Medicine And The Elderly
Flu/Cold—Never The Strain Shall Meet

The common cold is not as serious as the less common influenza, and they are caused by altogether different viruses. But they have some similarities and it’s not always easy to tell them apart. Because flu can be dangerous if unchecked, we need to learn whatever we can about this disease.

Raccoon-Borne Rabies Spreads

A recent rabies outbreak among raccoons in mid-Atlantic states is seen as a potential public health problem since raccoons live closer to humans than most other susceptible wild animals.

Sulfites: Preservatives That Can Go Wrong

Heretofore sprayed on fresh fruits and vegetables by some restaurants to keep them looking that way and used in some drug products for their preserving qualities, sulfites are undergoing FDA review as a result of reports that adverse reactions result for some people.

Prompt Drug Approvals, More Innovation Sought

FDA has rewritten its regulations on new drug development. The aim is to permit drugs to reach the market sooner and at less cost to the developers, without compromising standards of safety and effectiveness.

What The Experts Know About AIDS

Some basics on this disease—that’s causing near panic among some segments of the population—are given by U.S. Public Health experts closest to the problem.

Medicine And The Elderly

Older people as a group take more than their share of the nation’s drugs because they have more health problems. Aging creates additional problems having to do with proper selection of medicines and their proper use. Here are some background and tips for patients and those who administer drugs to them.

Screening Out Chest X-Rays

Routine chest X-raying is unrewarding in percentages of disease findings when considered against risks from X-ray exposure and the expense, a panel of experts finds. The panel recommended that much screening be discontinued.
Supplements For Fast Foods?

I was startled to see a recommendation that people should "supplement their diets with required nutrients if they frequently dine on fast foods" in Chris Lecos' article on fast food in your May issue ("What About Nutrients in Fast Foods?").

Is FDA really advising fast food fans to take vitamin supplements?

I doubt that such advice is really necessary. As our organization's recent report, Fast Food and the American Diet, points out, there is nothing uniquely deficient about fast food. However, as most consumers are well aware, the menus of fast food restaurants are limited. Foods that are good sources of certain nutrients (e.g., vitamin A) don't appear on many fast food menus. This doesn't mean that fast food fans need vitamin A supplements; it merely means that they should include vitamin-A rich foods in other meals.

Our report recommended that "meals eaten at fast-service restaurants should be incorporated into a varied diet that includes many other food choices." I think that such a recommendation is preferable to advising people to spend money on vitamin supplements that they most likely do not need.

Kathleen Meister
Research Associate
American Council on Science and Health

We readily agree with the American Council on Science and Health report that meals consumed at fast service restaurants "should be incorporated into a varied diet that includes many other food choices." The FDA Consumer article was not intended to imply that fast food patrons might have to take vitamin and mineral supplements nor to advise consumers "to spend money on vitamin supplements that they most likely do not need." Overall, the article makes the same point as Ms. Meister's letter, namely that some fast food menus are so limited that certain nutrients may be lacking in some meals, thus necessitating the inclusion of these nutrients in other meals, at home or in a restaurant. The sentence quoted by Ms. Meister from the final paragraph of the article was intended only to reinforce points made earlier in the article. For example, it was clearly stated that a balanced and varied diet will provide the essential nutrients for good health. Further, it was pointed out that obtaining all the required nutrients depends on what food combinations people eat away from home, how often they rely on certain food choices, and what other foods they eat the rest of the day.

Praise For Hazard Board

Two major factors in the effectiveness of the Health Hazard Evaluation Board are the group's uncompromising objectivity and impartial scientific approach. As the "Supreme Court" of food and drug hazard evaluation, the board is able to assess immediate public health risks with a responsiveness unequalled by other Government bodies. It is vital that the public as well as agencies such as USDA have access to an independent body of scientific review.

My experience with the FDA Bureau of Foods and the USDA Standards and Labeling Division received extensive national press coverage. But few of the reports were presented with the total accuracy and complete perspective of Mr. Lecos' article.

Carole S. Harris
Falls Church, Va.

Readers may recall that it was Mrs. Harris' child that choked on a meat product, triggering action by USDA and the Health Hazard Evaluation Board.
Clarification Of AAFCO

The statement that the Association of American Feed Control Officials is a national organization representing state officials made on page 24 of the June 1983 FDA Consumer is somewhat misleading. Actually the membership of the association is composed of the following:

1. The officers charged by law with execution of state, provincial, dominion and federal laws in the continent of North America, Hawaii and Puerto Rico regulating the production, labeling, distribution, and sale of animal feeds and livestock remedies.

2. The heads or chiefs of experiment stations, departments of agriculture, bureaus, division sections and laboratories and employees thereof charged by law with the examination of animal feeds and livestock remedies.

3. Research workers employed by state, provincial, dominion or federal agencies who are engaged in the investigation of animal feeds, livestock remedies or their component parts.

In addition, the statement made in the article “Food Fit For A Fido” on page 23 that The American Association of Feed Control Officials requires that each label contain _____ is also somewhat misleading in that the association has no authority to enforce feed laws or regulations. This rests with the agencies charged with such responsibilities. The Association does develop model laws and regulations as well as definitions and policies and encourages agencies to adopt them in the interest of uniform regulation.

Jack W. Van Stavern
AAFCO President

Liked Orphan Article

As a reader of FDA Consumer for many years, I am convinced that it is probably the finest of all government publications. We were delighted with your timely article, “Rx for Orphan Drugs” (September 1980), and are even more ecstatic with your most recent article, “A Future for Orphan Drugs” (April 1983). Although this last article was described by the writer as “medical science fiction,” it was well researched and as accurate an account of the future as can possibly be written.

... Volunteer agencies, researchers and individuals have formed a new consumer agency to address the needs of people with orphan diseases. The publicity surrounding the Orphan Drug Act’s passage into law caused an avalanche of inquiries from people with rare disorders who had previously been unable to obtain information about their disability or new methods of treatment. As a result National Organization for Rare Disorders (NORD) disseminates information throughout the world about rare disorders and orphan drugs.

One factor omitted from your article should be mentioned, even though it is not science fiction, but fact. Dr. Marion Finkel, director of the FDA’s Office for Orphan Product Development, has been the chief factor in the success of the FDA’s orphans drug program. She deserves a salute from FDA and consumers alike for her determination to end the needless suffering of rare disease victims. Of the 14 “adopted” orphan drugs listed in your article, she was personally responsible for the adoption of 12 of those drugs. Actually, 18 new orphan therapies were adopted between March 1982 and March 1983 as a result of Dr. Finkel’s work. Hundreds of thousands of lives have been saved and millions will be saved in the future.

I look forward to your April 1991 issue of FDA Consumer when you will be able to reprint the article “A Future for Orphan Drugs” as a factual narrative, rather than science fiction.

Abby S. Meyers
NORD Steering Committee
Director, Family and Professional Services
Tourette Syndrome Association
According to ancient legend, the Greek goddess Thetis heard a prophecy that her son, Achilles, would die in battle. To protect him, she attempted what might be called the first inoculation by dipping him head first into the magical River Styx. This made him invulnerable—except for the part of his body that Thetis held onto, his heel. Thus, we get the colorful phrase “Achilles heel” for a weak point in an otherwise strong person. In terms of an invasion route for many bacteria and viruses, our Achilles heel is located at the other end of the anatomy, the respiratory tract: the nose, throat, windpipe, bronchial tubes and lungs.

Every day, as we inhale some 500 cubic feet of air, equivalent to a large walk-in closet, all kinds of unwanted visitors tag along: dust particles and the mites that often accompany them, pollen, a variety of airborne debris, and numerous bacteria and viruses. The body has various defenses protecting its respiratory tract. Strong, rough hairs in the nostrils stop the largest of these unwelcome guests. Smaller invaders then encounter the equivalent of flypaper, a sticky film of mucus that traps bacteria and particles. These are then pushed by the continual beating of legions of tiny whip-like hairs, the cilia, back to the gullet where they descend into the digestive tract and are consumed. Bacteria that make it past these obstacles encounter a variety of other defense mechanisms which together prevent the many organisms we inhale every day from causing disease.

Despite these formidable barriers, occasional harmful bacteria or viruses do manage to gain a foothold. Among these can be any of 200 viruses in eight groups or families that produce the common cold. There are also three types of influenza virus: type A, the most frequently encountered and often the most severe; B, which commonly causes localized outbreaks and occasionally severe epidemics; and C, which occurs rarely. Among the influenza A viruses, there are numerous subtypes that exist in the animal kingdom, three of which are known to be capable of infecting man.

The spread of influenza viruses from person to person depends on whether an infected individual comes in contact with someone who is susceptible. It is thought that infection with one influenza virus leaves a person resistant indefinitely to infection with the exact same virus. When a strain of influenza virus appears in a population for the first time, outbreaks that occur are likely to be limited in size. Outbreaks that affect large numbers of individuals over a wide geographic area are referred to as epidemics, and worldwide epidemics affecting all age groups are called pandemics.

The capacity of influenza viruses to produce significant outbreaks year after year is the result of their diversity. Pandemics occur when viruses of an influenza A subtype emerge that have not been present for many years. Such pandemics occurred with the emergence of “Spanish flu” in 1918, “Asian flu” in 1957, and “Hong Kong flu” in 1968. The viruses that caused these pandemics were each representatives of different subtypes of influenza A.

In addition to the differences in types of variation seen in influenza and cold viruses, there are important differences in the types of disease they cause. The common cold is well-known as a self-limited illness that is usually no more than a nuisance for two or three days. By comparison, influenza is a major killer worldwide. The Spanish flu pandemic of 1918 was the worst pestilence that ever afflicted mankind. It has been estimated that more than 30 million people died in the United States, and perhaps billions died worldwide. In 1957, more than 50 thousand people died in the United States from Asian flu. Even in years between pandemics there are usually thousands of deaths in this country, mostly in elderly persons or those with chronic illnesses such as cystic fibrosis, asthma or heart disease.

It is this capacity to produce sudden, widespread epidemics of varying severity that once made influenza appear to be a mysterious affliction. Many theories were proposed to account for the speed and intensity of a flu epidemic. In 1657, the English physician Thomas Willis, remarking on the sudden way so many were afflicted with chills, aches and fever, attributed it to the malign influence of the stars—in Italian, influenza coeli, from which we get the word influenza. The word grippe, sometimes also la grippe, was once often used as a synonym for influenza. While this may seem like a precise French word for the harsh grip of the disease on the body, it actually comes from the Russian word krip, or hoarseness.

Those caught in influenza’s grip are far from caring how the disease was christened but are more concerned with how to get rid of it.

During the 1918 pandemic, the question of whether the early signs of respiratory distress signaled only another common cold or the dreaded onset of Spanish flu and a brush with death was of sharp and immediate concern. The Denver Post of Oct. 11, 1918, seeking to conserve the energies of that city’s physicians, who were exhausted from
dealing with so many desperately ill persons, tried to tell its
readers the difference between a cold and the flu. The be-
ing of a cold, the paper said, was not as sudden, its
aches not as severe, its fever not as high. And, the Post
added, a cold is distinguished by "chilliness rather than de-
finite chills." In terms of diagnosis outside a laboratory, the
truth is we haven’t really progressed much past the vague
advice in that 1918 newspaper. What is possible now that
wasn’t possible in 1918 is a sure way of knowing whether a
person has flu by laboratory testing for presence of the spe-
cific antibody associated with the flu virus. It’s also possible
to provide a precise list of symptoms that distinguish flu
from a cold. But the list deals with generalities and
averages.

One reason it’s so difficult to tell definitely from symp-
toms alone that a person has the flu or a cold is that humans
differ widely in how they react to these respiratory infec-
tions. Some may become quite ill from a cold; others may
exhibit only mild distress from the flu. In fact, there is no
single symptom that distinguishes flu from the common
cold—or even from the early stages of bronchitis or strep
throat. From controlled experiments with volunteers, the
best that can be said is the following:

- Regarding fever: colds rarely are accompanied by fever,
  except in children; flu usually begins with fever.
- Regarding onset: flu is swift and severe; colds tend to
  build more slowly.
- Regarding location: colds show localized symptoms such
  as sneezing, runny nose, etc.; flu has general symptoms
  such as weakness, muscular pain, chills, headache.
- Regarding other symptoms: 90 percent of flu victims have
  a dry, hacking cough; 60 percent have sore eyes; 50 percent
  have a flushed face and hot, moist skin. Such symptoms ap-
  pear less often in cold sufferers.

The point to note is that there is no absolute way to tell by
symptoms alone which infection a person is suffering from.
The best that can be said is that if a patient is suddenly
stricken with fever, chills, general weakness and headache
and muscular pains, accompanied by a severe cough, sore eyes
and flushed face, and if there is a flu outbreak in the area,
then he or she probably has influenza. But since children
and older persons differ in the severity of symptoms, and
since symptoms are further clouded by differences between
individuals—such as prior history of exposure to influenza,
genetic endowment, stress or personal health—it is simply
impossible to state on the basis of symptoms alone that a
respiratory infection is or is not the flu.

Unfortunately, even if we could tell from symptoms
whether a person has influenza, there is no medicine now
known to cure it, although some drugs are being studied.
Penicillin and other antibiotics have no effect on flu or other
viruses, although they may help fight certain complicating
infections, such as bronchitis and some types of pneumonia.
A physician is the best judge of when to use antibiotics.

Nevertheless, while influenza cannot yet be cured, it can
be prevented by vaccination. However, because flu virus of-
ten drifts or shifts into a form new to the body’s immune de-
fenses, inoculation against one flu strain does not necessari-
ly protect against the next epidemic. Such protection
requires inoculation with a vaccine specific for the strain or
strains currently circulating.

If flu can be only prevented, not cured, how can it be
reconceived, once caught? In the 1918 pandemic, nurses were in
greater demand than physicians, since the main need for flu
victims was tender loving care. That’s still the best treat-
ment. The patient should drink lots of water and fruit juice,
keep warm and comfortable, and remain in bed until temper-
atures returns to normal. To ease discomfort from muscle
pains or headaches, aspirin or a substitute may be taken by
an adult. An aspirin substitute (or aspirin, if directed by a
physician) may be taken by children. It’s important that the
patient be closely observed to detect signs of complications.
This includes just about every infectious respiratory tract
dsesease, such as acute bronchitis, pharyngitis, tonsillitis,
laryngitis, croup, sinusitis and pneumonia. Ordinarily such
complications don’t involve the digestive or intestinal sys-
tem. Therefore, influenza virus is seldom if ever responsible
for what is erroneously called “intestinal flu” or
“stomach flu.”

Finally, how serious is the flu? Obviously, as the Spanish
flu pandemic of 1918 shows, flu can be a life-threatening
disease. This is why, when a flu strain appeared in 1976 (the
“swine flu”) that seemed to resemble the 1918 flu virus,
the government geared up for inoculation of every Ameri-
can. This proved to be a false alarm. But new flu strains that
are far less virulent than that which caused the 1918 pan-
demic can still exact a huge toll in losses of life and in ill-
ness. For example, the Asian flu pandemic of 1957 caused
45 million cases of influenza in the United States alone.

In the absence of such potent influenza strains, the kinds of
influenza we usually encounter tend to produce moderate-
ately severe illnesses but are not serious health threats to most
healthy individuals. Complete recovery can be expected
within a week. For certain high-risk groups—old people,
children, the chronically ill, and pregnant women—any
form of flu can be a serious problem since the disease or its
complications may be life threatening. The mortality curve
of influenza—the death rate for each age group—usually
takes a U-shaped form on a graph, evidence of flu’s special
danger to the very young and the very old. (The single ex-
ception was the Spanish flu, which showed a W-shaped
form, attesting that millions in the prime and healthiest
years of life died either from the flu or its complications.)
There is also some evidence that pregnant women may have
more severe influenza than healthy, non-pregnant women.
Any pregnant woman who catches influenza should report it
promptly to her physician.

Special precautions are necessary with children who con-
tract influenza. It can strike with far more severity than in
an adult, and include fever above 104 degrees Fahrenheit,
along with such complications as convulsions, croup or
pneumonia. With both types of flu (as well as with chicken-
pox) there is danger for children from infancy to the late
ten years of a life-threatening illness called Reye syndrome (pronounced “rye”). Reye syndrome usually takes the fol-
lowing course: The child is recovering from a mild viral ill-
ness such as influenza. Suddenly, in rapid succession, the
child has vomiting, violent headaches, listlessness, irritabil-
ity (even combative ness), delirium, disturbed breathing,
More Diverse Than The Common Cold

Despite the fact that there are only three main types of influenza (A, B, and C), there are potentially an unlimited number of strains. Thus, this group of viruses is even more diverse than the common cold.

The influenza A viruses are the most subject to variation, and the variants are called subtypes. Each subtype is given a name that describes the major surface proteins of the virus and the proteins responsible for inducing immune responses that protect against infection with the same virus. The two major proteins are the hemagglutinin ("H") and the neuraminidase ("N"); thus, the viruses that caused the three pandemics of this century were designated H1N1, H2N2, and H3N2.

Before 1978, experience with influenza viruses had led to the belief that various strains of the same subtype would emerge in the years following a pandemic, each with a minor change in hemagglutinin. When the change was great enough, the virus would spread rapidly and cause epidemics. These changes occurring in viruses of one subtype are referred to as "drift," and probably occur through spontaneous mutation of the viral genes.

The emergence of a new subtype—which is a change from the strains of one subtype to ones of a completely different hemagglutinin subtype—is referred to as "shift." Although it was previously thought that "shift" also resulted from mutation, it is now clear that this is not the case. Viruses of different subtypes apparently exist in nature, but where they persist when they are not causing outbreaks in man is unknown.

At present, the strains causing important outbreaks belong to the H1N1 and H3N2 subtypes of influenza A viruses. However, the influenza B viruses are not to be sneezed at. The B viruses are subject to less variation than the A viruses, having only one major type and no subtypes; however, they do "drift," which results in the appearance of new strains from time to time, and the resulting epidemics can be devastating.

Influenza viruses do more to confound scientists than simply "change their spots." In 1977, an epidemic caused by "Russian flu" was a landmark event because the virus was of the H1N1 subtype, similar to the Spanish flu of 1918. This was the first documented epidemic caused by the reemergence of a subtype that had circulated previously. Perhaps equally significant were the events of 1978 when "Russian flu" and strains of the H3N2 subtype related to the Hong Kong flu both produced epidemics. Previously, all shifts resulted in the disappearance of the old subtype as the new subtype emerged.

Population surveys showed that within a season or two of the introduction of the Hong Kong virus (1968-69), the majority of people had antibodies to the strain in their blood, indicating that they had been infected although not all had experienced apparent illness.

Tracking The Flu 'Season'

Influenza occurs in the northern hemisphere mostly in the winter months; typically, outbreaks occur from November to April. Although flu is uncommon in summer, outbreaks have been documented in warm weather with virulent new strains. Influenza has appeared every winter since the U.S. Centers for Disease Control began keeping records on the illness.

Of course, flu statistics are not always complete or accurate because of the problem of differentiating between real influenza and colds or other infections. Choosing the best vaccine is also difficult. The vaccines have to be made in advance, even though experts are not sure what type flu will break out because the virus continues to mutate, or "shift."

CDC monitors outbreaks all over the world, trying to find out if there are new mutations. If there is a trend towards the emergence of one new strain, CDC will follow it closely. Although new virulent epidemic strains may appear every 5 to 10 years, experts cannot predict with certainty what the strain will be.

In the United States last year (winter 1982–83), according to confirmed laboratory cases, the flu outbreak peaked in late February to early March. In the last major pandemic—the Hong Kong flu (1968–69)—the flu "season" in the United States extended from September through March and peaked in December and January.

Every spring, representatives from CDC, FDA and advisory committees representing the medical community meet to determine what strains of influenza virus to put in the next season's vaccine based on the best available information.

—Evelyn Zamula

stiffness of arms and legs, and then coma. A parent should not wait until there is a full progression of these symptoms or enough of them to substantiate fear that the child has Reye syndrome. Immediate action is called for. The family physician should be called right away. If a physician cannot be reached, the child should be taken to a hospital emergency room. A Reye syndrome attack moves so fast, and the penalty for failure to respond with equal speed is so severe, that not a second should be lost.

The word "syndrome" is applied when medicine recognizes a fixed pattern of symptoms but doesn't fully understand their cause (or causes). Thus, no one yet knows what causes Reye syndrome. However, there are studies indicating that the appearance of Reye syndrome in children may be associated with (not the same as "caused by") aspirin and other drugs that contain salicylates (the chemical basis of aspirin). Therefore, the U.S. surgeon general has advised against giving aspirin and other salicylate-containing products to children with flu or chickenpox unless directed by the child's physician. This is why the Food and Drug Administration announced that it is considering a regulation which would require the labels on aspirin and other salicylate-containing products to warn against giving such products to children under 16 with flu or chickenpox without consulting a physician.

Medicine has come a long way from the time when influenza was blamed on an evil star. The only certainty is that even the mildest illness must be treated with respect, and the patient not only cared for but observed carefully.

Tim Larkin is a freelance writer.
Rabid in wild animals is not usually a major threat to human populations. When it spreads to animals who live near heavily populated areas, however, it can become a potential public health problem.

A recent outbreak of rabies in raccoons in the mid-Atlantic states has focused attention on such a possibility. (In epidemiological terms an "outbreak" is a clustering of disease cases involving animals or people in numbers and proximity greater than expected.) Since raccoons live in closer proximity to humans than most wild animals, public health officials have alerted people living in the affected area to avoid contact with animals that might be rabid.

The latest outbreak comes at a time of a generally stabilized picture of rabies incidence among wild animals in the United States. Total reported rabies cases in animals in the nation for 1982 were actually about 14 percent lower than in 1981. The most significant change was the marked increase in the number of rabid raccoons and a significant decrease in rabid skunks. Cases of rabies in cats exceeded those in dogs for the second year in a row.

At present, there are three concurrent animal rabies outbreaks in the United States. The one of longest duration began 25 years ago, with cases in raccoons in the southeastern states, particularly Florida, Georgia and Alabama. It is spreading slowly northward and westward. A second outbreak, involving primarily skunks in the midwestern states, appears to be waning after 10 years.

The third outbreak, occurring in raccoons in mid-Atlantic states, is relatively new and has continued for about two years. Virginia, West Virginia, Pennsylvania, Maryland and the District of Columbia are most affected.

This increase in wild animal rabies is a major public health concern and probably constitutes the greatest threat to humans of any rabies outbreak in the last 20 years. Raccoons are the largest reservoir of rabies in urban areas since dog rabies was controlled in this country in the mid-1950s. Since the outbreak threatens major cities such as Washington, D.C., Baltimore, Trenton and Philadelphia, the risk of exposure for humans is significant.

At present, there is no known method for controlling wildlife rabies. The best means available for protecting humans against exposure to the disease is to immunize pets, which might otherwise expose persons. When necessary, people at high risk—veterinarians, wildlife conservation personnel, staff of quarantine kennels, and laboratory and field personnel working with raccoons—should receive pre-exposure immunization. The presently available raccoons vaccine in the United States is human diploid cell rabies vaccine (HDCV), an inactivated virus vaccine prepared from virus grown in human cells. HDCV provides more immunity and has fewer side effects than the previously available duck embryo vaccine (DEV). (See "Taking The Bite Out Of Rabies" in the March 1981

FDA Consumer.) For pre-exposure immunization, HDCV is given in three intramuscular doses—the first two doses within a week of each other and the second two to three weeks later.

To prevent rabies in people who have been exposed to a rabid animal, immediate flushing of the animal bite wound is recommended; this should be followed by prompt medical consultation. If post-exposure treatment is recommended, rabies immune globulin (RIG) and vaccine (HDCV) should be given. RIG is given once at the beginning of treatment; five doses of HDCV are given over a 28-day period.

Vaccination of pets and avoiding exposure to possible rabid wildlife is the best available protection for humans against raccoon rabies. There have been no reported human fatalities as a result of raccoon exposure.

Two human rabies cases were reported in the United States in the first six months of 1983. One patient was an American citizen exposed to rabies in Africa. He died in Massachusetts earlier this year. The second case was a 5-year-old child in Michigan who may have been exposed to a rabid bat. She died in March of this year.

Human rabies cases remain at the usual low level for the United States. Usually no more than five cases per year are reported. There were no known human fatalities from rabies in 1974, 1980 and 1982.

Katherine Lord is a public affairs officer for the U.S. Centers for Disease Control in Atlanta, Ga.
Sulfites: Preservatives That Can Go Wrong

The scene could have been the opening of a "whodunit." The victim dies of a sudden severe attack of asthma. The mystery is—what caused the attack?

One thing is sure. The butler didn't do it.

The chef did—when he added bisulfite to the fresh vegetables in the salad.

This story isn't fiction, however. One man has died, reportedly after eating food containing sulfites, and there is considerable concern about an increasing number of reports of adverse reactions to these agents.

Sulfiting agents are used in a number of drug products and foods as antioxidants (preservatives). What they do is delay or prevent undesirable changes in color, flavor or texture, such as browning or discoloration due to oxidation. Because sulfites keep fruits and vegetables looking fresh, their use in restaurants has increased in the last few years with the increasing popularity of salad bars. They are used in other restaurant foods, especially seafood and potatoes. Sulfites also are used in many processed foods, including fruit drinks, beer, wine, baked goods, vegetables and dried fruits, and in the processing of some food ingredients, including gelatin, beet sugar, corn sweeteners and food starches.

Since 1959, six sulfiting agents have been listed by FDA as GRAS (Generally Recognized as Safe) for use in food: sulfur dioxide, sodium sulfite, sodium and potassium bisulfite, and sodium and potassium metabisulfite. The agency is currently reviewing their GRAS status.

FDA is aware of approximately 90 cases of adverse reactions, including the one death, reportedly caused by sulfites in foods. The reactions included nausea, diarrhea, anaphylactic shock (a severe allergic reaction), acute asthma attacks, and loss of consciousness. They occurred soon after the victims ate salads or other foods in restaurants, ate certain processed foods, drank wine or other beverages, or took medications. A few reports have also been received of adverse reactions experienced by food service personnel who handled sulfites.

While most of these cases occurred in people who have asthma, about 30 percent occurred in non-asthmatics with no known allergies. The number of people who could have a reaction to sulfites is not known, but it may be large. Because this type of reaction was not recognized previously, it is likely the cases that have been reported to FDA are just the tip of the proverbial iceberg.

FDA has taken a number of steps to protect those who are allergic to sulfites. Companies operating interstate conveyances (buses, trains, planes) and caterers that provide food for them have been advised that consumers must be notified if sulfiting agents are used on foods intended to be eaten raw. State officials who monitor restaurants, grocery stores, and other retail food establishments have also been asked to tell users of sulfiting agents to alert customers by posting conspicuous and easily readable signs, placards, labels or statements on menus. FDA also has contacted retail food trade associations, asking their members to either stop using sulfiting agents or inform consumers when they are used by appropriate labeling.

Sulfiting agents are used in a number of medications, including antiemetics (drugs to prevent nausea), cardiovascular drugs, antibiotics, psychotropic drugs, intravenous solutions, analgesics (painkillers), anesthetics, steroids and nebulized bronchodilator solutions (used for the treatment of asthma). However, sulfites are not used in metered-dose bronchodilator inhalers.

FDA is working with drug manufacturers to explore the feasibility of substituting other antioxidants in these drugs. A labeling statement on drugs that do contain sulfites is also being considered.

The fact that some bronchodilators contain sulfites poses some potential problems in the treatment of asthmatics. Doctors could have difficulty determining whether the patient is having a reaction to the sulfiting agent or is not responding to the medication. It also is possible that the bronchodilator medication may give some protection against the effects of the sulfites, and that asthmatics could be at greater risk from other sulfite-containing drugs.

FDA has asked doctors to report any confirmed or suspected reactions to sulfiting agents. Symptoms that may be a clue to an anaphylactic reaction include flushing, angioedema (recurring attacks of transient swelling in areas of the skin or mucous membranes), hives, wheezing and generalized itching. These may progress to swelling of the larynx, abnormally low blood pressure, cyanosis (a bluish discoloration of the skin), loss of consciousness and respiratory arrest. Consumers who are or may be sensitive to sulfiting agents should read the labels of packaged foods to see if the product contains any of these agents. Before ordering at a restaurant, they should ask if any foods have been treated with sulfites.

—Annabel Hecht and Judith Willis
Prompt Drug Approvals, More Innovation Sought

Encouraging drug innovation and making safe and effective therapies available more promptly—it’s a tall order. But that’s what’s promised and hoped for in FDA’s recently proposed revisions of its Investigational New Drug (IND) regulations. These are the rules that govern the clinical testing of new drugs before they are approved for marketing.

The revisions in the IND regulations are part of an overall revamping of FDA’s new drug approval procedures, initiated in 1978 to speed the approval process and make it less costly for both industry and the agency. Proposed revisions of the New Drug Application (NDA) regulations were published last year (see “Slashing Away At Red Tape In The Drug Approval Process,” FDA Consumer, February 1983).

The major thrust of the proposed IND changes is that different stages of the process would be regulated differently. For instance, safety concerns would predominate in the beginning stages to ensure that research subjects are not exposed to unreasonable risks, while FDA requirements and advice geared toward the development of an application to market a drug should wait until the drug has undergone the initial safety tests in human subjects and has shown some marketing potential. In all instances the term “drug” is meant to include drugs, antibiotics and biologic products.

All in all, it is estimated that the proposed streamlining of the IND process will save drug sponsors $3.3 million annually.

FDA’s involvement in clinical testing of drugs began just over 21 years ago. Before 1962, individuals or firms developing new drugs didn’t have to tell FDA that an experimental product was being given to human subjects. This meant that information on such studies didn’t get to the agency until they were all over. In August 1962, new regulations were proposed giving FDA stronger control over drugs during the investigational stage. FDA was to be fully informed about the initiation and progress of clinical studies. Adequate studies on animals were required to assure there would be no danger to humans given the drug in clinical trials. Manufacturers were required to report to FDA the names and qualifications of the investigators involved in the studies.

Following by a few months the broader Kefauver-Harris amendments to the Food, Drug, and Cosmetic Act, the Investigational New Drug regulations were adopted in final form on Jan. 8, 1963, with changes to conform to the new amendments.

Today, before tests involving humans can begin, the drug sponsor must file a “Notice of Claimed Investigational Exemption for a New Drug.” This not only enables FDA to keep tabs on the clinical studies, but allows the sponsor to ship the drug to investigators throughout the country without having to meet all of the labeling and other requirements for new drugs. (One of the happier proposed revisions is the elimination of this mouthful of words to be replaced with the more direct phrase “Investigational New Drug Application,” to be abbreviated IND, the acronym already in use.)

Before an IND is filed, the drug sponsor carries out short-term animal studies to determine whether the proposed new drug will be safe for humans and to predict the drug’s likely therapeutic potential.

After the IND is submitted to FDA, there is a 30-day holding period during which the agency reviews the submission to make sure that human subjects won’t be exposed to unreasonable risks. If FDA does not object in 30 days, the drug sponsor can go ahead with the next phase of testing. If there is concern about the safety of the drug, human testing can’t begin until the problems are resolved.

IND applications are also reviewed by Institutional Review Boards—groups of scientific, medical and lay persons usually associated with the institution where clinical research is done. One reason for this review is to assure that human subjects are given enough information to be able to give their informed consent for participation in the studies.

Clinical trials of new drugs progress through three phases:

Phase 1—short-term studies in a small number (20 to 80) of normal subjects and patients to determine how the drug works and its harmful effects, and to gain early evidence of its activity.
Phase 2—early controlled clinical studies to determine the proper dosage and to evaluate the effectiveness of the drug for a particular disease, carried out in a small number (several hundred) of patients who have that disease.

Phase 3—expanded controlled and uncontrolled studies to gather additional information about the effectiveness and safety of the drug so that appropriate labeling can be written. Several hundred to several thousand patients may be involved.

Long-term animal testing is often conducted during the human testing phases to provide additional information on the chronic toxicity of the drug.

FDA monitors the progress of an IND by reviewing IND amendments and annual reports submitted by the drug sponsor. Adverse drug experiences and important findings from the animal toxicity studies must be reported promptly. Agency officials may assist the drug sponsor in developing the overall clinical plan, usually at the end of Phase 2 studies, to assure that the end result will provide the information needed for the final approval of the product for marketing.

Although the IND regulations have remained fairly constant over the years, drug approval has grown more complex, calling for improvements in the overall system. Highlights of the proposed changes:

1. Greater freedom during the early phase of human research. Recognizing that many drugs do not go on to later testing, FDA proposes to give drug sponsors greater research freedom during Phase 1 testing by narrowing its review to safety of those persons who are test subjects. The proposal also allows clinical investigators to modify protocols on the basis of experience during the study without first notifying FDA. The amount of toxicology and chemistry information required will depend on the nature and extent of the proposed clinical studies.

2. Clearer format for IND submission. A new format, including a greatly simplified cover sheet, a brief overview of the investigational plan, and a brief introductory statement about the drug, will contribute to better organized submissions and more expeditious agency review.

3. Clarified amendment procedures. The proposal divides amendments to INDs into three categories, each with its reporting schedule: (1) protocol amendments, to be required only for new protocols and changes in existing protocols; (2) information amendments, to be submitted as additional data develops; and (3) IND safety reports, which are to be made as soon as practicable but no later than three working days after the sponsor learns of the event in the case of fatal or life-threatening experiences and no later than 10 working days in the case of other serious adverse experiences.

4. Creation of explicit “clinical hold” procedures. The proposed IND revisions spell out when clinical studies will be put on “hold.” During Phase 1 studies, clinical holds would be used only where there is an unreasonable and significant risk to human subjects. In later phases, studies could be delayed also for serious defects in study design.

5. Closer consultation between FDA and drug sponsors. FDA proposes to offer any IND sponsor an opportunity to hold an “end of Phase 2” conference to discuss overall plans for Phase 3 studies. At present, such conferences have been offered only for drugs identified as “breakthroughs,” that is, those providing significant or modest therapeutic advances.

6. Treatment use of investigational drugs. The proposal modifies agency proceedings and clarifies the conditions under which investigational drugs may be used for treatment of patients. The changes are designed to make investigational drugs more readily available to patients with serious diseases or conditions and for whom alternative therapies do not exist or cannot be used.

7. Exemptions for certain studies on marketed drugs. FDA proposes to exempt from IND requirements research on marketed drugs under circumstances where safety is not an issue and where the research is not being conducted for commercial purposes. This will reduce the burden on researchers and permit FDA resources to be devoted to more significant and potentially risky investigations.

Along with these proposed changes, FDA plans to issue guidelines on the IND application format and on testing requirements. The proposed changes were detailed in the June 9, 1983, Federal Register.

—Annabel Hecht
The number one priority of the U.S. Public Health Service has been a new disease called Acquired Immune Deficiency Syndrome, or AIDS. The first reported appearance of AIDS in the United States occurred in mid-1981. Between that time and Aug. 1, 1983, the Public Health Service received reports of more than 1,900 cases and over 750 deaths.

AIDS is a serious threat to the health of several specific groups in the American population, a public health problem that merits the highest level of concern. Today, researchers within the Public Health Service and in many major medical institutions are working to identify the cause of AIDS and to develop effective treatments and preventive measures.

Since it was first discovered, medical experts have learned a great deal about AIDS. Following, in question-and-answer form, is information prepared by the Public Health Service about AIDS.
**AIDS**

"Thus far, no cases have turned up among the thousands of friends, relatives and co-workers of AIDS patients; this strongly indicates that routine contact offers no risk."

"To date, no cases have been found where AIDS has been transmitted by casual or even close daily contact with AIDS patients or persons in the high-risk group."

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**Q. What is AIDS?**

*A.* AIDS is a serious condition characterized by a specific defect in natural immunity against disease. People who suffer from AIDS become susceptible to a variety of rare illnesses. These illnesses are not found in people whose immune systems are normal. If they occur, they are relatively mild. The two diseases most commonly found in AIDS patients are Pneumocystis carinii pneumonia, a lung infection caused by a parasite, and Kaposi's sarcoma, a rare form of cancer or tumor of the blood vessel walls.

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**Q. What are its symptoms?**

*A.* Many AIDS patients have some symptoms before being diagnosed. Some of these early signs are similar to those of many other illnesses such as a cold or flu. These symptoms may include fever, night sweats, swollen glands (enlarged lymph nodes)—in the neck, armpits or groin—unexplained weight loss, yeast infections, diarrhea, persistent coughs, fatigue and loss of appetite. Anyone with prolonged, persistent symptoms should consult a physician.

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**Q. Is AIDS widespread?**

*A.* There were 1,972 cases reported in the United States as of Aug. 1, 1983. In addition, over 120 AIDS cases were reported from 20 other countries. Although at present the number of cases is not extremely large, no one can predict how many people will develop the disease in the coming months and years.

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**Q. Who gets AIDS?**

*A.* Nearly 95 percent of the AIDS cases have occurred in people belonging to one of four distinct groups:

- Sexually active homosexual and bisexual men with multiple sex partners. This group accounts for about three-fourths of all reported cases.
- Haitian entrants into the United States (5 percent)
- Present or past abusers of intravenous drugs (17 percent)
- Persons with hemophilia (8 percent)

Thus far, no cases have turned up among the thousands of friends, relatives and co-workers of AIDS patients; this strongly indicates that routine contact offers no risk.

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**Q. What causes AIDS?**

*A.* Scientists have not discovered the cause of AIDS, but they suspect that it is caused by a virus, possibly one present in the blood and/or body fluids, such as semen. AIDS appears to be primarily transmitted through sexual contact.

The fact that AIDS also has been found in intravenous drug abusers leads investigators to suspect that AIDS can be transmitted by blood on contaminated needles that have been shared.

The best evidence for transmission of AIDS through blood products is the occurrence of AIDS in a small number of hemophilia patients receiving large amounts of factor VIII, a clotting substance in blood.

As of June 1983, 78 Haitian entrants had developed AIDS. Public Health Service and other doctors are studying this group and are working with the Haitian government to determine the course of the disease in that country.

Some patients cannot be placed in the high-risk groups, but researchers believe that most of these are linked by close physical contact to AIDS victims. Some of the women who have developed AIDS have been steady sex partners of men with AIDS or men who are at high risk of AIDS, or they have a history of drug abuse. Children who have developed a syndrome similar to AIDS may have been exposed to AIDS before or during birth.

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**Q. What are some theories about viruses linked to AIDS?**

*A.* Researchers have reported finding evidence of several viral infections in the blood of AIDS patients, including those of cytomegalovirus (CMV), Epstein-Barr virus (EBV), and human T-cell leukemia virus (HTLV).
"Reputable blood banks and other blood collection centers use sterile equipment and disposable needles. Thus, there is no chance that a needle used for one blood donor would be used for another."

"FDA has advised blood and plasma collection centers to provide information on AIDS to potential donors, asking those in high-risk groups to refrain from donation."

However, scientists are still uncertain if these viruses play a role in causing AIDS, or if they appear after the patient's immune system has been weakened by AIDS.

Q. How contagious is AIDS?
A. To date, no cases have been found where AIDS has been transmitted by casual or even close daily contact with AIDS patients or persons in the high-risk groups. For instance, family members other than sex partners of AIDS victims have not developed AIDS. Ambulance drivers, police and firemen who have provided emergency assistance to AIDS patients have not fallen ill. Nurses, doctors and health-care personnel have not developed AIDS from exposure to AIDS patients.

However, health-care providers and laboratory workers should follow careful procedures when handling any blood and tissue samples from patients with potentially transmissible diseases, including AIDS.

Q. How do persons with hemophilia get AIDS?
A. Many persons with hemophilia require extensive use of factor VIII, a blood product that helps blood to clot. Without effective clotting, even minor cuts can cause prolonged and dangerous bleeding.

For persons with hemophilia, the development of factor VIII has been an important medical advance. Factor VIII is extracted and concentrated from pooled blood plasma donated by thousands of people, and it appears that in some rare instances the plasma has carried AIDS.

To insure the safety of plasma derivatives, FDA has collaborated with the U.S. Centers for Disease Control in examining 200 separate lots of clotting factor concentrate manufactured by the four major U.S. manufacturers and found none that contained detectable infectious viruses.

Recently, FDA approved a new heat treatment similar to pasteurization for treating blood products such as factor VIII. This procedure will reduce the likelihood that blood products will be contaminated with infectious agents like hepatitis B and, possibly, AIDS.

Q. Can the hepatitis vaccine spread AIDS?
A. Concern has been expressed about the safety of hepatitis B vaccine (Heptavax-B) because the vaccine is made from the plasma of carriers of hepatitis B, many of whom may be in the same populations at high risk for AIDS.

However, the procedures used in the manufacture of hepatitis B vaccine are effective in inactivating viruses from every known group. Therefore, the risk of vaccine-induced infection by any transmissible agent that might cause AIDS is extremely remote, and is far outweighed by the potential benefit from hepatitis B vaccine to individuals at high risk for hepatitis B virus infection.

Q. Is there a danger of contracting AIDS from donating blood?
A. Absolutely not. Reputable blood banks and other blood collection centers use sterile equipment and disposable needles. Thus, there is no chance that a needle used for one blood donor would be used for another. The need for blood is always acute and people who are not in the high-risk groups are urged to continue to donate blood as they have in the past.

Q. Is there a test for AIDS in blood?
A. There is as yet no test to detect AIDS in blood. Public Health Service agencies are examining blood products with the aim of developing a screening test for AIDS. However, a totally satisfactory test may not be possible until the agent that causes AIDS is identified.

Q. How is AIDS treated?
A. Some AIDS patients with Kaposi's sarcoma are being
Scientific research often does not provide quick solutions to diseases as complex as AIDS. But, given the scope and sophistication of current investigative efforts, there is every reason to hope—and expect—that they will lead to rapid progress against this devastating illness.

Treated experimentally with forms of interferon—a virus-fighting protein produced by the body. While it has had some success against Kaposi’s sarcoma, interferon treatment does not appear to restore immune function. There are other treatments, such as radiation, drugs and surgery, for many of the illnesses suffered by AIDS patients. Many biomedical investigators continue to work on methods for treating the specific immune defects found in AIDS patients.

Q. Can AIDS be prevented?
A. The Public Health Service has recommended that the following steps be taken to prevent the spread of this disease:
- Sexual contact should be avoided with persons known or suspected of having AIDS.
- Avoid having multiple sexual partners and avoid sexual contact with others who do.
- Members of high-risk groups should refrain from donating blood.
- Physicians should order blood transfusions for patients only when medically necessary.

In addition, FDA has advised blood and plasma collection centers to provide information on AIDS to potential donors, asking those in high-risk groups to refrain from donation. Personnel have been advised to learn the early warning signs of AIDS.

Q. What is the federal government doing about AIDS?
A. The U.S. Public Health Service has declared AIDS a top priority. CDC in Atlanta has established a surveillance system to conduct epidemiologic investigations in an attempt to identify risk factors for AIDS. CDC also is carrying out extensive testing on blood and tissue from AIDS victims to find the specific cause of the disease.

At the National Institutes of Health in Bethesda, Md., 6 of the 11 research components are involved in multidisciplinary laboratory and clinical studies of AIDS. These studies are aimed at determining the causative agents of AIDS, evaluating the natural history of the disease, characterizing the immune deficiency of the patients, improving treatment for AIDS patients, and establishing the disease in animal models.

FDA is involved in several areas of research with NIH, including studies of the possible relationship of AIDS to cytomegalovirus (CMV) and Epstein-Barr virus (EBV). FDA also is collaborating with NIH investigators in studying the clinical effectiveness of gamma interferon in AIDS patients and its effects on the immune defects in AIDS. Other FDA work is aimed at increasing the safety of blood and blood products.

Research grants have also been awarded by NIH to investigators at medical and research institutions around the country. These studies are aimed at evaluating various treatment regimens, investigating the underlying cause of the disorder, studying the AIDS-associated diseases such as Kaposi’s sarcoma and opportunistic infections, developing an animal model for the disease, and developing a “surrogate” test for AIDS that may lead to a method for screening blood prior to transfusion.

Q. What is the hope for conquering AIDS in the future?
A. Scientific research often does not provide quick solutions to diseases as complex as AIDS. But, given the scope and sophistication of current investigative efforts, there is every reason to hope—and expect—that they will lead to rapid progress against this devastating illness. Meanwhile, the preventive measures mentioned earlier can help reduce the risk of contracting or transmitting AIDS.

Q. Is there one place where up-to-date information can be obtained?
A. The Public Health Service has established a toll-free AIDS hotline. The number is 800-342-AIDS. Collect calls will be accepted from Hawaii and Alaska on (202) 245-6867.
Success In A Test Tube

Laboratory tests by scientists at FDA and the National Institutes of Health suggest that a naturally occurring substance produced by normal people’s white blood cells may help fight the severe immunological deficiencies seen in AIDS victims.

The substance is interleukin-2, which is produced by normal lymphocytes (a kind of white blood cell), in response to viral infections or other foreign substances.

The scientists found that interleukin-2 increases the infection-fighting activity of impaired lymphocytes from AIDS patients—at least in the test tube. Whether it will help AIDS patients is not yet known. The substance is available only in very small quantities.

Nevertheless, the research may provide a hint about the nature of the disease and how it might be treated. Dr. Alain Rook of FDA’s National Center for Drugs and Biologics reported on the research to an American Society for Virology symposium in East Lansing, Mich., in July. Rook represented the group working on interleukin-2. The study also was published in the July 1983 Journal of Clinical Investigation.

AIDS patients have been found to have an extraordinarily high incidence of active infection from a virus called cytomegalovirus (CMV). A common virus of the herpes family generally of little consequence in healthy persons, CMV can lead to serious diseases such as pneumonia, encephalitis, and liver infection in persons with suppressed immunity.

The FDA and NIH scientists found that the blood of AIDS patients at the NIH Clinical Center has a pronounced deficiency in activities of certain types of lymphocytes, the “natural killer cells” (NK cells), that normally destroy virus-infected and tumor cells. Virus-specific killer cells, another type of lymphocyte that provides an important defense against virus infections, were also found to be deficient in the AIDS patients.

In the study, lymphocytes from six homosexuals who had AIDS and active CMV infections and those from uninfected heterosexuals were incubated with interleukin-2 or interferon, another disease-fighting substance produced by white blood cells.

As expected, both interferon and interleukin-2 enhanced the natural killer cell activity of the lymphocytes from the normal subjects, and these lymphocytes exhibited virus-specific killer cell activity without treatment. Interferon enhanced the NK cell activity of only one AIDS patient and failed to produce changes in virus-specific killer cells from any of the AIDS patients.

But exposure to interleukin-2 significantly enhanced both the NK cells and the virus-specific killer cell activity of the lymphocytes from all six AIDS patients. Thus, the laboratory study provides a basis for the initiation of human clinical trials for interleukin-2 in AIDS patients.
by Annabel Hecht

Every night before he went to bed grandpa would line up his drugs for the following day. There was the diuretic to reduce the accumulation of water in his tissues and the potassium supplement needed to replace that lost from the action of the diuretic. These tablets were to be dissolved in a glass of orange juice. Then there was digoxin to aid his ailing heart and another tablet to take when he felt faint. A minor tranquilizer helped him over bouts of anxiety. On top of it all were the antacids and laxatives he bought without prescriptions.

In his drug-taking habits grandpa was little different than most older Americans. The elderly—those 65 and over—constitute about 11 percent of the total population; yet they take about 25 percent of all drugs dispensed in the United States, both prescription and over-the-counter (OTC). It is the rare older patient who needs only one or two prescription drugs. For most, polypharmacy (a scientific way of saying "many drugs") is the rule, rather than the exception. A University of Florida College of Pharmacy survey, reported in 1980, found that elderly patients took an average of 8.4 drugs a month. Other studies have shown that older patients may be getting as many as 14 to 18 different drugs in the course of a year.

Nursing home patients have been reported to take as many as 20 to 30 drugs, giving credence to the charge that the elderly are overmedicated.

The reason why the elderly take so many drugs is not hard to understand. They are more likely than other age groups to have one or more chronic illnesses, including heart disease, high blood pressure, diabetes and arthritis. Few such diseases can be treated with just one drug. Medication for chronic ills usually must be taken over long periods, frequently for the rest of the patient’s life. Diuretics, drugs to treat high blood pressure, along with sedatives, hypnotics, tranquilizers, painkillers, laxatives, and drugs for heart conditions are the medications most frequently prescribed for the elderly.

The very fact that the elderly must take so many medications increases their chance of experiencing an adverse reaction—a chance three times greater than that of the younger patient. Such reactions may be severe enough to require hospitalization.

The reactions elderly patients may experience include stupor, confusion or even overexcitement from sedatives, intestinal bleeding from aspirin, lowered blood pressure from antipsychotics such as chlorpromazine (Thorazine), and fainting following use of antidepressants, diuretics, sedatives, tranquilizers, and some high blood pressure medications.

Taking many drugs also increases the potential for drug interactions. One drug can alter the effect of another, for instance, by speeding up or slowing down its metabolism in the liver. Two similar drugs taken together may produce an effect that is greater than would be expected. Such an effect is called potentiation.

The young as well as the old patient can experience adverse reactions, of course. The problems of the elderly, however, are compounded by the very process of growing old. With age there are certain physiological changes that can affect the way in which drugs behave in the body. In addition, such factors as diet, alcohol consumption, disease, weather conditions such as high heat and humidity, malnutrition, and even bed rest can alter the movement of drugs through the body.

Drugs usually enter the body by mouth or by injection. How well they will do their job depends first on how well they are absorbed. While there isn’t any clear evidence that age alone affects absorption, it has been suggested that decreased absorption might occur as a result of physiological changes such as decreased gastric acidity, a reduction in peristaltic activity (the wave-like contractions that move digested food through the intestines), a change in the time it takes food to leave the stomach, or a decreased intestinal blood flow.

Where age does make a difference is in drug distribution, the process by which drugs are delivered to various sites in the body. Drug distribution in the elderly is altered in part because of changes in the body’s composition. The total body water and lean body mass—essentially muscle and bone—decrease, while the proportion of fat increases even though there is no increase in total weight. This means that drugs normally distributed in lean body tissue, such as digoxin, will end up at higher concentrations in the
bloodstream. On the other hand, barbiturates (Nembutal and others), phenothiazines (Thorazine and others), and diazepam (Valium) are stored in fatty tissue. The increased fat in the elderly can serve as a reservoir for these drugs and prolong their "working" time.

Drug distribution also can be altered by age-related changes in the blood. Plasma proteins in the blood aid in transporting many drugs from the intestines throughout the body. A certain percentage of the drug is always bound (attached) to the protein. Only the unbound, or free, portion of the drug can work. Thus, binding is important in determining how much drug will be available to do its job. With age there is a decline in the amount of albumin, one of the blood proteins. Some drugs are highly bound to albumin, including the epilepsy drug Dilantin, Valium, and blood-thinning drugs (Dicumarol). A reduction in albumin will result in an increased amount of active drug, so what would normally be a therapeutic dose of the drug may prove to be a toxic one.

Still other problems may develop because drugs compete for these binding sites. When one drug is blocked at the binding site by a second drug, the amount of the first drug that is freely circulating increases, as does the potential for toxicity. For example, phenylbutazone, salicylates and sulfonamides can displace tolbutamide, leading to hypoglycemia (low blood sugar).

Metabolism is another function that changes with age. According to one expert, drug metabolism rates in the elderly are one-half to two-thirds the rates of middle-aged and younger patients.

Metabolism takes place primarily in the liver where drugs are changed into water-soluble form so they can be excreted. The capability of the liver to perform this vital function depends on blood flow to that organ. In the elderly this blood flow is decreased. Some drugs, including beta blockers, narcotics, nitrates, hydralazine and tricyclic antidepressants, pass through the liver before they reach the general circulation. Because of the reduced blood flow, smaller amounts of these drugs are metabolized and excreted. Consequently, the amount that enters the elderly person's system is higher than it should be.

Interactions of different drugs in the liver may cause still other problems for the elderly patient. One drug may stimulate the metabolism of another, thus decreasing its effectiveness. Phenobarbital has this effect on blood-thinning drugs. On the other hand, the antibiotic chloramphenicol slows the metabolism of these drugs, thereby increasing the magnitude and duration of their effects.

Finally, the body's processes for elimination of drugs can be impaired in the elderly because of changes that occur in the aging kidney, changes that are more dramatic than those in any other organ. The kidney becomes smaller, blood flow decreases, and the filtering capacity decreases. Such kidney impairment retards the elimination of water-soluble drugs such as digoxin, certain antibiotics, chlorpropamide, and hypotensive agents, leaving the elderly patient more prone to adverse drug reactions.

If this weren't enough, the elderly appear to be more sensitive to certain drugs. For instance, they seem to be more bothered by anticholinergic drugs—those that block the action of the sympathetic nervous system. These drugs can cause confusion, disorientation, hallucinations and delirium, as well as blurred vision, dry mouth, palpitations and constipation in the elderly. Some anticholinergics are medications for spastic colon, drugs for Parkinson's disease, some antihistamines, tricyclic antidepressants, and drugs to control irregular heartbeats.

Older patients seem to be more sensitive to Valium, thus requiring smaller doses than younger patients. Older patients may experience fainting and dizzy spells from drugs such as antidepressants that don't usually produce such effects in younger patients.

Nonprescription, or over-the-counter (OTC), drugs have a prominent place in the medicine cabinets of most elderly people. Analgesics (painkillers), antacids, cough and cold preparations, and laxatives are among the OTC drug products most frequently used by older people. While many people don't think of these as drugs, OTC drug products, too, can be the cause of adverse side effects in older patients.

Aspirin, for instance, can increase the effect of blood thinners and decrease sodium and chloride excretion—a matter of concern to those with congestive heart failure. Chronic use of aspirin may lead to iron deficiency anemia. Antacids can interfere with the absorption of some drugs, such as the antibiotic tetracycline, while chronic use of laxatives can lead to electrolyte and water balance disturbances.

While many elderly people may have some vitamin deficiencies, treatment with megadoses of vitamins is generally not recommended. One reason is their side effects. Too much vitamin C may raise uric acid levels and trigger gout in those disposed to this painful disease. Vitamin C can also cause false readings on certain urine tests essential to control diabetes. Too much vitamin A can be the cause of fatigue, malaise and lethargy.

It would seem that the best way to avoid adverse reactions in older patients is simply to reduce the amount and number of drugs they take. However, prescribing for the elderly, like life itself, is not simple. The changes that come with age often are gradual and patients, being individuals, do not necessarily age at the same rate. Drug manufacturers, for the most part, do not test their products in elderly patients, and there are no easy, clear-cut guidelines to determine how much or little of a drug a particular patient will need.

To solve some of these problems, FDA, encouraged by the American Association of Retired Persons and the National Institute on Aging, is looking into the development of guidelines for geriatric testing of drugs. The guidelines, which will not be binding on pharmaceutical manufacturers, will answer such questions as whether all new drugs will be covered or only those used to treat ailments most often seen in the elderly. The ethics of testing drugs in elderly people, who are more likely to have adverse reactions, also must be considered.

The British, too, are concerned about the problems of drugs and the elderly, according to Scrip, a British-based pharmaceutical newsletter. The Committee on Safety of Medicines, an advisory body to the UK Licensing Authority, has advised that product literature for drugs used to treat diseases of the elderly should contain specific advice on how to prescribe for the older patient.

Further, the committee said that in considering new drug applications the decision on whether to require studies specifically in elderly patients will be based on such factors as: how often the drug is likely to be used in the elderly, the difference between a safe dose and a toxic one, the route of elimination, possible drug interactions, and whether similar drugs have previously posed problems for the elderly.

Annabel Hecht is a member of FDA's publications staff.
Any Medicine Worth Taking
Is Worth Taking Correctly

"Compliance" is a bureaucratic sort of word, but when it is applied to taking medicine it becomes shorthand for "taking the right amount of medicine, in the right way, at the right time." Unfortunately, many elderly patients do not take their medicines as they should. Various studies of older patients indicate that 50 to 60 percent of them make medication errors or simply don't take their medicine at all.

Noncompliance extends to even younger groups. A recent nationwide survey conducted by the American Association of Retired Persons found that one-fifth of respondents over 55 did not take all the drugs prescribed for them, mainly because they felt they didn't need the drugs or just didn't like them.

The reasons older patients fail to take their medicines are a bit more complicated and involve a variety of physical, psychological, social and economic factors. Those who take a large number of drugs are most likely to have problems. The drugs themselves may look alike in size, shape and color. They frequently are taken in different doses at different times of the day—scheduling that would confuse even a younger patient. The number of drugs they take may be unnecessarily high because they have prescriptions from more than one doctor.

Impaired hearing and confusion may make it difficult for the elderly patient to comprehend oral instructions even when they are carefully explained. Impaired vision makes it hard to read drug labels and other patient information. Child-proof packaging can pose serious problems for those crippled with arthritis or other handicapping conditions.

Contrary to the popular belief that the vast number of "senior citizens" are being warehoused in institutions, only 5 percent are in hospitals or nursing homes. Actually, many older people are living alone, often in isolation with no one to turn to for help. Noncompliance is common among people who are socially isolated.

In addition, lack of transportation or fear of crime may even prevent some older people from getting out to a drugstore. The high cost of medications also stands in the way of full compliance. Elderly patients on limited incomes often delay having a prescription filled, or skip doses to make their medication go further.

Some of these compliance problems, though certainly not all, can be alleviated simply by making sure elderly patients are fully informed about all the medications they are taking. Here are some suggestions for older patients and their families, or those who are caring for the elderly, to help them use their medicines wisely.

- Always tell the doctor exactly what prescription and nonprescription drugs are being taken. This is especially important the first time the doctor is consulted.
- Be sure to tell the doctor about any problems that have occurred with particular drugs—dizziness, rashes, indigestion.
- If any new drugs are prescribed, ask what they are for and how they should be taken. Get the information in writing. Keep a list of all drugs prescribed, the name of the doctor, the date they were prescribed, and any special instructions for their use.
- Be sure to ask about side effects that might occur, special rules for storage, and food and beverages that should be avoided. The doctor may have some printed information that will give more details about the drug and what it will and will not do.
- Always call the doctor promptly if unusual reactions occur. If any drug seems to be doing more harm than good, the doctor should be consulted. He or she can then decide whether another drug will be just as effective.
- If tablets or capsules are hard to swallow, ask if the drug comes in a liquid form.
- When the prescription is filled, ask the pharmacist to label the drug container in large, clear letters giving the name of the drug and what it is to be used for.
- If child-proof caps are hard to open, ask for an easy-to-open container. But then be sure to keep all medicines out of the reach of children.
- Do not take a drug in the dark. Always have plenty of light to be sure the right medicine is being taken. If you use reading glasses, make sure you are wearing them.
- To avoid taking the wrong drug, never keep drugs on a bedside table, except those for emergency use, such as nitroglycerin.
- To help keep track of the different medicines being taken, draw up a chart or calendar showing the name of the drugs and the time of day they are to be taken. Include any special instructions. Space can be provided to check off when the dose has been taken. The National Institute on Drug Abuse has a publication to help older Americans use their medicines wisely. This kit contains a number of suggestions on how to keep track of medicines. The kit can be obtained by writing to Elder-Ed, P. O. Box 416, Kensington, Md. 20740.
An expert panel of physicians convened by FDA has decided that routine chest X-ray screening examinations are of little use and recommends that they be discontinued in most instances.

The panel said that "the yield of unsuspected disease" found through such examinations is of too little clinical value to justify the cost, the additional exposure to radiation, and the inconvenience to the subjects.

The panel noted that such X-ray examinations are not based on medical history, physical examination, or specific diagnostic testing. Instead, they have been done routinely to find unsuspected disease conditions in a few individuals, and then to refer these people to clinics or physicians for diagnosis and treatment. But in the rooting out of these few cases, many other people are exposed to radiation, plus inconvenience, without a counterbalancing health benefit.

Chest X-ray screening also adds greatly to the nation's medical expenses, since almost half of all X-ray examinations involve the chest. The annual cost for chest X-rays is more than $2 billion.

Routine chest X-rays traditionally have been made to uncover unsuspected diseases (tuberculosis, lung cancer, heart conditions) in apparently well persons. Such early detection, it was thought, would increase the cure rate for the diseases detected, avoid prolonged and expensive medical care, reduce the spread of disease, and generally improve the health of society.

But the panel of experts found that these were faulty assumptions. The yield of unsuspected chest diseases has been small. The panel concluded that "routine radiography in the general population is unproductive, and of
little value to the patient.’’ The panel issued five guidelines that are, in effect, recommendations on chest X-ray screening examination.

Following are excerpts from those five guidelines:

- All mandated (required) routine screening of unselected populations should be discontinued, unless a significant yield can be shown.
- All routine prenatal screening examinations for the detection of unsuspected disease should be discontinued.
- Routine chest X-rays should not be required solely because of admission to a hospital.
- Mandatory chest X-ray examinations for employment, repeated chest X-ray examinations upon admission to a long-term facility (nursing home or chronic disease hospital), repeated chest X-ray examinations of tuberculosis reactors (persons showing positive tuberculin skin tests), repeated chest X-ray examinations of asymptomatic tuberculosis patients (those with no symptoms) who have completed therapy, and routine periodic chest X-ray examinations during tuberculosis treatment all have been shown to be of insufficient clinical value to justify continued use.
- Routine nonselective pre-employment chest X-ray examinations and periodic examinations unrelated to job exposure should be discontinued.

The complete text of the referral criteria and rationale for their development is contained in a report titled “The Selection of Patients for X-Ray Examinations: Chest X-Ray Screening Examinations.” The report can be purchased from the Government Printing Office as GPO Publication 017-015-00210-1.

Panel recommendations did not cover instances where a physician examining an individual decides that a chest X-ray is necessary. The panel therefore emphasized that these recommendations do not preclude chest X-ray examinations based on individual history, physical examination, or specific diagnostic testing, or in selected populations known to have significant yields of previously undiagnosed disease.

Routine X-ray screening can be traced to the historic acceptance of X-ray examinations as good public health practice. In past years, mobile vans were sent into neighborhoods by city and state health departments, backed by publicity campaigns and often funded by federal or local government agencies. Public health clinics included chest X-rays as part of the examination of all patients coming into the clinic.

For example, until 1972 the New York City health code required chest X-rays for detection of tuberculosis of all food preparation workers, persons working in maternity and newborn services, pregnant women, and city parks department and school system employees. That requirement ended when tuberculosis ceased being a major public health threat.

But these were good faith programs. Given the knowledge of the times, they seemed justified. Parts of some cities did have high rates of tuberculosis, and X-ray screening was an accepted part of disease control. As other diagnostic techniques appeared, as more was learned about the hazards of radiation, and as the health of the American public improved, the rationale for mass screening was weakened. The findings of the panel report indicate that rationale has largely disappeared.

Chest X-rays are one of the most frequently performed procedures in occupational medicine. They are included in employee health appraisals, in screening persons who work with pulmonary irritants and carcinogens, in checking the health of job applicants, and in job placement. Yet, there has been little published data on their value in the work setting. In this area, the panel urged that chest X-rays be based on a job applicant’s clinical examination, occupational and medical history, and proposed work assignment.

The panel noted that even if chest X-rays are no longer required upon admission to a hospital, it is likely that patients who need them will be given them as part of the evaluation of their illness. The difference is that the X-ray then is done for a medical reason and not routinely. To avoid exposing a fetus to radiation, the panel suggested that the tuberculin skin test, known to be effective and without risk, be substituted for chest X-rays in examination of pregnant women.

The review panel was established following a 1978 national conference on X-ray usage. The conference recommended that physician panels be formed to consider particular issues in radiology. FDA’s National Center for Devices and Radiological Health was designated as the convener. A report on pelvimetry, an X-ray examination often performed on pregnant women in labor, was previously issued by the center. (See “X-rays For Childbirth: Risky, Costly, Not Always Helpful” in the February 1982 FDA Consumer.)

The chest X-ray panel included specialists in radiology, internal medicine, epidemiology, thoracic medicine, occupational medicine, and family practice. The panel held meetings between 1979 and 1981, and its members received advice from experts outside the panel itself.

Panel findings were reviewed by 19 medical organizations having an interest and role in chest X-ray examinations. They included the American Academy of Family Physicians, the American College of Radiology, the American Thoracic Society, the American Occupational Medicine Association, and the American College of Obstetricians and Gynecologists. The organizations called the panel findings “eminently sensible.” The groups endorsed the findings that related to their interest, and the endorsements were then compiled as the panel’s overall recommendations. Some health insurance programs have begun disallowing payment for chest X-ray examinations done on admission to a hospital unless ordered by a physician. And the American Cancer Society has stopped recommending annual chest X-rays on persons who have no symptoms of disease. There has been no statistical improvement in cancer detection or mortality that can be credited to routine screening, the society said.

The panel’s guidelines on chest X-rays do not apply to patients being seen by a physician for specific signs or symptoms, nor to those seen for a complete health examination. They also do not apply to groups known to be susceptible to certain chest or respiratory diseases, such as immigrants from Southeast Asia, who have high levels of tuberculosis. Periodic chest X-rays are also considered beneficial for miners, asbestos workers, and others whose jobs carry certain kinds of risk.

Richard C. Thompson is a member of FDA’s publications staff.
The Notebook: a potpourri of items gathered from FDA news releases, the Federal Register and other sources. The Federal Register (designated FR, with date of publication) is available in many public libraries.

- Ernest T. Krebs Jr., champion of laetrile, and his assistant, Malvina Cassesse, started serving six-month jail sentences in San Francisco County Jail in May. The pair were jailed for violating the terms of probation, which prohibited them from promoting laetrile as an alleviation or cure for cancer. The probation was imposed after a 1973 conviction for violating anti-quackery laws and for practicing medicine without a license.

- In England, the UK Licensing Authority has proposed limiting the availability of products containing amygdalin (e.g., laetrile), according to Scrip, an international pharmaceutical newsletter.

- All Sereine brand solutions for hard contact lenses were recalled in late May because some lots of the product had been found to be non-sterile. Recalled by the manufacturer, Optikem International, Denver, Colo., were Sereine Cleaner, Sereine Soaking and Cleaning Solution, Sereine Wetting Solution, and Sereine Wetting and Soaking Solution.

- There is no truth to reports that people who wear contact lenses can go blind or that the lenses can become permanently fused to the corneas of the eyes from looking at bright flashes of light such as those from an arc welder. The origins of the story have been traced to a 1977 report in the British Medical Journal of a welder who had witnessed an explosion of an electrical switch box and later was treated for a corneal ulcer after wearing his contact lenses for too long. The electrical flash played no part in the eye injury.

- AGREEMENTS: FDA, the Animal and Plant Health Inspection Service of USDA, and the National Institutes of Health, each of which has authority for fostering proper animal care and welfare procedures in lab tests that use animals, have signed an agreement to share information about the care of laboratory animals. Each agency has named a liaison officer to serve on a standing committee that will, among other tasks, deal with specific cases of serious noncompliance (FR June 3).

- FDA and the Environmental Protection Agency have signed an agreement coordinating regulation of drug/pesticide products for use on or in animals. The agreement clarifies existing responsibilities and shifts a small group of products from primary EPA jurisdiction to regulation solely by FDA (FR May 20).

- The World Health Organization has asked for information on the abuse and medical usefulness of 12 benzodiazipine, or “minor tranquilizer,” drugs to be used in considering international restrictions. The 12 are clorazepate, delorazepam, ethyl loflazepate, etifoxine, haloxazolam, loprazolam, lorazepam, pirenzepine, propizepine, tizabionium, tofisopam and zopiclone (FR May 27).

- OTC DRUGS: A 50-percent aqueous emulsion of corn oil is a safe and effective ingredient in cholecystokinetic drug products for use in diagnostic gallbladder studies, FDA said in its final monograph on this class of OTC drug products. The monograph, or standard, became effective June 11.

At the same time, the agency, in a tentative final monograph, said there are no effective OTC oral insect repellents that humans can take. If this proposed finding is adopted, such products will be eliminated from the OTC market six months after publication of a final rule. Both conclusions were based on the recommendations of the Advisory Review Panel on OTC Miscellaneous Internal Drug Products, one of 17 panels set up to evaluate ingredients in all OTC products (FR June 10).

- ALL ABOUT FOOD: A 1975 proposal that would have established provisions for nutrition labeling of fresh fruits and vegetables has been withdrawn by FDA because such labeling would be too costly (FR June 14).

The Federal Trade Commission has decided to terminate its trade regulation rule that would have regulated energy and weight control claims, fatty acid and cholesterol claims, and “natural food” claims in food advertising. Areas that would have been covered will continue to be scrutinized on a case-by-case basis (FR May 24).

Treasury’s Bureau of Alcohol, Tobacco and Firearms is taking another look at prior decisions concerning ingredient labeling on wine, distilled spirits, and malt beverages. In February, the United States District Court for the District of Columbia set aside the Treasury Department’s decision to repeal ingredient labeling for alcoholic beverages. Comments have been requested about the bureau’s option to manufacturers of giving consumers an address to write for ingredient information, about label disclosure when FD&C Yellow No. 5 is used, and the lead time required if the ingredient labeling rules are not rescinded (FR June 17).

A temporary permit has been issued to Ralston Purina Co., St. Louis, Mo., to market-test canned tuna in water seasoned with vegetable oil (FR June 7).
Updates

Whooping Cough Increase

A whopping 79 cases of whooping cough (pertussis) were reported in Maryland in 1982, a marked increase from the 1 to 18 cases reported annually during the previous 10 years. Maryland's experience, as well as that of the United States from 1979 to 1981, clearly indicates that whooping cough is still a serious illness in young children, according to the federal Centers for Disease Control.

The Maryland victims ranged in age from 7 weeks to 23 years. Fifty-seven percent of all patients and 68 percent of those less than 1 year were hospitalized. The average hospital stay was 8.6 days. While no deaths occurred, two of the infants developed seizures, and one developed brain inflammation.

Sixty-one percent of the patients 6 months and older had not received three doses of DTP (diphtheria-typhoid-pertussis) vaccine and can be said to have had potentially vaccine-preventable cases, CDC said in the June 17 Morbidity and Mortality Weekly Report. The report also noted that following a television presentation on pertussis vaccine side effects, DTP vaccine sales by one pharmaceutical company to doctors in Maryland decreased 45 percent in April, compared to the average monthly sales for the preceding three months. At the same time, sales of vaccine without the pertussis component increased.

The response of FDA Commissioner Arthur Hull Hayes Jr. to the television program on pertussis vaccine was printed in the July-August 1982 issue of FDA Consumer.

AFP Kits Unblocked

FDA has withdrawn a 1980 proposed rule that would have restricted the sale, distribution and use of alpha-fetoprotein (AFP) test kits for detection of spinal cord defects in unborn children. In withdrawing the proposal, the agency said such restrictions were not necessary to ensure the safe and effective use of the test kits. Four manufacturers have been informed that their test kits are “approvable” for sale to laboratories and medical personnel.

The AFP test measures the amount of the alpha-fetoprotein in the blood serum and amniotic fluid of pregnant women. This protein is shed in larger quantity by the fetus under certain circumstances. A positive result can mean exposed spinal cord problems such as spina bifida, a maldevelopment of the spinal column and/or spinal cord resulting in mild to severe disability. The test also may be positive in the case of twins or triplets, a threatened miscarriage, or a pregnancy that is further along than believed.

For approval of the test kits, manufacturers will be required to provide explanatory brochures for women undergoing the AFP test to explain the test’s limitations and tell what further tests, such as ultrasound or amniocentesis (an examination of a small amount of amniotic fluid), are needed to confirm any defects if a positive reading is made.

In addition, manufacturers will be required to follow at least 1,000 patients at each of five medical centers and report to FDA the results of the AFP and follow-up tests.

The four manufacturers are Wampole Laboratories, Cranbury, N.J.; Amersham Corp., Arlington Heights, Ill.; Abbott Laboratories, Chicago, Ill.; and Kallestad Laboratories, Austin, Texas. FDA’s withdrawal of the earlier proposal was published in the June 17 Federal Register. What the AFP test is all about was explained in “AFP: Sometimes An Ominous Clue,” in the April 1980 FDA Consumer.

AFP test kits are being studied as an aid in the diagnosis and management of certain kinds of tumors. This is separate from the use in pregnancy and is not affected by the June 17 action.

Bendectin Withdrawn

Worldwide production of Bendectin, the only drug approved for morning sickness in the United States, was ended June 9 by its manufacturer, Merrell Dow of Cincinnati. The decision was an independent one.

The firm took the action 13 days after a Washington, D.C., court jury awarded $750,000 to the family of a girl born with serious deformities of the right arm and hand after her mother had taken the drug. The company faces about 300 other lawsuits in federal and state courts.

In 1980, FDA and its Fertility and Maternal Health Drugs Advisory Committee carried out a review of scientific information about Bendectin’s safety, particularly its possible association with birth defects in the offspring of women who took it during pregnancy. The committee said existing data did not demonstrate such an association, but that two of the studies raised “residual uncertainty” that merited further study.

On the basis of an advisory committee recommendation, FDA called for patient information stressing that Bendectin be used only to treat significant nausea and vomiting that would not respond to more conservative treatment, such as eating crackers and drinking warm fluids.

Hair Fibers Banned

The sale of artificial hair fibers for scalp implantation was banned by FDA, effective June 3. In announcing the ban, the agency said no currently available type of hair fibers or synthetic hair-
implanting technique is safe or effective.

The ban applies to fibers of such synthetic materials as polyester, modacrylic and polyacrylic and also to some natural materials, such as human hair processed for hair implantation on another head. It does not apply to natural hair transplants in which a person’s own scalp hair and surrounding tissue are grafted on another part of the scalp.

The technique covered by the ban usually consisted of implanting hundreds to thousands of synthetic fibers in the scalp; it cost thousands of dollars, took two or three days, and was usually not done by physicians. Contrary to advertising claims, the fibers were not effective either in simulating natural hair or concealing baldness.

Within a short time after implantation, the fibers usually fell out, broke off, or were rejected by the body.

From December 1978 through February 1981, FDA received 166 complaints about the fibers and the Federal Trade Commission received 181. These included cases of infection, facial swelling, severe pain, scarring, and permanent loss of remaining real hair. Many cases required extensive medical and surgical treatment. In seven cases, surgical removal of portions of the scalp was necessary. In 21 cases, the fibers could not be removed and the patients’ scalps remained disfigured.

In March 1979, FDA issued a public warning about the implants. The October issue of FDA Consumer in that year also contained an article on the dangers of artificial hair implants.

At present, FDA is not aware of any person distributing synthetic hair fibers. If safe fibers are developed in the future, manufacturers could apply to FDA, and the ban would not preclude their approval.

**New Sunlamp Proposals**

FDA is proposing to amend its current standard for sunlamps to include lamps that emit ultraviolet-A (UVA) radiation.

In recent years, there has been a growth of commercial tanning facilities, 75 percent of which, by FDA estimates, use lamps that emit mostly UVA radiation. Because UVA radiation does not burn the skin under normal use, these new lamps are mistakenly being called “safer” than traditional sunlamps that emit ultraviolet-B (UVB) radiation.

But UVA exposures are not without hazards. Large doses of UVA, as much as 1,000 times more than with UVB radiation, are needed to produce a visible tan. Thus, the user is exposed to longer periods of radiation. UVA rays penetrate more deeply into the skin and can damage the fiber that normally keeps the skin resilient. UVA also may contribute to skin cancer. In addition, certain medications and cosmetics may increase a person’s sensitivity to UVA and, as with UVB, the rays could increase the risk of cataracts if absorbed by the lens of the eye.

FDA believes its current standard, in place since 1980, should apply to all sunlamp devices equally—UVA and UVB, home sunlamps, and those in commercial facilities. The proposed standard would still require each unit to be equipped with a timer that would automatically turn the lamp off after a certain maximum exposure time and a manual switch so the lamp can be turned off by the user at any time. The timer requirement would be changed to reflect the longer exposure times used with UVA lamps. In addition, goggles would be required to protect the eyes from the more penetrating UVA radiation as well as UVB rays.

FDA is also proposing a more explicit warning label that reads:

“DANGER—Ultraviolet radiation. Follow instructions. Avoid overexposure. As with natural sunlight, overexposure can cause eye and skin injury and allergic reactions. Repeated exposure may cause premature aging of the skin and skin cancer. FAILURE TO USE PROTECTIVE EYEWEAR MAY RESULT IN SEVERE BURNS OR LONG-TERM INJURY TO THE EYES. Medications or cosmetics may increase your sensitivity to the ultraviolet radiation. Consult physician before using sunlamp if you are using medications or have a history of skin problems or believe yourself especially sensitive to sunlight. If you do not tan in the sun, you are unlikely to tan from the use of this product.”

The proposed standards were the result of almost two years of work with sunlamp manufacturers, professional associations, consumer groups and other government agencies. They were published in the May 20 Federal Register.

**Pergonal Leads To Quinits**

Quintuplets were born June 21 to Pamela Pisner of Olney, Md., who had been treated with the infertility drug Pergonal. The circumstances that led to her treatment with the drug were described in a piece accompanying the article “Infertility, And How It’s Treated” in the June 1983 FDA Consumer. This magazine had an inside track on the story as Mrs. Pisner is a secretary in FDA’s Office of Health Affairs.

**Warning About Beds**

Electrically powered beds with automatic switches should be removed from high-risk areas such as pediatric and psychiatric wards. FDA has told hospitals and state health departments. In a letter mailed June 24, the agency said a hazard may be posed by such beds when young patients play with the controls to see the beds work. The Canadian government also has notified hospitals in Canada of the problem. Three children have been crushed to death in hospital accidents involving electrically powered beds since early 1982. In each case the child was caught...
between the stationary part of the bed and its moving frame after activating the switch that lowers the bed from the chest-high, or examining, position to the normal height.

The first accident occurred in January 1982 at Zeeland Community Hospital, near Grand Rapids, Mich., when a 3-year-old girl was caught in the bed framework while allegedly playing with the bed's controls and watching the bed work. The bed was an electrically powered model 840 made by Hil-Rom Manufacturing Co., Batesville, Ind. The model is equipped with a "walk-away-down" switch that allows nurses to walk away from the bed after tripping the switch without having to wait until the bed moves to the down position. This control had been promoted as a safety feature in the past because a fully lowered bed lessens the severity of a patient fall. In this model, the bed is raised and lowered by a scissorslike action of the metal underparts. The fatalities resulted when the youngsters were caught in these metal parts.

In October 1982, a 6-year-old boy was killed in Toronto, Canada, when caught in a bed made by Dominion Metalware Industries Ltd., a firm owned by Hil-Rom Manufacturing. On April 17, 1983, an 11-year-old boy was killed at Christ Hospital in Oak Lawn, Ill., also in a Hil-Rom model 840.

In its June letter, FDA said that nurses and other hospital personnel should be made aware of the potential for accidents with electrically powered beds. Hospitals have been asked to report injuries or other experiences with the beds to the Product Problem Reporting Program, U.S. Pharmacopeia, 12601 Twinbrook Parkway, Rockville, Md. 20852.

Hil-Rom Manufacturing Co. has also notified hospitals about the deaths and said the "walk-away-down" feature will be offered only as a special order option from now on.

Reprints Available

Reprints are available of three articles that appeared in the June 1983 issue of FDA Consumer. The articles "Doing Something About Menstrual Discomforts" and "Infertility, And How It's Treated" can be obtained in single copies by writing to the Consumer Information Center, Dept. J., Pueblo, Colo. 81009. "Food Fit For A Fido" can be obtained in single copies from the Food and Drug Administration, HFE-88, 5600 Fishers Lane, Rockville, Md. 20857. Multiple copies of all three articles 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.

Aspartame For Soda

Aspartame, the newest low-calorie sweetener, has been approved for use in carbonated beverages. Approval was announced by FDA July 1.

Aspartame, developed by G.D. Searle Co., Skokie, Ill., was approved in 1981 for use as a tablet for hot beverages and for use in cold cereals; as a dry-base sweetener for powdered beverages, instant coffee and tea, gelatins, puddings, fillings and dessert toppings; and as a flavoring agent in chewing gum.

Searle did not seek approval for use in carbonated beverages initially because the chemical tended to break down through prolonged contact with water. The company sought approval for beverage use in August 1982. An extensive evaluation of that petition by FDA showed the company had resolved technical problems that prevented the use of aspartame in a liquid medium.

Money For 'Orphan' Products

Approximately 15 to 30 grants, ranging from $20,000 to $70,000, will be awarded by FDA this year to support clinical trials on the safety and effectiveness of "orphan" products. Orphan products are drugs, biologics, medical devices (including laboratory diagnostics), foods for medical purposes, and veterinary products that are useful in treating rare disease but lack commercial sponsorship.

The grants are available to any public or private, profit or nonprofit organization, including state and local governments. Because funds are limited, large research projects involving many patients and long-term follow-up aren't being considered. The typical study to be considered for support may involve up to several dozen patients and will be directed to providing substantial evidence of the product's safety and effectiveness.

Reporting Device Problems

Manufacturers and importers of medical devices will be required to report to FDA all deaths or serious injuries associated with their products under regulations proposed by FDA. Published in the May 27 Federal Register, the proposal would also require reporting of any device malfunctions which, if they recurred, would be likely to cause or contribute to death or serious injury.

The proposed regulation is a substitute for a November 1980 proposal that would have required reports by distributors of the devices as well as by the manufacturers and importers. The earlier proposal would have required reports on devices that "may have caused" a death or injury or that "may have a deficiency that could result" in a death or injury.

The new proposal is narrower in that reports are required whenever the manufacturer or importer has information that "reasonably suggests or a person alleges and the manufacturer or importer is aware of the allegation" that a device has caused or contributed to a death or serious injury.
The diet aid business is as sensitive as a seismograph. The slightest bit of adverse publicity concerning its products can send tremors throughout this $200 million-plus industry. A real shock wave—such as the widely published accounts of deaths ascribed to liquid protein diet products—can wipe out some segments of it.

So it is not surprising that an article appearing on Feb. 4, 1983, in the Star Free Press (Ventura, Calif.) about a court settlement between the nation's largest manufacturer of lucrative over-the-counter diet drugs and the state of California did not tell the whole story.

The article did report that Thompson Medical Inc. of New York had agreed to revamp the advertising of its appetite suppressants containing phenylpropanolamine (PPA) to comply with an order handed down by Judge William Peck of the California Superior Court. The article said that the firm was ordered to state in its advertisements—when it used testimonials of persons who had lost a great deal of weight—that the weight losses cited might not be typical of losses for all persons using the product. Advertisements also would be required to state that weight-loss figures in controlled scientific studies averaged only one pound per week and that to lose weight, one had to eat less. (On April 26, Thompson announced that all the changes required by the California court would be made nationwide.)

The article also disclosed that the judge had ordered Thompson to pay $145,000 in fines—$80,000 in a rather unusual grant to the Ventura County Public Health Services Department, and the rest in court costs and civil penalties.

A California consumer group spotted the article and, suspecting that there was more to the agreement than met the eye, alerted a sister consumer advocacy group in Washington, D.C., the Center for Science in the Public Interest. As a result, the center submitted a freedom of information request to the state of California, asking for a copy of the agreement and of any correspondence between Thompson and California's Consumer Protection Unit, also called the fraud unit.

The response to the freedom of information request confirmed that the terms of the agreement were substantially what appeared in the newspaper article. It also brought to light a Feb. 10 letter, from the chairman of the board of the Thompson firm to the Ventura County district attorney, in which the firm made further concessions.

In return for an end to litigation, Thompson agreed in the letter to stop advertising that its PPA-based diet pills were safe unless it also advised consumers with high blood pressure and other health problems to consult their physicians before taking the pills; Thompson also agreed not to claim that the drugs had been endorsed as safe and effective by a U.S. government advisory panel until FDA published a final regulation; the firm also promised not to claim that the products contained no stimulants. The products involved included Dextrim, Prolamine, Appedrine and Control.

Although a 1978 report by FDA's advisory review panel on OTC drug products had recommended that diet aids containing PPA be considered both safe and effective, many medical experts have disagreed. FDA is under no obligation to follow the recommendations of its advisory panels and the agency is concerned that the panel has recommended a higher dosage of PPA than has previously been marketed over-the-counter. (See "Experts Weigh Reducing Potions" in the October 1979 FDA Consumer.)

About one-third of obese persons have high blood pressure or associated cardiovascular ailments that may be dangerously aggravated by PPA. Misuse and abuse of drug products containing PPA accounted for 10,000 cases reported by poison control centers and 1,000 emergency room visits in 1980.

For these and other reasons, the Center for Science in the Public Interest has urged FDA to complete its review of OTC weight-control drugs, saying it believes that until the final regulation is issued, manufacturers of PPA-based diet drugs will be able to promote their products with impunity. The group maintains that these drugs are no more than minimally effective and should be distributed, if at all, as prescription drugs.

Evelyn Zamula is a member of FDA's publications staff.
Malodorous Painkiller

The smell of mothballs might evoke the feel of soft fur or scratchy woolens. But it’s not a smell people are likely to associate with opening a bottle of pills—which is why a Cincinnati woman became concerned when her bottle of Midol, a drug used to relieve menstrual pain, exuded a strong odor of mothballs.

She brought the bottle to FDA’s Cincinnati district office, where laboratory analysis revealed that the product contained naphthalene. Naphthalene has toxic properties and is one of the main ingredients in mothballs.

An inspection at the manufacturing plant failed to find any clues to the cause of the product’s abnormal odor. However, when district investigators checked the drug warehouse where the product had been stored—Kauffman-Lattimer Co. in Columbus, Ohio—they found that a supply of mothballs had been stored near the drug.

Kauffman-Lattimer withdrew all lots of 30-count capsule bottles of Midol distributed during a six-month period. This included some 2,600 bottles that had been shipped to Ohio, northern Kentucky, eastern New York, and Pennsylvania. Other health-care products that had been stored in the same warehouse area at that time were analyzed but none contained naphthalene.

Don’t Bank On It

Dr. M. Figuero Centro de Salud, a blood bank center in Arecibo, Puerto Rico, has decided to close down rather than comply with FDA’s regulations for blood and blood products.

Citing a lack of funds to make corrective actions, the center’s medical director, Dr. Sigfried Aguilor Llanes, made the decision after he was issued a regulatory letter from FDA’s San Juan district office following a July 1982 inspection of the center.

The district’s inspection records show a history of violations of good manufacturing practice regulations and a continued regression of the center since it was initially inspected in 1977. In 1979 and 1980, the center was issued a notice of adverse findings following inspections, and on both occasions the director failed to respond or take corrective actions.

In the 1982 inspection that led to issuance of the regulatory letter, the conditions found included: the center’s use of blood bag collection sets with use date expired (sets contain anticoagulants subject to deterioration and must be used before a specified cutoff date); lack of privacy for medical history interviews; unclean premises and unscreened windows and doors; no procedure for identifying previously rejected donors; equipment not calibrated daily according to FDA regulations; and personnel unfamiliar with current blood bank regulations.

When the blood bank did not respond to the regulatory letter, the district conducted a follow-up inspection. Asked why he failed to respond to the letter, the director informed the investigator he had decided to close the center.

The investigator’s findings were re-
ported to the Puerto Rico Department of Health, which rescinded the center’s local license until the required corrections are made. There is another blood bank for the 120,000 residents of the town of Arecibo at the regional medical center and it is currently in compliance.

**X-Ray Violations**

Six violations of the federal X-ray safety performance standards plus an unusually high noncompliance rate cost a Massachusetts firm and its district service manager a total of $10,000 in fines early this year. CGR Medical Corp., a Needham Heights firm that installs and services diagnostic X-ray equipment throughout the New England area, and David P. Horgan, the firm’s district service manager for New England, were fined the $10,000 by the U.S. District Court of Massachusetts because the firm certified that X-ray equipment it had installed met federal standards when, in fact, it did not.

The action resulted from inspections made by FDA’s **Boston district** investigators and Massachusetts radiation control inspectors over four years, beginning in 1979. In February of that year a Massachusetts radiation control inspector visited Cooley-Dickinson Hospital, Northampton, Mass., to determine if equipment installed two months earlier by CGR met the performance standard that prescribes the maximum amount of radiation X-ray equipment may emit, among other safety features.

The inspector found that the fluoroscopic collimator—a device that controls the size of the X-ray beam—permitted a beam that was too large. As a result, patients could have been subjected to more radiation than was intended or was necessary for diagnosis. This also could have exposed critical organs not intended to be exposed.

FDA field testing of X-ray units installed by CGR in June 1979 at a Westfield, Mass., hospital revealed that the light field localizer—the system that aims the X-ray source at the patient and defines the area of the body to be exposed—was putting out only half as much light as required, 7 foot candles instead of 15. When the light is not bright enough, the operator must make the X-ray beam wider than normal to assure adequate exposure. Again, this exposes areas of the body not intended to be included.

FDA inspection of two other facilities in 1979 revealed similar defects. CGR was notified and advised to correct them. The firm submitted reports from service engineers certifying that all the defects had been corrected.

As a result of these developments and a finding that 39 percent of the firm’s 28 installations made from December 1978 through February 1980 were out of compliance, a complaint for civil penalties was filed against CGR at FDA’s request. Two more violations, uncovered in 1980 and 1981 while the case was pending, were included. The firm was fined $1,000 for each of the six violations and the district service manager was fined an additional $4,000.
On Being A Cosmetic

Paula Payne Products Co., a manufacturer of cosmetics in Charlotte, N.C., said its skin cream was a cosmetic. But FDA said it was a drug, and an illegal one at that.

What made "Soft Secret Skin Softener and Moisturizer" a drug was the presence of hydrocortisone acetate, an ingredient approved by FDA for use in drugs to treat minor skin irritations and itching. Hydrocortisone and hydrocortisone acetate have been marketed as prescription drugs since 1952 to treat skin conditions, and FDA recently agreed that these ingredients could be marketed in nonprescription form as single ingredients and at low concentrations. Neither hydrocortisone nor hydrocortisone acetate is permitted in cosmetics, however.

The company could sell the product only as a drug but the firm had not registered with FDA as a drug manufacturer and was not selling it as a drug. The product also contained several active ingredients, and hydrocortisone acetate has not been approved for nonprescription use in combination with other active ingredients.

An investigator from FDA’s Atlanta district discovered the problem during a routine inspection of the firm. The district sent the firm a regulatory letter explaining the problem and requesting that the violation cease. As a result, the company destroyed its remaining inventory of the product—32,000 one-ounce tubes and 3,463 12-ounce bottles, valued at approximately $30,000. The company then reformulated the product, omitting the hydrocortisone acetate.

Blood Bank Fails

Don’t go searching for Antibody Search of Florida. The firm is no more. It has admitted to FDA that it repeatedly violated federal regulations for blood bank operation and that it attempted to conceal these violations. The firm agreed with FDA that its license should be revoked.

Antibody Search operated a plasmapheresis center in Jacksonville, taking blood from paid donors, removing the plasma, then returning the blood to the donors. This “source plasma” was sold to pharmaceutical companies who had contracts with the firm, for use in drug manufacturing and research. The donors returned every few weeks to sell their plasma again.

Federal regulations are strict as to how these centers must operate. The staff must be qualified, the facility properly equipped, records properly kept, and procedures for taking blood carefully followed. Antibody Search failed in all of these requirements when it was last inspected by FDA’s Orlando district office. The agency moved to close down the center.

The firm had been found deficient in earlier FDA inspections, especially in its newly hired manager’s qualifications to direct such an operation. Company officials had promised to bring the center into compliance, but these promises, set against a history of failed inspections and attempts to conceal violations, were unconvincing. They had shown, said FDA, “a willful disregard for the conditions of licensure.”

The agency decided to revoke the center’s license and published this decision April 26 in the Federal Register. The firm waived its right to a hearing and asked that its establishment and product licenses be revoked. FDA obliged.

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

With this issue, FDA Consumer is returning the Notices of Judgment to the magazine under the heading Summaries of Court Actions. However, the items will no longer include portions of court opinions. Court opinions are published by either the West Publishing Company or the Commerce Clearing House Inc., which will also carry full texts of injunction opinions, temporary restraining orders (TROs), and any subsequent actions on TROs. Those texts can be obtained from Commerce Clearing House at 1301 Pennsylvania Ave., N.W., Washington, D.C. 20004. Future notices printed in the magazine will be indexed in the magazine’s annual index. These changes are being made to devote more space in FDA Consumer to regular editorial matter. As a result of the change, the magazine will have at least one more feature article than when opinions were being carried. All items that have been withheld since the last Notices of Judgment (in the March 1983 issue) will be carried in upcoming issues. When that backlog is cleared up, the items will appear in a standard, easier-to-read format.

SEIZURE ACTIONS

FOOD/Poisonous and Deleterious Substance

Charged 8-13-82: when returned from Fort Worth, Texas, after shipment by Farmers Cooperative Association, Okarche, Okla., the article contained a pesticide chemical (a mercurial compound) and no tolerance or exemption from a tolerance for such pesticide chemical in wheat had been prescribed; 402(a)(2)(B). Consent decree authorized release to the shipper for salvaging. (F.D.C. No. 63763; S. No. 82–210–548; N.J. No. 1)

FOOD/Contamination, Spoilage, Insanitary Handling

Mole en pasta, at Dallas, N. Dist. Texas.
Charged 6-14-82: when shipped from outside the state of Texas, the mole en pasta, labeled in part “Mole en Pasta... Hecho en Mexico por: Productos Dona Maria, S.A.,” contained insect and rodent filth—402(a)(3); and required label information was not in such terms as to render it likely to be read and understood, since such information was in Spanish rather than in English—403(f). Default decree ordered destruction. (F.D.C. No. 63682; S. No. 82–265–655; N.J. No. 3)

Mole en pasta, corn husks, and Mexican sauces in cans, bottles and jars, at Dallas, N. Dist. Texas.
Charged 6-14-82: when shipped from outside the state of Texas, the mole en pasta, labeled in part “Mole en pasta... Hecho en Mexico por productos Dona Maria, S.A.,” contained insect and rodent filth—402(a)(3); the corn husks, labeled in part “Industrializadora de Hoja de Maiz para Tamales del Llano... Ahuacatlan, Nayarit, Mexico,” contained insect-damaged corn husks and moldy corn husks—402(a)(3); one lot of Mexican sauce in jars contained insect filth and other lots of Mexican sauce in cans were unfit for food because of swollen cans—402(a)(3); and information required to appear on the labels of the mole en pasta and the corn husks was not in such terms as to render it likely to be read and understood, because such statements were in Spanish rather than in English—403(f). Default decree ordered destruction. (F.D.C. No. 63725; S. No. 82–267–926; N.J. No. 4)

Mozzarella cheese loaves, part skim, low moisture, at Amsterdam, N. Dist. N.Y.
Charged 7-23-79: while held by Cheese Corporation of America, Amsterdam, N.Y., who manufactured the article using interstate nonfat dry milk, the article contained metal particles and black plastic-like particles; 402(a). The article was claimed by the manufacturer and the action was transferred to the District of Massachusetts for trial with a similar action. Ultimately, a decree of summary judgment ordered the article destroyed. (F.D.C. No. 62373; S. No. 79–156–594; N.J. No. 5)

DRUGS/Human Use

Dimethyl sulfoxide (DMSO), at Fife, W. Dist. Wash.
Charged 12-18-81: when shipped from outside of the state of Washington, the article (which was intended for...
human drug use and which was accompanied by a pamphlet titled "Wonder Drug or Industrial Solvent? DMSO" that claimed DMSO was useful for arthritis, bursitis, burns, schizophrenics, manic depressives, psychotic alcoholics, neurosis, paranoia, tendinitis [sic], sprains, sinusitis, strains, athletic injuries, cancer, degenerative lumbar discs, gout, exzema [sic], tansillitis, pharyngitis, malignant thyroid, otitis media, nose or ear furuncles, aortic aneurism, pulmonary tuberculosis, emphysema, hiatal hernia, post operative complications, varicose veins, strokes, scleroderma, clotted hemorrhoids, baldness, herpes simplex and herpes progenitalis) was a new drug without an effective approved New Drug Application—505(a); and while held by B J’s Enterprises (Smoke Shop), Fife, Wash., the article’s labeling failed to bear adequate directions for use and was not exempted due to its new drug status—502(f)(1). Default decree ordered destruction. (F.D.C. No. 63419; S. No. 81–177–014; N.J. No. 6)

Metronidazole tablets, at Dallas, N. Dist. Texas.
Charged 4-28-81: when shipped by Premo Pharmaceutical Laboratories Inc., South Hackensack, N.J., the article was a new drug without an effective approved New Drug Application; and while held for sale, the article’s labeling lacked adequate directions for use and was not exempted due to its new drug status; 505(a), 502(f)(1).

The article was claimed by the shipper. Upon motion of the parties, the action was ordered transferred to the District of New Jersey for consolidation with a similar action. Subsequently, a consent decree condemned the article, and the article was ordered destroyed. (F.D.C. No. 63434; S. No. 81–265–970; N.J. No. 7)

MEDICAL DEVICES

X-Ray control panel, transformer and collimator, Tracery III, at Honolulu, Dist. Hawaii.
Charged 10-17-79: the article, which had been manufactured by Western States Supply Ltd., Pueblo, Colo., was dangerous to health when used as directed, because the article would emit radiation beyond the preset exposure time—502(j); the accompanying labeling was false and misleading in claiming compliance with the regulation’s standards, and in claiming that the devices would deliver the radiation exposure stated in the instruction manual—502(a); and the article’s quality fell below its purported quality—501(c).

Initially, the article was claimed by the owner and a consent decree of condemnation authorized release for bringing into compliance. After installation of a replacement component, the claimant found that the article was still defective. Pursuant to stipulation of the parties, the article was ordered destroyed. (F.D.C. No. 62539; S. No. 79–145–842; N.J. No. 8)

CRIMINAL ACTION

King’s Trading Inc., and Jar-Yu King, director and manager, Kansas City, W. Dist. Mo.
Charged 9-1-82 by grand jury: sweet and sour sauce in pouches (count 1) and rice (count 2) were held under insanitary conditions in a building accessible to residents, were exposed to contamination by rodents, and the rice was contaminated with rodent filth; 402(a)(3), 402(a) (4). The defendants pleaded not guilty. The action came on for trial by court and jury. The jury returned a verdict of guilty.

The corporation was sentenced to a $10,000 fine on count 1; imposition of sentence on the second count was suspended; and the corporation was placed on probation for four years. The individual was sentenced to one year imprisonment and a $10,000 fine on the second count; and sentencing on count 1 was suspended and the individual was to be placed on probation for three years to commence upon release from imprisonment. (F.D.C. No. 63629; S. No. 82–261–628; N.J. No. 9)

CIVIL CONTEMPT ACTION

Alpha Pharmacal Inc., and Donald W. Huber, president, St. Louis, E. Dist. Mo.
Charged 4-25-78 in a petition for order to show cause in civil contempt and for modification of injunction: that the defendants should be held in civil contempt because FDA inspections of the defendants’ plant revealed that the defendants continued to operate their plant in violation of the current good manufacturing provisions of the Federal Food, Drug, and Cosmetic Act and the decree of injunction; and that the defendants should cease operations unless and until the defendants engaged a qualified pharmaceutical expert to assist defendants in establishing current good manufacturing practices at the Alpha plant, which expert would then certify to FDA that the defendants were willing and able to come into compliance.

Pursuant to stipulation, the order to show cause was dismissed; the petition for a modification of the injunction was withdrawn without prejudice, since the defendants had engaged an acknowledged pharmaceutical manufacturing expert who advised FDA that the Alpha plant had achieved substantial compliance with the requirements of current good manufacturing practice; and the defendants agreed to pay costs to the government as compensation for conducting inspection of the Alpha plant, subsequent to the entry of the decree of permanent injunction, in the amount of $2,932.55. (Inj. No. 724; S. No. 77–84–828 et al.; N.J. No. 10)

INJUNCTION ACTIONS

Charged 8-11-78 in a complaint for injunction: that the defendants manufactured and distributed in interstate commerce four new drugs (a lotion of Benzoyl Peroxide 20% with Sulfur 10% for use in the treatment of acne; Vitamin A Acid lotion for the treatment of acne; Petrocort cream as a topical drug in treating skin dryness and scaling; and Hypopigmentation lotion for use in treatment of melasma) without effective approved New Drug Applications; that the defendants held for sale various drugs after shipment of one or more of their components in interstate commerce; that the circumstances used for such drugs’ manufacture, processing,
pacing, labeling and holding failed to conform with current good manufacturing practice; that, when shipped and while held for sale after interstate shipment of their components, the defendants' drugs were in violation of the law as follows: the labels of the Vitamin A Acid lotion and Petrocort cream lacked a quantity of contents statement; the labels of the Benzoyl Peroxide 20% with Sulfur and Petrocort cream lacked the name and quantity of each active ingredient; the labeling the lotion of Benzoyl Peroxide 20% with Sulfur, the Vitamin A Acid lotion, the Petrocort cream, and the Hypopigmentation lotion lacked adequate directions for use; and the labels of the Vitamin A Acid lotion and the Petrocort cream lacked the prescription legend; that FDA inspections disclosed a number of specified deviations from current good manufacturing practice; and that the defendants were well aware that their activities were in violation of the law; 501(a)(2)(B), 502(b)(2), 502(e)(1)(A)(ii), 502(f)(1), 503(b)(4).

Since the facts which formed the basis for the action occurred four months earlier, and balancing the equities, the court denied a government motion for a preliminary injunction. However, after hearing before the court, the court found for the government on a motion for a permanent injunction, enjoined the complained of violations, and ordered monthly inspections by an expert on drug good manufacturing practice for one year, or less as might be set by the court.

Subsequently, the defendants moved for relief from the monthly inspections and the defendant's motion for relief was granted. Meanwhile, the defendants had moved to withdraw their motion for relief. Accordingly, the court vacated its order granting the relief, permitted the withdrawal of the motion to grant relief, but authorized the defendants to refile their motion for relief under the terms of the court's order of injunction.

A second motion for relief from monthly inspections was filed by the defendants, and opposed by the government. Ultimately, the defendants advised the court that the firm had ceased the manufacture of pharmaceutical products and that the one-year period for monthly inspections had lapsed. Accordingly, the court granted the defendants' motion to withdraw their second motion for relief. (Inj. No. 823; S. No. 77–140–847 et al.; N.J. No. 11)

Alpha Pharmacal Inc., and Donald W. Huber, president, and Daryl L. Keith, board of directors member, St. Louis, E. Dist. Mo.

Charged 2-27-76 in a complaint for injunction: that the defendants, at their St. Louis, Mo., plant, manufactured, processed, packed, labeled, held for sale after interstate shipment of components, and distributed in interstate commerce various drugs; that the circumstance used for the manufacture, packing and storage of the cardiac pacemakers were not operated or administered in conformity with the applicable requirements; and that required information respecting pacemaker Models DU–15, DU–33, DU–19, and DB–20 had not been provided to FDA; 501(h), 501(f), 501(c), 502(j), 502(a), 502(o).

All of the individual defendants, except Winand J. Dautzenberg, denied the charges insofar as they might be directed to them and asserted a number of affirmative defenses including lack of venue and lack of jurisdiction over the individuals. Neither the corporation nor Winand J. Dautzenberg filed any answer to the charges; and the government moved for a default judgment against the corporation and that individual. Meanwhile, all of the officers of the corporation had resigned and there was no one authorized to consent to FDA's inspection of the corporation's books and records which were on the corporation's premises that the Internal Revenue Service had seized and padlocked. So that consignees, physicians, and others could be provided with information relative to potential health hazards believed to be associated with the defendants' devices, FDA applied for an order authorizing entry to the corporation's premises for inspection and copy of the books and records of the corporation. The court granted such an order to FDA and such entry and inspection was made.

Upon motion of the government, a default decree of permanent injunction was entered against the corporation and Winand J. Dautzenberg, enjoining the complained of violations. All of the pacemakers on hand were destroyed and all components were destroyed, salvaged or otherwise disposed of. Pursuant to stipulation between the government and William C. Morris, Herbert G. Taus, Austin S. Moscowitz, and Jack D. American Technology, William C. Morris, board chairman, Herbert G. Taus, board member, Austin S. Moscowitz, executive vice president, Winand J. Dautzenberg, engineering vice president, Jack D. Thrasher, clinical and regulatory affairs manager, Northridge, C. Dist. Calif.

Charged 6-26-80 in a complaint for injunction: that the defendant manufactured (using interstate components), packed, labeled, and distributed in interstate commerce cardiac pacemakers which were intended to be implanted in humans to monitor and stimulate the heart; that the circumstance used for the manufacture, packing and storage of the cardiac pacemakers were not operated or administered in conformity with the applicable requirements; and that required information respecting pacemaker Models DU–15, DU–33, DU–19, and DB–20 had not been provided to FDA; 501(h), 501(f), 501(c), 502(j), 502(a), 502(o).

The government subsequently petitioned to modify the decree of permanent injunction and also petitioned for an order to show cause in civil contempt (see N.J. No. 10 of this issue of FDA Consumer). However, an acknowledged qualified expert found that the firm was in substantial compliance and both such petitions were dismissed. (Inj. No. 724; S. No. 76–18–771 et al.; N.J. No. 12)

Charged 11-5-81 in a complaint for injunction: that on a number of specified occasions, the defendants had sold, without a prescription, various specified prescription veterinary drugs to an FDA investigator who had visited the firm on an undercover basis; that such prescription veterinary drugs lacked adequate directions for use and were not exempted as prescription veterinary drugs because they were not sold to or on order of a licensed veterinarian in the course of his professional practice; that despite warning, the defendants continued to sell prescription veterinary drugs to customers without a prescription; 502(f)(1).

A consent decree of permanent injunction perpetually enjoined the defendants from the complained of violation and enjoined the sale of any interstate prescription veterinary drug unless and until procedures were established to store all such prescription drugs in an area accessible only to firm’s employees, procedures were established whereby such drugs were sold only to or on the order of a licensed veterinarian for use in the course of his professional practice; records were established to demonstrate the propriety of every prescription drug sale; an accurate inventory of all such drugs was prepared and procedures were established to reconcile the inventory with the quantity of drugs sold; and defendants reported to FDA demonstrating that the above requirements had been met. (Inj. No. 986; S. No. 80-211-943 et al.; N.J. No. 14)


Charged 2-12-82 in a complaint for injunction: that the defendant operated a potato chip and snack food manufacturing plant in Akron, Ohio; that they received and stored interstate foods, such as potatoes, popcorn, corn grits, flavoring, sauerkraut and flame butter salt; that they processed and packaged potato chips, popcorn, cheese puffs and corn curls; that they manufactured ice; that they shipped foods to intrastate and interstate consignees; that the defendants’ foods were prepared, packed and held under insanitary conditions; that FDA inspections revealed a number of specified insanitary conditions; that FDA analyses disclosed a number of specified insanitary conditions; that FDA analyses confirmed the presence of insect and rodent defilement; and that the defendants had been repeatedly warned of the insanitary conditions and practices in their warehouses; 402(a)(3), 402(a)(4).

A consent decree of permanent injunction enjoined the defendants from the complained of violations, and enjoined the defendants from continued operations involving interstate foods unless and until methods, facilities, and controls were established and operated in conformity with practices which would assure that food was not contaminated with rodent, insect or other filth; unless and until each of the defendants’ warehouses was examined by a qualified expert and certified to be in compliance; and unless and until all foods on hand were examined for filth, necessary analyses were made, and all contaminated food was destroyed or otherwise brought into compliance.

Subsequently, the government petitioned for modification of the decree of injunction. Upon consent of the parties, the decree was modified to delete Savita R. Sardana, and to require: that the defendants employ a sanitarian to inspect each warehouse twice a month for a year afterwards, and one every other month thereafter; that the defendants maintain records of all foods reconditioned or destroyed; and that the FDA might require the defendants to close any of the defendants’ warehouses if the sanitarian’s reports were not prepared or, if based on the sanitarian’s report or FDA inspection, FDA determined that the defendants were not in substantial compliance. (Inj. No. 933; S. No. 79-206-202 et al.; N.J. No. 16)
THE WINNER

A reminder to wash one’s hands before eating won a top prize in a food safety poster contest sponsored by the U.S. Department of Agriculture. The poster was drawn by Melinda Hayes, 8, a third-grader at Mercy Montessori Center, Cincinnati, Ohio. Other first-prize winners in the contest were Jennifer Agnello, 7, a second-grader at Lewiston-Porter North Elementary School in Youngstown, N.Y., and Robert Lucci, 11, a sixth-grader at Campus North School in Buffalo. The third annual contest drew 70,000 entries this year.