td>
</tr>
<tr>
<td>Isocarboxazid</td>
<td>Marplan</td>
<td>30 to 80</td>
</tr>
<tr>
<td><strong>Triazolopyridines</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Trazodone</td>
<td>Desyrel</td>
<td>150 to 600</td>
</tr>
<tr>
<td><strong>Tetracycllic</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Maprotiline</td>
<td>Ludiomil</td>
<td>150 to 300</td>
</tr>
</tbody>
</table>

*In some cases, large male manic patients may require 4,800 mg/day and do not experience toxic effects at this dose.

"Depression is a very complicated disorder," says Dr.
Jack Blaine, a clinical psychopharmacologist at NIMH. "There are clearly several kinds of depression with overlapping boundaries and symptoms ranging from moderate to severe."

Some depressions are chronic in nature; others are episodic, incorporating cycles of mania and depression (bipolar); still others consist of recurrent depressions alternating with normal or near-normal moods (unipolar).

Although the exact way an antidepressant works is not clearly understood, the drugs do alleviate many of the symptoms.

"Antidepressants also shorten the course of depression," says Potter. These drugs help many people to function day-to-day, keep them out of hospitals, and help them to keep their jobs and relationships intact.

Most antidepressants fall into three major classes: lithium, tricyclic drugs, and MAO inhibitors.

Lithium
Lithium is the recommended drug for patients suffering from manic depression or bipolar depression. This is a truly incapacitating form of depression and scientists suspect that

Albrecht Durer's engraving "Melencolia I," showing a winged, seated personification of Melancholia, is said to have been occasioned by the artist's sorrow at the death of his mother in 1514. Source: Panofsky, E., Albrecht Durer, Vol. 1, Princeton University Press, Princeton, N.J. 1943.

Melancholy And The Muse

Depression seems to be an occupational hazard of many writers and other artists.

Novelist Virginia Woolf and poets Ann Sexton, Sylvia Plath and John Berryman all committed suicide after bouts with depression. Robert Lowell has written movingly of his depression and repeated hospitalizations.

Nor have musicians been immune to its ravages. Schumann wrote much of his piano music while depressed. He died in an asylum after an earlier attempt at suicide by drowning. Handel wrote his Messiah in less than a month during one of his manic or high states.

Whether or not writers had depression, they examined and wrote poignantly of the disorder that so dominates the lives it takes over.

Robert Burton, a 17th century philosopher and humorist, wrote, "All my griefs to this are jolly/naught so damn'd as melancholy." Shakespeare wrote of "the sad companion, dull-eyed melancholy."

F. Scott Fitzgerald, whose wife was institutionalized for mental illness, and who himself was an alcoholic, evokes the mood of depression in his essay The Crack-Up*:

But at three o'clock in the morning, a forgotten package has the same tragic importance as a death sentence, and the cure doesn't work—and in a real dark night of the soul it is always three o'clock in the morning, day after day.

In the novel, The Sorrows of Young Werther, the writer Goethe has his character speak in words reminiscent of modern-day patients who describe their depression:

God knows, I often get into bed with the desire, indeed at times with the hope, of not awaking again; and in the morning I open my eyes, see the sun again, and am wretched. O that I could be capricious, could put the blame on the weather, on a third party, on a frustrated undertaking, then I would only have to bear half the unendurable burden of ill humour. But woe is me! I feel too plainly that all the guilt is mine alone,—no, not guilt! Bad enough that in me the source of all my misery lies concealed, as formerly the source of all my joys . . . . My eyes are dried up, and my thoughts, no longer regaled with refreshing tears, draw my brow into anxious folds. I suffer much, for I have lost what was the sole rapture of my life, that holy, animating force with which I created worlds all about me; it is gone!

*F. Scott Fitzgerald in The Crack-Up, copyright 1945 by New Directions Publishing Co. Reprinted by permission of New Directions.
genes play a large role in its incidence. During the manic phase, persons experience incredible highs, have frenetic and sustained bursts of energy (individuals have been known to stay up days at a time), have an unrealistic sense of well-being, exercise poor judgment, are aggressive, and experience delusions of grandeur. During the depressive phase, the individual plunges to such depths, and to despair so intense, that he or she may commit suicide. A young peoples’ disease, this depression most often strikes those in their mid-20s.

Lithium, still a mysterious drug, brings down the euphoric highs of mania, but scientists do not understand why it also works against the depressive phase. The severity of the episodes, the potential impact of a future episode on an individual’s functioning, the attitude of the patient toward taking medication for long periods, and many other factors will determine whether and how long a patient continues on treatment.

One of the major problems in prescribing lithium is getting patients to stay on the drug. Dr. Jamison found in a study on lithium compliance that 50 percent of the patients stopped taking the drug against medical advice. Their reason for stopping: They missed the euphoric feelings and sense of well-being experienced during mild manic states.

Side Effects: According to the National Institute of Mental Health, “There is a narrow range between the therapeutic and toxic level.” Periodic blood tests are needed to monitor the lithium level. Because lithium is excreted from the body almost entirely by the kidneys, any injury or weakening of the kidneys may allow lithium to accumulate to dangerous levels in the body. Since too little sodium also has been implicated in lithium build-up, the use of diuretics and low-sodium diets can be especially harmful to the patient taking lithium. Other side effects include nausea, lethargy, thirst, hand tremors, greatly increased urination, and possible weight gain.

Tricyclics

The most widely used class of the antidepressant drugs, tricyclics are usually prescribed for patients with depression characterized by “endogenous” symptoms. These include insomnia, loss of appetite and weight, psychomotor retardation, loss of energy, decreased capacity to feel pleasure, suicidal thoughts, and thought patterns dominated by hopelessness, helplessness and excessive guilt. Usually known as “classic depression,” this depression most often strikes people in the late 30s or early 40s.

NIMH’s Dr. Potter says 80 percent of those on the right dosage of tricyclic drugs eventually get better. For those who don’t do well on a drug regimen, electroconvulsive treatment is sometimes recommended. There are even those who will spontaneously snap out of their depression after one or two episodes.

Side Effects: Tricyclics can be extremely toxic in excessive doses. Dr. Potter says coroners in metropolitan areas report that tricyclic drugs are a major culprit in deaths due to drug overdoses. Too high a dose also can produce irregularities in heartbeat. Other side effects include disturbed vision, sweating, dizziness, decreased or increased sexual desire, constipation, and edema.

MAO Inhibitors

These antidepressants are usually prescribed for people who have not responded to tricyclics or else have “atypi-cal” depression, a type of depression one psychiatrist described as “open to anyone’s definition.” Less common than classic depression, the condition includes high levels of anxiety and phobic and obsessive-compulsive symptoms. Some individuals also sleep and eat a lot—in contrast to the insomnia and loss of appetite associated with individuals who have classic depression.

MAO—monoamine oxidase—is an enzyme that breaks down neurotransmitter molecules into inactive substances. MAO inhibitors interfere with metabolic breakdown of amines. Therefore, amine levels increase in people taking these medications.

Side Effects: The combination of certain foods with MAO inhibitors can trigger very high blood pressure, rapid pulse, headaches, problems with vision, and sometimes paralyzing or fatal strokes. Foods high in the amines tyramine or histamine should be avoided. These foods include beer, red wines, chocolate, pickled fish, cheese and yogurt. Stimulants, caffeine and allergy pills should also be avoided.

Keeping persons on antidepressants long enough for the antidepressive effects to be felt often proves difficult. During the first two to four weeks the patient feels the side effects of the drug but has little relief from the depression. “Physicians often make the mistake of taking their patients off the drug too soon for its antidepressive effects to be felt, or not raising the dose to an adequate level to be effective,” says NIMH’s Dr. Blaine. “It may take as long as six weeks for the drug to work.”

Many physicians recommend that patients be kept on their drug regimen for six to eight months and even as long as a year. The relapse rate for patients taken off too early is 60 to 80 percent. A recent NIMH study showed that patients had to be almost completely symptom-free for approximately three months before the tricyclic drugs could be discontinued without excessive relapses. Because antidepressant side effects can be dangerous to a few and nearly intolerable to a larger number, drug companies have tried to come up with variations on existing drugs which have fewer side effects.

Several new antidepressants await marketing approval from FDA, but long-term clinical trials will be needed to test both their effectiveness and the lack of or presence of deleterious side effects.

Dr. Mitchell Baiter of NIMH, who has spent years conducting surveys of Americans’ use of prescription drugs, says, “We’re still looking for the perfect antidepressant.”

The benefits of psychotherapy also should be emphasized. For mild depression, psychotherapy is usually the best treatment. But even for those who take drugs to control their depression, psychotherapy plays a necessary role in their treatment. As one patient so eloquently describes it:

“I cannot imagine leading a normal life without lithium . . . Lithium keeps me in relationships, in my career, out of a hospital, and in psychotherapy. It keeps me alive too. But psychotherapy heals, it makes some sense of the confusion, it reins in the terrifying thoughts and feelings; it brings back hope, and the possibility of learning from it all. No pill can help me deal with the problem of not wanting to take pills, but no amount of therapy alone can prevent my manias and depressions. I need both.”

Judy Folkenberg is a science writer at the National Institute of Mental Health.
On Treating Warts With Spunk Water And Other Things

by Richard C. Thompson

"Talk about trying to cure warts with spunk water. You got to go all by yourself, Tom, to the middle of the woods, where you know there's a spunk-water stump, and just as it's midnight you back up against the stump and jam your hand in and say: 'Barley corn, barley corn, Injun-meal shorts; Spunk water, spunk water, swallow these warts,' and then walk away quick, eleven steps, with your eyes shut, and then turn around three times and walk home without speaking to anybody. Because if you speak the charm's busted...

"I've took off thousands of warts off of my hands that way, Huck. I play with frogs so much that I've always got considerable many warts. Sometimes I take 'em off with a bean."

"Bean's good. I've done that. You take and split the bean, and cut the wart so as to get some blood, and then you put the blood on one piece of the bean and take and dig a hole and bury it, 'bout midnight at the crossroads in the dark of the moon, and then you burn up the rest of the bean. The piece that's got the blood on it will keep drawing and drawing, trying to fetch the other piece to it, and so that helps the blood to draw the wart, and pretty soon off she comes."

"Yes, that's it, Huck. Though when you're burying it if you say 'Down bean; off wart: come no more to bother me!' it's better. But how do you cure 'em with dead cats?"

"You take your cat and go and get in the graveyard 'long about midnight when somebody that was wicked has been buried; and when it's midnight a devil will come, or maybe two or three, but you can't see 'em, you can only hear something like the wind; and when they're taking that feller away, you heave your cat after 'em and say, 'Devil follow corpse, cat follow devil, warts follow cat. I'm done with ye!' That'll fetch any wart."

—From The Adventures of Tom Sawyer by Mark Twain

Good reading but doubtful advice.

Spunk water, burnt beans and dead cats as such do nothing for warts. And Tom Sawyer's wrong about the frogs; neither they nor toads cause warts. All warts are viral infections of the skin. Their medical name is "verruca," and most often they are defined by their location on the body.

Common (vulgaris) warts occur on the hands and fingers, sometimes on
the face, and occasionally on mucous membranes of the mouth and larynx. 
Vulgaris warts that appear around or beneath the nails are known as per- 
ungal warts and are often found in persons who bite their nails or pick at 
their cuticles.

Flat warts (verruca plana) occur— 
sometimes in groups—on the hands, 
wrists and knees, or on the face, neck 
and back. They may follow the line of 
razor cuts and nicks. Venereal warts 
(condyloma acuminata) occur on or 
near the genitalia and anus. Plantar 
warts (verruca plantaris) are found 
only on the soles of the feet.

Of those several kinds, only vulgaris 
and plantar warts should be self-treated 
with nonprescription drugs, and only if 
they are on accessible body sites. All 
or other warts—and plantar and vulgaris 
warts that are problems or persist- 
ent—should be seen by a physician.

Both plantar and vulgaris warts are 
easily recognized. The vulgaris wart 
is small, raised, hard and grayish, with a 
rough surface. The plantar wart is flat, 
may be either hard (callused) or soft, 
and sometimes resembles a corn. Plant- 
tars can be painful and can interfere 
with walking, since the entire body weight compresses on them. Several 
plantars growing close together form a 
mosaic wart.

The Handbook of Nonprescription 
Drugs, compiled by the American 
Pharmaceutical Association, places 
plantar and common warts in the same 
therapeutic category as corns and call-
luses, since all are superficial condi-
tions of the skin that require essentially 
the same kinds of treatment.

In its section on wart treatment, the 
Essential Guide to Nonprescription 
Drugs (D. Zimmerman, Harper 1983) 
states reassuringly that “the more com- 
mon kinds of warts—those that arise 
on the hands, feet, face and some other 
body surfaces—are not dangerous. 
They are not early cancer; they do not 
develop into cancers; and they never 
invade layers of tissue beneath the 
skin.”

Warts are most common in children 
and young adults, and usually appear 
on the hands, fingers, face and the 
soles of the feet. The peak incidence 
for warts is age 12 through 16. The 
medical theory is that adults have 
fewer warts because of immunity ac-
quired in childhood.

Three conditions must exist for a 
person to develop warts:
• The infective papilloma virus must 
be present.
• There must be a way, such as a cut 
or abrasion, for the virus to enter the 
skin.
• The person’s immunity system (de-
fense against infection) must be defi-
cent or suppressed. Immunity can be 
lowered by chronic or temporary ill-
ness or by a person’s being on certain 
medications, such as the steroid drugs 
used to treat allergies and rheumatism.

The incubation period (time it takes 
for warts to appear after infection) is 
usually three to four months, although 
it may take as much as a year. They 
first show as tiny, smooth, skin lesions 
that slowly grow and enlarge. Repeated 
irritation of a wart will aggravate that 
growth and enlargement. Some physi-
cians suggest deliberate irritation as a 
means of stimulating antibody produc-
tion and speeding the eventual disappear-
ance of the wart. 

The wart cycle appears to follow a 
predictable pattern. The papilloma 
virus enters the skin through a cut or 
abrasion and moves into the cell nucle-
us. After settling in, the virus takes 
over the cell’s reproductive function 
and causes the now-infected cell to be-
gin producing a warty growth instead of 
normal new skin cells. If the in-
fected person is healthy and immune 
systems are intact, the body will begin 
manufacturing antibodies against this 
viral infection even as it is occurring. 
Then the wart may disappear in a mat-
ter of months. But if the immune sys-

stem has been suppressed by medication 
or is busy fighting off another illness, 
the wart may not only keep growing, it 
may also spread warts to other loca-
tions on the body.

The process can be halted at any 
time, even at the beginning, by having 
a physician excise (cut away) the warty 
growth, or freeze it with liquid nitro-
gen, or burn it off with an acid com-
pound. If the wart is either the plan-
tar or common (vulgaris) variety, the 
per- 
sion can attempt to treat it with an over-
the-counter medication, such as one 
containing salicylic acid.

Even without treatment, warts do not 
stay with a person forever. The body’s 
own defense system deals with warts as 
it does with any infection, and in time 
usually overcomes them. About a third 
will clear up within a year; two-thirds 
within two years; and almost all within 
five years.

Because they are caused by a virus, 
warts are contagious. They can spread 
by direct contact, one person infecting 
another. They can be spread indirectly, 
from such locations as swimming pool 
areas and showers. They can even 
spread from an existing site on the 
body to other body locations, as often 
happens when children scratch a wart. 
Because of this possibility of reinfec-
tion, many medical experts think it is 
better to have warts removed rather 
than waiting for them to disappear. But 
some say destroying a wart when it 
first appears may be undesirable, be- 
cause the desired immunity has not yet 
taken hold.

Warts contain their highest concen-
tration of virus particles when they are 
about six months old. From that point 
on they seem to feel the effects of 
the antibodies working against them. 
Growth will slow, and unless there has 
been reinfection, they will begin to 
disappear.

An increase in plantar warts noted in 
England beginning in 1970 may have 
followed an increase in the number and 
use of swimming pools in that country. 
The warm pool water softens the horny 
skin layers on the soles of the swimm-
ers’ feet, and the abrasive action of 
poolside running and diving scrapes off 
bits of skin from those softened areas. 
If someone at a pool has a plantar wart, 
the virus particles in such scrapings 
could infect other persons using the
pool. From this English experience came a larger speculation that an area of heavy traffic around a pool can be contaminated by even one person with plantar warts.

Because warts are apparently self-limiting, some medical scientists question whether any treatment is needed. Exceptions would be for cosmetic reasons, or if the wart is subject to unwanted irritation or is painful because it is on a weight-bearing surface.

Dr. Rees B. Rees, emeritus professor of dermatology at the University of California School of Medicine in San Francisco, seems more certain that treatment is required. He writes in Modern Medicine magazine (June 1983) that, although warts are largely a nuisance, "they should not be ignored just because they seem to be benign. They should be treated whenever possible, both for the patient's well-being and for epidemiologic reasons since the virus is so easily transmitted and the lesions so widespread."

Dr. Rees suggests that a wart vaccine may be possible. He notes that a group of researchers recently skin-tested persons with various types of warts, using an HPV (human papilloma virus) antigen obtained from plantar warts. Half the patients (10 of 22) showed regression or disappearance of their warts within a month after the testing. This, he says, raises the possibility of there being a wart vaccine "in the foreseeable future."

Getting back to Tom Sawyer. Tom may not have been all that wrong. There have been cases cited in medical journals (some of them both anecdotal and scientific) where the power of suggestion appeared helpful in getting rid of warts, especially in younger children. It seemed somehow to enhance the body's natural immunity. This is also mentioned in dermatology textbooks, with reports of medical hypnosis being used as an adjunct to conventional wart therapy.

Richard C. Thompson is a member of FDA's publications staff.

How To Shrink Warts

An FDA review panel looking at nonprescription wart treatments found only one product—salicylic acid—to be both safe and effective. Applied to the wart, this ingredient acts as a keratolytic (skin peeler) that destroys the outer surface and causes the wart to disappear. Salicylic acid is available without prescription as "wart paint" and in other formulations to treat common and plantar warts.

Treatment should continue as long as the wart keeps shrinking in size, for up to 12 weeks. The paint should be applied to the wart very carefully, with the surrounding area protected by petroleum jelly or salve so that no harm is done to healthy skin.

The panel found other wart remedies, such as lactic acid and acetic acid, to be safe but not effective, and such substances as camphor and menthol were found neither safe nor effective.

Wart treatments available from physicians, usually dermatologists, include freezing the wart with liquid nitrogen (cryotherapy); removing it surgically; or using salicylic acid, bleomycin sulfate, podophyllin and other prescription medications. Single-dose X-ray treatment (the Pipkin procedure) is used less now than it once was.

If there is any doubt as to the kind of wart, a physician should be consulted before self-treatment is attempted. And wart self-treatment should never be used on unwanted moles or other skin blemishes.
The woman flicks on the TV set and settles down to watch her favorite soap opera. However, she’s about 60 seconds too early and instead of the start of her favorite program, she sees a commercial for a prescription drug to treat high blood pressure. With typical Madison Avenue allure, the ad may prompt the woman—if she is a hypertensive patient—to ask her doctor about getting on the drug.

Or, it may provide her with information about hypertension—information that leads to her having a blood pressure check which uncovers a potentially dangerous health situation.

Still another reaction to the ad might be that she is confused or misled. After all, the ad lasted a mere minute. Is that long enough to tell her all she needs to know about a drug that can be prescribed only by a physician?

It is also possible, of course, that the advertisement—like so many commercials—may simply pass through the consumer’s mind without any of the gray matter bothering to record it.

The situation is hypothetical. Women (and men) do watch soap operas. But such an ad has not yet appeared on television. Whether TV and other media will be used to advertise prescription drugs directly to consumers is one of the hottest issues to confront the Food and Drug Administration in years.

The issue confronts FDA because since 1963 FDA has had statutory authority to regulate prescription drug advertising. To date, however, that advertising has largely been limited to health professional audiences.

It is a hot issue because the stakes are high. Not only are hundreds of millions of dollars involved but also traditional health practicing methods. Indeed, physicians may find themselves faced with a more educated (or thoroughly brainwashed, depending on your viewpoint) patient who won’t accept the doctor’s word for what drug is best.

However, before the conclusion-jumping gets out of hand, it is best to point out that the issue is more complicated than may first appear. Selling an anti-hypertension drug is not like selling an antiperspirant. In the first place, Congress has passed a law setting certain standards for prescription drug advertising. Those standards include the requirement that all such advertising carry a “brief summary” of prescribing information. That summary has to include information relating to a drug’s side effects, including adverse reactions, precautions, contraindications and effectiveness.

Now, when a 24-hour deodorant is advertised, no mention is made of the fact that it won’t work for 24 seconds in a drop forge foundry. Or when a nonprescription cough syrup is touted on TV, there is no note that it contains 50 percent alcohol and shouldn’t be mixed with ordinary, everyday booze. But if a TV commercial boasts of a prescription drug’s ability to ease symptoms of a disease, that commercial must—under current regulations—also include information about the drug’s side effects and any precautions that must be followed when taking it.

That information is known as the “brief summary” of prescribing information and is already found with each drug advertisement in a professional journal. This “brief summary” material can take considerable space, as much as half a page of relatively small type in a magazine ad. Despite the brief summary requirement, drug companies spend an estimated $600 million a year to advertise their prescription products to health professionals. It goes without saying that advertising to consumers through newspapers, radio and television could gobble up hundreds of millions more.
More About ZOVIRAX®

DESCRIPTION: ZOVIRAX is the brand name for acyclovir, an antiviral drug active against herpes viruses. ZOVIRAX Ointment 5% is a formulation for topical administration. Each gram of ZOVIRAX Ointment 5% contains 50 mg. of acyclovir in a polyethylene glycol base.

INDICATIONS AND USAGE: ZOVIRAX (acyclovir) Ointment 5% is indicated in the management of initial herpes genitalis and in limited non-life-threatening mucocutaneous Herpes simplex virus infections in immunocompromised patients. In clinical trials of initial herpes genitalis, ZOVIRAX Ointment 5% has shown a decrease in healing time and in some cases a decrease in duration of viral shedding and duration of pain. In studies of immunocompromised patients with mainly herpes labialis, there was a decrease in duration of viral shedding and a slight decrease in duration of pain.

By contrast, in studies of recurrent herpes genitalis and of herpes labialis in non-immunocompromised patients, there was no evidence of clinical benefits; there was some decrease in duration of viral shedding.

Diagnosis: Whereas cutaneous lesions associated with Herpes simplex infections are often characteristic, the finding of multinucleated giant cells in smears prepared from lesion exudate or scrapings may assist in the diagnosis. Positive cultures for Herpes simplex virus offer a reliable means for confirmation of the diagnosis. In genital herpes, appropriate examinations should be performed to rule out other sexually transmitted diseases.

CONTRAINDICATIONS: ZOVIRAX Ointment 5% is contraindicated for patients who develop hypersensitivity or chemical intolerance to the components of the formulation.

WARNINGS: ZOVIRAX Ointment 5% is intended for cutaneous use only and should not be used in the eye.

PRECAUTIONS: General: The recommended dosage, frequency of applications, and length of treatment should not be exceed (see Dose and Administration). There exist no data which demonstrate that the use of ZOVIRAX Ointment 5% will either prevent or correct viral transmission to other persons or prevent recurrent infections when applied in the absence of signs and symptoms. ZOVIRAX Ointment 5% should not be used for the prevention of recurrent HSV infections. Although clinically significant viral resistance associated with the use of ZOVIRAX Ointment 5% has not been observed, this possibility exists.

Drug Interactions: Clinical experience has identified no interactions resulting from topical or systemic administration of other drugs concomitantly with ZOVIRAX Ointment 5%.

Carcinogenesis, Mutagenesis, Impairment of Fertility: Acyclovir was tested in lifetime bioassays in rats and mice at single daily doses of 50, 150, and 450 mg/kg/day given by gavage or by subcutaneous injections. These studies show no statistically significant difference in the incidence of benign and malignant tumors produced in drug-treated as compared to control animals. Nor did acyclovir induce the occurrence of tumors in drug-treated animals as compared to controls. In 2 in vitro cell transformation assays used to provide preliminary assessment of potential genotoxicity in advance of these more definitive lifetime bioassays in rodents, conflicting results were obtained. Acyclovir was positive at the highest dose used in one system and the negative results were obtained in another transformation system.

No chromosome damage was observed at maximum tolerated parenteral doses of 100 mg/kg/day in rats or Chinese hamsters; higher doses of 500 and 1000 mg/kg were clastogenic in Chinese hamsters. In addition, an activity was found in a dominant lethal study in mice. In 9 of 11 microbial and mammalian cell assays, no evidence of mutagenicity was observed. In 2 mammalian cell assays (human lymphocytes and L5178Y mouse lymphoma cells in vitro), positive response for mutagenicity and chromosomal damage occurred, but only at concentrations of 1000 times the plasma levels achieved in man following topical application.

Acyclovir does not impair fertility or reproduction in mice or rats at oral doses up to 450 mg/kg/day or in rats at subcutaneous doses up to 25 mg/kg/day. In rabbits given a high dose of acyclovir (50 mg/kg/day, a.c.), there was a statistically significant decrease in implantation efficiency.

Pregnancy: Teratogenic Effects. Pregnancy Category C. Acyclovir has been known to cause a statistically significant increase in implantation efficiency in rabbits, when given at subcutaneous doses providing mean plasma levels of drug 2.2 times those expected from use in patients with normal renal function.

Reproduction studies were negative for impairment of fertility or harm to the fetus in mice given oral doses, and in rats given subcutaneous doses providing mean plasma levels of drug 64 times and 4 times (respectively) greater than those expected from use in patients with normal renal function.

Acyclovir was not teratogenic after subcutaneous administration of up to 50 mg/kg/day during the period of organogenesis in rats and rabbits; doses up to 450 mg/kg given daily by gavage to mice were not teratogenic. There are, however, no adequate and well-controlled studies in pregnant women. Acyclovir should be used during pregnancy only if the potential benefit justifies the potential risk to the fetus.

Nursing Mothers: It is not known whether this drug is excreted in human milk. Because many drugs are excreted in human milk, caution should be exercised when ZOVIRAX is administered to a nursing woman.

ADVERSE REACTIONS: Because ulcerated genital lesions are characteristically tender and sensitive to any contact or manipulation, patients may experience discomfort upon application of ointment. In the controlled clinical trials, mild pain (including transient burning and stinging) was reported by 103 (28.3%) of 364 patients treated with acyclovir and by 115 (31.1%) of 370 patients treated with placebo; treatment was discontinued in 20 of these patients. Other local reactions among acyclovir-treated patients included pruritus in 15 (4.1%), rash in 1 (0.3%), and vulvitis in 1 (0.3%). Among the placebo-treated patients, pruritus was reported by 17 (4.6%) and rash by 1 (0.3%).

In all studies, there was no significant difference between the drug and placebo group in the rates or type of reported adverse reactions nor were there any differences in abnormal clinical laboratory findings.

OVERDOSAGE: Overdose by topical application of ZOVIRAX Ointment 5% is unlikely because of limited transcutaneous absorption (see Clinical Pharmacology).

DOSAGE AND ADMINISTRATION: Apply sufficient quantity to adequately cover all lesions every 3 hours 6 times per day for 7 days. The dose size per application will vary depending upon the total lesion area but should approximate a one-half inch ribbon of ointment per 4 square inches of surface area. A finger cot or rubber glove should be used when applying ZOVIRAX to prevent autoinoculation of other body sites and transmission of infection to other persons. Therapy should be initiated as early as possible following the onset of signs and symptoms.

Help for herpes... Now available at your nearby

In health care, Peoples makes the difference.
"Not only are hundreds of millions of dollars involved but also traditional health practicing methods."

Which is one—but only one—of the arguments that opponents of Rx advertising make. They say that in the end it is the consumer who will have to pay for the cost of advertising. It is acknowledged that the consumer pays for the cost of other advertising but, the argument goes, the consumer has the clear option on that purchase. With a prescription drug, the final decision actually rests with the prescriber, the physician.

However, proponents of Rx advertising to consumers make an argument that the ads could result in a more informed consumer who would make better use of drugs, thus cutting down on costly noncompliance in drug-taking.

On the other side of that reasoning is the contention that the advertising will make people ask for drugs they really don't want or need. And therein lies the crux of the issue: Will Rx advertising result in consumers learning about medicines or will it result in them yearning for unneeded medications?

Proponents of the idea also argue that prescription drug advertising to the public could result in speedier availability and use of important medical advances. But opponents fear that the ads could result in patients being confused by the inherent oversimplification of advertising, particularly radio and TV advertising. One health official shares that concern, saying he fears that ads will "trivialize" prescription drugs.

Direct-to-consumer advertising of prescription drugs has come to the forefront in recent years because some pharmaceutical firms have said that they want to use that route to sell their products. Several ventures have been made into the area, but none of them has fully explored the use of commercial television and radio.

But this year major advertising plans have been developed that would include testing commercials on live television. However, FDA has asked for a moratorium on all Rx advertising to consumers. That moratorium was called for in February of this year to allow for a public discussion of the issue and to conduct research before a decision is made. Under the terms of the moratorium, two types of ads are being permitted: (1) ads designed solely to communicate price information about a product—in such ads no mention is made of what the product is used for or how; and (2) so-called institutional ads in which a public health subject, such as diabetes, is discussed but no mention is made of a specific product.

After the call for the moratorium, FDA held meetings in Washington, D.C., and across the country. Those meetings were attended by more than 900 people representing industry, advertisers, consumers and health professionals. A majority of the consumers opposed advertising prescription drugs. Generally, they didn't accept the idea that advertising would educate, and they feared the ads would lead to overmedication.

Health professional organizations were also wary. In a meeting with FDA officials, representatives of major groups expressed reservations almost to a man. When shown proposed TV ads made up by two drug firms, the professionals also found the ads too promotional as well as "objectionable." However, at the time of the meeting (May 23) none of the organizations had taken a formal stand on the issue.

In June, the American Medical Association, representing more than 200,000 doctors, passed a resolution on Rx advertising at its annual meeting in Chicago. The AMA resolution noted that surveys of physicians indicated that advertising aimed at prevention of disease would be acceptable but advertising of treatment of disease would not be. The AMA further noted that it had a "generally negative attitude" on the subject but concluded by giving its support to FDA's moratorium and to proposals for testing the impact of the prescription drug ads on consumers.

Two drug firms that have shown an interest in direct-to-consumer advertising are Ciba-Geigy and Merck Sharp &
Selling an anti-hypertension drug is not like selling an antiperspirant.

Dohme. At the May meeting with health professionals, the two firms came out with somewhat different conclusions as to the role that Rx advertising can and should play. Merck tried some print advertisements that met FDA regulations on its vaccine for pneumonia. Sales of the vaccine dropped off sharply after its initial introduction, and the company, according to Tom Beckett, the firm's executive director of marketing communications, felt that only a small percentage of patients who should be getting the vaccine were. So Merck went to consumer advertising for the product.

The firm ran ads in the October 1981 Reader's Digest, in Modern Maturity magazine, and in newspapers. Physicians were notified in advance that the ads would appear. Merck got a favorable reaction to the ad from 63 percent of the doctors that it surveyed.

Yet, after the advertising campaign was over, Merck said it had 'serious reservations' about direct-to-consumer advertising and the firm suggested that it be used only in rare instances. If the advertising is to be permitted, Beckett offered these suggestions:

- There should be a clear public health need for the product.
- Any advertising should point out that the physician makes the determination on when a drug is to be prescribed.
- The ads should enhance, not interfere with, the doctor-patient relationship.

Merck also recommended that pharmaceutical firms be encouraged to pre-clear ads with FDA and that the agency establish and enforce guidelines for such advertising.

Ciba-Geigy would be more comprehensive in its advertising. Felton Davis, the firm's senior vice president for government and public affairs, said that advertising of prescription drugs to consumers should include labeling information for patients about the drug as well as directions for obtaining a brochure that would provide additional information on the condition for which the drug is being prescribed.

The firm would, for example, offer a toll-free phone number or a place to which readers or viewers could write for more information about the condition to be treated by the drug. Davis sees no difficulty in developing patient labeling to go along with the drug dispensed.

Ciba-Geigy also believes that actual market-testing of certain ads, with FDA approval, is necessary before a final policy can be made. Ciba-Geigy wants to put its test ads on commercial television in selected test cities. The firm says that way it could measure whether the ads help to educate consumers, whether they promote or inhibit patient-doctor relations, and—of course—whether the ads increase sales.

FDA will do its testing using fictitious drugs under controlled testing circumstances. The agency's TV and magazine ads will seek to find out if the brief summary information can be adequately communicated. Then FDA will test 10 versions of the adverse information, ranging from minimal mention of possible side effects to the full prescribing information written in nontechnical language.

FDA will test the ads on individuals, using a simulated TV program and a mock magazine, both of which would be shown to audiences picked by random selection.

FDA is also considering regulations that would set the standards for testing of direct-to-consumer Rx advertising by drug firms. Those standards would allow for some limited market-testing of live television commercials.

The agency will analyze the test results and weigh them along with the comments from the various consumer, industry and professional groups before making its decision on whether or not soap opera fans (and other Americans) will see prescription drugs 'promoted' (or 'explained') through advertisements.

Roger W. Miller is editor of FDA Consumer.
When it comes to inflicting pain, a little bitty kidney stone can go a long way. When a stone begins to act up, the person who has it can only hope fervently it will go as soon as possible. The distance a stone must travel to make its way out of the kidney, down the connecting tube (ureter) to the bladder, and out through the urethra is only a couple of feet, but to the person furnishing the geography it can seem like miles.

Each year, one in every thousand adults is hospitalized with one or more kidney stones. They are found in 1 percent of autopsies. The exquisite pain that announces that a kidney stone has stuck temporarily in a system that nature intended only for liquids is so devastating it can make strong men weep and walk the floor. Women compare it to the pain of childbirth.

More men than women have kidney stones, and they are rare among children and blacks. The predisposition to form stones can run in families. Dehydration can contribute to stone formation. There are geographic differences in kidney stone incidence, bringing into use the term "stone belts," stone epidemics. "Kidney stones vary in size from a grain of sand to a coconut. Most of the smaller ones find their way out of the system but some get stuck along the way and cause trouble. Some stones, called staghorn for their shape, are too large to pass from the kidney and can't be removed except by major surgery. They may occupy large areas of the urine-collecting chambers of that organ and be shaped by its interior contours.

In the medical books kidney stones are described as renal stones, urinary stones, calculi, or uroliths, and kidney stone disease is referred to as nephrolithiasis. Doctors who treat patients with stones may prescribe medicine to deal with pain or infection or to produce changes in the urinary acidity or alkalinity (pH). The patient may be directed to drink lots of water and other liquids or avoid certain foods. The diet-water precautions may be extended indefinitely if the patient's system seems to have a proclivity for developing stones.

FDA recently approved a new "orphan" drug called sodium cellulose phosphate for treating Type I absorptive hypercalciuria, a condition that occurs mostly among males, particularly middle-aged men. In absorptive hypercalciuria, excessive calcium is absorbed by the intestine, resulting in too much of it in the urine, which causes recurring production of kidney stones. Types II and III of the condition are not treatable with the new drug, which acts by binding calcium in the gastrointestinal tract so that it's excreted instead of being absorbed by the body. The new drug is an "orphan" because it's composed of natural substances and is unpatentable, hence less profitable to manufacture.

All kidney stones are bad news, but the worst are those that lodge in some part of the ureter, causing the urine to back up and obstruct the kidney's functions. In the kidney itself the stone can get stuck somewhere in the system of chambers or areas where the urine collects before it's discharged into the ureter. In the ureter, the trouble spot is usually at one of three narrow points on the way to the bladder. A stone that reaches the bladder sometimes passes out of the body without further trouble. But stones are sometimes found in the bladder too, either having arrived through the ureter or formed in the bladder itself.

Kidney stones lead to infection, which can inflame and irritate and eventually destroy the kidney. This can happen rather quickly if infection and obstruction exist together. Stones also can prolong an existing infection, and some are produced as a result of infection.

The kinds, intensity and locations of pain caused by stones depend somewhat on the location of the stone in the urinary system. The worst pain comes when a stone gets hung up in the ureter.

A stone that partially obstructs but continues to move down the urinary system appears to cause the greatest pain. Pain typically begins in the flank area and extends laterally around the abdomen, radiating to the groin and genitals. Onset can be abrupt, colicky and almost unbearable. The patient can find no position that will bring relief. As the stone moves through the ureter, the pain continues to radiate laterally.

If the stone lodges in the ureter for any length of time, inflammation can set in, along with pain at this locality. Severe colic may return once the stone gets near the bladder, and the pain may extend to the inner side of the thigh. The urge to urinate may be powerful. Bloody urine, nausea and vomiting are other symptoms of kidney stone troubles. Sometimes there will be abdominal distention. If infection is present, there may be chills and fever and bladder irritation. Along with all this there may be a constant ache in the back and flank.

Kidney stones are formed in four chief ways: (1) from an increase in concentration and excretion of stone crystalloid substances in the urine—calcium, oxalate, uric acid, cystine, xanthine and, rarely, phosphate; (2) from changes in the urine that favor stone formation, such as increased concentrations of salts and organic compounds, a changed ratio of urinary magnesium/calcium, or increased urinary pH from diet, medications or infections; (3) from precipitation of insoluble substances out of the urine onto calcific plaques or other substances such as infectious material; and (4) structural disorders.

Calcium is a component in 80 to 90 percent of kidney stones and is often combined with oxalate (oxalic acid), found in about 65 percent of stones. Hypercalciuria is the name given to excessive excretion of calcium in the urine. This condition results most often from abnormally increased activity of the parathyroid glands, called hyperparathyroidism.
Hypercalciuria may occur in some adults who drink a quart or more of milk a day, or who take in excessive calcium from other foods. The major calcium foods are cheese and milk. It’s known that milk and proteins can cause increased body absorption of calcium from the intestine. Hyperparathyroidism and some other disease conditions—especially those that keep the patient from moving about to get exercise—can result in hypercalciuria.

In excess excretion of oxalate, the problem is not so much related to diet as to the body’s own production of that substance. Some other conditions, such as genetic disorders, disease and poisoning, contribute to overexcretion of oxalate.

Excess excretion of uric acid crystals that form stones is a metabolic abnormality and results from various diseases or disorders, almost always gout. Allopurinol is a drug that has been used to reduce the body’s production of uric acid. Stones made up of xanthine, silicon dioxide and other substances are fairly rare. Cystine stones, which result from an inherited defect, also are somewhat rare.

Stones of “struvite” (magnesium ammonium phosphate) are caused by an infection that raises the alkaline level in the urine. Most staghorn stones are formed of struvite.

Stones range from soft to hard and may be rounded or have jagged edges (jackstones). They may also vary in consistency or texture. When recovered from the system, they are assayed to determine how to treat that particular patient to prevent this kind of stone from forming again. All except uric acid stones are visible on X-ray if they’re big enough to spot and if there is no intervening bone in the photograph. Other diagnostic methods help confirm and identify types.

Patients who tend to form kidney stones are always given water or other liquids to maintain a high urine production to keep stone-forming substances well diluted. Fluids are taken at bedtime and upon arising. Appropriate antibiotics are given to combat infection. For patients with stones other than those formed by uric acid or cystine, the urine should be high alkalinity (pH of 7.0 or higher). The presence of a kidney stone reduces the system’s resistance to bacterial infection, particularly if the stone obstructs urine flow.

Obstruction and infection together can destroy the kidney, as can prolonged kidney distention from backed-up urine when a stone blocks the pelvic junction of the kidney and ureter, or the ureter itself.

Of the stones that get out of the kidneys and into the ureter, around 80 percent pass through the system. Such a blessed event is to be encouraged by physical activity on the patient’s part, plentiful fluid intake, and sometimes anti-spasmodic medication that relaxes the ureter to facilitate passing of the stone. Much kidney stone therapy consists of watchful waiting for the stone to pass. If it doesn’t, and infection persists or the pain’s intensity does not abate, it must be removed.

This is done in one of three ways: manipulating the stone, breaking or shattering it into smaller pieces that will be carried out, or by surgically removing it.

If a stone must be removed, doctors prefer taking it out whole to breaking it up if there is no substantially increased risk. When a stone is broken into fragments any piece or particle that remains in the urinary system provides something solid upon which crystalloid materials in the urine can precipitate to form a larger stone, a little like the grain of sand or other detritus in an oyster that eventually grows up to be a pearl.

Surgical removal of stones is resorted to only if obstruction, intense pain or infection cannot be dealt with successfully without the incision. In kidney surgery, an incision is made, the kidney opened, and the stone plucked out. Removal of a staghorn stone from the kidney is a major operation, usually performed on younger patients, who may have stronger constitutions and the most to gain from the risk involved. The large structure is broken up and the pieces removed one by one. In one such procedure, a nephroscope, a tubular device inserted through an incision in the kidney pelvis for viewing the kidney recesses during surgery, may be used to remove remaining fragments by means of a suction tube inserted through a channel in the nephroscope.

Stones lodged in the ureter often can be removed with a cystoscope, another viewing instrument inserted through the urethra, thence into the bladder. Further instruments can be inserted through the cystoscope into the ureter. The stone is withdrawn by means of an instrument passed through a tube on the cystoscope and pushed past the stone. This instrument has wires that can be formed into a small basket that captures the stone for withdrawal. Forceps also can be inserted through the cystoscope and into the bladder to grasp and remove or break stones lodged there.

Fluoroscopy is helpful in coordinating location and retrieval of stones, and liquid is often pumped through the tube to flush the pieces of stone out of the system.

Other methods are being tested in Europe to remove stones from the kidney. In one, called percutaneous nephrolithotomy, a long hollow needle is placed into the kidney through an incision in the patient’s back. The needle track is widened to admit a nephroscope through which wires or forceps are inserted and the smaller stones then removed. Larger stones are broken up by ultrasound vibration or by electrohydraulic shocks before removal by suction. These devices and methods have been developed over the past five years, although ultrasonic disintegration of stones was performed in the United States as early as 1953.

In West Germany a non-surgical procedure called extracorporeal lithotripsy is under development for removal of stones from the kidney. Electric shocks are delivered to break the stone while the patient is in a tub of water. The position of the stone is pinpointed in three dimensions by two special X-ray machines. By use of an ellipsoidal reflector the effect of the shocks is concentrated at the stone. Some 500 to 1,000 shocks of short duration are administered to break up an average size kidney stone. The fragments then pass out in the urine over the next few days.

As of the beginning of this year, several hundred patients have been reported as successfully treated. The method apparently does not work as well, if at all, for removal of stones from the ureter, and at the present time the setup is quite expensive, the equipment costing over a million dollars.

Harold Hopkins is editorial director of FDA Consumer.
As far as the experts were concerned, the Mark Eden breast developer was a bust even before the promoters of the device caved in and agreed to an out-of-court settlement. Still, over a period of almost 19 years, thousands of women had paid millions of dollars for a device that was supposed to (but didn’t and couldn’t) increase the size of their breasts.

The promoters, Eileen and Jack Feather, agreed to a million-dollar non-tax-deductible settlement and to a pledge that they would stop peddling the bust developer as well as some weight-loss devices. The only way the Feathers can get such products back on the market is by proving to the Food and Drug Administration that their devices are “safe and effective” for their intended use.

Jack and Eileen Feather are also top officials of Cambridge Plan International of Monterey, Calif., the firm that sells the Cambridge diet plan. Their son, Vaughn, is chief executive officer of the firm.

The U.S. Postal Service and the U.S. attorney’s office had used results of a University of Arizona research study on the Mark Eden device to support mail fraud charges against the Feathers, whose advertisements were found for years in numerous women’s magazines and weekly tabloids. The study of Arizona coeds proved what the experts had thought all along—that the device provided no measurable gain in bust size.

U.S. Attorney Joseph P. Russoniello of the northern district of California was ready to go to trial with charges that the Mark Eden promoters were using the mails to defraud when the Feathers agreed to an out-of-court settlement last May. The agreement included a $1.1 million payment to the Postal Service by the Feathers in exchange for the government dropping the mail fraud charges. The settlement money is not deductible from the Feathers’ or the Mark Eden company’s income taxes.

The Feathers had been indicted in May 1982 over advertising not only for the bust developers but also for two other products related to weight loss, Astro-Trimmer and Slim-Skins.

Astro-Trimmer is a belt-like device to be worn while exercising. According to instructional literature, it had to be hooked around doorknobs to be used.

Slim-Skins relied on a household vacuum cleaner to do the “weight-reducing” work. A special adapter hose was provided to connect the vacuum cleaner to the knickers that were to be worn while doing certain exercises. (See accompanying article.)
How The Knickers Work

The following is from the instruction booklet for Slim-Skins, titled: “Total Inch Reduction Program for the Sensational New Slim-Skins”:

Your Slim-Skins are a marvel of ease and simplicity to use. Their ingenious design allows you to convert your own household vacuum cleaner into the most exciting and effective inch reducing machine imaginable. First, get out your vacuum cleaner. Plug it into the electrical outlet nearest to where you plan to do your Slim-Skins Program. Now you simply slip on your Slim-Skins directly over your bare skin, keeping the pullstrings in front. Tie the laces at the waist and knees firmly—but not too tight. The Slim-Skins should always be worn directly over bare skin; any garment such as pants, slacks, shorts, even light underwear coming between your skin and the Slim-Skins will detract from the real inch trimming potential of this marvelous reducer. After putting on your Slim-Skins, then connect the white universal adapter hose, which is included, by attaching the short nozzled end to the white ring extending from the Slim-Skins. Then attach the longer nozzle on the other end to the hose of your own vacuum cleaner. Push the nozzle in until it forms a firm bond. It’s just that simple!

Dr. Jack H. Wilmore, former head of the physical education department of the University of Arizona, conducted the research on the Mark Eden device and is among the experts who say that attempts to increase bust size are usually unproductive.

“Mark Eden took the tack that its product would raise the breast platform muscles, the pectorals, giving the appearance of a bigger bust,” Dr. Wilmore says. But he adds that women do not have the same predisposition to muscle bulking that men do.

“A high level of the male hormone testosterone is needed to increase muscle girth,” he notes. “That’s why the average woman can ‘pump iron’ regularly and experience only a minimal increase in chest size through development of the muscle platform behind the breast.”

The female breast consists of fatty and glandular tissues. Obesity, pregnancy and lactation are more or less natural ways that the size may be affected. The introduction of hormones and the injection of some substance such as silicone are less natural. However, those two choices carry risks that many medical experts consider unacceptable.

In the settlement the Feathers made no admission of liability for the devices but agreed that they would cease manufacturing and selling them and similar products. The settlement also specified that the court could prevent any entry of the Feathers into such business unless the Feathers could establish to the satisfaction of FDA that the devices were safe and effective for their intended use.

The Arizona research project was initiated by the Postal Service. Volunteers were obtained through the university’s newspaper, the Arizona Daily Wildcat, which published a brief article outlining the research and asking for women to aid in the work. More than 280 women responded. Seventeen women were selected for the experimental group and another seventeen for a control group.

The procedures for each of the three testing sessions were identical. They began with breast photography from the side and front views, both in full inhalation and exhalation positions, and with arms extended to the side at a 60 degree angle to standardize positions. The photography session was followed by a water displacement test to determine each woman’s breast volume, each woman assuming a prone position on a sheet of plywood that allowed the breasts to be positioned, depending on their size, in either a one- or two-liter glass beaker.

Finally, a series of measurements were taken, including a bust measurement without clothing and one with a bra or bathing suit top. These measurements were also taken after the training session at the end of the first day, at the beginning of the second day, and at the conclusion of the second, third, fifth, sixth, twelfth and eighteenth days.

Those taking part in the three-week experimental exercise program used the Mark Eden II device, two plastic bars that were connected by a metal spring at one end with two sponge rubber pads on each of the other ends for the hands. The women grasped the device by the pads, extended their arms and opened and closed the device against the resistance of the spring.

The Postal Service attorney in the case was Tom Ziebarth of the USPS Consumer Protection Division. He had been involved in litigation with the Feathers for 16 years. It was Ziebarth who suggested that Dr. Wilmore of the University of Arizona conduct the coed study.

Although the Feathers' past products are now banned from the market, the experts say that women should be cautious about using any products that promise to radically alter body dimensions. They urge women to take into account the costs—both psychological and financial—that such changes may bring.

Lou Eberhardt is a media relations officer with the U.S. Postal Service.
FDA has proposed regulations for labeling infant formulas that, among other things, specify the format for declaring nutrients, require the declaration of water and carbohydrate levels and iron content, and call for a pictogram showing the major steps for preparation of the formula. At the same time, the agency issued a final rule spelling out quality control and nutrient and labeling requirements for infant formulas to treat unusual medical or dietary problems. These formulas are exempt from some requirements of the Infant Formula Act of 1980 (FR July 12).

Drug products containing more than 75 milligrams of the antihistamine diphenhydramine hydrochloride in a single package and in an oral dosage form will need child-resistant packaging, under a rule proposed by the Consumer Product Safety Commission (FR July 11).

On May 25 a shipment of old radium sources completed a journey from an EPA facility in Alabama to a storage site in Hanford, Wash., under the eye of FDA and EPA. The sources, including implantable radium-containing gold and platinum needles once used to treat cancer, were collected from physicians, hospitals, universities and industries across the country and transported in special lead-lined containers, each weighing several tons.

Gamma radiation at doses up to 1 megarad can be used to control microbial contamination of spices, natural flavorings and dehydrated vegetable seasonings under an FDA rule that became effective July 5, 1983. Comprehensive regulations for food irradiation will be proposed in the near future (FR July 5).

Ciba Vision Care has petitioned FDA to allow the use of polymers containing Reactive Blue 21, Reactive Black 5, Reactive Yellow 15 and Reactive Orange 78 in coloring contact lenses (FR July 5).

Sales of nonprescription drugs totaled $6.7 billion in 1983, a 12 percent increase over the $6 billion sold in 1981, according to the market firm of Charles H. Kline & Co. The firm projects that figure will reach $7 billion by 1987.

The Public Health Service's Office of Health Technology Assessment is gathering information on the safety, clinical effectiveness, appropriateness and use of streptokinase infusion as a treatment for acute heart attacks. Written material should be sent to Dr. Rita Chow, Office of Health Technology Assessment, Park Building, 5600 Fishers Lane, Rockville, Md. 20857 (FR June 30).

L-ascorbic acid (vitamin C) did not cause cancer in male and female rats or mice, but allyl isovalerate (a synthetic fragrance and flavoring ingredient) caused mononuclear-cell leukemia in male rats and lymphoma in female mice, according to newly released reports from the National Toxicology Program of the Department of Health and Human Services (FR July 13 and July 25).

A proposed rule that would have allowed hospital emergency room personnel to dispense controlled substances to non-patients when alternate pharmacy services are not available has been withdrawn by the Drug Enforcement Administration. It was decided there is no need for the rule at this time (FR June 28).

Proposed consent agreements filed by the Federal Trade Commission would prohibit Amana Refrigeration Inc. and Foote, Cone & Belding Advertising Inc. from saying that Amana microwave ovens passed independent laboratory testing in 1980 and were rated "best quality" in a 1980 consumer survey. Statements regarding FDA's microwave oven warning label exemption are not affected (FR July 18).

A new U.S. Department of Agriculture rule says the administrator of the Food Safety and Inspection Service can approve new substances and new uses for approved substances in or on meat or poultry, provided the substance is an FDA-approved food additive, color additive, or a GRAS substance (FR July 19).

Manufacturers of products to diagnose or treat allergies will be required to supply FDA with the name and address of suppliers of allergenic source materials (mold, feathers, hair) under a new FDA proposal (FR July 15).

FDA is proposing to affirm that wheat and corn gluten and zein are generally recognized as safe as direct food ingredients. Wheat gluten is important in making bread; corn gluten is used as a texturizer; and zein, one of the components of corn gluten, is used as a coating material on confectionery pieces, nuts and enriched rice (FR July 12).
When A Book Is A Label

Back on July 7, 1981, a U.S. marshal seized a quantity of the industrial solvent DMSO (dimethyl sulfoxide) and 75 copies of a book titled The Persecuted Drug: The Story of DMSO at DMSO Inc., Buffalo, N.Y. While the seizure was in progress, television crews from three Buffalo stations arrived to videotape the action. A month later, the New York Civil Liberties Union, attempting to intervene on behalf of the widow of the book’s author, challenged FDA’s action, alleging that seizure of the books was unconstitutional because it violated the First Amendment guarantee of a free press. A routine seizure thus became a highly publicized affair.

The seizure had been made at the request of FDA’s Buffalo district office. Early in February, the district learned about DMSO Inc. from the Erie County Health Department and from an ad in a local newspaper offering DMSO for sale. The Buffalo district staff suspected the company might be illegally selling DMSO for use as a drug.

Dimethyl sulfoxide, a chemical byproduct of the paper manufacturing process, is used principally as an industrial solvent. It is approved by FDA for limited use in human and veterinary medicine—as a topical application for horses and dogs to reduce acute swelling due to trauma and in a solution for treatment of humans who have a rare chronic disorder of the bladder called interstitial cystitis. FDA has also authorized certain investigational uses. Use of industrial grade DMSO to treat medical conditions is considered especially hazardous because the product may contain toxic impurities.

DMSO has been illegally promoted for treatment of other disease conditions, including arthritis and psoriasis, even though the product has never been proved safe and effective for these uses. Use of industrial grade DMSO to treat medical conditions is considered especially hazardous because the product may contain toxic impurities.

When two Buffalo district investigators who were assigned to the case went to DMSO Inc., they found signs in the windows saying “Arthritis Backache? . . . DMSO the Miracle Working Solvent . . .” and “The Story of DMSO by Pat McGrady.” Michael Grassia, president of the company, told the investigators his firm was repackaging DMSO from bulk drums into consumer-size plastic containers for retail and wholesale distribution. He said he was selling the McGrady book, The Persecuted Drug: The Story of DMSO, but currently had none in stock. He also was selling gallon bottles of distilled water. Apparently, the water, the book and the DMSO were the only items he was selling. When one of the investigators asked about one of the signs in the window, Grassia removed it.

In the next few months, the Buffalo district staff saw several more advertisements for the company’s DMSO, including one promoting both the chemical and McGrady’s book. Grassia called the Buffalo district office to ask how far his promotions could go without pushing the DMSO into drug status. He was told that associating his product with the McGrady book, which listed therapeutic uses for DMSO, would make the product a misbranded drug.

The McGrady book is a history of dimethyl sulfoxide, from its discovery and use as an industrial solvent to its current controversial status as both an approved and unapproved drug. One chapter recounts a drug company’s investigations into medical uses for the chemical in the 1960s and specifically describes the company’s instructions for testing DMSO for a variety of conditions, including bursitis, arthritis, low back strain and sinusitis. The chapter, basically a summary of directions given by the company to its clinical investigators, includes methods of application, precautions, and possible adverse reactions.

In May 1981, another Buffalo investigator went to DMSO Inc., this time posing as a customer. He questioned Grassia about medical uses for DMSO. Grassia said that because of New York laws he was allowed only to recommend the product as a solvent; he then handed the investigator a copy of the McGrady book and said that it contained instructions and precautions for use. Three customers came in, and the investigator heard Grassia telling them about using DMSO on his back after diluting it with distilled water and again recommending the McGrady book for answers to medical questions. The investigator bought some DMSO, some distilled water and the book.

The Buffalo district took action to have the product and book seized. DMSO Inc., FDA contended, was selling DMSO for therapeutic purposes for which the drug lacked adequate directions for use and for which the drug was not generally recognized as safe and effective. It was, therefore, a new drug lacking approval and was misbranded. The agency further contended that the McGrady book, although innocuous in itself, was being used by DMSO Inc. as labeling which misrepresented the DMSO and caused it to be an unapproved new drug. It is not FDA’s policy to initiate seizure of books or other literature from such places as bookstores; however, the agency usually recommends seizure of any point-of-sale labeling that causes regulated products to be in violation of the law. Such material is seized both as evidence and to prevent the labeling from being used to misbrand the product.

So, when a U.S. marshal accompanied by a Buffalo district investigator, officially seized the DMSO, 75 copies of the McGrady book also were taken. Also seized were one full 55-gallon drum of DMSO, two partially filled drums, 257 four-ounce bottles, 78 eight-ounce bottles, and 31 sixteen-ounce bottles.

The New York Civil Liberties Union (NYCLU) sought to intervene on behalf of Grace McGrady, the widow of the author. The NYCLU moved to dismiss the action as it involved the books, alleging that the seizure violated the First Amendment guarantee of a free press. DMSO Inc. contested the seizure of both the books and chemical, as owner of the products, and denied the violations.
FDA’s primary interest was in stopping the illegal sale of the DMSO, so the agency requested that the court release the books from seizure, and the court agreed. Because of the litigation, however, FDA began to re-examine its policy on seizure of labeling. The agency pledged to make no future seizures of the McGrady book from DMSO Inc., pending completion of this policy review.

Several months after the books were released from seizure, they were donated to the Erie County Public Library because DMSO Inc. failed to claim them. However the NYCLU still urged the court to rule on the First Amendment issue, arguing that the question was still relevant and that FDA had abused its authority by seizing the books.

District Court Judge John T. Curtin disagreed, saying that because FDA had agreed to make no further seizures of the book from DMSO Inc. and because the agency had reassessed and revised its policy on the seizure of books as labeling, the issue of the books’ seizure was moot. Under the new policy, FDA will no longer request seizure of books, even if they constitute labeling under the Food, Drug, and Cosmetic Act. Instead, if FDA believes that a book’s use as labeling presents a significant consumer deception requiring legal action, the agency will request that the Department of Justice file a complaint for injunction against that use of the book. An injunction proceeding will assure that there is an opportunity for a hearing prior to the imposition of any restrictions on the use of the book in question.

Over a year after DMSO Inc. failed to respond to the government’s interrogatories, Judge Curtin entered a default decree stating that the DMSO was an unapproved new drug and was misbranded, and it was therefore condemned.

—Carol Ballentine

Hot Picks

How can a grain company have no grain? When is a medical device a cosmetic? Give up? Then read on.

At first glance, Harmon Grain Products Inc., McCook, Neb., would appear to be a company that handles grains. Actually, the company manufactures flavored toothpicks, which might be thought of as a medical device but are classified by FDA as a cosmetic because of their cleansing and freshening effect in the mouth. In one instance, however, the effect was just the opposite.

When FDA’s Buffalo district office received consumer complaints that five school children had suffered adverse reactions from Hot Cinnamon Flavored Toothpicks manufactured by the Nebraska firm, samples of the toothpicks were analyzed by the Buffalo laboratory. The concentration of cinnamaldehyde (oil of cinnamon) was found to range up to 29 percent. Cinnamaldehyde in this amount can cause burning of the mouth.

Alerted to these findings, the Kansas City district office inspected and collected toothpick samples from the Nebraska firm. Assays of these samples by the Kansas City laboratory found levels of cinnamaldehyde consistent with those found in Buffalo.

The cinnamon flavor is imparted to the toothpicks by soaking them in a solution containing cinnamaldehyde. Advised of the laboratory findings, Harmon Grain Products reformulated the soaking solution and recalled all outstanding stocks of cinnamon-flavored toothpicks.

Lead Leads To Trouble

Two women in Sioux Falls, S.D., inherited some equipment for distilling water and decided to go into business as the Ven-Sioux Distilled Water Co. They ran into trouble when a pipe broke on their distillation equipment but soon had it fixed. Unfortunately, the lead-based solder used to repair the apparatus led to other problems.

A representative from the Sioux Falls health department came knocking on the Ven-Sioux company door to say that the gallon bottles of distilled water sold by the company contained unacceptable high levels of lead. The health department had found lead in the water ranging from 0.10 to 0.17 milligrams per liter—well above the 0.05 milligrams per liter tolerance set by FDA. The health official told the women they would have to stop distribution until the problem could be identified and would have to recall all possibly contaminated bottles.

The Ven-Sioux company complied and, with help from city officials, identified the recently repaired pipe as the source of the problem. This was dealt with by rewelding of the distillation equipment. The women also notified two local newspapers and radio and television stations of the recall. Approximately 200 bottles were recovered and destroyed in a local landfill.

Cologne Le Fluorocarbon

It’s not often that an FDA seizure smells so sweet, but the Orlando district recently reported a flagrant, but fragrant, violation of the law. A distributor’s stock of Worth’s “Je Reviens Eau de Cologne” and “Ivoire de Balmain Eau de Toilette” was seized after an analysis of samples revealed they contained Freon 114, a chlorofluorocarbon (CFC) whose use is banned in the United States in cosmetics and other products.

A few years ago the public was shaken by scientists’ reports that the use of CFCs as propellants in aerosol products could reduce the ozone shield, a gaseous belt extending 10 to 30 miles above the earth that filters out harmful ultraviolet radiation from the sun. Responding to this concern, FDA, along with the Consumer Product Safety Commission and the Environmental Protection Agency, banned all nontoxic uses of CFCs in self-pressurized containers in 1978. The products primarily affected were deodorants, antiperspirants, hair sprays, colognes and fragrances, regulated by FDA;
pesticides and industrial products, regulated by EPA; and household cleaners and air fresheners, under the jurisdiction of CPSC.

When they first came on the market, chlorofluorocarbons had a lot to recommend them. They were cheap, non-flammable and efficient. When mixed with the product to be propelled and sprayed into the air, they readily converted from a liquid to a gas—and therein lies the problem.

When released into the environment in the gaseous form, CFCs slowly diffuse upward until they reach the stratosphere, where the ultraviolet radiation from the sun decomposes them, freeing chlorine atoms that act to decrease the concentration of ozone. This depletion of the stratospheric layer of ozone allows more ultraviolet radiation to reach the earth. This type of radiation can lead to an increase in skin cancers. (See “Cancer Of The Skin Keeps Erupting” in the June 1983 FDA Consumer.) The radiation has the potential for changing temperature and climate, influencing the growth and development of certain plant and animal species, and threatening the balance of delicate terrestrial and aquatic ecosystems.

U.S. industry is well aware of restrictions on the use of CFCs, as are most foreign manufacturers. In fact, French perfume manufacturers package their products under two labels—one intended for the American market, which complies with the FDC Act and the Fair Packaging and Labeling Act, and the other for the world market.

Recently, however, the Orlando district received complaints that perfumes containing CFCs were being distributed in the area. Somehow, French perfumes intended for sale in South and Central America were being diverted to the United States. An inspection of Cosmetics Inc., Hialeah, Fla., revealed that this was the case, and FDA seized $3,760.46 worth of perfumes.

Turning Turtle

An inspector from FDA’s Mobile, Ala., resident post visited the B&B Pet Shop in Mobile after receiving a report that the store was selling small turtles. The report came from the Mobile County Health Department, which also said that a sample of water from the store’s turtle tank contained *Salmonella* bacteria.

*Salmonella* bacteria, which can cause gastrointestinal infections in humans, are commonly found in all turtles. Accordingly interstate commerce in pet turtles is restricted by FDA because of the high incidence of transmission of *Salmonella* organisms to children and to others who handle turtles as pets.

At the pet shop, the FDA inspector was told by the owners that they had gone out of the pet turtle distribution business and had released all unsold turtles into a pond near their house.

FDA prohibits the sale or distribution of viable turtle eggs and turtles less than 4 inches except for marine turtles and turtles for scientific study. Before the ban, small turtles had been popular children’s pets. Unfortunately, children are more likely than adults to contract salmonellosis from turtles because they are less apt to follow sanitary precautions after handling them as pets.

Raw-Milk Cheese

Soft-ripened cheeses made from raw (unpasteurized) milk have become popular in Europe, and that popularity has carried over to what Europeans consider their export markets. One result is that these cheeses are beginning to appear at U.S. ports of entry. But unpasteurized cheese, whether foreign or domestic, may not be sold in this country unless it has been aged at 35 degrees Fahrenheit for at least 60 days, which makes bacteria that may be present harmless.

This law dates back to a generation ago when brucellosis, a cattle disease transmissible to humans, was a common animal illness. Although much less prevalent, it still occurs, and FDA believes that public health protection requires that the regulation be enforced. Europeans seem less concerned, claiming that diseases have been largely eliminated from their dairy herds.

The agency’s New York import district routinely samples European soft-ripened cheese that may have been made from raw, unpasteurized milk (*lait cru*). It has found and detained several lots of such cheese, notably Camembert and Brie. An enzyme called phosphatase is present in cheese that has been made with raw milk, and the import laboratory found the enzyme in 10 of 105 samples tested.

To help resolve the problem, the FDA import district held a meeting this past summer, attended by representatives of the American Cheese Association, the French Embassy’s commercial staff, and French soft-cheese manufacturers. To ensure that their products could be offered for sale in the United States, French health officials agreed to inspect their country’s soft-cheese
operations, and the manufacturers themselves agreed to pay closer attention to their pasteurization processes.

A Taste For Raccoon

The owner of a fish market in Stamford, Conn., is said to have a taste for raccoon. No one could argue with that as a personal preference. But when he took 37 frozen raccoon carcasses from North Carolina to Connecticut with the intention of selling the meat commercially, he ran into trouble with two health agencies.

The Stamford Health Department discovered the frozen raccoon carcasses, eviscerated but with the hides intact, during a routine inspection of the fish market. Suspecting a possible hazard to health, the department embargoed the lot and contacted FDA, which has jurisdiction over wild game marketed as food.

An investigator from the agency's Bridgeport resident post checked with FDA headquarters and learned that although raccoon is considered an edible game animal, mostly in rural areas of the South, the current rabies epidemic on the eastern seaboard throws some doubt on the safety of eating the animals. (See "Raccoon-Borne Rabies Spreads," in the September 1983 FDA Consumer.)

Rabies is an acute infectious viral disease of the central nervous system. Symptoms in humans include a short period of mental depression, restlessness, malaise and fever. Restlessness increases to uncontrollable excitement, followed by excessive salivation and paralysis. The disease is usually fatal to mammals. Although human infection is generally the result of a bite from a rabid animal, such as a bat or dog, handling the flesh of a rabid animal also presents a risk. Freezing will not kill the virus.

Although no brain tissue samples were analyzed to verify if the animals were infected, experts at FDA and the U.S. Centers for Disease Control agreed that the raccoons should be disposed of because of the potential health hazard. The carcasses could not be buried because animals, such as dogs or rats, might unearth the bodies. FDA and CDC recommended incineration.

The Bridgeport investigator gave this information to the Stamford Health Department, which destroyed the carcasses in the Stamford incinerator.

Paying For Ice

Consumers who earlier this year purchased 5-pound boxes of frozen scallops from the Kam Kue Seafood Corp., Jersey City, N.J., may have paid for some frozen water.

During a recent inspection of the seafood repacker, FDA's New York import district inspectors were checking the weight of each box in an eight-carton lot of frozen scallops when they discovered the boxes were 4 ounces lighter than the 5 pounds stated on their labels.

When a sample box collected by the inspectors was weighed upon thawing at the district laboratory, it was nearly a pound short. This was attributed to the excessive "glaze" (or ice) contained in the box of scallops.

Because the labels on the boxes were inaccurate as to contents, and misleading to consumers, the article was misbranded under FDA regulations. Based on these findings, the district filed for seizure of the lot. In May, the products, valued at almost $500, were seized by a U.S. marshal.

Squeaky Clean?

Investigators from FDA's Philadelphia district recognized trouble during a routine inspection of Eastern Candy Co., Philadelphia, when they found rodent excreta in some of the firm's equipment—the starch mogul, the enrober and the cooling tunnel.

A starch mogul is a large machine, usually holding hundreds of pounds of molding starch for shaping or forming certain types of candy. An enrober coats articles of food with chocolate or other food toppings. The cooling tunnel cools the coated articles of food until the coating solidifies. Rodent or insect filth in these machines is more than likely to end up in the finished food products.

The investigators also saw rodent footprints in trays of molding starch and found widespread evidence of contamination—rodent-gnawed candy, rodent pellets throughout the building, live beetles in boxes of candy, and a multitude of structural flaws (such as broken windows) that would allow insects, rodents and birds to enter the plant. The investigators collected samples of salt-water taffy, chocolate-covered pretzels, and assorted candies that were analyzed by the district laboratory and found to contain insect and rodent filth.

The district warned the company that it was violating the Food, Drug, and Cosmetic Act and should clean up its business. However, a follow-up inspection a month later found the same sort of insanitary conditions, including boxes of Easter eggs with insect holes.

The district requested that the company be enjoined from manufacturing candy under insanitary conditions. The company signed a consent decree of permanent injunction agreeing to clean and repair its facilities and rid the premises of insects and rodents. Under the terms of the injunction, the firm was restricted from resuming operations until it was inspected and approved by the district. Twice the company asserted it was ready to resume production and the district withheld approval upon finding evidence of rodent and insect contamination. But the third time, the district found the plant was clean and the company was back in business.

—This small sample of reports from the field was compiled and edited by Annabel Hecht, Carol Ballentine, Michael Herndon, Richard Thompson and Evelyn Zamula.
Snarmy of 
Court Actions

SEIZURE ACTIONS

FOOD/Poisonous and Deleterious Substance

Charged 10-15-82: when shipped by American Roland Food Corp., New York, N.Y., from East Rutherford, N.J., the article, labeled in part “CEB Pink Pepper From Reunion Island Packed by CEB,” bore and contained a poisonous and deleterious substance (pink pepper berries) which rendered it injurious to health—402(a)(1). Default decree ordered destruction. (F.D.C. No. 63860; S. No. 82–283–739; N.J. No. 1)

FOOD/Contamination, Spoilage, Insanitary Handling

Mole en pasta, at Dallas, N. Dist. Texas.
Charged 3-23-82: when shipped from Mexico, the article, labeled in part “Mole en pasta—Dona Maria . . . Hecho en Mexico por: Productos Dona Maria, S.A.,” contained insect and rodent filth—402(a)(3); and the label information was not as required, because such information was in Spanish rather than in English—403(f). Default decree ordered destruction. (F.D.C. No. 63668; S. No. 82–267–613; N.J. No. 2)

Mole en pasta, at Dallas, N. Dist. Texas.
Charged 3-25-82: when shipped from Mexico, the article, labeled in part “Mole en pasta . . . Hecho en Mexico por: Productos Dona Maria, S.A.,” contained insect and rodent filth—402(a)(3); and the label information was not as required, because such information was in Spanish rather than in English—403(f). Default decree ordered destruction. (F.D.C. No. 63676; S. No. 82–267–616; N.J. No. 3)

Pepper, black, peppermill-grind, at Fort Worth, N. Dist. Texas.
Charged 10-8-82: when shipped by McCormick & Co., Inc., Hunt Valley, Md., the article was short weight (approximately 3.3 percent); 403(e)(2). Default decree ordered destruction. (F.D.C. No. 63832; S. No. 82–267–712; N.J. No. 4)

Charged 8-25-82: while held for sale, the article contained insect filth; 402(a)(3). Consent decree authorized release to Sesame Products, Inc., Paris, Texas, for salvaging. (F.D.C. No. 63785; S. No. 82–296–930; N.J. No. 5)

FOOD/Economic and Labeling Violation

Table syrup, at Jackson, S. Dist. Miss.
Charged 5-7-82: when shipped by Norris Bros., West Monroe, La., the article, labeled in part “Ole Grady’s Sorghum Syrup, Cane Molasses & Sugar Syrup Table Syrup . . . Grady Williams, Jr. Star Route Leaf, Miss. . . Good ‘N’ Thick,” had had corn syrup substituted in part for the article—402(b)(2); the article’s labeling was false and misleading as to its ingredients—403(a)(1); and the article failed to conform to the definition and standard of identity for table syrup, since it failed to bear the name of each ingredient and failed to bear the product name as required—403(g)(2).

Subsequently, FDA discovered an error in interpretation of analytical laboratory results so that there was no information or evidence that the article contained any corn syrup. Accordingly, a consent decree authorized release of the article to the dealer and it was agreed that future sales of products containing the same ingredients would bear labels complying with 21 U.S.C. 343(g)(2) and 21 CFR 168.180(d)(3) requiring that the percentages of the ingredients be declared parenthetically as part of the product’s name. (F.D.C. No. 63710; S. No. 82–235–833; N.J. No. 6)

DRUGS/Human Use

Counterfeit caffeine, phenylpropanolamine HCl & ephedrine sulfate stimulant capsules, counterfeit doxylamine succinate combination analgesic capsules, empty imprinted capsules, fourteen offset imprinting rollers, and two capsule imprinting machines, at Central Islip, E. Dist. N.Y.
Charged 9-30-81: while held by Jerome Stephens Pharmaceuticals, Inc., Central Islip, N.Y., the drugs were counterfeit drugs, since without authorization they bore
the imprint of a drug manufacturer, processor, packer or distributor other than the actual manufacturer, processor, packer or distributor; and the capsule imprinting machines had been used in making counterfeit drugs; 201(g)(2).

The dealer claimed the capsule imprinting machines (a Delta model and a Harnett model). The Harnett model imprint machine was also claimed by the Long Island Trust Company, Garden City, N.Y., who claimed a security interest in the machine. Ultimately, a consent decree was entered into by parties. The decree ordered the destruction of all 14 offset imprinting rollers, ordered the sale of the Delta model imprinting machine, and ordered the release of the Harnett model imprinting machine to the security-interest claimant, with the provision that such machine be removed from the dealer’s premises and that no agreement respecting continued use by the dealer be entered into by the security-interest claimant. (F.D.C. No. 63540; S. No. 81–194–072 et al.; N.J. No. 7)

Counterfeit capsules and tablets, nine offset imprinting rollers, and one capsule imprinting machine, at Hauppauge, E. Dist. N.Y.
Charged 9-30-81: while held by LNK International Inc., Hauppauge, N.Y., the drugs were counterfeit drugs, since without authorization they bore the imprint of a drug manufacturer, processor, packer or distributor other than the actual manufacturer, processor, packer or distributor—201(g)(2); and the equipment had been used or designed for use in making counterfeit drugs—201(g)(2).

The dealer claimed the imprinting machine, asserting that several months previously the dealer had been notified by FDA that “the manufacture, distribution and sale of the products involved herein were legally questionable”; that the dealer had immediately terminated production and switched the use of the imprinting machine to the production of other products; and that the claimant requested the return of the imprinting machine for use in its regular course of business involving the production of legal pharmaceuticals.

A consent decree of condemnation ordered the destruction of the counterfeit drugs and the offset imprinting rollers, and authorized the release of the capsule imprinting machine to the claimant. The consent decree also enjoined the claimant to cease the manufacture and distribution of drug products upon FDA notice that the drug product was a counterfeit or imitation, that the claimant file specified reports for three years concerning over-the-counter drug products containing certain ingredients; that the claimant maintain specified current good manufacturing records; and that the claimant send information copies of the decree to its customers. (F.D.C. No. 63541; S. No. 81–270–425; N.J. No. 8)

Dexamethasone sodium phosphate injection (10 mg./ml.), at Skokie, N. Dist. Ill.
Charged 9-15-81: when shipped by Carter Glogau Laboratories, Inc., Glendale, Ariz., the article was a new drug without an effective approved New Drug Application; 505(a).

The article was claimed by the shipper who denied the charge and demanded a jury trial. The shipper advised that New Drug Applications had been approved for other dosage units of dexamethasone sodium phosphate injection and that the firm was actively working to obtain approval of the 10 mg./ml. product. Subsequently, the court dismissed the action without prejudice and with leave to reinstate. Ultimately, the claimant voluntarily destroyed the article. (F.D.C. No. 63534; S. No. 81–291–535; N.J. No. 9)

Nitrofurantoin suspension, at Columbus, S. Dist. Ohio.
Charged 8-20-82: when shipped by Performance Products, Inc., St. Louis, Mo., the article was a new animal drug and no approval of a New Animal Drug Application was in effect with respect to its use or intended use; 501(a)(5). Default decree ordered destruction. (F.D.C. No. 63774; S. No. 82–273–169; N.J. No. 10)

Charged 8-16-82: when the liquid was shipped by Na-
tional Pharmaceutical Mfg. Co., Baltimore, Md., and while the capsules were held by Dunhall Pharmaceuticals, Inc., Gravette, Ark. (who manufactured the capsules using interstate pentylenetetrazole), the articles were new drugs without effective approved New Drug Applications—505(a); and the labeling of the capsules lacked adequate directions for use and was not exempted due to the article's new drug status—502(f)(1). Default decree ordered destruction. (F.D.C. No. 63782; S. No. 82-341-394; N.J. No. 11)

DRUGS/Veterinary

Counterirritant & absorbent veterinary lotion, at Colton, C. Dist. Calif. Charged 7-8-82: when shipped by Carter-Luff Chemical Co., Inc., Gloversville, N.Y., the article was a new animal drug and no approval of a New Animal Drug Application was in effect with respect to its use or intended use—501(a)(5); and the circumstances used for the articles' manufacture, processing, packing and holding failed to conform with current good manufacturing practice—501(a)(2)(B). Consent decree ordered destruction. (F.D.C. No. 63736; S. Nos. 82-306-002/3; N.J. No. 12)

Scarlet Oil veterinary fluid, Blood Stop powder, other veterinary drug stocks, and stocks of drug components, at Olathe, Dist. Kan. Charged 11-14-80: while held for sale after manufacture (or, in the case of drug components, while being held for manufacture) by Chemvet Laboratories, Inc., Olathe, Kan., the circumstances used for the manufacture, processing, packing and holding failed to conform with current good manufacturing practice—501(a)(2)(B). A default decree ordered destruction. The responsibility for the disposition of the articles was subsequently transferred to FDA, because distribution of the articles required elaborate compliance with applicable toxic and hazardous waste laws. Subsequently, the court inquired as to the failure of FDA to destroy the articles. FDA consulted with the Environmental Protection Agency which arranged for the recycling and diversion of some of the hazardous articles, by a university, as teaching aids and not for consumption by man or animals. FDA moved for a supplemental order to modify the order of destruction to permit such disposition. The court modified its order of destruction to release certain specified articles to the specified university. With the cooperation of the Kansas Department of Health and Environment, more than half of the remaining articles (i.e., 37,000 pounds of non-hazardous goods) were disposed of at a landfill. Pursuant to a supplemental order of destruction, all of the articles deemed to be hazardous substances, as well as some additional non-hazardous substances, were transferred to the university. The remaining 25,000 pounds of non-hazardous goods were ultimately disposed of at a landfill. (F.D.C. No. 63214; S. No. 80-251-122 et al.; N.J. No. 13)
And my good health begins with me. That's why I try to eat properly, get plenty of rest, and exercise.

But no matter how well I take care of myself, there are times when I just don't feel right.

And I start thinking about how to get better.

When I need medicine, my first step is to get the right information.

If non-prescription medicine is called for, I make sure I read the labels thoroughly before I make my selection; then I follow directions carefully.

If a prescription medicine is necessary, I make sure that my doctor gives me all the information I need.

Reading the labels, understanding and following directions; these are the right steps to take when you take medicine.

After all, your good health begins with you.

Michal Margulies—Dancer

The Council On Family Health
A public service by the manufacturers of medicines.