JOSE CERDA

Box 5:

Rohy Pnol
Bratton NYC Police Commissioner
Methamphetamine
Mutli-Cultural Programs
Immigration – Fraternal Order of Police Firearm related juvenile use of drugs

ENCLOSURES FILED OVERSIZE ATTACHMENTS 16957

VANA 14148

ROHYPNOL: THE DATE RAPE DRUG

BACKGROUND

Rohypnol, also known as "Roofies", is the brand name of the drug flunitrazepam. It is used in some countries to treat insomnia or anxiety but is illegal to produce or prescribe in the United States. Referred to as the "date rape drug", Rohypnol-- tasteless, odorless and easily dissolved in alcohol-- has increasingly been used by rapists to incapacitate their victims. Its use is also growing in popularity among young people.

WHAT THE CLINTON ADMINISTRATION HAS DONE:

1. Customs Crackdown at the Ports of Entry

On March 5, 1996, Secretary Rubin and Customs Commissioner Weise directed the U.S Department of Customs to seize all Rohypnol coming across the border. The Customs Service is now confiscating any amount of Rohypnol brought into the country by travelers, commercial shipments, or through the mail.

2. President Clinton's Anti-Gang and Youth Violence Act of 1996

In May of this year, President Clinton submitted legislation to Congress to further fight the scourge of Rohypnol. Among the other provisions to keep kids drug-free, the bill would give the Attorney General emergency authority to reclassify certain emerging drugs such as Rohypnol on the list of controlled substances-- thereby stiffening the penalties for their use.

3. President Clinton's Commitment to Sign H.R. 4137 Into Law

President Clinton will sign into law H.R. 4137, the Drug-Induced Rape Prevention and Punishment Act of 1996. The bill will criminalize the use of Rohypnol-- or any illegal drug-- used with the intent to facilitate a violent crime. Enactment of the legislation will mean tougher penalties for such crimes, with criminals who use Rohypnol on their victims particularly targeted. The bill will also commission a six-month Drug Enforcement Agency study to determine whether Rohypnol should be reclassified.

Rophynol (row-hip-nole)

(flunitrazepam)

Known as "quaalude of "90s" in some parts of the country.

Background

- benzodiazepine sedative (same family as Valium, Xanax, Halcion); manufactured by Roche Pharmaceuticals
- not legally available in U.S.; approved medicine in most other parts of the world
- prescribed as sedative (short-term treatment of insomnia & sleep disorders)
- Names: "rophies" "ropies" "roaches" "R2" "getting roached"
- Oral or pills crushed and put in joints

Effects

- 10 times more potent than Valium; sedative/disinhibition effects are amplified in combination with alcohol
- 2mg tablet = drunken-like feelings, euphoria, disinhibition, muscle relaxation, slowed coordination, hangover. High doses = stupor. Unique property is its ability to cause amnesia (memory loss), particularly in combination with alcohol. This is a characteristic of many benzodiazepines. Late 1980s, cases of Halcion causing memory loss as long as 48 hours after use.
- Onset 20-30 minutes; lasts about 8 hours
- Risks: like all benzodiazepines, can produce dependence, rebound insomnia, withdrawal after extended use. Long-half life (slow elimination from body) = residual effects that can be dangerous if users take additional doses. Generally low OD potential, but high doses/drinking can cause significant respiratory & cardio depression.

National Trends

- fastest growing drug problem among adolescents in south Florida; "epidemic" began over summer of 1993
- Other "hotspots": southern Texas
- Users: club drug (young adults); alcohol extender (teenagers); ease comedown from crack/speed (street population in treatment)
- implicated in "date rape" cases in Florida

Arizona

- First reports to CEWG in April 1995 of coming in over the border; Tucson, Yuma; mainly adolescents/teenagers taking it in combination with alcohol
- 4 ERs in Yuma reported during September 1995; all kids
- 41 DEA actions through November 1995
- CEWG: no current reports of availability outside southern Arizona; use appears centered among high school students, so would expect eventual spread north

INTERVENTION SPECIALISTS EVAC

EAST VALLEY ALCOHOLISM COUNCIL, INC. • 554 S. Bellview • Mesa, Arizona 85204
Administrative Services (602) 962-7922 • Clinical Services (602) 962-7711

FAX TRANSMISSION

DATE: 1-23-96 **TIME:** 12:45

AGENCY/CO. NAME:

ATTENTION: Dwight Vick

FAX NUMBER: 202-456-7028

TRANSMISSION CONSISTS OF 3 **PAGES INCLUDING COVER.**

PROBLEMS? CALL 602-962-7922

EVAC'S FAX NUMBER IS 602-844-8449

MESSAGE: Dwight - Per our conversation, here is the info. Talk to you soon.

John Hohman
Program Director
EVAC

People who attended the meeting:

Ross Deck
Edward Jurith
Representatives from HHS
Roche legal council
member - Robert T. Angarola - Carter Drug Czar
Don Kaiser - lawyer from Swiss office, now in Washington

Rohypnol is produced by the Switzerland-based company, Roche. It is an international company with more than 80 production plants around the world. Two of their companies produce the drug, Rohypnol. They are located in Mexico City, Mexico and Bogota, Columbia.

Kaiser presented the information. The Roche company heard of the drug's presence in late 1994. Hospital emergency rooms, treatment centers, and detoxification centers in Florida were admitting people with this drug in their blood stream or on their person. At first the company was not concerned. As these calls increased, the company began to worry as well. They did not know how it entered the country. Several options were explored.

At first, Roche thought the people using the drug had obtained the drug through legal means. Kaiser mentioned the FDA and Customs agents allow someone to fill a prescription in another country as long as they do not have more than a 90-day supply. Foreign travelers use the drug as a sleep aid when travelling abroad and drank too much. Since this drug is legal by prescription in 62 foreign countries, this was of no major concern to Roche.

The drug entered the U.S. through Florida with Caribbean- and Northeastern-based construction companies. Arriving to help

rebuild Miami after Hurrican Andrew, the construction workers were working long hours and needed a drug to help them sleep heavily. They brought and took Rohypnol as prescribed. Eventually, the drug was mixed with alcohol to double the effects of the drugs. It became popular in bars and entered the street scene. However, Rohypnol was not the only drug to be abused in the area. Emergency rooms, detoxification centers and drug treatment facilities overflowed with people who were depressed and/or overworked after the hurricane.

Roche is auditing its Mexican and Columbian plants internally for leaks. This is a strong possibility since the pills appear in bubble wrapping. Their audits show that no employee or groups of employees are removing the supplies or products outside of their facilities.

Roche hired a drug research organization from Haight-Asbury in San Francisco to interview users in South Texas. Their findings showed that three types of people are more likely to take Rohypnol: opiate addicts, habitual users, first-time users. Opiate addicts use the drug to detoxify from all opiates. Basically, it stops most withdrawal symptoms. It is also a bridge drug. They use it until they can obtain more opiates. If used more than two weeks, the addict has simply switched addictions - from opiates to Rohypnol. Habitual users will use anything to get a "fix", including Rohypnol. The most predominate user is the first-time, naive user. They are usually kids who are rebelling against their parents. Roche stated their studies show most of the kids could not pick out Rohypnol from

the pill charts they were shown.

The company expects to use the Haight Asbury to conduct research in the South Florida area. However they expect some drug connection. There will be few similarities between the Florida and Texas epidemics.

The company has agreed to limit access to pharmacies in or near Mexican border towns. In South Texas, the Haight Asbury study determined there is no major syndicate involvement in the distribution of Rohypnol. The users go to a Mexican physician located near a pharmacy and obtain a prescription. They take it to the nearest full-service pharmacist and get the pills. Most orders are not over 100 pills and are easily hidden from Customs agents (who would not be concerned about a prescription drug from Mexico in the first place). The company states they do not conclusively know how it is currently entering the Florida region.

Roche is negotiating with Mexican officials in an effort to regulate the Rophynol market. Their biggest concern is their lack of understanding the Mexican laws. The company fears any serious involvement with the Columbian government. They do no want their employees or investigators to die.

My Thoughts on Rhynopol

Roche used this as a meeting to prevent any further media damage or government action this drug.

They are scared that Roche will be associated with the production of a "date-rape drug". I think they are willing to regulate themselves so they can prevent damage control and government intervention. There were two cases in South Texas and Florida where the woman was raped after being exposed the Rohypnol. The kids call this violent activity, and getting high off the drug, as "roaching". The word Roche is printed on the tablet and the people mispronounce it.

I have some serious misgivings about the validity and reliability of their research. First, they brought outsiders into South Texas to interview kids and users on the amount of the drug they used. Students are not generally honest about their use. They will lie to "look tough" or to cover up real usage amounts. While they did hire former users to interview them, these former users are outsiders to the South Texas. The interviewers are not familiar with the lifestyles and people. The interviewees will see them as "suckers" so they are more likely to lie than if it were someone they could identify with at the time.

I asked the Roche representatives what were the other pills the users were shown. They all responded that various types were shown. Since generic forms of Rohypnol are just as easily available in Mexico as the Roche pill itself, I asked if they

were pictured. There were no definitive answers. Furthermore, they stated they did not know if these users were taking the generic forms; yet, their findings in South Texas were conclusive. They did not know who the producers of the generic Rophynol market. Their only response was that 50 percent of men and 15 percent of the women could pick out the Roche pill. This made no sense to me and it was obvious I would get no further answers at this session.

They were constantly referring to the drug as an oral drug. I asked them if their research showed that Rohypnol was smoked. Their studies did not show this occurrence at all. They stated the drug has no effect on the body once it is heated above 110 degrees. I stated the kids are still doing it and its use is increasing. When I called my friends in Phoenix, I learned some people crush the pill and mix it with marijuana. This is the second most common method of ingestion.

The drug is not fatal unless the person ingests large amounts of alcohol and Rohypnol at the same time over a long period of time. Several people believe it is a loss leader by the black markets. They are attempting to gain more customers and they are targeting the three groups mentioned above.

The Roche representatives stated they were the first company in American history to offer self-regulation to the government. They will work with the Mexican government to control the drug in border towns and foreign governments to prevent any leaks. They are also working with the Columbian government to prevent possible leaks from their country. The representatives agreed

this would be difficult since the Columbian government is under siege. I agree. There was a brief mention of the product being shipped from other Central American or South American countries. No substantive investigations into this possibility were mentioned.

This issue has become a race issue. Throughout 20th Century America, drug use has been a race issue. Opiate smoking was regulated in California because it was a Chinese tradition. The Chinese experienced racism throughout the region. No other opiate use was controlled. Marijuana and cocaine were regulated by state and local governments in an effort to control Hispanic and black populations. Once these problems involved white, middle-class Americans, federal involvement was demanded. When this was a South Florida/Caribbean problem, it was not a problem. When the drug entered Floridian, middle-class white American kids and young adults at dance bars, it became a problem.

At this point in time, national citizen forces are not strongly aligned on this issue. Their influence at this time is not a factor in the policy making process. With media attention, this will grow without question.

One salient, yet silent, factor in drug policy formulation is the alcohol and pharmaceutical industries. Tighter controls on these industries mean more money will be spent on drugs in the black market. Roche's meeting today falls along those lines. The only anomaly is Roche's advocating a mostly self-regulation measure. Roche is courting the Federal government in an effort to gain control of the situation without governmental action.

In my opinion, it boils down to this - the Roche Company is afraid the American public will perceive this as the crack cocaine of the 1990s and the date rape pill. They gathered these groups of government employees together to encourage them to implement the company's wishes.

My Recommendations

- **Take no legislative action at this time.** If the WH attempts to control Rohypnol, it must look at controlling other benzodiazepines like valium. After the Maxine Water's arguments on crack cocaine vs. cocaine sentencing, it would renew old arguments.

- **All action should originate from the Executive Branch.**

- **Publicity should be avoided.** Children watch television. If the media portrays this as the "crack of the 1990s", demand will increase. Many people will want to see what it is like and will try it. This could result in higher Rohypnol addiction rates than we are currently experiencing.

- **The President should instruct the Secretary of State** to contact his counterpart within the Mexican government. Since most of the South Texas business appears to be "mom-and-pop" store purchases in Mexico, the U.S. should encourage them to place stricter controls on the Rohypnol and its generic products in or near border towns.

- **The President should instruct the Secretary of the Treasury** to notify Customs agents of the increased use of this drug and it is made accessible through their ports of entry. Roach Pharmaceutical cited several instances where they asked people to purchase the drug and smuggle it over the

border. Others were asked to declare it. In all cases, no action was taken by Customs.

- **The President should instruct the Secretary of Health and Human Services** to prepare a pamphlet for immediate distribution to all teachers, school administrators, treatment facilities, and emergency room personnel on this drug, its increased use among youth, and subsequent symptoms. Its use among habitual addicts should be mentioned as well. These groups are more likely to report is presence because of his involvement. Presidential attention to this issue will provide more reliable data available for study.

- **Roche should be encouraged to apply for a patent on the drug.** The only reason Rohpynol is not available on the American market today is due to its direct competition with valium. If they applied and received the rights to market the drug in the U.S., Roche could increase their profits on the drug by selling at a higher price in the United States than they would receive for Rohypnol in Mexico. The drug would be less alluring and the government could control its purity. The Federal government will monitor the drug.

  Rohypnol is not a drug like cocaine or heroin; therefore, it does not require a Schedule 1 rating. This will free the law enforcement agencies to monitor the influx of more serious drugs, like heroin and cocaine.

- **If this becomes the "Crack of the 1990s", executive action will prove to the American people during an election year that President Clinton has made every attempt to control this problem without media attention. Media attention could attract children to the drug, making all actions counterproductive.**

If these policies are implemented, I think it will be a win-win situation for all involved. I would like to discuss these options with you.

Thank you for the excellent oppotunity. I want to participate in any and all of these opportunities that occur.

People who attended the meeting:

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My Recommendations

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- **After further consideration, Senator Biden is more correct that I initially thought him to be.** I still think a low-key approach to the problem is the Administration's best alternative. Media attention will increases youth demand for the drug. The country's best method to deter use is to deter youth attention while gaining the attention of community leaders such as school teachers, law enforcement agencies, and treatment facilities.

  If legislative means are necessary, Rohypnol should be given a Schedule 1 rating if treatment and educational funding is provided. I think this could resurrect Cong. Waters' arguments on cocaine and crack cocaine. If the Administration supports her statements, they can rely on a 1991 Minnesota case where the legal distinction between the two drugs and jail time was addressed.

  If no treatment funding is provided, the Federal government should list it as a Schedule 2 drug. Therefore, Federal, state and local governments could tax the drug and use the revenues for treatment and education initiatives.

Used this way, Rohypnol could be the country's first controlled drug that viewes addiction as a public health problem rather than as a law enforcement one. Most opponents to this will cite this is a European measure and drugs are still prevelant in those countries. The argument can be counterattacked by stating the U.S. has the highest estimated addiction rates among all industrialized nations in the world. Furthermore, we have established this precedence in America with drug-addicted pregnant women. This statement will shut up the opposition. No one wants to publicly oppose children, particularly in an election year.

- **The supply-siders, like Roche and William Bennett, will encourage punishment for possession of the drug.** This may be a good offer. Unfortunately, these groups want to lock them up and throw away the key. The drug sellers serve one-third of their time and are released, due to jail overcrowding. This is a downside to listed Rohypnol as a Schedule 1 drug. Intensive treatment and educational funding must be provided to prevent the spread of this now "fad" drug.

- **There is no mention in the Biden Report or with the ONDCP meeting of treatment funding for these addicted children.**

- **There is no mention of cooperation of cooperative efforts**

between state and local governments on this issue.

- **All action should originate from the Executive Branch.**

- **Publicity should be avoided**. Children watch television. If the media portrays this as the "crack of the 1990s", demand will increase. Many people will want to see what it is like and will try it. This could result in higher Rohypnol addiction rates than we are currently experiencing.

- **The President should instruct the Secretary of State** to contact his counterpart within the Mexican government. Since most of the South Texas business appears to be "mom-and-pop" store purchases in Mexico, the U.S. should encourage them to place stricter controls on the Rohypnol and its generic products in or near border towns.

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- **Like the Secretary of State and HHS, the Attorney General should contact the appropriate agencies within her jurisdiction to control the spread of Rohypnol.**

- **Roche should be encouraged to apply for a patent on the drug.** The only reason Rohpynol is not available on the American market today is due to its direct competition with valium. If they applied and received the rights to market the drug in the U.S., Roche could increase their profits on the drug by selling at a higher price in the United States than they would receive for Rohypnol in Mexico. The drug would be less alluring and the government could control its purity. The Federal government will monitor the drug.

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LEVEL 1 - 16 OF 29 STORIES

The Tampa Tribune

September 12, 1995, Tuesday, FINAL EDITION

SECTION: NATION/WORLD, Pg. 8

LENGTH: 508 words

HEADLINE: What are kids doing out at 4 a.m.?

BODY:

It's 4 o' clock Sunday morning. Do you know where your kids are?

That's the wake-up call that the parents of 2,500 mostly teenagers should have gotten this weekend when police and sheriff's deputies busted up a "rave" party in downtown Tampa.

"Rave" clubs are the latest youth fad, drawing young people after bar closing hours to while away the morning dancing, lounging and generally having "fun."

Within minutes of the bust at the Parthenon club, 13 people had been arrested - seven for possessing illegal drugs. Hundreds more appeared to be under the influence of something other than loud music.

The smell of cigarettes, marijuana and alcohol hung in the air. Police confiscated LSD, marijuana, ecstasy and Rohypnol.

LSD, as nearly everyone knows, is a hallucinogenic drug popular during the '60s and currently experiencing a revival. Ecstasy is a powerful and very addictive drug that has been available for years.

And, Rohypnol is one of the newer drugs on the underground market. A sedative similar to Halcion and Valium, it mimics alcohol intoxication. Nicknamed "roofies," the pills sell for $ 3 to $ 5 each and are growing in popularity. Rohypnol is the drug Broward County prosecutors say a rapist used earlier this year to sedate women he met in bars and later attacked.

No responsible parent would want a son or daughter trying these dangerous drugs. But one has to wonder how many of these kids have responsible parents.

Among those arrested were 17-year-olds from Tampa, Pinellas Park and St. Petersburg. Police suspect others in the crowd were 16, 15 and possibly even 14. Party-goers interviewed by The Tampa Tribune said they've seen children as young as 12 at some "rave" parties.

Hellooooo. Is an adult present at these kids' homes?

Tampa has a curfew that was supposed to put an end to such shenanigans, but

everyone knows it is largely ignored. City officials say they are sitting helplessly on their hands until some high court somewhere says curfews are legal. So much for bold leadership.

Courts haven't stopped cities like Phoenix, Washington, D.C., Atlanta, Boston, Buffalo, Dallas, Denver, New Orleans, Newark and Orlando from adopting and enforcing curfews. Indeed, those cities have seen a significant drop in juvenile crimes such as auto thefts ever since the kids were forced to stay off the streets in the middle of the night.

Parents who can't see to it that their kids get home by midnight or shortly after don't get a lot of sympathy here. Certainly parenting is hard work. Saying no, being firm, taking away the car keys isn't easy. But it has to be done to assure the kids' survival.

As for the dance clubs that put on the "raves," the police are well within their jurisdiction to do just what they did at Parthenon over the weekend: shut them down. Police cited faulty wiring and unsafe conditions in order to close the place. They can also go a step further and declare them a public nuisance. This community doesn't need a business that entices kids to stay out all night.

TYPE: EDITORIAL; EDITORIALS

LOAD-DATE: September 14, 1995

LEVEL 1 - 17 OF 29 STORIES

TEXAS MONTHLY

September, 1995

SECTION: STATE WIDE REPORTER; Pg. 88

LENGTH: 839 words

HEADLINE: A New Low

BYLINE: HELEN THORPE; Edited by David McCormick

HIGHLIGHT:
Across the state, kids are getting seriously messed up on a dirt-cheap downer from Mexico.

BODY:
ROB IS A JITTERY NINE-teen-year-old bean pole who lives in Houston. He doesn't work or go to school, but he spends a lot of time in the city's nightclubs, where he frequently buys a potent sedative called Rohypnol. A single two-milligram pill has more intoxicating power than a six-pack of beer. "I was at Numbers, a club down the street," says Rob, sitting in front of a youth center on Westheimer. "I took two Rohypnol and I was like --" he rolls his eyes, tilts his head, and lets his tongue hang out of his mouth. "I went outside and there were these two cops in the parking lot. I said, 'Excuse me, Mr. Beers, I haven't had any officers tonight.'"

Although Rohypnol is illegal in the United States, it is available by prescription in Mexico, and importing it is no trouble at all: Lately the drug has become a fad among teenagers around the state. Rohypnol is manufactured by the Swiss pharmaceutical giant Hoffman-La Roche and was introduced in the seventies in Europe and South America, where it is prescribed as a means to relax patients before surgery and as a treatment for insomnia. Beginning in the eighties, hard-core drug users in Europe started using it to come down from cocaine or metham-phetamine highs. Now thrill-seeking teenagers in Texas, Florida, and other parts of the South have discovered the drug. To them, it's ideal because it makes them feel drunk but doesn't make them throw up, doesn't show up in the most common urine tests, and is dirt cheap. One pill can cost anywhere from $ 1 to $ 5. But the pills are far from harmless; early last year, the late grunge rock star Kurt Cobain slipped into a coma after taking Rohypnol and drinking champagne while on tour in Italy, though he was revived after his stomach was pumped.

So many teenagers have been taking it that the Texas Commission on Alcohol and Drug Abuse (TCADA) issued a warning to drug treatment centers about the pills in May. On the street the drug has many nicknames; teenagers know it as rope, ribs, or roaches. Law-enforcement authorities call it Mexican Valium because of its similarities to that drug, but Rohypnol is estimated to be ten times stronger and has some novel attributes. Another of its many names is "the forget pill," because Rohypnol typically causes complete short-term amnesia. It also reduces inhibitions. Rob says, "You take it -- you black out. The next day

people tell you what you did, and you're like, 'Wha-a-a-a-t?'" In rare cases Rohypnol can also induce aggression, rages, hallucinations, or psychoses. Many teenagers take it while drinking, which greatly increases the impairment of their motor abilities. Statewide, there have been two suspected fatal overdoses.

Rohypnol first became popular in border towns. According to figures compiled by the TCADA, law enforcement along the border reported 31 cases involving the drug in 1991. Last year there were 197 cases. Nilda Gomez, a drug abuse counselor who works with teenagers in Brownsville, says Rohypnol is everywhere she turns. "What's so surprising is that it used to be fifteen-year-olds who were doing drugs, but now it's thirteen-, twelve- and even eleven-year-olds," says Gomez.

The use of Rohypnol gradually spread north, and today drug counselors in Houston, San Antonio, Dallas, and Austin know of people who have taken Rohypnol. The drug is said to have a moderate to high risk of addiction. Eight months ago Annette, a self-possessed sixteen-year-old, was buying Rohypnol regularly in clubs along Sixth Street in Austin. (Her name has been changed to protect her privacy.) She now lives in Odyssey House, a residential treatment facility in Houston for teenagers. As she sits on a sofa there, wearing a white T-shirt and white cotton pants, her honey-colored hair twisted into a bun, Annette looks like an extra in Beverly Hills 90210. but she recites a family history of abuse and chemical dependency. "I'm the kind of person who wouldn't take one or two," she says of her experiences with Rohypnol. "I would take three or four and drink at the same time. We used to call them 'run-trip-and-falls.'" Sometime last year Annette took enough Rohypnol to obliterate four full days. She came to at her boyfriend's house, with a hospital band around her wrist. "A friend of mine from San Antonio had run away, and she wanted to do some because she'd never tried them. We got a lot. The last thing I remember is my friend turning to me and saying, 'Annette, we need to go.' And then it just goes black.

"Four days later I woke up -- well, not really woke up, because I hadn't been asleep. I had gone to another friend's apartment, and I had had sex with somebody -- this is what they told me -- and I had had a tampon in, and it had gotten stuck up inside me, so I had to go to the emergency room. I lost track of my friend, and she didn't know anybody in Austin."

Clearly, playing drugstore cowboy is no game. Rohypnol is more than an easy way to get wasted -- it's an easy way to waste a life.

GRAPHIC: Picture, Known as "the forgot pill,"-Rohypnol reduces inhibitions and causes short-term amnesia. ANDREW YATES

LANGUAGE: ENGLISH

LEVEL 1 - 18 OF 29 STORIES

The Tampa Tribune

June 23, 1995, Friday, FINAL EDITION

SECTION: FLORIDA/METRO, Pg. 6

LENGTH: 359 words

HEADLINE: Radio host blamed for drug mishap

BYLINE: WILLIAM YELVERTON; Tribune Staff Writer

DATELINE: CLEARWATER

BODY:

Prosecutors are holding radio personality Ron Bennington of "Ron and Ron" fame responsible for leaving an illegal drug where his young daughter could find it.

The 10-year-old girl was hospitalized overnight in March. She fell asleep and couldn't be roused after taking medicine from a box marked "children's Tylenol."

An investigation determined the child had taken an undetermined amount of Rohypnol - a powerful narcotic similar to Valium - that was in the Tylenol container.

Pinellas sheriff's spokeswoman Marianne Pasha said Bennington told a deputy someone in Miami had given him the Rohypnol a year ago. His daughter was taken to All Children's Hospital in St. Petersburg for observation but was home the next day, Pasha said.

"Ron felt very bad about the whole situation," Pasha said.

Bennington, 36, who with Ron Diaz has a popular show on WSUN, was charged earlier this month with culpable negligence in the March 6 incident at his Seminole home. He has filed a written plea of not guilty.

Bennington agreed to enter a pretrial intervention program, said Rebecca Graham, assistant county court director for Pinellas State Attorney Bernie McCabe.

The program is a form of probation for first-time, nonviolent offenders. If participants complete the program and stay out of trouble, charges are dropped.

Bennington could not be reached for comment Thursday.

His daughter, Gail, was taken to a Seminole hospital the night of March 6 after her mother couldn't rouse her, Pasha said.

Julie Bennington told a deputy who was called to the hospital that she feared the girl was having an allergic reaction to children's Tylenol. The mother had told the girl to take the Tylenol earlier that night when she wasn't feeling well.

At the request of emergency workers at the hospital, Julie Bennington telephoned her husband and told him to bring in the box and package, Pasha said.

Ron Bennington was charged June 8. He was not arrested. Instead he was issued a summons. His wife was not charged.

Although Rohypnol, also known as "roofies," "rufies" and Roche, is illegal, Bennington was not charged with a drug offense.

GRAPHIC: PHOTO,
Ron Bennington

TYPE: FOCUS ON FLORIDA

LOAD-DATE: July 3, 1995

LEVEL 1 - 19 OF 29 STORIES

THE DALLAS MORNING NEWS

June 15, 1995, Thursday, HOME FINAL EDITION

SECTION: NEWS; Pg. 1A

LENGTH: 1065 words

HEADLINE: Dangerous sedative being smuggled across border Mind-altering drug reduces inhibitions, can cause amnesia

BYLINE: Rebecca Howland, Staff Writer of The Dallas Morning News

BODY:

Law enforcement officials say they are alarmed at the growing popularity of a dangerous and potent sedative being smuggled across the Mexican border and now making its way north through the state.

Rohypnol - commonly called Roach, Rophie or the Forget Pill on the street - is a hypnotic or mind-altering drug that reduces users' inhibitions and can cause amnesia, especially when taken with alcohol.

The drug reportedly has been used in gang initiations and date-rape cases in which the woman can't remember the next day what happened, say drug treatment and law enforcement officials.

The drug - which officials say is about 10 times stronger than Valium - is illegal in the United States. But in other countries anyone can get Rohypnol with a doctor's approval, and in some, including Mexico and Colombia, it is often sold over the counter.

The drug is most often seen among males ages 13 to 18 and is

frequently used in gang initiations, officials in South Texas say.

Law enforcement officials and medical experts say use of the drug in South Texas is skyrocketing, and there is increasing incidence of it in Austin, Houston and Dallas. The drug is often sold on the street for 50 cents to $ 3 a pill, officials said.

Use of the drug has also increased dramatically in southern Florida, especially in Miami, since 1992. Officials there said it is streaming into the United States from Colombia.

Hoffmann-LaRoche, a Switzerland-based pharmaceutical company that manufactures the drug, produces Rohypnol in plants in Colombia and Mexico.

Although selling Rohypnol over the counter is technically illegal worldwide, it happens frequently in the two countries, which do not effectively enforce regulations, officials from the World Health Organization said.

The drug is used as a sleeping aid to combat severe insomnia or to sedate psychotic patients, said Al Wasilewski, director of public policy and communications for Hoffmann-LaRoche. It is also prescribed to patients about to undergo surgery and who are not going to receive full anesthesia. After taking the drug, the patient would not remember the uncomfortable procedure.

Mr. Wasilewski declined to comment about whether or not Hoffmann-LaRoche would consider discontinuing its production of the drug, although he said the company is "very concerned" about the abuse.

Rohypnol "happens to have that attraction to a certain subset of the population that will abuse anything. . . . It is an unbelievable thing to hear that these drugs which have a good therapeutic use are being abused in this way," Mr. Wasilewski said.

Hoffmann-LaRoche never sought approval from the Food and Drug Administration to distribute Rohypnol in the United States, he said.

"There was already a significant number of similar sedative hypnotics" in the United States, he said. "There was no need to add another one to the pie."

Steve Mithos, the director of program services for the Palmer Drug Abuse treatment center in McAllen, said more than half of the teenagers he sees are "getting roached."

"It's pretty widespread, and in the last six months, it's really grown," he said. "Now, about 15 percent of the kids I see list it as their primary drug of choice, not just something they take once in a while."

Sean, a 19-year-old in treatment for drug abuse in Dallas and who asked not to be identified by his last name, said Rohypnol began "hitting it big" on Dallas' club and party scene last year.

Sean estimated that half of his friends had experimented with the drug or were using it regularly. "It's everywhere," he said.

"If you just go down and see a doctor in Mexico and get a prescription, you can carry five boxes across the border, no problem," he said. "Each box has 50 or 100 pills in it."

Sean estimated he'd taken the pills 10 or 11 times.

"It's real mellow. I just felt like I didn't want to move," he said.

Although Sean described feeling "under control" while on the drug, he recounted experiencing amnesia after mixing the drug with alcohol, and described several "incidents" in which men "took advantage of women sexually because the women didn't know what they were doing."

The drug can also trigger belligerent and aggressive behavior, Mr. Mithos said.

One of Mr. Mithos' patients is on probation for manslaughter, he said.

"The guy doesn't even remember shooting anyone. He's neat, a real nice guy. You wouldn't think he would do something like that, but he was loaded on Roaches."

In Austin and Houston, law enforcement officials say the drug is rapidly growing in popularity and is most often seen in conjunction with "heavier" drugs such as heroin or crack cocaine.

"We're seeing (Rohypnol) all over the place," said Tony Arnold, a forensic chemist for the Austin Police Department.

"People are using the hyperactive drugs, and when they finally burn out, then they use the Rohypnol to go to sleep," Mr. Arnold said, estimating that one out of every five cases he sees involves the drug.

A few months ago, nobody had heard of the drug, Mr. Arnold said.

"At first, most of the cops thought they were 2-milligram Valiums," he said. Hoffmann-LaRoche also produces Valium, a small, blue pill stamped with the number "10" in a circle. Rohypnol differs in color - it is white - and is marked by "2" instead of "10." The numbers refer to the dosage of the active ingredient in milligrams.

Many law enforcement officials in Dallas said that while they had encountered the small white pills several times during the past year, they were not overly concerned that it was getting out of control.

But Martin Pracht, who works for the Drug Enforcement Administration in Dallas, said officials are underestimating the drug's spread.

"Rophies are much more dangerous and potent than what people are giving them credit for," Mr. Pracht said. "You'd be crazy to say this will not be a problem" in Dallas.

"It's just taking a while to get up here and increase in popularity. But it will," he said.

Because the drug has never been legal in the United States, detecting it is difficult, Mr. Pracht said. The drug is not listed in the commonly-used Physician's Desk Reference, and police and medical officers do not know what symptoms to look for.

Customs officials on the border said it is difficult to stop such smuggling because officers search for materials that look like contraband.

GRAPHIC: CHART(S): (DMN) Rohypnol.

LANGUAGE: ENGLISH

LOAD-DATE: July 13, 1995

LEVEL 1 - 21 OF 29 STORIES

November 29, 1994

SECTION: NATIONAL NEWS; Section D; Page 17

LENGTH: 256 words

HEADLINE: 'Roofies' give Florida teens a cheap high Popular drug makes its users feel drunk

BYLINE: By Donna Pazdera FORT LAUDERDALE SUN-SENTINEL

BODY:
Fort Lauderdale, Fla. - It's just a $ 5 hit. But wash it down with a beer and you might do something embarrassing - or downright scary.

You might crumple to the ground. Or urinate on yourself.

Or stop breathing.

Technically, the drug is called Rohypnol. Those more familiar with the little white pills call them "roofies."

If you haven't heard of them yet, you will, drug abuse specialists and police say.

"It will be as popular as crack because it is so cheap," said Dave Marcus, case manager at Spectrum Program Inc., a drug treatment center for adolescents in Pompano Beach, Fla.

High schoolers are particularly fond of roofies because they are cheap and because they make them feel very, very drunk, Marcus said.

The pills sell for $ 3 to $ 5 apiece. Teenagers generally buy the drug off-campus and take it at weekend parties. Sometimes they pop one in the morning before school, making them incoherent all day.

"It's like the poor man's Quaalude," Marcus said, referring to a sedative drug that was popular in the 1970s.

It's not known how many people are abusing Rohypnol, but in Broward County, Fla., nearly one in five clients at two drug treatment centers for adolescents have used them.

In Palm Beach County, Fla., officials say roofies are slowly becoming popular with teenagers and young adults.

Rohypnol, manufactured by Roche, a U.S. pharmaceutical company, is not legal in the United States. It is used in Central and South America to sedate patients for surgery, said Al Wazaluski, a Roche spokesman.

LANGUAGE: ENGLISH
LOAD-DATE: December 1, 1994

LEVEL 1 - 21 OF 29 STORIES

November 29, 1994

SECTION: NATIONAL NEWS; Section D; Page 17

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1994 The Atlanta Journal and Constitution, November 29, 1994

LANGUAGE: ENGLISH
LOAD-DATE: December 1, 1994

LEVEL 1 - 22 OF 29 STORIES

Times Publishing Company
St. Petersburg Times

November 29, 1994, Tuesday, Tampa Edition

SECTION: TAMPA TODAY; TAMPA BAY & STATE; Pg. 5B

DISTRIBUTION: TAMPA TODAY; TAMPA BAY AND STATE

LENGTH: 511 words

HEADLINE: Tranquilizer hooks teens, drug users

BYLINE: SUSAN CLARY

BODY:

It's just a few dollars a hit. But wash it down with a beer and you might do something embarrassing - or downright scary.

You might crumple to the ground. Or urinate on yourself.

Or stop breathing.

Technically, the drug is called Rohypnol. Those more familiar with the little, white pills call them "Roofies."

If you haven't heard of them yet, you will, drug abuse specialists and police say.

"They have become the Quaaludes of the '90s," said Dr. Sven Norman, referring to a sedative that was popular in the 1970s. "One of the reasons they are abusing it is they get the desired effect. It causes drowsiness and a pretty significant intoxication."

Norman, director of the Florida Poison Information Center at Tampa General Hospital, said the center first heard of the drug earlier this year.

Experts say it is popular with three groups. Teenagers use it to intensify the effects of alcohol. Heroin users like it because it enhances the sedating effects of lower-purity heroin. Cocaine abusers use it to parachute down from a binge.

"It is extremely dangerous," Norman said. "When combined with alcohol, it can be life-threatening."

The tranquilizer is a small, white tablet imprinted with the letters RH. Experts say the drug is several times more powerful than Valium. Users call the pills "roofies," "ruffies" or "Roche," (pronounced Ro-shay) after the company that makes them.

The drug's side effects include hallucinations, respiratory problems, sleep disturbances and anxiety.

While the drug is widely used in South Florida, law enforcement officials in the Tampa Bay area said they have yet to see any cases.

"I'm not saying it doesn't exist around here, but it's not a problem. Not yet," said Lt. Bob Guidara, commander of the Tampa Police Department QUAD Squad.

St. Petersburg police spokesman Bill Doniel said the same is true in his city but noted that new drugs in South Florida often migrate here.

Roofies have become especially popular with high schoolers because they are inexpensive - 50 cents to $ 8 each. When taken alone, they make users feel very sleepy. The effect is intensified when combined with alcohol.

Rohypnol is manufactured by Roche, a U.S. pharmaceutical company, but is not legal here. It is used in Central and South America to sedate patients for surgery, said Al Wazaluski, a Roche spokesman.

- Information from the Associated Press was used in this report.

TEEN DRUG

NAME: Rohypnol (Roofies)

WHAT IT LOOKS LIKE: Little white pills.

PRICE: Inexpensive - $ 3 to $ 5 each.

WHAT IT DOES: Used alone, roofies make users feel very sleepy. Combined with alcohol, the effect intensifies. Described as 10 times stronger than Valium. Side effects include hallucinations, respiratory problems, sleep disturbances, anxiety and possible addiction.

MANUFACTURER: Rohypnol is manufactured by Roche, a U.S. company, but is not legal here. Authorities think the drug is being brought in from South America.

LANGUAGE: ENGLISH

LOAD-DATE: November 30, 1994

LEVEL 1 - 23 OF 29 STORIES

THE PHOENIX GAZETTE

November 29, 1994 Tuesday, Final

SECTION: FRONT; Pg. A2

LENGTH: 351 words

HEADLINE: NEW, CHEAP DRUG CATCHING ON WITH TEENS

DATELINE: FORT LAUDERDALE

BODY:

It's just a $5 hit. But wash it down with a beer and you might do something embarrassing -- or downright scary.

You might crumple to the ground. Or urinate on yourself.

Or stop breathing.

Technically, the drug is called Rohypnol. Those more familiar with the little white pills call them roofies.

If you haven't heard of them yet, you will, drug abuse specialists and police say.

"It will be as popular as crack because it is so cheap," said Dave Marcus, case manager at Spectrum Program Inc., a drug treatment center for adolescents in Pompano Beach, Fla.

In Arizona, however, the drug is unknown, police said.

"We've never even heard of it, but if it gets popular in other areas of the country, it will get here sooner or later," said Lt. Rick Knight, a state Department of Corrections narcotics detective.

High schoolers are particularly fond of roofies because they are cheap and because they make users feel very, very drunk, Marcus said.

The pills sell for $3 to $5 apiece. Teenagers generally buy the drug off-campus and take it at weekend parties. Sometimes they pop one in the morning before school, making them incoherent all day.

"It's like the poor man's Quaalude," Marcus said, referring to a sedative drug that was popular in the '70s.

It's not known how many people are abusing Rohypnol, but in Broward County, Fla., nearly one in five clients at two drug treatment centers for adolescents have used them.

Rohypnol is manufactured by Roche, a U.S. pharmaceutical company. The drug is

not legal in the United States. It is used in Central and South America to sedate patients for surgery, Al Wazaluski, a Roche spokesman, said.

School officials say many teenagers get the drug at parties, where it is given away by a dealer who is looking for customers.

The drug, sold in tablet form, has been described as 10 times stronger than Valium. Used alone, roofies make users feel very sleepy. Combined with beer, the effect is intensified.

The drug also is crushed and snorted to cushion the crash from a cocaine or crack high, said Hollywood Police Sgt. Mark May.

LANGUAGE: ENGLISH

LOAD-DATE: December 13, 1994

LEVEL 1 - 13 OF 29 STORIES

Star Tribune

October 24, 1995, Metro Edition

SECTION: Variety; Pg. 1E

LENGTH: 538 words

HEADLINE: FYI;
Kissing Keanu and telling

BODY:
Noting that after 25 takes of a kissing scene with Keanu Reeves for "Bram Stoker's Dracula," Winona Ryder "reportedly left the set in tears," YM (Young and Modern) magazine has harvested the following smooching critiques:

"Keanu's so sure of himself, but I was back there spraying Binaca and hoping that I wouldn't offend him." - Sandra Bullock, costar in "Speed."

"He was pretty scruffy . . . but he had a sexy smell." - Ione Skye, costar in "River's Edge."

"Kissing scenes are pretty complicated, but we tried to enjoy them." - Aitana Sanchez-Gijon, costar in "A Walk in the Clouds."

"He's a very good kisser. . . . He's definitely blessed." - Lori Petty, costar in "Point Break."

- San Francisco Chronicle

'Spanish fly' becomes real

Rohypnol, an illicit sedative-hypnotic drug most commonly abused in Florida and Texas, has made its way to Minnesota. It is used for medicinal purposes in other parts of the world, but not approved in the United States. Primary users are adolescents who combine it with alcohol and other drugs. Because of its amnesialike effects, it is also being used as a "date rape" drug, according to a drug alert issued by Carol Falkowski, research coordinator for the Chemical Dependency Division of the Minnesota Department of Human Services.

In southern Minnesota, abuse of the drug has been suspected in several cases in which a drug was placed in alcoholic beverages of young females who are subsequently exploited sexually, said Falkowski. Victims have no recall of events following sedation. Rohypnol has a bitter taste when added to a beverage and is about 10 times more potent than Valium. For more information on

Rohypnol, call the Minnesota Prevention Resource Center at (800) 247-1303.

- Hazelden Foundation

Today Costumed guides will lead visitors by candlelight through Historic Fort Snelling. The living-history players will be preparing for winter.

When: 7 to 9 p.m. today

Where: Historic Fort Snelling, Hwy. 5 and 55, near the Minneapolis-St. Paul International Airport.

Admission: Adults, $ 6; seniors, $ 5; ages 6 to 15, $ 4.

Call: 725-2413

Same space, whole new place

The old Rupert's in Golden Valley has been remodeled and reincarnated as the Metropolitan, an elegant room to rent for events and concerts. The Metropolitan, on Interstate Hwy. 394, is owned by upscale Twin Cities restaurateurs, the D'Amico Brothers. The space underwent a $ 1 million renovation. It seats 730 people for concerts at tables on various tiers.

A site for wedding and bar mitzvah parties, it also will be open to the public for the "Live at the Met" concert series in the next few weeks. October Project, an arty pop band featuring poetic singer Mary Fahl, will kick off the series tonight. Lowen & Navarro, an adult-pop duo, will do the Met Nov. 21, and jazz vocalist Dee Dee Bridgewater will sing there Nov. 26.

What: October Project.

When: 8 p.m. today.

Where: The Metropolitan, 5418 Wayzata, Blvd., Golden Valley.

Admission: $ 14 to $ 20.

Call: 989-5151.

GRAPHIC: Photograph

LANGUAGE: ENGLISH

LOAD-DATE: October 25, 1995

LEVEL 1 - 14 OF 29 STORIES

THE ORLANDO SENTINEL

October 3, 1995 Tuesday, METRO

SECTION: LOCAL & STATE; Pg. C5

LENGTH: 494 words

HEADLINE: ST. CLOUD MAN DIES FROM ILLEGAL DRUG;
POLICE SAID THE 20-YEAR-OLD OVERDOSED ON THE ILLEGAL SEDATIVE SMUGGLED FROM SOUTH AMERICA.

BYLINE: By Henry Pierson Curtis of The Sentinel Staff

DATELINE: KISSIMMEE

BODY:

A St. Cloud man may be one of the first victims in Florida to die from an overdose of an illegal sedative smuggled from South America.

Stacy McCormack died sometime Sunday after swallowing more than a dozen tablets of Rohypnol, a drug commonly called "roofies," Kissimmee police said.

The sedative is 10 times more powerful than Valium and is becoming known as the "Quaalude of the '90s," a reference to the drug widely abused in the 1970s. Rohypnol has become increasingly popular in the past few years among high school students mixing it with beer for a cheap high, drug abuse authorities said Monday.

Spokesmen for the Florida Poison Information Centers said Monday that no Rohypnol-related deaths had been reported previously to offices in Miami, Tampa and Jacksonville. It's possible that previous fatalities have not been reported by medical examiners to the statewide network, they said.

"We've just been lucky that kids who take it are just slumped over their desks in school and not driving. It's just a matter of time (until) we're going to have a couple," said Dr. Susan Sandbeck, deputy director of the Florida Poison Information Center in Miami. "It's fast acting; it's intense. It's a great buzz . . . but all you have to do is get a kid who vomits or get a kid who is driving a car and it's deadly."

McCormack, 20, was found dead about 10:30 p.m. Sunday on a couch in a friend's apartment on Central Avenue in Kissimmee. He had gone to sleep about 7 a.m. after taking "roofies" and watching movies, Kissimmee police Detective Warren Shepard said.

McCormack, who worked construction and had been in robust health, apparently choked on his own vomit after falling asleep, police reported. Several of his friends told police that McCormack began taking Rohypnol several months ago and had taken as many as 14 tablets at one time.

The Orange-Osceola Medical Examiner's Office said the cause of McCormack's death will not be known for several weeks - until toxicology tests are completed. The office is investigating a second possible Rohypnol-related death, a spokeswoman said.

The victim of that overdose was a Brevard County woman who died last week in an Orlando-area motel room. Additional information about the death could not be obtained Monday from the Orange County Sheriff's Office.

Rohypnol is the brand name of flunitrazepan, a sedative sold in Europe, South America and Asia by Roche, a Swiss pharmaceutical company. Its sedation lasts about an hour and it is used to calm patients for minor surgery in physicians' offices, pharmacists said.

In interviews Monday, several people said Rohypnol sells for $5 a tablet in Orlando-area nightclubs. Authorities said it began appearing in mid-1989 in South Florida and that most shipments appear to come from Colombia.

Rohypnol abuse can cause hallucinations, slowed reflexes and altered depth perception. Overdoses can cause respiratory arrest or death from aspirating vomit.

LANGUAGE: ENGLISH

LOAD-DATE: October 4, 1995

LEVEL 1 - 26 OF 29 STORIES

South China Morning Post

June 3, 1994

SECTION: NEWS; Pg. 7

LENGTH: 1120 words

HEADLINE: Doctor in the clear over drug accusation

BYLINE: By STEVE BALL

BODY:

A DOCTOR who, after a barely two-minute consultation, sold an addictive drug demanded by a patient he had never seen before was last night cleared of professional misconduct by the Medical Council.

Dr Yu Hon-biu supplied 10 tablets of the tranquilliser Rohypnol to an undercover policewoman on July 27, 1990, almost without question, the Medical Council heard.

But the council decided the evidence against Dr Yu was not sufficient to prove a charge of misconduct in supplying the drug.

Dr Yu said ''I may have been slightly negligent'', but that was not the same as misconduct.

Rohypnol, chemical name Flunitrazepam, is a commonly abused drug and, since October 7, 1990, has been listed as a dangerous drug.

But Dr Yu denied the drug was addictive. ''It is not a drug of dependency,'' he told the council.

Dr Yu based his knowledge mainly on a book written before Rohypnol was invented. He came to the council with his copy of the third edition of Goodman and Gilman's Pharmacological Basis of Therapeutics, published in 1965, while Dr Yu was at medical school.

Council chairman Professor Rosie Young Tse-tse pointed out that the book was almost 30 years old. Dr Yu said: ''But what was written there was facts.''

''In 1965,'' Professor Young said.

''Still facts,'' replied Dr Yu, who graduated in 1968.

In his final submission to the council, Dr Yu put his hand on his Goodman and Gilman's and said: ''If you say that is not the authority then I don't have any more to submit.''

Professor Young pointed to a passage in the Eighth edition of Goodman and Gilman's, published in 1990, which warned that tranquillisers were potentially

addictive with unpleasant and sometimes dangerous side effects.

The council heard that at around 4 pm on July 27, 1990, police constable Yeung Miu-hung went to Dr Yu's surgery in Ferry Street, Kowloon, and said: ''I want Rohypnol.''

It was Ms Yeung's first visit to the clinic, but Dr Yu did not ask her about her previous medical history.

Instead, he simply asked her ''Insomnia?''. Ms Yeung replied ''Yes'', and she told the council Dr Yu then stared at her in such a way as if to suggest: ''How many tablets would you like?''

She asked for 10 and Dr Yu charged her $ 4 for each tablet. There was no charge for the consultation.

Dr Yu did not tell Ms Yeung how the tablets should be taken. He did not write out a prescription and the tablets were supplied separately by the clinic nurse, who was not a registered nurse, based on Dr Yu's patient notes.

Cross-examining, Senior Crown Counsel Lynda Shine said: ''As a professional doctor you did not know anything about this patient's medical history.''

Dr Yu agreed, but objected when Ms Shine said his conduct had been ''cursory and unprofessional'' and the drug prescription had not been bona fide.

Dr Yu said he did not need to ask any more questions. ''She said she was an insomniac, that was enough.''

Council member Dr David Fang then asked Dr Yu if there could have been any other reason for lack of sleep other than insomnia. Dr Fang said: ''For instance, she might have had a brain tumour.''

Dr Yu did not answer that question, but later said: ''I did not know of any organic cause of insomnia.''

During the hearing, Dr Yu frequently referred to the drug manufacturers' leaflet on Rohypnol as evidence of the drug's effectiveness for all types of insomnia.

The leaflet said that it was not advisable to prescribe the drug for someone who was in the first stages of pregnancy. Dr Yu admitted that he did not ask Ms Yeung whether she was pregnant.

LANGUAGE: ENGLISH

LOAD-DATE: June 15, 1994

LEVEL 1 - 12 OF 29 STORIES

The Scotsman

November 14, 1995, Tuesday

SECTION: Pg. 2

LENGTH: 1960 words

HEADLINE: Fresh drug menace surfaces

BYLINE: Severin Carrell Home Affairs Correspondent

BODY:

FEARS are growing that a potent sleeping tablet blamed for drug deaths in Europe and the United States may be replacing temazepam among users and addicts in Scotland.

Drugs agencies and police have received reports that heroin addicts and regular drugs users in Greenock, Glasgow, Dundee and Stirling have begun abusing Rohypnol, a strong sedative used mainly for insomnia, in conjunction with other substances and alcohol.

Batches of the drug, known to users as Wallbangers or Roofies, have been seized by Strathclyde police for the first time.

About 2000 have been impounded in two recent hauls.

One English force has also begun investigating counterfeit Rohypnol imports.

Rohypnol has caused controversy in the Netherlands, Germany, and the US over drugs deaths, illness due to breathing problems and acts of violence by users who had taken the stronger, two-milligramme tablet which is sold in Europe.

One of the world's largest pharmaceutical firms, Roche, has voluntarily stopped making the stronger tablet and replaced it with much lower dosage, one-milligramme pills similar to those sold in the United Kingdom.

Dr Donald Uges, a specialist in forensic toxicology and drug analysis from Groningen in Holland, said the drug became popular among Dutch football hooligans as it promoted aggression and among drug addict prostitutes as it sedated them before sex.

Heroin addicts take it to boost the effects of poor quality heroin, and cocaine users use it to smooth out withdrawal.

He added doctors and drug addicts had stopped using or dispensing the drug recently because it was so dangerous if taken with other drugs or alcohol.

"You won't be happy when Rohypnol is in your country," Dr Uges told The Scotsman yesterday.

"Rohypnol is even worse and more dangerous than temazepam."

The drug was withdrawn from National Health Service lists in 1985 after the Government began its "selected list" of the cheapest generic drugs. But its use in private prescriptions has remained high, with boxes of 30 costing pharmacists £ 4.08.

Rusty Murray, chair of a voluntary drug users group in Dundee, said he knew of about 20 to 30 addicts and users in the city who took Rohypnol regularly, plus others in areas of Glasgow.

They acquired purple, diamond-scored, one-milligramme pills from doctors by buying them on private prescription, took them personally or sold them off to other users or dancers at raves for £ 3 or £ 4 each - securing a substantial profit.

Despite fears the tablets would be ground down and injected, like temazepam tablets, most swallowed them in quantities of up to 10 or 15 at a time.

Illegally imported European- strength pills sold for up to double that price.

He said: "Once people get the feeling for them, they will just take off. You will find they will become more and more known because doctors won't be prescribing temazepam."

The Scottish Drugs Forum has learnt that drugs workers in Inverclyde had found the different strengths on sale in the area, selling for as little as 50p each. They came on sale early this year, and had begun showing up in Stirling.

Dave Liddell, the agency's director, said it was too soon to predict if Rohypnol would replace temazepam after the clampdown on its availability and ban on gel-filled capsules by ministers in October.

But he added: "It's something we view with concern. In some senses, there's an inevitability about something replacing temazepam. There is no surprise in relation to this, unless we get to grips with reducing the overall demand for drugs."

LANGUAGE: ENGLISH

LOAD-DATE: November 14, 1995

LEVEL 1 - 9 OF 29 STORIES

The Tampa Tribune

December 2, 1995, Saturday, FINAL EDITION

SECTION: NATION/WORLD, Pg. 14

LENGTH: 500 words

HEADLINE: Menace of the "date rape drug'

BODY:

It is hard to fathom how the drug scene in America could degenerate any further. Recently a Detroit woman was reported to have sold her 15-year-old son to a drug dealer in exchange for crack cocaine. Police say the boy spent six months as a sex slave and drug runner before being rescued.

That little horror is just one more in an endless series of degradations involving crack. But a new drug is making the rounds now, with its own peculiar brand of evil. Rohypnol, known on the street as "roofies," is not just a drug of the slums, although it is used there by gang members. It is also traded in bars, dance parties and other gatherings of young people. Police in California call it "the date rape drug."

Rohypnol, the brand name for flunitrazepam, is used in other countries to treat anxiety and insomnia and to sedate surgery patients. It is illegal to possess it in the United States without a foreign prescription. In a story in the Orange County Register, a spokesman for the Swiss manufacturer, the F. Hoffmann-La Roche & Co. pharmaceutical firm, said the drug must be getting into the United States through the mail or across the border from Mexican pharmacies.

Local police also report the drug's appearance in our area. Pinellas County sheriff's investigators recently arrested three men in Seminole who had 38 of the tablets, along with other drugs, guns and $ 22,000 in cash. "We're starting to see it hand over fist," said Lt. Michael Platt of the Pinellas narcotics-intelligence unit.

The drug is diabolically well-suited for rape, because it can be slipped into someone's drink at a bar, and within 15 to 30 minutes that person slips into a state of amnesia lasting up to eight hours. "It's like, "I think I got raped, but I don't remember,' " Platt said.

The victim is in danger of more than sexual assault, though. When combined with alcohol, the drug can be fatal.

If being young weren't cruel and complicated enough these days, now young women have to worry about whether some creep is slipping a knock-out pill into her drink at a party. Counselors advise people to refuse a drink offered by a stranger, and never to leave one's drink unattended.

This is a law enforcement problem, of course, but it is more than that. Here the women's rights movement and the most ardent social and religious conservatives ought to find common ground. The level of decadence and disregard for human worth required to drug and rape a young woman ought to arouse the wrath of every rational person.

It would be simple if the manufacturer could just stop making the drug, but that seems unlikely. Washington ought to press researchers to consider other ways of accomplishing the same medicinal results, perhaps altering the formula or form of the drug. Shipping and dispensation should be more rigorously controlled too.

Still, the problem is not so much with the manufacturer. America's drug problem is just one more symptom of the moral breakdown of much of society.

TYPE: EDITORIAL; EDITORIALS

LOAD-DATE: December 4, 1995

LEVEL 1 - 11 OF 29 STORIES

Chicago Tribune

November 27, 1995 Monday, EVENING UPDATE EDITION

SECTION: NEWS; Pg. 2; ZONE: C; EVENING. People.

LENGTH: 347 words

HEADLINE: NEW DRUG FINDS WAY INTO DATE-RAPE SCENARIO

BODY:

A drug used in date rapes is knocking on the nation's door, according to narcotics experts in the U.S.

The drug, Rohypnol, is described by law enforcement as a sedative 10 times more powerful than Valium and is manufactured by the F. Hoffmann-La Roche & Co. pharmaceutical firm, based in Basel, Switzerland. Not approved for use in the United States, it has been a legal prescription drug for several years in most of the world and is available in Europe and Latin America.

On the street, users call the small, white pills "roofies" and "Roche." The substance has also been referred to as "the date-rape drug" and "the Quaalude of the '90s," after another oft-abused sedative. Rohypnol is drawing the attention of narcotics experts across the country.

It is being smuggled into the United States, usually in its original wrapping, through Colombia and Mexico, according to Bob Nichols, an assistant state prosecutor in Ft. Lauderdale, where illegal use of roofies in this country first became noticed.

Nichols has been involved in five sexual-battery cases connected to roofies in the last five months.

"The pattern with the rapes is that high school and college kids and gang members are slipping it into drinks at nightclubs and pickup joints," Nichols said.

Police in South Florida and Southern California report an increase in the number of women filing complaints that they felt drugged after drinking just a drink or two, and then waking up to find they had been raped.

Drug counselors and law-enforcement officers are bracing for the arrival of roofies, which typically cost $1 to $5 for a single, 2-milligram pill. The pill is also taken by cocaine users who want to parachute down less harshly from a cocaine high.

Reports of Rohypnol abuse have surfaced in Florida, Texas and other parts of the Southwest.

Jennifer Trenshaw, health educator at the University of Southern California Health Center, had a word of advice for people, especially women:

Don't leave your drink unattended, and don't accept a drink from a stranger.
LANGUAGE: ENGLISH

LOAD-DATE: January 15, 1996

LEVEL 1 - 7 OF 29 STORIES

The New York Times

December 9, 1995, Saturday, Late Edition - Final

SECTION: Section 1; Page 6; Column 1; National Desk

LENGTH: 1313 words

HEADLINE: In South, Drug Abusers Turn to a Smuggled Sedative

BYLINE: By MIREYA NAVARRO

DATELINE: MIAMI, Dec. 8

BODY:

A prescription drug sold abroad is becoming the fastest-growing abused drug among young people in Florida and one that has found its way to a dozen other states, law-enforcement officials say.

Manufactured by Hoffmann-La Roche, the Swiss pharmaceutical company, and sold by prescription in about 60 countries as Rohypnol, the pills are not made or approved for use in the United States. But Drug Enforcement Administration officials say the police in Florida, Texas and other Southern states are reporting an increase in smuggled shipments from Colombia, a Hoffmann-La Roche distribution site for other Latin American countries, and from Mexico, where some pharmacies sell Rohypnol over the counter.

The Federal Drug Enforcement Agency has reported Rohypnol seizures in at least 13 states but says its distribution and abuse has been concentrated in Texas and Florida, where some law enforcement officials say the pills threaten to become "the Quaaludes of the '90s."

Lee P. Brown, the White House drug policy director, said today that Rohypnol was an emerging drug that his office was tracking closely but that "it has by no means become a national problem."

But in Florida, drug counselors say Rohypnol has found a thriving market among teen-agers who have made it the latest addition to the drug scene at nightclubs and in schools. School officials in South Florida say Rohypnol, considered a bargain at $5 or less a pill, has become almost as widely used as marijuana and LSD among students.

Officials in Dade County, where the sedative first surfaced in 1989, have become concerned enough that they have begun routine testing for Rohypnol in cases where the driver appears drunk but registers low alcohol levels. The medical examiner's office will soon begin to test for Rohypnol in cases in which women say they might have been raped but do not remember.

In Texas, where Hoffman-La Roche is financing an epidemiological study to examine why Rohypnol is being abused, researchers say it is mostly taken by users of other drugs who find it more potent than other sedatives. Cocaine

addicts say Rohypnol helps them come down more smoothly from their high; heroin users say it offsets their withdrawal symptoms.

Known among American users as "roofies," from the mispronunciation of the brand name, and sometimes as "roach" or "rope," Rohypnol is a benzodiazepine, a class of sedatives that includes Valium. Marketed in 1- or 2-milligram dosages, it induces muscle relaxation, short-term amnesia and sleep. Its effect, felt within 15 to 20 minutes and lasting eight hours or more, is similar to that of alcohol in that it helps loosen inhibitions before sedation takes hold.

Frequent users can develop tolerance and get addicted, requiring treatment. In Miami, officials at the Up Front Drug Information Center said its hot line had received calls from teen-age girls who said they had grown dependent on Rohypnol and wanted help.

When combined with alcohol or other drugs, drug experts say, it can cause respiratory depression and death. Kurt Cobain, the grunge rock singer, collapsed and slipped into a brief coma a month before his suicide last year after ingesting Rohypnol with champagne in a hotel room in Rome.

While in Europe and Latin America Rohypnol is mainly known as a sleeping aid and pre-surgery anesthetic (although it is also abused), many here learned of its existence in startling ways. Drug information hotlines started to hear from parents wondering about the pills they had just found in their child's pocket. Teachers called paramedics because a student had passed out.

At Miami Palmetto Senior High School, the school newspaper reported, a junior was taken to the hospital when a friend noticed she missed her mouth while eating nachos.

Now, 20 percent of the patients at the adolescent drug abuse program at Jackson Memorial Hospital say they have taken Rohypnol, doctors there said. In Dade County schools, 21 cases of Rohypnol possession or use have been reported to police since they began tracking the drug five months ago.

In Broward County, north of here, prosecutors say they handled two rape cases recently and are investigating two others where men gave the drug to women and then sexually assaulted them. In one case, the pill was slipped into the woman's drink while she visited the defendant. The man then bragged he had done the same to a dozen other women.

"When they wake up, they're completely naked and the defendant is sitting next to them in his underwear," said Assistant State Attorney Bob Nichols, adding that both defendants pleaded guilty and went to prison. "These girls are all in therapy because they can only imagine what happened."

Since Dade County began testing drunk drivers for Rohypnol, 35 drivers have tested positive for the drug, making roofies the most popular among caught drivers after marijuana and cocaine, said Dr. Lee Hearn, director of the toxicology laboratory at the county's medical examiner's office.

"Police are reporting that they stop them for driving really badly and when they open the door, they fall out," he said.

Its low price and harmless look, bubble-wrapped like so much medicine, may

explain some of the drug's popularity, drug counselors and police said. At Miami Palmetto High, Rene C., a 16-year-old junior, said he liked it because "it gets you drunk." Maria B., an 18-year-old senior, said she only took roofies on special occasions to feel relaxed.

"You don't hear anything bad about it, like heroin or crack, where people die or anything," she said.

They were able to obtain Rohypnol from both classmates and friends, the students said. In Florida, Rohypnol is mainly smuggled through the mail and delivery packages or in luggage, DEA officials say. In Texas, the drug comes in through border crossings, often legally. A recent survey by the University of Texas College of Pharmacy in Austin found that 43 percent of those declaring prescription drugs in customs forms at the border brought Rohypnol. Only Valium was declared more frequently.

The Food and Drug Administration generally allows people to bring drugs sold abroad but not approved here but only for their personal use, defined as a three-month supply. But once in, the drug is considered illegal by law enforcement officials. They said Rohypnol was a controlled substance and its possession punishable by both fines and prison.

D.E.A. officials have reported seizures of more than 50,000 pills at a time in both Texas and Louisiana, and they say they are concerned about the involvement of cocaine and marijuana traffickers in Rohypnol's distribution. So are drug counselors, who say they worry that it may be used by dealers to hook children on other drugs.

"We feel South Florida is a test market for this drug," said James Hall, of Up Front Drug Center here.

Alfred J. Wasilewsky, a spokesman for Hoffmann-La Roche's affiliate in the United States, said the company was working on altering Rohypnol's dosage to try to make it less attractive. He said the presence of similar products in the market dissuaded the company from seeking approval to sell the drug in the United States.

In South Florida, school officials have added roofies to their group counseling and classroom discussions. In Texas, the state's Commission on Alcohol and Drug Abuse is about to send out 10,000 fliers on the drug to school nurses and has added a question about Rohypnol to its survey of 100,000 4th to 12th-graders about drug use, which is given every other year.

But the Miami Palmetto Senior High School principal, Leonard Glazer, noted that alcohol, not roofies, remained the biggest problem in schools.

"I think we tend to overlook that in the high school scene, alcohol is the introducer," he said. "Once your inhibitions have been lowered by alcohol, you're more likely to experiment."

GRAPHIC: Photo: The fastest-growing abused drug in Florida is the Rohypnol pill, made by Hoffmann-La Roche.

Map: "A CLOSER LOOK: Abusing a Sedative"
Siezures by law-enforcement agencies of the prescription sleeping pill Rohypnol, which is not approved for sale in the United States, have risen sharply in certain states. Map of continental U.S. shows states where the greatest quantities of Rohypnol have been siezed, along with other states where the drug has been siezed. (Source: Drug Enforcement Administration)

LANGUAGE: ENGLISH

LOAD-DATE: December 9, 1995

LEVEL 1 - 6 OF 29 STORIES

Rocky Mountain News

December 10, 1995, Sunday

SECTION: NEWS/NATIONAL/INTERNATIONAL; Ed. B; Pg. 2A

LENGTH: 400 words

HEADLINE: New drug threatens U.S. youth
Florida, Texas report rising use of Rohypnol, prescription sedative sold abroad, illegal in U.S.

BYLINE: Mireya Navarro; The New York Times

DATELINE: MIAMI

BODY:

A prescription drug sold abroad is becoming the fastest- growing abused drug among young people in Florida and one that has found its way to a dozen other states, law-enforcement officials say.

Manufactured by Hoffmann-La Roche, the Swiss pharmaceutical company, and sold by prescription in about 60 countries as Rohypnol, the pills are not made or approved for use in the United States.

But federal Drug Enforcement Agency officials say the police in Florida, Texas and other Southern states are reporting an increase in smuggled shipments from Colombia, a Hoffmann-La Roche distribution site for other Latin American countries, and from Mexico, where some pharmacies sell Rohypnol over the counter.

The DEA has reported Rohypnol seizures in at least 13 states but says its distribution and abuse has been concentrated in Texas and Florida, where some law enforcement officials say the pills threaten to become ''the Quaaludes of the '90s.''

Lee P. Brown, the White House drug-policy director, said Friday that Rohypnol is an emerging drug that his office is tracking closely but that ''it has, by no means, become a national problem.''

But in Florida, drug counselors say Rohypnol has found a thriving market among teen-agers who have made it the latest addition to the drug scene at nightclubs and in schools.

School officials say Rohypnol has become almost as widely used as marijuana and LSD.

In Texas, where Hoffman-La Roche is financing an epidemiological study to examine why Rohypnol is being abused, researchers say it is taken mostly by users of other drugs who find it more potent than other sedatives.

Known among American users as ''roofies,'' from the mispronunciation of the brand name, and sometimes as ''roach'' or ''rope,'' Rohypnol is a benzodiazepine, a class of sedatives that includes Valium. The drug induces muscle relaxation, short-term amnesia and sleep.

LANGUAGE: English

LOAD-DATE: December 13, 1995

LEVEL 1 - 5 OF 29 STORIES

Rocky Mountain News

December 10, 1995, Sunday

SECTION: NEWS/NATIONAL/INTERNATIONAL; Ed. F; Pg. 95A

LENGTH: 374 words

HEADLINE: New drug takes hold among teens
Florida, Texas report surging use of Rohypnol, sold legally in 60 countries but not U.S.

BYLINE: Mireya Navarro; The New York Times

DATELINE: MIAMI

BODY:

A prescription drug sold abroad is becoming the fastest- growing abused drug among young people in Florida and has found its way to a dozen other states, law-enforcement officials say.

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LANGUAGE: English

LOAD-DATE: December 12, 1995

LEVEL 1 - 4 OF 29 STORIES

THE DALLAS MORNING NEWS

December 17, 1995, Sunday, BULLDOG EDITION

SECTION: NEWS; Pg. 40A

LENGTH: 1655 words

HEADLINE: Police suspect illegal sedative used in date rapes

BYLINE: Julio Laboy, Orange County Register

DATELINE: SANTA ANA, Calif.

BODY:

SANTA ANA, Calif. - It started out as a casual get-together for a 25-year-old student but ended in rape, humiliation and the harrowing revelation that a drug used in date rapes is knocking on the nation's door.

The drug, Rohypnol, is described by law enforcement as a sedative 10 times more powerful than Valium and is manufactured by the F. Hoffmann-La Roche & Co. pharmaceutical firm, based in Basel, Switzerland. Not approved for use in the United States, it has been a legal prescription drug for several years in most of the world and is available in Europe and Latin America.

The sale and introduction of the drug into interstate commerce in the United States is illegal; virtually the only people who can possess it legally in this country are those who have prescriptions written in other countries.

On the street, users call the small, white pills "roofies" and "Roche." The substance has also been referred to as "the date rape drug" and "the Quaalude of the '90s," after another oft-abused sedative. Rohypnol is drawing the attention of narcotics experts across the country.

It is being smuggled into the United States, usually in its original wrapping, through Colombia and Mexico, according to Bob Nichols, an assistant state prosecutor in Fort Lauderdale, Fla., where illegal use of roofies in this country first was noticed.

Mr. Nichols has been involved in five sexual-battery cases connected to roofies in the last five months.

"I don't know why it's suddenly on the scene. It's been around awhile," Mr. Nichols said. "The pattern with the rapes is that high school and college kids and gang members are slipping it into drinks at nightclubs and pick-up joints."

That is what one Orange County, Calif., woman, an English major at the University of California, San Diego, thinks happened to her Sept. 29.

The student attended a concert that night with a male friend.

The two were not romantically involved, she said.

She had three glasses of wine that night. At least one glass of wine was consumed in the parking lot of the San Diego theater where the concert was taking place.

That's when the student started feeling strange. She doesn't remember the concert. She doesn't remember how she got home. She doesn't remember getting into bed. The last thing she does recall is waking up the next morning naked and in a pool of vomit.

"I was so sick when I woke up," she said. "I could hardly hold my head up. I couldn't remember anything. I noticed there was vomit on the bed and stuck on my hair. I was lying in it. I could have choked on it and died. He was naked and I was naked. He said we made love."

The woman was crushed. Their relationship had never been an intimate one, she said. The Orange County Register , which generally doesn't publish the names of sexual-abuse victims, is withholding her name from publication.

The woman, who works as a part-time language teacher and as a waitress, thinks that her companion slipped a roofie into her wine that night and that it erased her memory, an effect described by pharmacologists and in medical reports.

Struggling to overcome the nightmare, the woman is seeing a therapist and is taking a vacation out of the country to escape the everyday reminders of that ill-fated night. She agreed to share her story because, she said, "I didn't do anything wrong."

She wants to turn a negative experience into a positive one. She wants to warn other young women about roofies.

"My friends had no clue about this drug," she said. "This stuff is scary. You can't be cautious enough."

She called a rape hotline after spending two lonely days knee-deep in guilt and self-doubt. She then went to a therapist at Kaiser Permanente in San Diego.

"Some people were saying I got drunk. But I didn't. I just had wine," the student said. "I was telling the therapist that I couldn't believe it. I was crying. I was confused. As I started telling her my story she said, Hold on. I know what this is.' "

The student learned from the therapist that her situation resembled a drugging and that an epidemic of similar cases had arisen in the past six months.

"She said they all were feeling sluggish and drunk on dates that ended in rape," the student said.

That's when the student first heard about roofies.

"We have seen many date-rape cases," Kaiser Permanente spokesman Jim McBride said. "Many of those patients report being drugged. Our therapists believe

these stories are credible. It's real. It's happening."
The woman then notified the San Diego Police Department.

Investigators are looking into the matter.

Police Sgt. Joanne Archambault of the sex-crimes unit said she cannot comment on rape cases because of privacy reasons, but she confirmed that the student's report had been taken.

"Recently, lots of girls have been coming in saying they were drugged or passed out after having one or two drinks," Sgt. Archambault said. "We even talked to the Poison Control Center about it."

Orange County drug counselors and law-enforcement officers are bracing for the arrival of roofies, which typically cost $ 1 to $ 5 for a single, 2-milligram pill.

"I would assume that because of the movement of things in the San Diego-Los Angeles-Orange County corridor, that yes, it may be here," said Bill Edelman, division manager in charge of alcohol and drug programs at the Orange County Health Care Agency. Reports of Rohypnol abuse have surfaced in Florida, Texas and other parts of the Southwest, he said.

Jennifer Trenshaw, health educator at the University of Southern California Health Center, sai she advised people, especially women, not to leave their drinks unattended and not to to accept drinks from strangers.

The UCSD student who says she was raped remembers going to the bathroom twice during the concert. She left her drink with her date.

The student described all the classic circumstances and side effects of a roofie mixed with alcohol, Mr. Edelman said.

"It's a sedative. It's a drug that can be enhanced when it is combined with alcohol or opiates," Mr. Edelman said.

Rohypnol, the brand name for Flunitrazepam, is used in other countries to treat anxiety and insomnia and to sedate surgery patients, according to pharmacologists and drug-information centers.

Patients on the drug appear drunk. When it's combined with alcohol, the effects can be deadly.

"These guys using this to get girls are like those people who like to do things with dead bodies," Mr. Edelman said. "It's sick.

Maybe we need to think about a campaign about how this drug is used in bars."

Al Wasilewski, a spokesman for the pharmaceutical company's U.S. division, said the drug is being illegally mailed into the United States. He also said that some Mexican pharmacies near the U.S. border are illegally selling the drug over the counter. He said Hoffmann-La Roche has never sought approval to market the drug in the United States.

"It's a legitimate product sold for legitimate use in those countries where it's registered," Mr. Wasilewski said.He disagreed with law-enforcement officials who have described the drug as being 10 times more powerful than Valium but acknowledged that taken in equal doses, Rohypnol will act more quickly and more powerfully than Valium.

"They are two different drugs designed to do two different things," Mr. Wasilewski added. "It was about a year ago when we began to see just more than sporadic abuse of Rohypnol."

Hoffmann-La Roche has initiated studies to learn more about how the drug is being abused, where it's coming into the United States, and where in the country it is most likely to be found. The company is trying to track its movement throughout the country and recently helped set up a task force with members drawn from federal and local law-enforcement agencies, academics and drug-counseling centers, Mr. Wasilewski said. The company has also disseminated alerts to the health-care industry and police departments.

Hoffmann-La Roche has divisions in Mexico City and Bogota, Colombia, where Rohypnol is manufactured for the Latin American market.

"We're doing everything that is possible for Roche to get this product off the streets," Mr. Wasilewski said. "We're confident that the diversion of Rohypnol is not occurring internally from our sites in Mexico and Colombia."

Dr. Jim Adams, associate professor of molecular pharmacology and toxicology at USC's School of Pharmacy, said Flunitrazepam can make someone lose control of motor and neurological functions.

Respiration is also affected. When it's mixed with alcohol, he said, a coma can easily follow. Vomiting also can occur, and if a victim is unconscious, he or she runs the risk of drowning in the discharge.

The drug reacts with brain cells to quickly diminish nervous system operations, said Dr. Edward Newton, a consultant to the Los Angeles Regional Poison Control Center. The area the center serves includes Orange County.

"It depresses neurological activity in the brain," Dr. Newton said. "People do die if they take too much."

It is difficult to determine a lethal dose of Rohypnol because reactions to sedatives differ among individuals, and when taken alone it is not difficult to manage, according to the Up Front Drug Information and Education Center in Miami. An overdose is more likely when Rohypnol is mixed with alcohol or other drugs. The speed with which the overdose will take place depends on how much alcohol a person has consumed.

A roofie will sedate its user quickly. Sedation occurs 15 to 30 minutes after ingestion and lasts about eight hours, USC's Ms. Trenshaw said. If an overdose occurs, the need for medical care is urgent.

An added problem with Rohypnol is that it causes amnesia for most of the sedation period, especially during a patient's first consumption. That makes prosecution of abuse cases difficult, Ms. Trenshaw said.

LANGUAGE: ENGLISH
LOAD-DATE: December 18, 1995

LEVEL 1 - 1 OF 29 STORIES

Star Tribune

January 16, 1996, Metro Edition

SECTION: Variety; Pg. 1E

LENGTH: 654 words

HEADLINE: FYI;
'Date-rape' drug

BYLINE: Dave Matheny; Staff Writer

BODY:

Rohypnol, a potent sedative-hypnotic drug, has made its way to Minnesota. Rohypnol is a sleeping pill used in Mexico but not approved for use in the United States. It has been abused primarily by young people who combine the drug with alcohol. Because of its amnesialike effects it also is being used as a date rape drug, according to a drug alert issued by the Minnesota Department of Human Services.

In southern Minnesota, abuse of the drug has been suspected in several cases in which some is placed in alcoholic beverages of young women who are subsequently exploited sexually. Victims have no recall of the events following sedation. Rohypnol has a bitter taste when added to a beverage and is about 10 times more potent than Valium. For more information on this drug, call the Minnesota Prevention Resource Center at 427-5310 (metro) or (800) 247-1303.

- Hazelden Foundation

Saddam happens

Five years ago today, the Gulf War suddenly became real, as Allied jets swept into Iraq. We're indebted to "War Slang" by Paul Dickson (Pocket Books hardcover; $ 25) for the following information. There is something appealing about slang that grows up around particular pursuits or disciplines, especially hazardous ones: It reflects how we adapt to hardship and even to the possibility of being killed.

Dickson includes sections on specialized slang from the Civil War up through the present. Here are a few from the Gulf War:

- Diver: CNN reporter Charles Jaco, known for diving off camera during Scud alerts.

- Homer: A member of the Iraqi army (based on bumbling Homer Simpson).

- Little Hollywood: Area near the swimming pool of the Dharhran hotel, from which TV correspondents frequently delivered their live reports, often wearing

helmets, flak jackets and goggles, while the camera crews wore T-shirts. Mysterious blue domes seen in the background actually were pool cabanas and storage sheds.

- Poor man's defense: The Iraqi tactic of filling the sky with randomly aimed gunfire, as was seen over Baghdad almost nightly.

- Saddam Happens: Bumper sticker seen on the back of a tank.

- Speed bumps: At first, the handful of U.S. troops on the Saudi Arabian side of the border, facing the massed Iraqi forces on the other side; if the Iraqis had attacked, the Americans saw themselves as little more than speed bumps. Later the term was applied to Iraqi soldiers. (By the time the war ended, Iraqi troops had been killed by Allied forces at a ratio of about 1,000 to one. In fact, the Pentagon later said that more Americans would have died if the troops had remained stateside during the same period, largely from road accidents.)

- W.T.O.: The Washington Theater of Operations - an ironic reference.

In a subsection titled "Murphy's Laws for Grunts," Dickson includes a list of 29 laws. A sampling:

- When in doubt, empty your magazine.

- If the enemy is in range, so are you.

- Tracers work both ways.

- The easy way is always mined.

- Dave Matheny

This week

Thinking about the warm

One way to take the edge off of winter is to go to a big indoor place where they pretend it's some other season - summer, for example. Actually, the annual Minnesota Sportsmen's Boat, Camping and Vacation Show isn't just for warm-weather activities, but that's what comes to mind for most folks: Boats, RVs, hunting and fishing stuff is what it's about. As usual there are displays and demonstrations, including a live trout pond and stage shows.

- What: 1996 Minnesota Sportsmen's Boat, Camping and Vacation Show

- When: Today, 5 to 10:30 p.m.; noon to 10:30 p.m. tomorrow through Friday; 10 a.m. to 10:30 p.m. Saturday; 10 a.m. to 6:30 p.m. Sunday.

- Where: St. Paul Civic Center, St. Paul.

- Admission: $ 6 adults, $ 2 children under 12; preschoolers free.

GRAPHIC: Illustration

LANGUAGE: ENGLISH

LOAD-DATE: January 17, 1996

code of federal regulations

CFR Index and Finding Aids

Revised as of January 1, 1995

UNITED STATES CODE ANNOTATED

Title 21

Food and Drugs

§§ 1 to 800

1995
Supplementary Pamphlet

Covering Years 1973 to 1994

Replacing 1994 pocket part in back of 1972 bound volume

Includes the Laws of the
103rd CONGRESS, SECOND SESSION (1994)

For close of Notes of Decisions
See page III

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tiality for harmful effects through excessive use to the merely average man and even to those below the average. National Nutritional Foods Ass'n v. Weinberger, D.C.N.Y.1973, 366 F.Supp. 1341, affirmed 491 F.2d 845.

Commissioner is not required to set over-the-counter limit beyond which drug may be obtained only by prescription, at maximum which consumer might withstand; substantial margin of safety may be used. National Nutritional Foods Ass'n v. Weinberger, D.C.N.Y.1973, 366 F.Supp. 1341, affirmed 491 F.2d 845.

11. Elements of offense

Where federal law prohibits dispensing of a drug without a prescription, propriety of securing and adjusting that drug without a prescription does not depend upon user's knowledge of the particular dangers involved. Lindsay v. Ortho Pharmaceutical Corp., C.A.N.Y.1980, 637 F.2d 87.

12. Jurisdiction

Reason Food and Drug Administration has primary jurisdiction to determine whether drug sought to be marketed constitutes "new drug" subject to this chapter is expertise of Federal Drug Administration in resolving technical and scientific questions. Biotics Research Corp. v. Heckler, C.A.Nev.1983, 710 F.2d 1375.

13. Persons liable

Under "bulk supplier doctrine," bulk supplier of polytetrafluoroethylene (PTFE) to manufacturer of jaw joint implant, which was regulated by the Food and Drug Administration (FDA), did not have any duty to warn of possible dangers of PTFE in implant, and thus, patients could not recover from supplier for injuries allegedly received as result of implant, on breach of duty to warn theory; FDA approved PTFE as appropriate medical device for use in a medical implant, and before filling the order, supplier informed manufacturer of its lack of knowledge of whether use of device in implants was appropriate. Veil v. Vitek, Inc., D.N.D.1992, 808 F.Supp. 229.

R.C. Ohio §§ 3715.01(A)(5)(a), (A)(6)(a), (B)(2) do not apply to the administration of a drug or device by a licensed member of the medical profession. Morse v. Riverside Hospital, 1974, 339 N.E.2d 846, 44 Ohio App.2d 422.

Complaint brought by patient who contracted hepatitis during a blood transfusion did not state a valid claim for relief against hospital and blood bank based upon negligence by reason of a violation of R.C. Ohio § 3715.01(A)(5)(a), (A)(6)(a), (B)(2), inasmuch as provisions thereof did not apply to administration of a drug or device by a licensed member of medical profession. Morse v. Riverside Hospital, 1974, 339 N.E.2d 846, 44 Ohio App.2d 422.

18. —— Weight and sufficiency

Public promotion of high dosage quantities of vitamins A and D for the cure, mitigation, treatment, and prevention of a variety of ailments, when coupled with the fact that there exists little, if any, evidence of known nutritional requirements above the levels of 10,000 IU per dosage unit of vitamin A and 400 IU per dosage unit of vitamin D was sufficient to demonstrate that Food and Drug Administration requirements that preparations of vitamins A and D above those levels be restricted to prescription sale and be labeled accordingly was not arbitrary or capricious. National Nutritional Foods Ass'n v. Mathews, D.C.N.Y.1976, 418 F.Supp. 394.

Although evidence sufficient to support finding that high potency preparations of certain vitamins had no demonstrated usage as a food, at least for all but an extremely small percentage of the population, above levels established in Food and Drug Administration regulations requiring that high potency preparations be available for sale only by prescription and be labeled accordingly, might not, standing alone, be sufficient to sustain the regulations, it was a relevant and important data in favor of the regulations. National Nutritional Foods Ass'n v. Mathews, D.C.N.Y.1976, 418 F.Supp. 394.

19a. Witnesses

Commissioner of food and drugs would not be called at "Overton-type" hearing, which was being held to determine whether the Food and Drug Administration acted rationally in requiring that preparations of vitamins A and D in excess of specified dosages be restricted to prescription sale and be labeled accordingly, for cross-examination by those opposing the actions taken by the Food and Drug Administration. National Nutritional Foods Ass'n v. Mathews, D.C.N.Y.1976, 418 F.Supp. 394.

21. State regulation or control

Lethal injection statute was not preempted by Federal Drug Abuse Prevention and Control Act (DAPCA) or Federal Food, Drug and Cosmetic Act (FDCA); Statute's single goal was merely to effect execution of lawfully condemned inmates, in contrast to the federal Acts' concerns over deleterious effects of unregulated usage of controlled substances by individual citizens, and statute could not violate federal law, inasmuch as federal government utilized lethal injection method of execution. State v. Deputy, Del.Super.1994, 644 A.2d 411.

§ 355. New drugs

(a) Necessity of effective approval of application

No person shall introduce or deliver for introduction into interstate commerce any new drug, unless an approval of an application filed pursuant to subsection (b) or (j) of this section is effective with respect to such drug.

(b) Filing application; contents

(1) Any person may file with the Secretary an application with respect to any drug subject to the provisions of subsection (a) of this section. Such person shall submit to

the Secretary as a part of the application (A) full reports of investigations which have been made to show whether or not such drug is safe for use and whether such drug is effective in use; (B) a full list of the articles used as components of such drug; (C) a full statement of the composition of such drug; (D) a full description of the methods used in, and the facilities and controls used for, the manufacture, processing, and packing of such drug; (E) such samples of such drug and of the articles used as components thereof as the Secretary may require; and (F) specimens of the labeling proposed to be used for such drug. The applicant shall file with the application the patent number and the expiration date of any patent which claims the drug for which the applicant submitted the application or which claims a method of using such drug and with respect to which a claim of patent infringement could reasonably be asserted if a person not licensed by the owner engaged in the manufacture, use, or sale of the drug. If an application is filed under this subsection for a drug and a patent which claims such drug or a method of using such drug is issued after the filing date but before approval of the application, the applicant shall amend the application to include the information required by the preceding sentence. Upon approval of the application, the Secretary shall publish information submitted under the two preceding sentences.

(2) An application submitted under paragraph (1) for a drug for which the investigations described in clause (A) of such paragraph and relied upon by the applicant for approval of the application were not conducted by or for the applicant and for which the applicant has not obtained a right of reference or use from the person by or for whom the investigations were conducted shall also include—

(A) a certification, in the opinion of the applicant and to the best of his knowledge, with respect to each patent which claims the drug for which such investigations were conducted or which claims a use for such drug for which the applicant is seeking approval under this subsection and for which information is required to be filed under paragraph (1) or subsection (c) of this section—

(i) that such patent information has not been filed,

(ii) that such patent has expired,

(iii) of the date on which such patent will expire, or

(iv) that such patent is invalid or will not be infringed by the manufacture use, or sale of the new drug for which the application is submitted; and

(B) if with respect to the drug for which investigations described in paragraph (1)(A) were conducted information was filed under paragraph (1) or subsection (c) of this section for a method of use patent which does not claim a use for which the applicant is seeking approval under this subsection, a statement that the method of use patent does not claim such a use.

(3)(A) An applicant who makes a certification described in paragraph (2)(A)(iv) shall include in the application a statement that the applicant will give the notice required by subparagraph (B) to—

(i) each owner of the patent which is the subject of the certification or the representative of such owner designated to receive such notice, and

(ii) the holder of the approved application under subsection (b) of this section for the drug which is claimed by the patent or a use of which is claimed by the patent or the representative of such holder designated to receive such notice.

(B) The notice referred to in subparagraph (A) shall state that an application has been submitted under this subsection for the drug with respect to which the certification is made to obtain approval to engage in the commercial manufacture, use, or sale of the drug before the expiration of the patent referred to in the certification. Such notice shall include a detailed statement of the factual and legal basis of the applicant's opinion that the patent is not valid or will not be infringed.

(C) If an application is amended to include a certification described in paragraph (2)(A)(iv), the notice required by subparagraph (B) shall be given when the amended application is submitted.

(c) Period for approval of application; period for, notice, and expedition of hearing; period for issuance of order

(1) Within one hundred and eighty days after the filing of an application under subsection (b) of this section, or such additional period as may be agreed upon by the Secretary and the applicant, the Secretary shall either—

(A) Approve the application if he then finds that none of the grounds for denying approval specified in subsection (d) of this section applies, or

(B) Give the applicant notice of an opportunity for a hearing before the Secretary under subsection (d) of this section on the question whether such application is approvable. If the applicant elects to accept the opportunity for hearing by written request within thirty days after such notice, such hearing shall commence not more than ninety days after the expiration of such thirty days unless the Secretary and the applicant otherwise agree. Any such hearing shall thereafter be conducted on an expedited basis and the Secretary's order thereon shall be issued within ninety days after the date fixed by the Secretary for filing final briefs.

(2) If the patent information described in subsection (b) of this section could not be filed with the submission of an application under subsection (b) of this section because the application was filed before the patent information was required under subsection (b) of this section or a patent was issued after the application was approved under such subsection, the holder of an approved application shall file with the Secretary the patent number and the expiration date of any patent which claims the drug for which the application was submitted or which claims a method of using such drug and with respect to which a claim of patent infringement could reasonably be asserted if a person not licensed by the owner engaged in the manufacture, use, or sale of the drug. If the holder of an approved application could not file patent information under subsection (b) of this section because it was not required at the time the application was approved, the holder shall file such information under this subsection not later than thirty days after September 24, 1984, and if the holder of an approved application could not file patent information under subsection (b) of this section because no patent had been issued when an application was filed or approved, the holder shall file such information under this subsection not later than thirty days after the date the patent involved is issued. Upon the submission of patent information under this subsection, the Secretary shall publish it.

(3) The approval of an application filed under subsection (b) of this section which contains a certification required by paragraph (2) of such subsection shall be made effective on the last applicable date determined under the following:

(A) If the applicant only made a certification described in clause (i) or (ii) of subsection (b)(2)(A) of this section or in both such clauses, the approval may be made effective immediately.

(B) If the applicant made a certification described in clause (iii) of subsection (b)(2)(A) of this section, the approval may be made effective on the date certified under clause (iii).

(C) If the applicant made a certification described in clause (iv) of subsection (b)(2)(A) of this section, the approval shall be made effective immediately unless an action is brought for infringement of a patent which is the subject of the certification before the expiration of forty-five days from the date the notice provided under paragraph (3)(B) is received. If such an action is brought before the expiration of such days, the approval may be made effective upon the expiration of the thirty-month period beginning on the date of the receipt of the notice provided under paragraph (3)(B) or such shorter or longer period as the court may order because either party to the action failed to reasonably cooperate in expediting the action, except that—

(i) if before the expiration of such period the court decides that such patent is invalid or not infringed, the approval may be made effective on the date of the court decision,

(ii) if before the expiration of such period the court decides that such patent has been infringed, the approval may be made effective on such date as the court orders under section 271(e)(4)(A) of Title 35, or

(iii) if before the expiration of such period the court grants a preliminary injunction prohibiting the applicant from engaging in the commercial manufacture or sale of the drug until the court decides the issues of patent validity and infringement and if the court decides that such patent is invalid or not infringed, the approval shall be made effective on the date of such court decision.

In such an action, each of the parties shall reasonably cooperate in expediting the action. Until the expiration of forty-five days from the date the notice made under paragraph (3)(B) is received, no action may be brought under section 2201 of Title

28 for a declaratory judgment with respect to the patent. Any action brought under such section 2201 shall be brought in the judicial district where the defendant has its principal place of business or a regular and established place of business.

(D)(i) If an application (other than an abbreviated new drug application) submitted under subsection (b) of this section for a drug, no active ingredient (including any ester or salt of the active ingredient) of which has been approved in any other application under subsection (b) of this section, was approved during the period beginning January 1, 1982, and ending on September 24, 1984, the Secretary may not make the approval of another application for a drug for which the investigations described in clause (A) of subsection (b)(1) of this section and relied upon by the applicant for approval of the application were not conducted by or for the applicant and for which the applicant has not obtained a right of reference or use from the person by or for whom the investigations were conducted effective before the expiration of ten years from the date of the approval of the application previously approved under subsection (b) of this section.

(ii) If an application submitted under subsection (b) of this section for a drug, no active ingredient (including any ester or salt of the active ingredient) of which has been approved in any other application under subsection (b) of this section, is approved after September 24, 1984, no application which refers to the drug for which the subsection (b) application was submitted and for which the investigations described in clause (A) of subsection (b)(1) of this section and relied upon by the applicant for approval of the application were not conducted by or for the applicant and for which the applicant has not obtained a right of reference or use from the person by or for whom the investigations were conducted may be submitted under subsection (b) of this section before the expiration of five years from the date of the approval of the application under subsection (b) of this section, except that such an application may be submitted under subsection (b) of this section after the expiration of four years from the date of the approval of the subsection (b) application if it contains a certification of patent invalidity or noninfringement described in clause (iv) of subsection (b)(2)(A) of this section. The approval of such an application shall be made effective in accordance with this paragraph except that, if an action for patent infringement is commenced during the one-year period beginning forty-eight months after the date of the approval of the subsection (b) application, the thirty-month period referred to in subparagraph (C) shall be extended by such amount of time (if any) which is required for seven and one-half years to have elapsed from the date of approval of the subsection (b) application.

(iii) If an application submitted under subsection (b) of this section for a drug, which includes an active ingredient (including any ester or salt of the active ingredient) that has been approved in another application approved under subsection (b) of this section, is approved after September 24, 1984, and if such application contains reports of new clinical investigations (other than bioavailability studies) essential to the approval of the application and conducted or sponsored by the applicant, the Secretary may not make the approval of an application submitted under subsection (b) of this section for the conditions of approval of such drug in the approved subsection (b) application effective before the expiration of three years from the date of the approval of the application under subsection (b) of this section if the investigations described in clause (A) of subsection (b)(1) of this section and relied upon by the applicant for approval of the application were not conducted by or for the applicant and if the applicant has not obtained a right of reference or use from the person by or for whom the investigations were conducted.

(iv) If a supplement to an application approved under subsection (b) of this section is approved after September 24, 1984, and the supplement contains reports of new clinical investigations (other than bioavailability studies) essential to the approval of the supplement and conducted or sponsored by the person submitting the supplement, the Secretary may not make the approval of an application submitted under subsection (b) of this section for a change approved in the supplement effective before the expiration of three years from the date of the approval of the supplement under subsection (b) of this section if the investigations described in clause (A) of subsection (b)(1) of this section and relied upon by the applicant for approval of the application were not conducted by or for the applicant and if the applicant has not obtained a right of reference or use from the person by or for whom the investigations were conducted.

(v) If an application (or supplement to an application) submitted under subsection (b) of this section for a drug, which includes an active ingredient (including any ester or salt of the active ingredient) that has been approved in another application under subsection (b) of this section, was approved during the period beginning January 1, 1982, and ending on September 24, 1984, the Secretary may not make the approval of an application submitted under this subsection and for which the investigations described in clause (A) of subsection (b)(1) of this section and relied upon by the applicant for approval of the application were not conducted by or for the applicant and for which the applicant has not obtained a right of reference or use from the person by or for whom the investigations were conducted and which refers to the drug for which the subsection (b) application was submitted effective before the expiration of two years from September 24, 1984.

(d) Grounds for refusing application; approval of application; "substantial evidence" defined

If the Secretary finds, after due notice to the applicant in accordance with subsection (c) of this section and giving him an opportunity for a hearing, in accordance with said subsection, that (1) the investigations, reports of which are required to be submitted to the Secretary pursuant to subsection (b) of this section, do not include adequate tests by all methods reasonably applicable to show whether or not such drug is safe for use under the conditions prescribed, recommended, or suggested in the proposed labeling thereof; (2) the results of such tests show that such drug is unsafe for use under such conditions or do not show that such drug is safe for use under such conditions; (3) the methods used in, and the facilities and controls used for, the manufacture, processing, and packing of such drug are inadequate to preserve its identity, strength, quality, and purity; (4) upon the basis of the information submitted to him as part of the application, or upon the basis of any other information before him with respect to such drug, he has insufficient information to determine whether such drug is safe for use under such conditions; or (5) evaluated on the basis of the information submitted to him as part of the application and any other information before him with respect to such drug, there is a lack of substantial evidence that the drug will have the effect it purports or is represented to have under the conditions of use prescribed, recommended, or suggested in the proposed labeling thereof; or (6) the application failed to contain the patent information prescribed by subsection (b) of this section; or (7) based on a fair evaluation of all material facts, such labeling is false or misleading in any particular; he shall issue an order refusing to approve the application. If, after such notice and opportunity for hearing, the Secretary finds that clauses (1) through (6) do not apply, he shall issue an order approving the application. As used in this subsection and subsection (e) of this section, the term "substantial evidence" means evidence consisting of adequate and well-controlled investigations, including clinical investigations, by experts qualified by scientific training and experience to evaluate the effectiveness of the drug involved, on the basis of which it could fairly and responsibly be concluded by such experts that the drug will have the effect it purports or is represented to have under the conditions of use prescribed, recommended, or suggested in the labeling or proposed labeling thereof.

(e) Withdrawal of approval; grounds; immediate suspension upon finding imminent hazard to public health

The Secretary shall, after due notice and opportunity for hearing to the applicant, withdraw approval of an application with respect to any drug under this section if the Secretary finds (1) that clinical or other experience, tests, or other scientific data show that such drug is unsafe for use under the conditions of use upon the basis of which the application was approved; (2) that new evidence of clinical experience, not contained in such application or not available to the Secretary until after such application was approved, or tests by new methods, or tests by methods not deemed reasonably applicable when such application was approved, evaluated together with the evidence available to the Secretary when the application was approved, shows that such drug is not shown to be safe for use under the conditions of use upon the basis of which the application was approved; or (3) on the basis of new information before him with respect to such drug, evaluated together with the evidence available to him when the application was approved, that there is a lack of substantial evidence that the drug will have the effect it purports or is represented to have under the conditions of use prescribed, recommended, or suggested in the labeling thereof; or (4) the patent information prescribed by subsection (c) of this section was not filed within thirty days after the receipt of written notice from the Secretary specifying the failure to file such information; or (5) that the at the application contains any untrue statement of a material fact: *Provided*, That if the Secretary (or in his absence the officer acting as Secretary) finds that there is an imminent hazard to the public health, he may suspend the approval of such application immediately, and give the applicant prompt notice of his action and afford the applicant the opportunity for an expedited hearing under this subsection; but the authority conferred by this proviso to suspend the approval of an application shall not be delegated. The Secretary may also, after due notice and opportunity for hearing to the applicant, withdraw the approval of an application submitted under subsection (b) or (j) of this section with respect to any drug under this section if the Secretary finds (1) that the applicant has failed to establish a system for maintaining required records, or has repeatedly or deliberately failed to maintain such records or to make required reports, in accordance with a regulation or order under subsection (k) of this section or to comply with the notice requirements of section 360(k)(2) of this title, or the applicant has refused to permit access to, or copying or verification of, such records as required by paragraph (2) of such subsection; or (2) that on the basis of new information before him, evaluated together with the evidence before him when the application was approved, the methods used in, or the facilities and controls used for, the manufacture, processing, and packing of such drug are inadequate to assure and preserve its identity, strength, quality, and purity and were not made adequate within a reasonable time after receipt of written notice from the Secretary specifying the matter complained of; or (3) that on the basis of new information before him, evaluated together with the evidence before him when the application was approved, the labeling of such drug, based on a fair evaluation of all material facts, is false or misleading in any particular and was not corrected within a reasonable time after receipt of written notice from the Secretary specifying the matter complained of. Any order under this subsection shall state the findings upon which it is based.

[See main volume for text of (f) to (i)]

(j) Abbreviated new drug applications

(1) Any person may file with the Secretary an abbreviated application for the approval of a new drug.

(2)(A) An abbreviated application for a new drug shall contain—

(i) information to show that the conditions of use prescribed, recommended, or suggested in the labeling proposed for the new drug have been previously approved for a drug listed under paragraph (6) (hereinafter in this subsection referred to as a "listed drug");

(ii)(I) if the listed drug referred to in clause (i) has only one active ingredient, information to show that the active ingredient of the new drug is the same as that of the listed drug;

(II) if the listed drug referred to in clause (i) has more than one active ingredient, information to show that the active ingredients of the new drug are the same as those of the listed drug, or

(III) if the listed drug referred to in clause (i) has more than one active ingredient and if one of the active ingredients of the new drug is different and the application is filed pursuant to the approval of a petition filed under subparagraph (C), information to show that the other active ingredients of the new drug are the same as the active ingredients of the listed drug, information to show that the different active ingredient is an active ingredient of a listed drug or of a drug which does not meet the requirements of section 321(p) of this title, and such other information respecting the different active ingredient with respect to which the petition was filed as the Secretary may require;

(iii) information to show that the route of administration, the dosage form, and the strength of the new drug are the same as those of the listed drug referred to in clause (i) or, if the route of administration, the dosage form, or the strength of the new drug is different and the application is filed pursuant to the approval of a petition filed under subparagraph (C), such information respecting the route of administration, dosage form, or strength with respect to which the petition was filed as the Secretary may require;

(iv) information to show that the new drug is bioequivalent to the listed drug referred to in clause (i), except that if the application is filed pursuant to the approval of a petition filed under subparagraph (C), information to show that the active ingredients of the new drug are of the same pharmacological or therapeutic

class as those of the listed drug referred to in clause (i) and the new drug can be expected to have the same therapeutic effect as the listed drug when administered to patients for a condition of use referred to in clause (i);

(v) information to show that the labeling proposed for the new drug is the same as the labeling approved for the listed drug referred to in clause (i) except for changes required because of differences approved under a petition filed under subparagraph (C) or because the new drug and the listed drug are produced or distributed by different manufacturers;

(vi) the items specified in clauses (B) through (F) of subsection (b)(1) of this section;

(vii) a certification, in the opinion of the applicant and to the best of his knowledge, with respect to each patent which claims the listed drug referred to in clause (i) or which claims a use for such listed drug for which the applicant is seeking approval under this subsection and for which information is required to be filed under subsection (b) or (c) of this section—

(I) that such patent information has not been filed,

(II) that such patent has expired,

(III) of the date on which such patent will expire, or

(IV) that such patent is invalid or will not be infringed by the manufacture, use, or sale of the new drug for which the application is submitted; and

(viii) if with respect to the listed drug referred to in clause (i) information was filed under subsection (b) or (c) of this section for a method of use patent which does not claim a use for which the applicant is seeking approval under this subsection, a statement that the method of use patent does not claim such a use.

The Secretary may not require that an abbreviated application contain information in addition to that required by clauses (i) through (viii).

(B)(i) An applicant who makes a certification described in subparagraph (A)(vii)(IV) shall include in the application a statement that the applicant will give the notice required by clause (ii) to—

(I) each owner of the patent which is the subject of the certification or the representative of such owner designated to receive such notice, and

(II) the holder of the approved application under subsection (b) of this section for the drug which is claimed by the patent or a use of which is claimed by the patent or the representative of such holder designated to receive such notice.

(ii) The notice referred to in clause (i) shall state that an application, which contains data from bioavailability or bioequivalence studies, has been submitted under this subsection for the drug with respect to which the certification is made to obtain approval to engage in the commercial manufacture, use, or sale of such drug before the expiration of the patent referred to in the certification. Such notice shall include a detailed statement of the factual and legal basis of the applicant's opinion that the patent is not valid or will not be infringed.

(iii) If an application is amended to include a certification described in subparagraph (A)(vii)(IV), the notice required by clause (ii) shall be given when the amended application is submitted.

(C) If a person wants to submit an abbreviated application for a new drug which has a different active ingredient or whose route of administration, dosage form, or strength differ from that of a listed drug, such person shall submit a petition to the Secretary seeking permission to file such an application. The Secretary shall approve or disapprove a petition submitted under this subparagraph within ninety days of the date the petition is submitted. The Secretary shall approve such a petition unless the Secretary finds—

(i) that investigations must be conducted to show the safety and effectiveness of the drug or of any of its active ingredients, the route of administration, the dosage form, or strength which differ from the listed drug; or

(ii) that any drug with a different active ingredient may not be adequately evaluated for approval as safe and effective on the basis of the information required to be submitted in an abbreviated application.

(3) Subject to paragraph (4), the Secretary shall approve an application for a drug unless the Secretary finds—

(A) the methods used in, or the facilities and controls used for, the manufacture, processing, and packing of the drug are inadequate to assure and preserve its identity, strength, quality, and purity;

(B) information submitted with the application is insufficient to show that each of the proposed conditions of use have been previously approved for the listed drug referred to in the application;

(C)(i) if the listed drug has only one active ingredient, information submitted with the application is insufficient to show that the active ingredient is the same as that of the listed drug;

(ii) if the listed drug has more than one active ingredient, information submitted with the application is insufficient to show that the active ingredients are the same as the active ingredients of the listed drug, or

(iii) if the listed drug has more than one active ingredient and if the application is for a drug which has an active ingredient different from the listed drug, information submitted with the application is insufficient to show—

(I) that the other active ingredients are the same as the active ingredients of the listed drug, or

(II) that the different active ingredient is an active ingredient of a listed drug or a drug which does not meet the requirements of section 321(p) of this title,

or no petition to file an application for the drug with the different ingredient was approved under paragraph (2)(C);

(D)(i) if the application is for a drug whose route of administration, dosage form, or strength of the drug is the same as the route of administration, dosage form, or strength of the listed drug referred to in the application, information submitted in the application is insufficient to show that the route of administration, dosage form, or strength is the same as that of the listed drug, or

(ii) if the application is for a drug whose route of administration, dosage form, or strength of the drug is different from that of the listed drug referred to in the application, no petition to file an application for the drug with the different route of administration, dosage form, or strength was approved under paragraph (2)(C);

(E) if the application was filed pursuant to the approval of a petition under paragraph (2)(C), the application did not contain the information required by the Secretary respecting the active ingredient, route of administration, dosage form, or strength which is not the same;

(F) information submitted in the application is insufficient to show that the drug is bioequivalent to the listed drug referred to in the application or, if the application was filed pursuant to a petition approved under paragraph (2)(C), information submitted in the application is insufficient to show that the active ingredients of the new drug are of the same pharmacological or therapeutic class as those of the listed drug referred to in paragraph (2)(A)(i) and that the new drug can be expected to have the same therapeutic effect as the listed drug when administered to patients for a condition of use referred to in such paragraph;

(G) information submitted in the application is insufficient to show that the labeling proposed for the drug is the same as the labeling approved for the listed drug referred to in the application except for changes required because of differences approved under a petition filed under paragraph (2)(C) or because the drug and the listed drug are produced or distributed by different manufacturers;

(H) information submitted in the application or any other information available to the Secretary shows that (i) the inactive ingredients of the drug are unsafe for use under the conditions prescribed, recommended, or suggested in the labeling proposed for the drug, or (ii) the composition of the drug is unsafe under such conditions because of the type or quantity of inactive ingredients included or the manner in which the inactive ingredients are included;

(I) the approval under subsection (c) of this section of the listed drug referred to in the application under this subsection has been withdrawn or suspended for grounds described in the first sentence of subsection (e) of this section, the Secretary has published a notice of opportunity for hearing to withdraw approval of the listed drug under subsection (c) of this section for grounds described in the first sentence of subsection (e) of this section, the approval under this subsection of the listed drug referred to in the application under this subsection has been withdrawn

or suspended under paragraph (5), or the Secretary has determined that the listed drug has been withdrawn from sale for safety or effectiveness reasons;

(J) the application does not meet any other requirement of paragraph (2)(A); or

(K) the application contains an untrue statement of material fact.

(4)(A) Within one hundred and eighty days of the initial receipt of an application under paragraph (2) or within such additional period as may be agreed upon by the Secretary and the applicant, the Secretary shall approve or disapprove the application.

(B) The approval of an application submitted under paragraph (2) shall be made effective on the last applicable date determined under the following:

(i) If the applicant only made a certification described in subclause (I) or (II) of paragraph (2)(A)(vii) or in both such subclauses, the approval may be made effective immediately.

(ii) If the applicant made a certification described in subclause (III) of paragraph (2)(A)(vii), the approval may be made effective on the date certified under subclause (III).

(iii) If the applicant made a certification described in subclause (IV) of paragraph (2)(A)(vii), the approval shall be made effective immediately unless an action is brought for infringement of a patent which is the subject of the certification before the expiration of forty-five days from the date the notice provided under paragraph (2)(B)(i) is received. If such an action is brought before the expiration of such days, the approval shall be made effective upon the expiration of the thirty-month period beginning on the date of the receipt of the notice provided under paragraph (2)(B)(i) or such shorter or longer period as the court may order because either party to the action failed to reasonably cooperate in expediting the action, except that—

(I) if before the expiration of such period the court decides that such patent is invalid or not infringed, the approval shall be made effective on the date of the court decision,

(II) if before the expiration of such period the court decides that such patent has been infringed, the approval shall be made effective on such date as the court orders under section 271(e)(4)(A) of Title 35 or

(III) if before the expiration of such period the court grants a preliminary injunction prohibiting the applicant from engaging in the commercial manufacture or sale of the drug until the court decides the issues of patent validity and infringement and if the court decides that such patent is invalid or not infringed, the approval shall be made effective on the date of such court decision.

In such an action, each of the parties shall reasonably cooperate in expediting the action. Until the expiration of forty-five days from the date the notice made under paragraph (2)(B)(i) is received, no action may be brought under section 2201 of Title 28 for a declaratory judgment with respect to the patent. Any action brought under section 2201 shall be brought in the judicial district where the defendant has its principal place of business or a regular and established place of business.

(iv) If the application contains a certification described in subclause (IV) of paragraph (2)(A)(vii) and is for a drug for which a previous application has been submitted under this subsection continuing such a certification, the application shall be made effective not earlier than one hundred and eighty days after—

(I) the date the Secretary receives notice from the applicant under the previous application of the first commercial marketing of the drug under the previous application, or

(II) the date of a decision of a court in an action described in clause (iii) holding the patent which is the subject of the certification to be invalid or not infringed,

whichever is earlier.

(C) If the Secretary decides to disapprove an application, the Secretary shall give the applicant notice of an opportunity for a hearing before the Secretary on the question of whether such application is approvable. If the applicant elects to accept the opportunity for hearing by written request within thirty days after such notice, such hearing shall commence not more than ninety days after the expiration of such thirty days unless the

Secretary and the applicant otherwise agree. Any such hearing shall thereafter be conducted on an expedited basis and the Secretary's order thereon shall be issued within ninety days after the date fixed by the Secretary for filing final briefs.

(D)(i) If an application (other than an abbreviated new drug application) submitted under subsection (b) of this section for a drug, no active ingredient (including any ester or salt of the active ingredient) of which has been approved in any other application under subsection (b) of this section, was approved during the period beginning January 1, 1982, and ending on September 24, 1984, the Secretary may not make the approval of an application submitted under this subsection which refers to the drug for which the subsection (b) application was submitted effective before the expiration of ten years from the date of the approval of the application under subsection (b) of this section.

(ii) If an application submitted under subsection (b) of this section for a drug, no active ingredient (including any ester or salt of the active ingredient) of which has been approved in any other application under subsection (b) of this section, is approved after September 24, 1984, no application may be submitted under this subsection which refers to the drug for which the subsection (b) application was submitted before the expiration of five years from the date of the approval of the application under subsection (b) of this section, except that such an application may be submitted under this subsection after the expiration of four years from the date of the approval of the subsection (b) application if it contains a certification of patent invalidity or noninfringement described in subclause (IV) of paragraph (2)(A)(vii). The approval of such an application shall be made effective in accordance with subparagraph (B) except that, if an action for patent infringement is commenced during the one-year period beginning forty-eight months after the date of the approval of the subsection (b) application, the thirty-month period referred to in subparagraph (B)(iii) shall be extended by such amount of time (if any) which is required for seven and one-half years to have elapsed from the date of approval of the subsection (b) application.

(iii) If an application submitted under subsection (b) of this section for a drug, which includes an active ingredient (including any ester or salt of the active ingredient) that has been approved in another application approved under subsection (b) of this section, is approved after September 24, 1984, and if such application contains reports of new clinical investigations (other than bioavailability studies) essential to the approval of the application and conducted or sponsored by the applicant, the Secretary may not make the approval of an application submitted under this subsection for the conditions of approval of such drug in the subsection (b) application effective before the expiration of three years from the date of the approval of the application under subsection (b) of this section for such drug.

(iv) If a supplement to an application approved under subsection (b) of this section is approved after September 24, 1984, and the supplement contains reports of new clinical investigations (other than bioavailability studies) essential to the approval of the supplement and conducted or sponsored by the person submitting the supplement, the Secretary may not make the approval of an application submitted under this subsection for a change approved in the supplement effective before the expiration of three years from the date of the approval of the supplement under subsection (b) of this section.

(v) If an application (or supplement to an application) submitted under subsection (b) of this section for a drug, which includes an active ingredient (including any ester or salt of the active ingredient) that has been approved in another application under subsection (b) of this section, was approved during the period beginning January 1, 1982, and ending on September 24, 1984, the Secretary may not make the approval of an application submitted under this subsection which refers to the drug for which the subsection (b) application was submitted or which refers to a change approved in a supplement to the subsection (b) application effective before the expiration of two years from September 24, 1984.

(5) If a drug approved under this subsection refers in its approved application to a drug the approval of which was withdrawn or suspended for grounds described in the first sentence of subsection (e) of this section or was withdrawn or suspended under this paragraph or which, as determined by the Secretary, has been withdrawn from sale for safety or effectiveness reasons, the approval of the drug under this subsection shall be withdrawn or suspended—

(A) for the same period as the withdrawal or suspension under subsection (e) ed this section or this paragraph, or

(B) if the listed drug has been withdrawn from sale, for the period of withdrawal from sale or, if earlier, the period ending on the date the Secretary determines that the withdrawal from sale is not for safety or effectiveness reasons.

(6)(A)(i) Within sixty days of September 24, 1984, the Secretary shall publish and make available to the public—

(I) a list in alphabetical order of the official and proprietary name of each drug which has been approved for safety and effectiveness under subsection (c) of this section before September 24, 1984;

(II) the date of approval if the drug is approved after 1981 and the number of the application which was approved; and

(III) whether in vitro or in vivo bioequivalence studies, or both such studies, are required for applications filed under this subsection which will refer to the drug published.

(ii) Every thirty days after the publication of the first list under clause (i) the Secretary shall revise the list to include each drug which has been approved for safety and effectiveness under subsection (c) of this section or approved under this subsection during the thirty-day period.

(iii) When patent information submitted under subsection (b) or (c) of this section respecting a drug included on the list is to be published by the Secretary, the Secretary shall, in revisions made under clause (ii), include such information for such drug.

(B) A drug approved for safety and effectiveness under subsection (c) of this section or approved under this subsection shall, for purposes of this subsection, be considered to have been published under subparagraph (A) on the date of its approval or September 24, 1984, whichever is later.

(C) If the approval of a drug was withdrawn or suspended for grounds described in the first sentence of subsection (e) of this section or was withdrawn or suspended under paragraph (5) or if the Secretary determines that a drug has been withdrawn from sale for safety or effectiveness reasons, it may not be published in the list under subparagraph (A) or, if the withdrawal or suspension occurred after its publication in such list, it shall be immediately removed from such list—

(i) for the same period as the withdrawal or suspension under subsection (e) of this section or paragraph (5), or

(ii) if the listed drug has been withdrawn from sale, for the period of withdrawal from sale or, if earlier, the period ending on the date the Secretary determines that the withdrawal from sale is not for safety or effectiveness reasons.

A notice of the removal shall be published in the Federal Register.

(7) For purposes of this subsection:

(A) The term "bioavailability" means the rate and extent to which the active ingredient or therapeutic ingredient is absorbed from a drug and becomes available at the site of drug action.

(B) A drug shall be considered to be bioequivalent to a listed drug if—

(i) the rate and extent of absorption of the drug do not show a significant difference from the rate and extent of absorption of the listed drug when administered at the same molar dose of the therapeutic ingredient under similar experimental conditions in either a single dose or multiple doses; or

(ii) the extent of absorption of the drug does not show a significant difference from the extent of absorption of the listed drug when administered at the same molar dose of the therapeutic ingredient under similar experimental conditions in either a single dose or multiple doses and the difference from the listed drug in the rate of absorption of the drug is intentional, is reflected in its proposed labeling, is not essential to the attainment of effective body drug concentrations on chronic use, and is considered medically insignificant for the drug.

(8) The Secretary shall, with respect to each application submitted under this subsection, maintain a record of—

(A) the name of the applicant,

(B) the name of the drug covered by the application,

(C) the name of each person to whom the review of the chemistry of the application was assigned and the date of such assignment, and

(D) the name of each person to whom the bioequivalence review for such application was assigned and the date of such assignment.

The information the Secretary is required to maintain under this paragraph with respect to an application submitted under this subsection shall be made available to the public after the approval of such application.

(k) Records and reports; required information; regulations and orders; access to records

(1) In the case of any drug for which an approval of an application filed under subsection (b) or (j) of this section is in effect, the applicant shall establish and maintain such records, and make such reports to the Secretary, of data relating to clinical experience and other data or information, received or otherwise obtained by such applicant with respect to such drug, as the Secretary may by general regulation, or by order with respect to such application, prescribe on the basis of a finding that such records and reports are necessary in order to enable the Secretary to determine, or facilitate a determination, whether there is or may be ground for invoking subsection (e) of this section. Regulations and orders issued under this subsection and under subsection (i) of this section shall have due regard for the professional ethics of the medical profession and the interests of patients and shall provide, where the Secretary deems it to be appropriate, for the examination, upon request, by the persons to whom such regulations or orders are applicable, of similar information received or otherwise obtained by the Secretary.

(2) Every person required under this section to maintain records, and every person in charge or custody thereof, shall, upon request of an officer or employee designated by the Secretary, permit such officer or employee at all reasonable times to have access to and copy and verify such records.

(l) Public disclosure of safety and effectiveness data

Safety and effectiveness data and information which has been submitted in an application under subsection (b) of this section for a drug and which has not previously been disclosed to the public shall be made available to the public, upon request, unless extraordinary circumstances are shown—

(1) if no work is being or will be undertaken to have the application approved,

(2) if the Secretary has determined that the application is not approvable and all legal appeals have been exhausted,

(3) if approval of the application under subsection (c) of this section is withdrawn and all legal appeals have been exhausted,

(4) if the Secretary has determined that such drug is not a new drug, or

(5) upon the effective date of the approval of the first application under subsection (j) of this section which refers to such drug or upon the date upon which the approval of an application under subsection (j) of this section which refers to such drug could be made effective if such an application had been submitted.

(m) "Patent" defined

For purposes of this section, the term "patent" means a patent issued by the Patent and Trademark Office of the Department of Commerce.

(As amended Aug. 16, 1972, Pub.L. 92-387, § 4(d), 86 Stat. 562; Sept. 24, 1984, Pub.L. 98-417, Title I, §§ 101, 102(a)-(b)(5), 103, 104, 98 Stat. 1585, 1592, 1593, 1597; May 13, 1992, Pub.L. 102-282, § 5, 106 Stat. 161; Aug. 13, 1993, Pub.L. 103-80, § 3(n), 107 Stat. 777.)

HISTORICAL AND STATUTORY NOTES

1993 Amendments

Subsec. (j)(6)(A)(ii). Pub.L. 103-80, § 3(n)(1)(A), corrected a typographical error in the original by substituting "Secretary" for "Secretry".

Subsec. (j)(6)(A)(iii). Pub.L. 103-80, § 3(n)(1)(B), inserted a comma after "published by the Secretary".

Subsec. (k)(1). Pub.L. 103-80, § 3(n)(2), struck out ": Provided, however, That regulations" and inserted in lieu thereof a period and "Regulations".

1992 Amendments

Subsec. (j)(8). Pub.L. 102-282, § 5, added par. (8).

1984 Amendment

Subsec. (a). Pub.L. 98–417, § 102(b)(1), added "or (j)" following "pursuant to subsection (b)".

Subsec. (b)(1). Pub.L. 98–417, § 103(a), designated the existing provisions of subsec. (b) as par. (1) thereof and redesignated existing cls. (1) through (6) of par. (1) as so redesignated as cls. (A) through (F) thereof, respectively.

Pub.L. 98–417, § 102(a)(1), added requirement that the applicant file with the application the patent number and the expiration date of any patent which claims the drug for which the applicant submitted the application or which claims a method of using such drug and with respect to which a claim of patent infringement could reasonably be asserted if a person not licensed by the owner engaged in the manufacture, use, or sale of the drug, that the applicant amend the application to include such information if an application is filed under this subsection for a drug and a patent which claims such drug or a method of using such drug is issued after the filing date but before approval of the application, and that, upon approval of the application, the Secretary publish the information submitted.

Subsec. (b)(2), (3). Pub.L. 98–417, § 103(a), added pars. (2) and (3).

Subsec. (c)(1). Pub.L. 98–417, § 102(a)(2), designated the existing provisions of subsec. (c) as par. (1) thereof and in par. (1) as so designated redesignated former pars. (1) and (2) as subpars. (A) and (B), respectively.

Pub.L. 98–417, § 102(b)(2), substituted "subsection (b) of this section" for "this subsection".

Subsec. (c)(2). Pub.L. 98–417, § 102(a)(2), added par. (2).

Subsec. (c)(3). Pub.L. 98–417, § 103(b), added par. (3).

Subsec. (d)(6). Pub.L. 98–417, § 102(a)(3)(A), added cl. (6) relating to the failure of the application to contain the patent information prescribed by subsec. (b) of this section. Former cl. (6) was redesignated (7).

Subsec. (d)(7). Pub.L. 98–417, § 102(a)(3)(A), redesignated former cl. (6) as (7).

Subsec. (e). Pub.L. 98–417, § 102(a)(3)(B), added, in the first sentence covering the grounds for withdrawal of approval by the Secretary, a new cl. (4) relating to the failure to file the patent information prescribed by subsec. (c) of this section within 30 days after the receipt of written notice from the Secretary specifying the failure to file such information, and redesignated the former cl. (4) as (5).

Pub.L. 98–417, § 102(b)(3), inserted, in the provisions of the second sentence preceding cl. (1) of the enumeration of clauses covering the grounds for withdrawal of approval by the Secretary, the phrase "submitted under subsection (b) or (j) of this section" after "withdraw the approval of an application".

Pub.L. 98–417, § 102(b)(4), substituted, in cl. (1) of the second sentence covering the grounds for withdrawal of approval by the Secretary, the phrase "under subsection (k) of this section or to comply with the notice requirements of section 360(k)(2) of this title" for "under subsection (j) of this section or to comply with the notice requirements of section 360(j)(2) of this title".

Subsec. (j). Pub.L. 98–417, § 101, added subsec. (j). Former subsec. (j) was redesignated (k).

Subsec. (k). Pub.L. 98–417, § 101, redesignated former subsec. (j) as (k).

Subsec. (k)(1). Pub.L. 98–417, § 102(b)(5), substituted "under subsection (b) or (j) of this section" for "pursuant to this section".

Subsecs. (*l*), (m). Pub.L. 98–417, § 104, added subsecs. (*l*) and (m).

1972 Amendment

Subsec. (e). Pub.L. 92–387 inserted "or to comply with the notice requirements of section 360(j)(2)" in clause (1) of the second sentence relating to the maintenance of records.

Change of Name

The Department of Health, Education, and Welfare was redesignated the Department of Health and Human Services, and the Secretary of Health, Education, and Welfare or any other official of the Department of Health, Education and Welfare was redesignated the Secretary or official, as appropriate, of Health and Human Services, with any reference to the Department of Health, Education, and Welfare, the Secretary of Health, Education, and Welfare, or any official of the Department of Health, Education, and Welfare, in any law, rule, regulation, certificate, directive, instruction, or other official paper in force on the effective date of Pub.L. 96–88, as prescribed by section 601 of Pub.L. 96–88, Title VI, Oct. 17, 1979, 93 Stat. 696, set out as a note under section 3401 of Title 20, Education, deemed to refer and apply to the Department of Health and Human Services or the Secretary of Health and Human Services, respectively, except to the extent such reference is to a function or office transferred to the Secretary of Education or the Department of Education under Pub.L. 96–88, Title III, §§ 301 to 307, Oct. 17 1979, 93 Stat. 677 to 681. See section 3441 to 3447 and 3508 of Title 20.

Effective Date of 1984 Amendment

Section 105 of Pub.L. 98–417 provided that:

"(a) The Secretary of Health and Human Services shall promulgate, in accordance with the notice and comment requirements of section 553 of title 5, United States Code [section 553 of Title 5, Government Organization and Employees], such regulations as may be necessary for the administration of section 505 of the Federal Food, Drug, and Cosmetic Act [this section], as amended by sections 101, 102, and 103 of this Act [enacting subsec. (j) of this section and amending subsecs. (a) to (e) and (k)(1) of this section and section 360cc(a) and (b) of this title], within one year of the date of enactment of this Act [Sept. 24, 1984].

"(b) During the period beginning sixty days after the date of the enactment of this Act [Sept. 24, 1984], and ending on the date regulations promulgated under subsection (a) take effect, abbreviated new drug applications may be submitted in accordance with the provisions of section 314.2 of title 21 of the Code of Federal Regulations and shall be considered as suitable for any drug which has been approved for safety and effectiveness under section 505(c) of the Federal Food, Drug, and Cosmetic Act [subsec. (c) of this section] before the date of the enactment of this Act [Sept. 24, 1984]. If any such provision is inconsistent with the requirements of section 505(j) of the Federal Food, Drug, and Cosmetic Act [subsec. (j) of this section], the Secretary shall consider the application under the applicable requirements of such section. The Secretary of Health and Human Services may not approve such an abbreviated new drug application which is filed for a drug which is described in sections 505(c)(3)(D) and 505(j)(4)(D) of the Federal Food, Drug, and Cosmetic Act [subsecs. (c)(3)(D) and (j)(4)(D) of this section], except in accordance with such section."

Effective Date of 1972 Amendment

Amendment by Pub.L. 92–387 effective on the first day of the sixth month beginning after Aug. 16, 1972, see section 5 of Pub.L. 92–387, set out as a note under section 360 of this title.

Federal Policy Regarding the Export of Banned or Significantly Restricted Substances

For provisions relating to the applicability of the term "banned or significantly restricted substance", as defined, and the Federal policy regarding the export of banned or significantly restricted substances, see section 1–101 of Ex. Ord. No. 12264, Jan. 15, 1981, 46 F.R. 4659, set out as a note under section 2403 of Title 50, Appendix, War and National Defense.

Legislative History

For legislative history and purpose of Pub.L. 92–387, see 1972 U.S. Code Cong. and Adm. News, p. 2963. See, also, Pub.L. 98–417, 1984 U.S. Code Cong. and Adm. News, p. 2647; Pub.L. 102–282, 1992 U.S. Code Cong. and Adm. News, p. 103.

CROSS REFERENCES

Patents, extension of patent term, see 35 USCA § 156.

FEDERAL PRACTICE AND PROCEDURE

Review of administrative decisions in courts of appeals, see Wright, Miller, Cooper & Gressman: Jurisdiction § 3941.

WEST'S FEDERAL PRACTICE MANUAL

Application for use of new drug, see § 3688.

CODE OF FEDERAL REGULATIONS

Formal evidentiary public hearing, see 21 CFR 12.1 et seq.

New animal drugs, see 21 CFR 510.3.

New animal feed drugs, see 21 CFR 558.3.

New drugs for human use, see 21 CFR 310.100 et seq.

LAW REVIEW COMMENTARIES

A survey of law regarding the liability of manufacturers and sellers of drug products and medical devices. Bryan J. Maedgen and Sheree Lynn McCall, 18 St. Mary's L.J. 395 (1986).

Brother can you spare a drug: Should the experimental drug distribution standards be modified in response to the needs of persons with Aids? 19 Hofstra L.Rev. 191 (1990).

Developing, testing, and marketing an AIDS vaccine: Legal concerns for manufacturers. Alison Joy Arnold, 139 U.Pa.L.Rev. 1077 (1991).

Drug Price Competition and Patent Term Restoration Act of 1984: Is it a healthy long term solution? Note, 21 Rutgers L.J. 147 (1989).

From dog food to prescription drug advertising: Litigating false scientific establishment claims under the Lanham Act. Charles J. Walsh and Marc S. Klein, 22 Seton Hall L.Rev. 389 (1992).

Getting new drugs to people with AIDS: A public policy response to Lansdale. Marsha N. Cohen, 18 Hastings Const.L.Q. 471 (1991).

Long-range planning in environmental and health regulatory agencies. Richard N.L. Andrews, 20 Ecology L.Q. 515 (1993).

More gold and more fleece: Improving the legal sanctions against medical research fraud. James T. O'Reilly, 42 Admin.L.Rev. 393 (1990).

OMB involvement in FDA drug regulations: Regulating the regulators. Comment, 38 Catholic U.L.Rev. 175 (1988).

Right of privacy in choosing medical treatment: Should terminally ill persons have access to drugs not yet approved by the Food and Drug Administration? 20 John Marshall L.Rev. 696 (1987).

The Drug Price Competition and Patent Term Restoration Act of 1984. James J. Wheaton, 35 Catholic U.L.Rev. 433 (1986).

LIBRARY REFERENCES

Regulation of drugs and pharmacists generally, see Drugs and Narcotics ⇐ 1, 11, et seq.

Regulation of drugs and pharmacists generally, see C.J.S. Drugs and Narcotics § 27 et seq.

NOTES OF DECISIONS

1. Constitutionality

A single administrative proceeding in which each manufacturer of drug challenged on ground of efficacy may be heard is constitutionally permissible measured by requirements of procedural due process. Weinberger v. Hynson, Westcott and Dunning, Inc., Va.1973, 93 S.Ct. 2469, 412 U.S. 609, 37 L.Ed.2d 207.

Defendant could be indicted for violations of recordkeeping regulations promulgated by Food and Drug Administration (FDA) for new drug investigations, as FDA had authority to create regulations and delegation of that authority to FDA satisfied constitutional concerns of nondelegation doctrine. U.S. v. Garfinkel, C.A.8 (Minn.) 1994, 29 F.3d 451.

This section requiring new drug approval does not deny equal protection to person suffering from Down's Syndrome or their parents and custodians. Duncan v. U.S., D.C.Okl.1984, 590 F.Supp. 89.

This chapter's statutory scheme for gaining approval for new drug applications in order to permit introduction into interstate commerce of such new drug does not require Food and Drug Administration to approve or disapprove any new drug in absence of application and is constitutional as exercise of Congress's power to set standards in order to protect public from unsafe drugs, even though drug application may involve costs which are so substantial as to cause persons appropriately situated to forego compliance with this chapter. Gadler v. U.S., D.C.Minn. 1977, 425 F.Supp. 244.

2. Construction

Even if a substance is also a food, it may be subjected to requirements of this chapter if it is used in the diagnosis, cure, mitigation, treatment or prevention of diseases in man or other animals; intended use is an important aspect in determining whether the substance is a drug. Rutherford v. U.S., C.A.Okl.1976, 542 F.2d 1137, on remand 424 F.Supp. 105.

A consistent construction of this chapter by the Food and Drug Administration for 30 years and a construction which accords with the literal language of this chapter may only be changed by Congress itself. USV Pharmaceutical Corp. v. Richardson, C.A.Va.1972, 461 F.2d 223, affirmed 93 S.Ct. 2498, 412 U.S. 655, 37 L.Ed.2d 244.

New drug provisions must be construed broadly to meet congressional purpose to keep inadequately tested medical and related products which might cause widespread danger to human life out of interstate commerce. U.S. v. General Nutrition, Inc., W.D.N.Y.1986, 638 F.Supp. 556.

Definition of "new drug," within meaning of this section, which provided that such drugs could not be marketed prior to approval by Food and Drug Administration of either new drug application or abbreviated new drug application, must be liberally construed in order to effectuate policy of this chapter, which is protection of public health and safety. U.S. v. Articles of Drug . . . HORMONIN, D.C.N.J.1980, 498 F.Supp. 424, affirmed 672 F.2d 902, 904.

3. —— With other laws

Reach of scientific inquiry under subsec. (d) of this section defining general contours of "substantial evidence" respecting efficacy of drug for purposes of refusal or approval of a new drug application, and under section 321 of this title defining a "new drug," subject to provisions of this chapter, as a drug not generally recognized among experts as effective as well as safe for its intended uses, is precisely the same. Weinberger v. Bentex Pharmaceuticals, Inc., S.C. 1973, 93 S.Ct. 2488, 412 U.S. 645, 37 L.Ed.2d 235.

Court would presume that Congress was aware that this chapter would effect the earning potentiality of a drug patentee and chose to permit that effect when it tightened requirements for obtaining approval for new drugs. Roche Products, Inc. v. Bolar Pharmaceutical Co., Inc., C.A.Fed.1984, 733 F.2d 858, certiorari denied 105 S.Ct. 183, 469 U.S. 856, 83 L.Ed.2d 117.

Orders which do not deny or withdraw a new-drug application are reviewable under Administrative Procedure Act, sections 551 et seq. and 701 et seq. of Title 5, if they declare a "new drug" status. North American Pharmacal, Inc. v. Department of Health, Ed. and Welfare, C.A.8, 1973, 491 F.2d 546.

Provision of section 321 of this title defining a "new drug" as any drug not generally recognized among qualified experts as safe and effective for use under conditions prescribed, recommended, or suggested in labeling thereof should

be read with provision of this section requiring a new drug application to contain a full description of methods used in, and facilities and controls used for, manufacture, processing, and packing of drug and, as so read, should be construed as requiring premarketing approval for a new drug product of any manufacturer even if product purports to be a generic or "me-too" copy of a recognized drug. Pharmadyne Laboratories, Inc. v. Kennedy, D.C.N.J.1979, 466 F.Supp. 100, affirmed 596 F.2d 568.

Issues which were presented in complaint challenging Food and Drug Administration's administering of this section and section 357 of this title, governing withdrawal of approval of antibiotic and nonantibiotic drugs upon finding of lack of substantial evidence that the drugs have effect they are represented to have under conditions of use prescribed, recommended or suggested in labeling, and which did not deal with agency discretion were subject to review under the Administrative Procedure Act, sections 551 et seq. and 701 et seq. of Title 5. American Public Health Ass'n v. Veneman, D.C.D.C.1972, 349 F.Supp. 1311.

4. Purpose

In enacting 1962 amendments to this chapter which direct Food and Drug Administration to refuse approval for a new drug application and to withdraw any prior approval if substantial evidence that drug is effective for its intended use is lacking, Congress intended test for establishing efficacy to be a rigorous one; Congress intended that clinical impressions of practicing physicians and poorly controlled experiments would not constitute an adequate basis for establishing efficacy. Weinberger v. Hynson, Westcott and Dunning, Inc., Va.1973, 93 S.Ct. 2469, 412 U.S. 609, 37 L.Ed.2d 207.

Drug Price Competition and Patent Term Restoration Act has the general purposes of increasing the availability of low-cost drugs by expanding the generic drug approval procedure and of encouraging new drug research by restoring some of the patent term lost while drug products undergo testing and await FDA premarket approval. Glaxo Operations UK Ltd. v. Quigg, C.A.Fed. (Va.) 1990, 894 F.2d 392.

This chapter and underlying regulations governing approval of marketing of new drugs were not intended to provide patent-like protection for a seller who has gained approval of a pioneer new drug application. Upjohn Mfg. Co. v. Schweiker, C.A.Mich.1982, 681 F.2d 480.

Purpose of this section relating to new drugs is to protect public against danger to human life arising from use of unsafe and ineffective drugs by assuring that, before any drug is marketed, it will have been carefully reviewed by Food and Drug Administration experts, and Congress' exclusion of generally recognized drug products from definition of "new drug" is very narrow one, which is not intended to permit pharmaceutical manufacturer to substitute its opinion regarding safety or effectiveness of a drug for that of the Food and Drug Administration or to require court to develop its own body of scientific knowledge in substitution for that of the FDA. Premo Pharmaceutical Laboratories, Inc. v. U.S., C.A.N.Y.1980, 629 F.2d 795.

4a. Retroactive effect

Drug, with respect to which a new drug application had been filed under this chapter as originally enacted which permitted evaluation of a new drug solely on grounds of unsafety, was not exempt from 1962 amendments to this chapter, which directs the Food and Drug Administration to withdraw any prior approval if substantial evidence that the drug is effective for its intended use is lacking, by virtue of "grandfather clause" of 1962 amendments to this chapter, notwithstanding contention that when drug became generally recognized as safe and was no longer a "new drug," its new drug application ceased to be effective. Weinberger v. Hynson, Westcott and Dunning, Inc., Va.1973, 93 S.Ct. 2469, 412 U.S. 609, 37 L.Ed.2d 207.

This section contemplates that drugs whose new drug applications became effective prior to adoption thereof will be on basis of adequate and well-controlled investigations; withdrawal proceedings cannot be thwarted by a showing of general recognition of effectiveness based merely on expert testimony and reports with respect to investigations and clinical observations regardless of the controls used. Weinberger v. Hynson, Westcott and Dunning, Inc., Va.1973, 93 S.Ct. 2469, 412 U.S. 609, 37 L.Ed.2d 207.

Efficacy requirements of this section were not designed to be prospective only. Weinberger v. Hynson, Westcott and Dunning, Inc., Va.1973, 93 S.Ct. 2469, 412 U.S. 609, 37 L.Ed.2d 207.

If, on October 9, 1962, laetrile was marketed for exactly the same uses for which it is presently being sold and was generally recognized by qualified experts as safe for those uses, it is exempt, under grandfather clause contained in 1962 amendment to this chapter [set out as a note under section 321 of this title], from the test of general recognition by experts as being safe and effective for its claimed uses. Rutherford v. U.S., C.A.Okl.1976, 542 F.2d 1137, on remand 424 F.Supp. 105.

Where new drug application had been approved and no proceedings had been commenced by the Secretary to withdraw approval, drug manufacturer's purported withdrawal prior to day immediately preceding effective date of 1962 effectiveness amendment [set out as a note under section 321 of this title] to this chapter was ineffective for purpose of determining whether drugs qualified for permanent "grandfather clause" exemption from enlarged definition of a "new drug" included in amendments. USV Pharmaceutical Corp. v. Richardson, C.A.Va. 1972, 461 F.2d 223, affirmed 93 S.Ct. 2498, 412 U.S. 655, 37 L.Ed.2d 244.

Manufacturer, whose marketing approval for its drug was outstanding and had not been legally withdrawn on date of 1962 amendment to this chapter was not entitled to claimed benefit of section 107 of Pub.L. 87–781, set out as a note under section 321 of this title, applicable to drugs not covered by an effective marketing order on day immediately before enacting date of amendments. Hynson, Westcott & Dunning, Inc. v. Richardson, C.A.4, 1972, 461 F.2d 215, modified on other grounds 93 S.Ct. 2469, 412 U.S. 609, 37 L.Ed.2d 207.

5a. Generally

While this chapter provides the Food and Drug Administration with sanctions, such as civil injunction proceedings, criminal penalties, and in rem seizure and condemnation, to enforce prohibition against sale in commerce of any article without an effective new drug application, this chapter does not create a dual system, one administrative and the other judicial. CIBA Corp. v. Weinberger, N.J.1978, 98 S.Ct. 2495, 412 U.S. 640, 37 L.Ed.2d 230.

Food and Drug Administration was not compelled to pursue new drug procedure in the laetrile situation in the absence of an application. Rutherford v. U.S., C.A.Okl.1976, 542 F.2d 1137, on remand 424 F.Supp. 106.

Where it was well-known that liver damage was among adverse effects on humans from prolonged use of drug, drug manufacturer, which was neither sponsor nor promoter of drug, was not liable for death of user from liver damage on theory that drug had not been properly tested for dangerous and harmful side effects it would produce. Brick v. Barnes-Hines Pharmaceutical Co., Inc., D.C.D.C.1977, 428 F.Supp. 496.

5b. Offenses within section

Cancer patient's purchase of Laetrile in Mexico and subsequent transportation of that drug to Minnesota for his personal use constituted introduction of Laetrile into interstate commerce and was prohibited by this section prohibiting introduction or delivery for introduction into interstate commerce any new drug, unless approval of application by Food and Drug Administration is effective with respect to such drug; this section does not purport to apply only to manufacturers or distributors, but plainly states that "no person shall introduce or deliver for introduction into interstate commerce any new drug." Gadler v. U.S., D.C.Minn.1977, 425 F.Supp. 244.

5c. Authority of Secretary

Although this section requiring Secretary of Health, Education and Welfare [now Secretary of Health and Human Services] to disapprove a new drug application if he or she finds that proposed labeling is false or misleading reflects Congress' continuing concern that drug labeling should be both truthful and complete, it cannot fairly be read to encompass authority for requiring the delivery of written material to patient at time of dispensing and these provisions, as contrasted with mislabeling provisions of this chapter, apply only at moment of shipment in interstate commerce and not to action subsequent to shipment in interstate commerce. Pharmaceutical Mfrs. Ass'n v. Food and Drug Administration, D.C.Del.1980, 484 F.Supp. 1179.

In deciding that phenformin hydrochloride posed an imminent hazard, Secretary was authorized to create within suspension order voluntary system of limited distribution to those small number of patients for whom it might be determined that drug's benefits outweighed its risks and was also authorized to delay implementation of order for 90 days. Forsham v. Califano, D.C.D.C.1977, 442 F.Supp. 203.

6. Rules and regulations

Strict and demanding standards in regulations issued under this subchapter, which standards bar anecdotal evidence indicating that doctors "believe" in efficacy of a drug, are amply justified by legislative history of its provisions. Weinberger v. Hynson, Westcott and Dunning, Inc., Va.1973, 93 S.Ct. 2469, 412 U.S. 609, 37 L.Ed.2d 207.

Food and Drug Administration (FDA) may impose regulations on development of drugs but authorized regulations must be for purpose of conditioning investigational drug exemptions which will apply only to drugs intended for use by qualified experts investigating the safety and effectiveness of the drug, but regulations may not require clinical investigators to submit investigational reports directly to FDA. U.S. v. Garfinkel, C.A.8 (Minn.) 1994, 29 F.3d 451.

Amendment to Food and Drug Administration's over-the-counter drug review regulations, creating 12-month period for comment on temporary final monographs, which consumers alleged served only to delay implementation of Food, Drug, and Cosmetic Act's safety and efficacy requirements by further postponing publication of final monographs, was consistent with Act, and was designed to facilitate gathering of supplemental information to promote efficiency, and thus was not arbitrary, capricious or otherwise improper. Cutler v. Hayes, 1987, 818 F.2d 879, 260 U.S.App.D.C. 230.

Authority granted by subsec. (i) of this section allowing the Secretary of Health and Human Services to establish "other conditions relating to the protection of public health" with respect to maintaining accurate drug records is insufficient legislative guidance for the issuance of regulations which, if violated, would furnish the basis for criminal liability. U.S. v. Smith, C.A.Cal.1984, 740 F.2d 734.

The fact-finding procedures employed by Food and Drug Administration in approving British drug manufacturer's new drug application and rejecting American drug manufacturer's petition urging denial of the application was adequate, since Administration followed applicable statutory and regulatory criteria for approving the application, and engaged in informal fact-finding procedures to gather evidence concerning the safety and effectiveness of the drug. Upjohn Mfg. Co. v. Schweiker, C.A.Mich.1982, 681 F.2d 480.

Where drug manufacturer failed to comply with this chapter and regulations governing the manufacturing, sampling and labeling of proposed new drug, new drug application could not be approved. Edison Pharmaceutical Co., Inc. v. Food and Drug Admin., Dept. of Health, Ed. and Welfare, 1979, 600 F.2d 831, 195 U.S.App. D.C. 17.

Only those studies of effectiveness of drug that meet the standards particularized in 21 C.F.R. 130.14 pertaining to adequate and well-controlled studies are acceptable in determining whether there is substantial evidence to support the claims of effectiveness for any drug. Sterling Drug Inc. v. Weinberger, C.A.2, 1974, 503 F.2d 675.

In rejecting evidence submitted in support of new drug application, Food and Drug Administration should make its criticisms express and detailed and cite pertinent regulations and evidentiary flaws. Cooper Laboratories, Inc. v. Commissioners, Federal Food and Drug Administration, 1974, 501 F.2d 772, 163 U.S.App.D.C. 212.

Under regulation pursuant to this section, as it existed prior to 1960 a drug company had the option of filing a supplemental application for a proposed change in the conditions under which such drug is to be used instead of a new drug application when a new drug application has already been approved, thereby eliminating the need to duplicate parts of the application previously approved, rather than mere option of filing a supplemental application or not. Hoffman v. Sterling Drug, Inc., C.A.Pa.1973, 485 F.2d 132, on remand 374 F.Supp. 850.

Regulations whereby new drug application would not be accepted for filing if incomplete on its face by omission of required material and which called for notice to the applicant and, in later regulation, provided for requested filing over protest were reasonable and valid. Durovic v. Richardson, C.A.Ill.1973, 479 F.2d 242, certiorari denied 94 S.Ct. 232, 414 U.S. 944, 38 L.Ed.2d 168, rehearing denied 94 S.Ct. 611, 414 U.S. 1088, 38 L.Ed.2d 494.

Food and Drug Administration's (FDA) regulation concerning waiver of in vivo bioequivalence testing for approval of generic drugs in certain circumstances did not exceed FDA's authority under Hatch-Waxman Amendments which govern FDA's approval of applications for generic versions of pioneer drugs, where FDA regulation did not attempt to waive bioequivalence determinations but, rather, regulation permitted waiver of discrete, specific form of in vivo testing for those categories of drugs where in vivo bioavailability or bioequivalence of drug product could be considered self-evident based on other data. Federal Food, Drug, and Cosmetic Act, § 505(j)(7)(B), as amended, 21 U.S.C.A. § 355(j)(7)(B). Fisons Corp. v. Shalala, D.D.C. 1994, 860 F.Supp. 859.

It is not a crime for protocol investigators to fail to maintain adequate and accurate records; although statute expresly authorizes promulgation of regulations requiring drug manufacturers or sponsors of clinical investigations to maintain and submit reports setting forth the results of clinical tests involving experimental drugs to Food and Drug Administration (FDA), statute's general regulatory authority is insufficient legislative guidance for issuance of regulations which, if violated, would furnish basis for criminal liability. U.S. v. Garfinkel, D.Minn.1993, 822 F.Supp. 1457.

Regulation promulgated by the Food and Drug Administration (FDA), which interpreted "feasibility" exception to statutory prohibition against administration of unapproved drugs to permit administration of such drugs in specific combat circumstances, was not arbitrary, capricious, or manifestly contrary to statute. Doe v. Sullivan, D.D.C.1991, 756 F.Supp. 12, affirmed 938 F.2d 1370, 291 U.S.App.D.C. 111.

Regulations adopted by the Food and Drug Administration for policing the nation's over-the-counter drug market were unlawful to the extent that they affirmatively sanctioned continued marketing of Category III drugs in the absence of an administrative determination that the products were generally recognized by experts as safe and effective. Cutler v. Kennedy, D.C.D.C.1979, 475 F.Supp. 838.

While Food and Drug Administration is to be given administrative flexibility to make regulations and determine new drug status of individual drugs or classes of drugs, argument that Food and Drug Administration lacks administrative resources to insurer compliance with this section, cannot be permitted to postpone to some indefinite future date implementation of required preclearance approval of new drug applications. Hoffmann-LaRoche, Inc. v. Weinberger, D.C.D.C.1975, 425 F.Supp. 890.

The Food and Drug Administration does not have unbridled discretion to do what it pleases in determining whether product is a "new drug" since its procedures must satisfy the rudiments of fair play. National Ethical Pharmaceutical Ass'n v. Weinberger, D.C.S.C.1973, 365 F.Supp. 735, affirmed 503 F.2d 1051.

6a. Application, cancellation of

Where new drug application applicant fails to produce adequate and well-controlled studies showing efficacy, summary disposition of application is authorized. Cooper Laboratories, Inc. v. Commissioner, Federal Food and Drug Administration, 1974, 501 F.2d 772, 163 U.S.App. D.C. 212.

While an applicant for approval to market a new drug may withdraw his application during pendency thereof, he has no such right after approval of the application by the Secretary; at that point only the Secretary can withdraw the approval. USV Pharmaceutical Corp. v. Richardson, C.A.Va.1972, 461 F.2d 223, affirmed 93 S.Ct. 2498, 412 U.S. 655, 37 L.Ed.2d 244.

Criteria which were used by Secretary of Health, Education, and Welfare in deciding to suspend new drug applications for phenformin hydrochloride on ground that drug posed an "imminent hazard" did not improperly reflect intent of Congress nor were they at substantial variance with Food and Drug Administration regulation. Forsham v. Califano, D.C.D.C.1977, 442 F.Supp. 203.

Under this section authorizing Secretary of Health, Education, and Welfare to suspend new drug application for a drug which poses an "imminent hazard," meaning of "imminent hazard" is not to be restricted to a concept of crisis. Forsham v. Califano, D.C.D.C.1977, 442 F.Supp. 203.

6b. Exhaustion of remedies

Failure of consumers of over-the-counter drugs to exhaust their administrative remedies before challenging Food and Drug Administration's regulations implementing Food, Drug and Cosmetic Act program concerning new over-the-counter drugs did not require dismissal of action in view of Food and Drug Administration's waiver of issue by failing to raise objection and futility of pursuing administrative remedies. Cutler v. Hayes, 1987, 818 F.2d 879, 260 U.S.App.D.C. 230.

When Food and Drug Administration has primary jurisdiction to determine status of product, one seeking to contest agency's determination must exhaust all administrative remedies before seeking judicial review. Biotics Research Corp. v. Heckler, C.A.Nev.1983, 710 F.2d 1375.

Food and Drug Administration and California State Department of Health Services had primary jurisdiction to determine whether persons could traffic in new drug; thus, if plaintiff wished to obtain Laetrile to use in the nutritional program for prevention of cancer, he had to exhaust his administrative remedies prior to seeking judicial relief. Carnohan v. U.S., C.A.Cal.1980, 616 F.2d 1120.

Alleged statements by Food and Drug Administration (FDA) employees that they intended to waive bioequivalence testing for certain abbreviated new drug applications and that they intended to treat impurity analysis for generic drugs differently were not final agency actions and, therefore, could not be challenged under Administrative Procedure Act. Fisons Corp. v. Shalala, D.D.C.1994, 860 F.Supp. 859.

Soap manufacturer was required to exhaust his administrative remedies with Food and Drug Administration regarding to determination of whether soap was "safe and effective" for particular purpose for which it had already been marketed, and whether it was therefore not subject to new drug hearings. Farquhar v. Food and Drug Admin., D.C.D.C.1985, 616 F.Supp. 190.

Drug manufacturer which marketed drug under trademark and which filed pioneer new drug application for that drug could maintain action challenging Food and Drug Administration's approval of new drug application to British manufacturer and distributor of drug called "ibuprofen," even though manufacturer had not exhausted its administrative remedies where, to obtain withdrawal of British manufacturer's application, manufacturer would have to show that drug was not safe or not effective and that avenue would have been fruitless. Upjohn Mfg. Co. v. Schweiker, D.C.Mich.1981, 520 F.Supp. 58, affirmed 681 F.2d 480.

Where substantive questions as refined in proceedings required decision as to whether Finkel memorandum to effect that Food and Drug Administration would approve post-1962 duplicate new drug applications in reliance on published reports without fresh clinical investigations or available raw data should be issued as a rule or as a general statement of policy, exempt from notice and comment requirement, questions should have been confronted squarely and decided by the Food and Drug Administration before judicial review was sought and, thus, case would be dismissed for failure to exhaust administrative remedies. Hoffmann-La Roche, Inc. v. Harris, D.C.D.C.1979, 484 F.Supp. 58.

District court's assertion of jurisdiction over action for determination as to whether drug was a "new drug" would be premature prior to refusal of Food and Drug Administration to issue declaratory order Carolina Brown, Inc. v. Weinberger, D.C.S.C.1973, 365 F.Supp. 310.

6c. Reapplication

Unless pharmaceutical manufacturer can show that its drug product is generally recognized, among experts qualified by scientific training and experience to evaluate safety and effectiveness of drugs, as safe and effective for use under conditions prescribed and that, being so recognized, it has been used to material extent or for material time under such conditions, manufacturer must file with Food and Drug Administration a new drug application and establish by substantial evidence to satisfaction of Food and Drug Administration that drug is safe and effective for its intended uses. Premo Pharmaceutical Laboratories, Inc. v. U.S., C.A.N.Y.1980, 629 F.2d 795.

Food and Drug Administration acted reasonably in interpreting term "drug" as used in provisions of Federal Food, Drug and Cosmetic Act requiring information to be filed on "any patent which claims the drug for which the applicant submitted the application," to mean "drug product" for which new drug application was filed. Pfizer, Inc. v. Food and Drug Admin., D.Md.1990, 758 F.Supp. 171.

7. Necessity of approval

Durovic v. Richardson, 327 F.Supp. 386, [main volume] affirmed 479 F.2d 242, certiorari denied 94 S.Ct. 232, 414 U.S. 944, 38 L.Ed.2d 168, rehearing denied 94 S.Ct. 611, 414 U.S. 1088, 38 L.Ed.2d 494.

Drug that had same active ingredient as Food and Drug Administration-approved drug product, which had been marketed for many years, but which had different inactive ingredients, could not be marketed without obtaining approval of new drug application from Food and Drug Administration, where it was not generally recognized among qualified experts as safe and effective for use under conditions stated in labeling, there was no published scientific literature as to drug to enable qualified experts to make necessary determination, experts had sharp differences of opinion, both as to methods used and results claimed, and, although manufacturer had sold 16,500,000 tablets there was no evidence that drug had been used to material extent or for any substantial period of time. Premo Pharmaceutical Laboratories, Inc. v. U.S., C.A.N.Y. 1980, 629 F.2d 795.

Constitutional rights of privacy and personal liberty do not give individuals the right to obtain Laetrile free of lawful exercise of government police power. Carnohan v. U.S., C.A.Cal.1980, 616 F.2d 1120.

Regional compounding centers which performed same function that doctors would otherwise have performed by taking chemotherapeutic drugs approved by the FDA and diluting and repackaging them into single-dosage units ready to be used by patients did not fall within the "repackaging" or "bioequivalent product" exceptions to federal premarketing approval requirements. U.S. v. Baxter Healthcare Corp., N.D.Ill.1989, 712 F.Supp. 1352.

New drug approval requirement applies to patients or users of a new drug as well as to manufacturers of it. Duncan v. U.S., D.C.Okl. 1984, 590 F.Supp. 39.

Options available to Food and Drug Administration such as good manufacturing practice regulations and section 351 of this title did not adequately protect the public so as to obviate need for preclearance, as "new drugs", generic drugs having the same active ingredients and in some cases the same inactive ingredients as in their FDA-approved pioneer counterparts. U.S. v. Premo Pharmaceutical Laboratories, Inc., D.C.N.J.1981, 511 F.Supp. 958.

Food and Drug Administration's policy of permitting new drugs that were chemically equivalent to pioneer drug for which full new drug application was in effect to be marketed without approved new drug application contravened clear statutory requirement of preclearance, was not within intendment of 1962 amendments to this section and legislative scheme they embody, and, by permitting marketing of large classes of such drugs, violated its own regulations. Hoffmann-La Roche, Inc. v. Weinberger, D.C.D.C. 1975, 425 F.Supp. 890.

Manufacturer of drug called "PAX," which was a "new drug" within the meaning of this section, would be preliminarily enjoined from introducing and delivering such drug into interstate commerce from foreign trade zone unless and until approval of an application filed pursuant to this section was effective with respect to such drug. U.S. v. Yaron Laboratories, Inc., D.C.Cal.1972, 365 F.Supp. 917.

7a. Exemptions

Phrase "any drug," in "grandfather clause" of Drug Amendments of 1962, set out as a note under section 321 of this title, which exempts from effectiveness requirements any drug which on date preceding enactment was commercially used or sold in the United States, was not a "new drug" as defined in this chapter as originally enacted, and was not covered by an effective application for a new drug under this chapter as originally enacted, is used in the generic sense, so that "me-toos," those drugs similar or identical to drugs with effective new drug applications, whether products of same or different manufacturers "covered" by an effective new drug application, are not exempt from efficacy requirements. USV Pharmaceutical Corp. v. Weinberger, Va.1973, 93 S.Ct. 2498, 412 U.S. 640, 37 L.Ed.2d 230.

Exemption under the "grandfather clause" of the Drug Amendments of 1962, set out as a note under section 321 of this title, is afforded only for drugs that never had been subject to new drug regulation. Weinberger v. Hynson, Westcott and Dunning, Inc., Va.1973, 93 S.Ct. 2469, 412 U.S. 609, 37 L.Ed.2d 207.

Food and Drug Administration (FDA) is required to promulgate regulations allowing for exemptions from operation of new drug application process which will apply only to drugs intended solely for investigational use, by experts to investigate safety and effectiveness of drugs, and those exemptions must be conditioned on imposition of informed-consent provisions on manufacturers or sponsors. U.S. v. Garfinkel, C.A.8 (Minn.) 1994, 29 F.3d 451.

As an exemption to a comprehensive regulatory statute concerned with public safety, grandfather clause of 1962 amendments to this subchapter is to be strictly construed, and party seeking to grandfather in pre–1962 drug bears burden of proof as to each condition. U.S. v. Articles of Drug Consisting of following: 5,906 Boxes, C.A.Puerto Rico 1984, 745 F.2d 105, certiorari denied 105 S.Ct. 1358, 470 U.S. 1004, 84 L.Ed.2d 379.

Grandfather clause exempting certain drugs from requirement under this chapter of providing effectiveness makes no distinction between pioneer and "me-too" drugs but exempts only that generic class of drugs which on October 9, 1962, were not covered by an effective new drug application. Smithkline Corp. v. Food and Drug Administration, 1978, 587 F.2d 1107, 190 U.S.App.D.C. 210.

Where there was similarity in formula between drug marketer's citrus bioflavonoid drugs subject to new drug applications and its "me-too" drugs, both the NDA'd and the "me-too" drugs would be treated alike and neither could qualify for exemption under the "grandfather clause" from 1962 effectiveness amendment [set out as a note under section 321 of this title] to this chapter. USV Pharmaceutical Corp. v. Richardson, C.A.Va.1972, 461 F.2d 223, affirmed 93 S.Ct. 2498, 412 U.S. 655, 37 L.Ed.2d 244.

In light of health risks associated with estrogenic drug products, drug product which was fixed combination of three unconjugated estrogens was not apt subject for exemption from requirement that expert consensus as to general recognition of the product's safety and effectiveness be founded upon substantial evidence in order for the product to transcend "new drug" status. U.S. v. Articles of Drug . . . HORMONIN, D.C.N.J.1980, 498 F.Supp. 424, affirmed 672 F.2d 902, 904.

Practice of pharmacy exemption from sanctions of this chapter was not applicable where corporation disseminated information to solicit applications for membership in its organization and, as a result of such memberships, prescriptions for its products were referred to single pharmacy that specialized in compounding the drug. U.S. v. Sene X Eleemosynary Corp., Inc., D.C.Fla.1979, 479 F.Supp. 970.

Where there had been no completed tests or investigations to determine either the efficacy or safety of animal drugs, they were never generally recognized as safe and effective for the uses intended, and thus "grandfather clause" exemption from the effectiveness requirement of this section was not applicable. U.S. v. 14 Cases More or Less, "Naremco Medi-Matic Free Choice Poultry Formula", D.C.Mo.1974, 374 F.Supp. 922.

7b. Defenses

Producer and distributor of nutritional, personal care and related products, and its officers and employees, all of whom were prosecuted for

allegedly "misbranding" drug could not complain that drug was improperly classified as prescription drug where they did not avail themselves of procedures to make its arguments before appropriate agency and waited until they had been prosecuted to make arguments in district court. U.S. v. General Nutrition, Inc., W.D.N.Y.1986, 638 F.Supp. 556.

Cancer patient's right to privacy would not protect his importation for personal use of new drug Laetrile in violation of this section prohibiting introduction into interstate commerce of any new drug unless approval of application by Food and Drug Administration is effective with respect to such drug. Gadler v. U.S., D.C.Minn. 1977, 425 F.Supp. 244.

8. Interstate commerce

In order for a court properly to condemn a drug item, a nexus must be shown between drug item and commerce so as to invoke federal jurisdiction; on the one hand, in a case in which a drug is found to be misbranded, it may be condemned when introduced into or while in interstate commerce or while held for sale after shipment in interstate commerce; on the other hand, if a drug is confiscated because it is an unapproved "new drug," it must be shown to have been introduced or delivered for introduction in interstate commerce before it may be condemned. U.S. v. Articles of Drug, C.A.Pa. 1978, 585 F.2d 575.

A drug is "in interstate commerce" for purposes of this section, if one of its components previously traveled in interstate commerce, and if finished drug itself is destined in ordinary course of business for interstate distribution; therefore, since ingredients of drugs seized from pharmaceutical laboratory traveled in interstate commerce, were manufactured in usual course of laboratory's business, and were intended for interstate distribution, there was sufficient nexus with interstate commerce to justify their seizure. U.S. v. Articles of Drug . . . WANS, D.C. Puerto Rico 1981, 526 F.Supp. 703.

Within subsec. (a) of this section, "into interstate commerce" necessarily encompasses introduction of items into flow of shipments and transportation within United States, even if the final destination of the drug is not within the United States. U.S. v. An Article of Drug Consisting of 197 Boxes, More or Less, each Containing 150 Capsules, D.C.Tex.1981, 520 F.Supp. 467.

9. New drug, determination of status as

Although drug marketer in 1961 had stated in a letter to director of new drug branch of bureau of medicine in the Food and Drug Administration that a certain class of products were no longer considered to be new drugs, and marketer in 1961 had stopped filing supplemental information as required by regulation with regard to products for which new drug applications had become effective, marketer's new drug applications had not been withdrawn prior to 1962 so that its products were no longer covered by an effective application for purposes of "grandfather clause" in Drug Amendments of 1962, set out as a note under section 321 of this title. USV Pharmaceutical Corp. v. Weinberger, Va.1973, 93 S.Ct. 2498, 412 U.S. 640, 37 L.Ed.2d 230.

Parties cannot confer jurisdiction to determine "new drug" status of a drug; only Congress can do so. Weinberger v. Bentex Pharmaceuticals, Inc., S.C.1973, 93 S.Ct. 2488, 412 U.S. 645, 37 L.Ed.2d 235.

Whether a particular drug is a "new drug," so as to require an effective new drug application before it may be introduced into commerce, depends in part on expert knowledge and experience of scientists based on controlled clinical experimentation and backed by substantial support in scientific literature. Weinberger v. Bentex Pharmaceuticals, Inc., S.C.1973, 93 S.Ct. 2488, 412 U.S. 645, 37 L.Ed.2d 235.

Issue whether drugs were generally recognized as safe and effective and thus not "new drugs" within this chapter and whether the drugs were exempt from new effectiveness requirements by reason of grandfather clause in the Drug Amendments of 1962, set out as a note under section 321 of this title, were kinds of issues peculiarly suited to initial determination by the Food and Drug Administration with its specialized competence and expertise, and district court's referral of these issues to the Administration was appropriate. Weinberger v. Bentex Pharmaceuticals, Inc., S.C.1973, 93 S.Ct. 2488, 412 U.S. 645, 37 L.Ed.2d 235.

Food and Drug Administration has jurisdiction to determine jurisdictional question whether a particular drug is a "new drug" so as to acquire an effective new drug application before drug may be introduced into commerce. Weinberger v. Hynson, Westcott and Dunning, Inc., Va.1973, 93 S.Ct. 2469, 412 U.S. 609, 37 L.Ed.2d 207.

Toothpaste manufacturer failed to show by substantial evidence that potassium nitrate made contribution to claimed effect of treating dentin hypersensitivity and could not rely solely upon laboratory testing profiles for toothpastes with single active ingredient of sodium MFP to prove anticaries effectiveness; therefore, toothpaste combining sodium MFP and potassium nitrate was "new drug" for which application had to be filed and approved before marketing. U.S. v. Articles of Drug, C.A.7 (Ill.) 1987, 826 F.2d 564.

Food and Drug Administration memorandum, concerning approval of new drug applications for generic versions of drugs first marketed after 1962 that are based on reports in the scientific literature to establish the drug's safety and effectiveness, was consistent with published regulations of the Administration; the memo did not conflict with regulation requiring an applicant to submit reports of all clinical tests sponsored or received by the applicant, nor did it conflict with regulation stating that certain summaries of safety and effectiveness data do not constitute full reports of investigations. Burroughs Wellcome Co. v. Schweiker, C.A.N.C.1981, 649 F.2d 221.

Requirements of "new drug" section of this chapter, namely, general safety and effectiveness recognition, were met once the Government admitted that all of manufacturer's drugs were the same generically as a drug already approved as safe and effective and it was not necessary, therefore, for the Government to perform bioavailability, bioequivalence, and other qualified controlled tests to establish safety and efficacy. U.S. v. Articles of Drug, C.A.Pa.1978, 585 F.2d 575.

Acceptance by the Federal Trade Commission of the Food and Drug Administration determination that drug used by weight reducing clinic was a new drug when used for the treatment of obesity, and thus that the fact should be disclosed to consumers, was supported by substantial evidence and was reasonable. Simeon Management Corp. v. F.T.C., C.A.9, 1978, 579 F.2d 1137.

Although substantial evidence of effectiveness for the labeled use is required for a drug to be generally recognized as effective, such substantial evidence may exist long before the drug is generally recognized as effective for that use; approval of a new drug application does not, alone, remove the approved drug from new drug status. Simeon Management Corp. v. F.T.C., C.A.9, 1978, 579 F.2d 1137.

In the absence of evidence as to how laetrile was marketed before passage of 1962 amendment to this chapter requiring drugs to be recognized as effective, court could not determine whether drug was subject to the new requirement or was grandfathered in. Rutherford v. U.S., C.A.Okl.1976, 542 F.2d 1137, on remand 424 F.Supp. 105.

"New drug" for purposes of this section is a substance which is generally recognized by scientific experts as safe and effective for use under the conditions prescribed or suggested in the labeling thereof unless, prior to 1962, it was subject to the requirements of the Food and Drugs Act of 1906, Act June 30, 1906, Ch. 3915, 34 Stat. 768. Rutherford v. U.S., C.A.Okl.1976, 542 F.2d 1137, on remand 424 F.Supp. 105.

Fact that label contained a contraindication of use in cases of "known or suspected malignancies" did not preclude consideration of danger of activation of latent cancer of prostate in determining whether drug marketed by claimant was a new drug within this subchapter especially in light of evidence that in four out of five cases a patient may have latent cancer of the prostate though not known or suspected. U.S. v. 1,048,000 Capsules, More or Less, "Afrodex," C.A.Tex.1974, 494 F.2d 1158.

The newness of a drug within meaning of provision of this section relating to introduction into interstate commerce of any "new drug" may arise by reason of a new or different recommended use for the drug even though the same drug may not be a "new drug" when used for another disease. Hoffman v. Sterling Drug, Inc., C.A.Pa.1973, 485 F.2d 132, on remand 374 F.Supp. 850.

Affidavits in declaratory judgment action established that drug intended for use in management of malignant tumors had not, either before or after the Drug Amendments of 1962, set out as note under section 321 of this title, achieved general recognition among qualified experts as safe and effective for such use, so as to be exempt from requirement of new drug application. Durovic v. Richardson, C.A.Ill.1973, 479 F.2d 242, certiorari denied 94 S.Ct. 232, 414 U.S. 944, 38 L.Ed.2d 168, rehearing denied 94 S.Ct. 611, 414 U.S. 1088, 38 L.Ed.2d 494.

Where drug was offered for use in the management of malignant tumors, "grandfather clause" in the Drug Amendments of 1962, set out as note under section 321 of this title, had no effect on it, in determining whether a new drug application was required. Durovic v. Richardson, C.A.Ill.1973, 479 F.2d 242, certiorari denied 94 S.Ct. 232, 414 U.S. 944, 38 L.Ed.2d 168, rehearing denied 94 S.Ct. 611, 414 U.S. 1088, 38 L.Ed.2d 494.

Drug is a "new drug," and thus is subject to seizure if shipped in interstate commerce without prior approval of a new drug application, unless it is presently regarded by qualified experts as both safe and effective for its intended use or unless it was generally regarded by qualified experts on the October 9, 1962, effective date of the "grandfather clause" exemption as safe for intended use. U.S. v. An Article of Drug * * * "Bentex Ulcerine", C.A.Tex.1972, 469 F.2d 875, certiorari denied 93 S.Ct. 2772, 412 U.S. 938, 37 L.Ed.2d 397.

Fact that pre-1962 new drug application drugs became generally recognized as safe on or before effective date of 1962 effectiveness amendments [set out as a note under section 321 of this title] to this chapter did not establish that such drugs were no longer covered by an effective new drug application and, thus, exempt, under the permanent "grandfather clause", from the amendment. USV Pharmaceutical Corp. v. Richardson, C.A.Va.1972, 461 F.2d 223, affirmed 93 S.Ct. 2498, 412 U.S. 655, 37 L.Ed.2d 244.

Hair care products which were intended to prevent or cure baldness or thinning hair and which had not been generally recognized as safe and effective for their intended use were "new drugs" and, as such, were subject to regulation by Food and Drug Administration (FDA). U.S. v. Kasz Enterprises, Inc., D.R.I.1994, 855 F.Supp. 534.

Before a product can be exempted from statutory new drug preclearance procedures it must be generally recognized by qualified experts as safe and effective for its intended use, and "general recognition" requirement does not involve actual safety or effectiveness of product, rather it is product's reputation in scientific community that is relevant. U.S. v. 225 Cartons, More or Less, of an Article of Drug, D.N.J.1988, 687 F.Supp. 946.

Drug manufacturer's application for approval of oral dosage of injectable calcium product, even if properly termed "paper" new drug application or abbreviated new drug application, was not subject to competing manufacturer's exclusivity rights where former's application did not refer to latter's oral product or to any investigations which were conducted by or for the latter; hence, effective date of approval of former's application was not delayed by 1984 amendments to Federal Food, Drug, and Cosmetic Act. Burroughs Wellcome Co. v. Bowen, E.D.N.C. 1986, 630 F.Supp. 787.

Government can prove lack of "general recognition" of drug as safe and effective for recommended uses so as to require filing of new drug application by proving absence of material fact as to any of following issues: general recogni-

tion in fact among nation's experts that seized drugs are safe and effective for intended use, existence of adequate and well-controlled studies which constitute substantial evidence of safety and effectiveness required for approval of new drug application, and generally available scientific literature substantiating expert consensus of safety and effectiveness. U.S. v. Articles of Drug, N.D.Ill.1985, 624 F.Supp. 776, affirmed 826 F.2d 564.

Food and Drug Administration Compliance Policy Guide did not bar enforcement action against manufacturer of toothpaste grounded on its introduction into interstate commerce without approved new drug application where language of Guide at issue was not statement of policy or interpretation constituting advisory opinion and where Guide discussed action to be taken by Food and Drug Administration personnel only and did not purport to address behavior by anyone outside Administration. U.S. v. Articles of Drug ... Promise Toothpaste for Sensitive Teeth, D.C.Ill.1984, 594 F.Supp. 211.

Generic drugs manufactured without submission to and approval by Food and Drug Administration of a new-drug application or abbreviated new-drug application were "new drugs" for purpose of application requirement where although active ingredients and in some cases inactive ingredients as well were the same as those in FDA-approved, pioneer counterparts there was expert testimony that such drugs were not generally recognized among qualified experts as safe and effective and even assuming identity of ingredients quantitatively and qualitatively, there were potentially significant differences in manufacturing processes between the generic and pioneer products. U.S. v. Premo Pharmaceutical Laboratories, Inc., D.C.N.J. 1981, 511 F.Supp. 958.

Pharmaceutical manufacturer is not permitted to substitute its judgment as to whether drug product is "new drug" for that of Food and Drug Administration, nor is the court required to develop its own body of scientific knowledge in substitution for the Administration. U.S. v. Articles of Drug . . . HORMONIN, D.C.N.J. 1980, 498 F.Supp. 424, affirmed 672 F.2d 902, 904.

Decision as to whether drug X-Otag Plus shipped by defendants in interstate commerce was a "new drug" and subject to requisite approval before being held for sale in interstate market was to be made by Food and Drug Administration, as agency entrusted by Congress with necessary expertise to make well-informed decisions on issue, and was not a decision which was within jurisdiction of district court in enforcement and injunction proceedings brought against defendants by United States. U.S. v. X-Otag Plus Tablets, D.C.Colo.1977, 441 F.Supp. 105, affirmed in part, remanded in part on other grounds 602 F.2d 1387.

Plaintiff who was dying from cancer of the pancreas and who sought to enjoin the Food and Drug Administration from preventing importation or interstate transportation of Laetrile for purposes of his own consumption raised statutory questions as to classification of Laetrile as a "new drug" sufficiently serious to make them fair grounds for litigation. Rizzo v. U.S., D.C.N.Y.1977, 432 F.Supp. 856.

Food and Drug Administration does not have unbridled discretion to do what it pleases in determining whether a product is a new drug, and its procedures must satisfy rudiments of fair play. Rutherford v. U.S., D.C.Okl.1977, 429 F.Supp. 506.

Where shelf life of drug had been exceeded and, beyond the Food and Drug Administration approved shelf life, it was a drug of unknown effectiveness, it was, in effect, a "new drug" without Administration approval and had to be presumed dangerous. Blanton v. U.S., D.C.D.C. 1977, 428 F.Supp. 360.

Food and Drug Administration has complete authority to determine which drugs are "new" and require an approved new drug application in order to be sold to the public. U.S. v. Marcen Laboratories, Inc., D.C.N.Y.1976, 416 F.Supp. 453, affirmed 556 F.2d 562.

Kit designed for use for performing in home, "preliminary screening test" by which human female may obtain indication of probability that she is or is not pregnant was not "drug" within meaning of this section requiring that "new drug" may be marketed in interstate commerce without first filing "new drug application." U.S. v. Article of Drug—OVA II, D.C.N.J.1975, 414 F.Supp. 660, affirmed, 535 F.2d 1248.

The actual safety or efficacy of a drug is irrelevant as to whether its safety and efficacy is generally recognized among qualified experts, and an announcement by the Food and Drug Administration or any other person as to the actual effectiveness of a drug is not determinative, and is irrelevant, to the ultimate issue of whether a drug is a "new drug." National Ethical Pharmaceutical Ass'n v. Weinberger, D.C.S.C.1973, 365 F.Supp. 735, affirmed 508 F.2d 1051.

In determining whether a drug is "new drug" there must be determination of whether drug has mustered the requisite scientifically reliable evidence of safety and effectiveness before they are in position to drop out of active regulation by ceasing to be "new drug." National Ethical Pharmaceutical Ass'n v. Weinberger, D.C.S.C. 1973, 365 F.Supp. 735, affirmed 508 F.2d 1051.

Where drug which consisted of 14 mgs. of chemical ingredient 9-aminoacridine hydrochloride and binder of 14 mgs. of polyvinylpyrrolidone and which was marketed as prescription drug for alleviation of various vaginal infections had much larger dosage than used in other aminoacridine medication for vaginal infections, was in tampon form rather than gel tablet and cream form, and had binder, drug was "new drug" and not exempt from seizure based on claim of misbranding. U.S. v. Article of Drug "Mykocert", D.C.Ill.1972, 345 F.Supp. 571.

9a. Components

Federal Trade Commission order purporting to remedy wrongs which Commission has found not to have been committed should be set aside, but portion of its order applying to "unusual or special ingredient representations" for all of plaintiff's over-the-counter drugs was reasonably related to violation made by misrepresenting that plaintiff's analgesics did not contain aspirin.

Bristol-Myers Co. v. F.T.C., C.A.2, 1984, 738 F.2d 554, certiorari denied 105 S.Ct. 960, 469 U.S. 1189, 83 L.Ed.2d 966.

Before two or more drugs may be recombined in single product, manufacturer must demonstrate by adequate and well-controlled investigations that each additional component provides specific benefit to patient that warrants increased risk. U.S. v. 225 Cartons, More or Less, of an Article of Drug, D.N.J.1988, 687 F.Supp. 946.

With respect to combination drug, it must be demonstrated that the combination of ingredients is generally recognized as safe and effective in order for the drug to transcend "new drug" status. U.S. v. Articles of Drug . . . HORMONIN, D.C.N.J.1980, 498 F.Supp. 424, affirmed 672 F.2d 902, 904.

Although each of the components of a drug may be generally recognized as safe and effective, a new drug is created when they are combined together in a new and different formulation. U.S. v. An Article of Drug Labeled "Entrol-C Medicated," D.C.Cal.1973, 362 F.Supp. 424, affirmed 513 F.2d 1127.

9b. Exclusive marketing period

A new drug developer's interpretation of the phrase "active ingredient (including any ester or salt of the active ingredient)" as permitting a drug company to obtain an extended period of market exclusivity for the new drug by applying for an approval of the acid first, followed by the salt, but not under the reverse sequence, was not a reasonable interpretation of the statute giving developers of new drugs a specified period of market exclusivity. Abbott Laboratories v. Young, 1990, 920 F.2d 984, 287 U.S.App.D.C. 190, certiorari denied 112 S.Ct. 76, 116 L.Ed.2d 49.

Generic manufacturer of drug products containing controlled released propranolol HCl, which had filed abbreviated new drug application, was entitled to 180 days of exclusivity from date of first commercial marketing of manufacturer's product, even though relevant patent holder chose not to sue manufacturer for patent infringement. Inwood Laboratories, Inc. v. Young, D.D.C.1989, 723 F.Supp. 1523.

Federal Food, Drug, and Cosmetic Act, § 505(j)(4)(D)(ii), as amended, 21 U.S.C.A. § 355(j)(4)(D)(ii), establishing five-year exclusive marketing period following approval of new drug application for nonantibiotic drug in which no abbreviated new drug application may be filed to market generic version of such drug did not apply to provide manufacturer of new antibiotic drug with exclusive marketing period during which Food and Drug Administration could not approve competitor's generic version of pioneer antibiotic drug, particularly where Congress had refused to amend language of provision pertaining to approval of antibiotic drugs [Federal Food, Drug, and Cosmetic Act, § 507, as amended, 21 U.S.C.A. § 357] to create similar exclusivity period. Glaxo, Inc. v. Heckler, D.C.N.C. 1985, 623 F.Supp. 69.

9c. Active ingredient

In the context of a statute that gave developers of new drugs a specified period of market exclusivity depending primarily on pharmaceutical novelty, the phrase "active ingredient (including any ester or salt of the active ingredient)" was ambiguous, as the phrase could refer to either the active ingredient of the original approved drug or to the active ingredient in the new drug. Abbott Laboratories v. Young, 1990, 920 F.2d 984, 287 U.S.App.D.C. 190, certiorari denied 112 S.Ct. 76, 116 L.Ed.2d 49.

12. Submission of investigative reports

Claimant failed to demonstrate that the Food and Drug Administration committed a clear error of judgment or acted arbitrarily and capriciously in denying claimant's request for relabeling of medical device known as "Diapulse" device, in light of the FDA's thorough examination of claimant's supporting documents and characterization of studies as either concerning basic biological phenomena which offered little more than encouragement for follow-up studies, studies with animals which were only indicative as to efficacy of device, studies in humans concerning medical conditions differing from those proposed by claimant, and studies conducted with devices substantially different from "Diapulse." U.S. v. An Article of Device ... Diapulse, C.A.7 (Ill.) 1985, 768 F.2d 826.

For purpose of determining whether a new drug is effective, substantial evidence consisting of well-controlled scientific testing is required and isolated case reports, random experience and reports lacking details needed to permit scientific evaluation are not to be considered. Edison Pharmaceutical Co., Inc. v. Food and Drug Admin., Dept. of Health, Ed. and Welfare, 1979, 600 F.2d 831, 195 U.S.App.D.C. 17.

Substantial evidence supported finding of the Commissioner, made in connection with refusal to approve new drug application, that studies submitted by drug manufacturer to prove the efficacy of new drug were replete with inaccuracies and ambiguities and lacked protocol and statistical analysis and that, therefore, the studies were not "adequate and well controlled" within the meaning of this section and did not establish the efficacy of the new drug. Edison Pharmaceutical Co., Inc. v. Food and Drug Admin., Dept. of Health, Ed. and Welfare, 1979, 600 F.2d 831, 195 U.S.App.D.C. 17.

Studies conducted on manufacturer's old formulation of Fiorinal with Codeine were not well-controlled clinical investigations of products using manufacturer's new formulation in which phenacetin was replaced with increased dosages of aspirin, and thus extrapolation of data derived from studies of old formulation could not be used to obviate need for new drug application for new formulation; manufacturer did not submit any data to indicate bioequivalence of new formulation with old formulation. U.S. v. 225 Cartons, More or Less, of an Article of Drug, D.N.J.1988, 687 F.Supp. 946.

In determining validity of approval of duplicate new drug application, law does not require any single study, viewed in isolation, to provide total support for Food and Drug Administration's action, but rather, record must be viewed as whole, taking into account cumulative and reinforcing nature of evidence. Upjohn Mfg.

Co. v. Schweiker, D.C.Mich.1981, 520 F.Supp. 58, affirmed 681 F.2d 480.

In determining whether allegedly misbranded drug came under grandfather clause exemption from requirement of "effectiveness," court could properly consider reprints of professional medical studies of the drug published by doctors in medical journals, and "dear doctor" letters printed by claimant which were distributed to physicians in promoting the sale of the drug. U.S. v. 1,048,000 Capsules, More or Less, "Afrodex", D.C.Tex.1972, 347 F.Supp. 768, affirmed 494 F.2d 1158.

13. Testing of drugs

Commissioner of Food and Drug Administration did not err in requiring drug manufacturers to show that their oral proteolytic enzymes were therapeutically effective in order to satisfy requirement for FDA approval that drugs be effective by showing of clinical, rather than merely statistical, significance. Warner-Lambert Co. v. Heckler, C.A.3, 1986, 787 F.2d 147.

Dismissal without prejudice of post-office proceeding against manufacturer of hair and scalp products did not collaterally estop Food and Drug Administration from denying efficacy of the treatment, since issue in post-office case concerned accuracy of advertising while issue before Food and Drug Administration was whether data submitted constituted adequate and well-controlled studies, and since dismissals without prejudice do not constitute a final determination. Brandenfels v. Heckler, C.A.9, 1983, 716 F.2d 553.

Under this chapter, before a new drug intended for human use can be marketed in interstate commerce, the drug must be clinically tested to establish that it is both safe and effective. Edison Pharmaceutical Co., Inc. v. Food and Drug Administration, Dept. of Health, Ed., and Welfare, 1979, 600 F.2d 831, 195 U.S.App.D.C. 17.

In proceeding on new drug application, substantial evidence supported conclusion of the Commissioner that, though it might be unethical to conduct such a study comparing two groups of cardiac patients, double-blind controlled testings of the new drug and one of its components could ethically be performed on noncardiac patients and that such testing was necessary before the drug could be administered to cardiac patients. Edison Pharmaceutical Co., Inc. v. Food and Drug Administration, Dept. of Health, Ed., and Welfare, 1979, 600 F.2d 831, 195 U.S.App.D.C. 17.

That multiinvestigator clinical trials testing effectiveness of combination drug which contained Dexedrine and amobarbital and which was labelled for use with obese patients involved subjects who were anxious, obese patients so that trials provided no assurance that Dexedrine, in amounts contained in drug, produced in nonanxious, obese patients side effects capable of being remedied by amobarbital did not render trials deficient under Food and Drug regulation requiring suitability of subjects so as to authorize summary, denial of new drug application in that present labeling of drug could be altered to recommend use with anxious, obese patients. Smithkline Corp. v. Food and Drug Administration, 1978, 587 F.2d 1107, 190 U.S.App.D.C. 210.

Regulation promulgated by Food and Drug Administration with respect to "new drugs" indicates that newness is a function of the novelty of a particular formulation, including the novel composition, combination, dosage, or administration and, though regulation extends so far as to encompass new uses for a drug or new methods of application, it does not encompass a scope so broad as to require bioavailability and bioequivalence tests once a drug is established as being the same generically as a drug already approved safe and effective. U.S. v. Articles of Drug, C.A.Pa.1978, 585 F.2d 575.

Even if reliance on a single well-known active ingredient like gentian violet lowered test for general recognition of efficacy and safety, animal drugs and food additive, which government sought to condemn, could not be properly deemed to be generally recognized as safe or effective, in absence of any adequate, well controlled, completed test of safety or efficacy of these combinations. U.S. v. Articles of Food and Drug Consisting of Coli-Trol 80, F4C-60 Feed Grade, Entrol-S Medicated, Entrol-P, C.A.Ga.1975, 518 F.2d 743.

That pain is difficult, or even impossible, to measure quantitatively does not entail infeasibility of controlled tests for determining drug's efficacy so as to establish grounds for waiver of regulations requiring efficacy of drug to be established by controlled investigation. Cooper Laboratories, Inc. v. Commissioner, Federal Food and Drug Administration, 1974, 501 F.2d 772, 163 U.S.App.D.C. 212.

Where drug manufacturer's submission did not set forth clearly and concisely the specific provision or provisions in regulations which were inapplicable to research dealing with drug's efficacy and did not specify or define alternative procedures which should be used to test drug's efficacy, neither Food and Drug Administration nor court could waive regulations requiring that efficacy of drug be established by controlled investigation. Cooper Laboratories, Inc. v. Commissioner, Federal Food and Drug Administration, 1974, 501 F.2d 772, 163 U.S.App.D.C. 212.

That causal connection between chloroquine phosphate and chloroquine retinopathy was not even suspected in the long term use by humans of the drug at the time manufacturers tested the drug would not relieve them of negligence in failing to conduct animal studies to show the connection between the drug and the disease. Hoffman v. Sterling Drug, Inc., C.A.Pa.1973, 485 F.2d 132, on remand 374 F.Supp. 850.

The safety and efficacy of combination drug involved in misbranding action cannot be equated with the safety of the components separately or in combination with different ingredients; the fact that one individual component of combination drug may be generally recognized as safe and effective is not relevant to the issue whether the combination itself is so recognized. U.S. v. 1,048,000 Capsules, More or Less, D.C.Tex.1972, 347 F.Supp. 768, affirmed 494 F.2d 1158.

Raw manufacturer of DES could not be vertically liable for distribution of DES tablets where tablet manufacturer bore responsibility of conducting separate test to determine adverse effects of drug. George v. Parke-Davis, 1987, 733 P.2d 507, 107 Wash.2d 584.

13a. Clinical studies

Food and Drug Administration bulletin, which provided that physician may, as part of practice of medicine, prescribe different dosage for patient without obtaining approval of the FDA, related to drugs which already had received FDA approval, and did not support contention of claimant, who sought relabeling of medical device known as "Diapulse" device, that differing conditions of use between studies and relabeling proposal were irrelevant, in light of statutory criteria contained in Federal Food, Drug, and Cosmetic Act, [§§ 505(d), 513(a)(3)(B)(i, ii)] as amended, 21 U.S.C.A. §§ 355(d), 360c(a)(3)(B)(i, ii)], which provides that scientific studies must be such that it could fairly and responsibly be concluded that drug or device will have effect it purports or is represented to have under conditions of use prescribed, recommended or suggested in labeling or proposed labeling thereof. U.S. v. An Article of Device ... Diapulse, C.A.7 (Ill.) 1985, 768 F.2d 826.

Food and Drug Administration had established that published clinical studies on Fiorinal with Codeine Nos. 1 and 2 did not establish requisite recognition of product or contribution of its components so as to obviate need for new drug application with respect to drugs; manufacturer submitted no studies with respect to Fiorinal with Codeine No. 1, most studies submitted were conducted with old formulation of Fiorinal with Codeine Nos. 2 and 3, and studies failed to measure efficaciousness of certain components of drugs. U.S. v. 225 Cartons, More or Less, of an Article of Drug, D.N.J.1988, 687 F.Supp. 946.

13b. Breast implants

Food and Drug Administration (FDA) report on risks of silicone gel breast implants was sufficiently reliable to be admissible hearsay as product of factual investigation conducted by FDA pursuant to its statutory authority. Toole v. McClintock, M.D.Ala.1991, 778 F.Supp. 1543.

14. Approval of drug—Administrative agency

Food and Drug Administration has jurisdiction to decide with administrative finality, subject to types of judicial review provided, the "new drug" status of individual drugs or classes of drugs. Weinberger v. Bentex Pharmaceuticals, Inc., S.C.1973, 93 S.Ct. 2488, 412 U.S. 645, 37 L.Ed.2d 235.

Even though a drug manufacturer does not have any new drug application in effect and is not seeking approval of any drugs, the Food and Drug Administration may make a declaratory order that a drug is a "new drug" so as to acquire an effective new drug application before drug may be introduced into commerce; power of the Administration to decide threshold jurisdictional question whether the drug is a "new drug" is not only an incident to its power to approve or withdraw approval of a new drug application. Weinberger v. Hynson, Westcott and Dunning, Inc., Va.1973, 93 S.Ct. 2469, 412 U.S. 609, 37 L.Ed.2d 207.

Trial court's order that drug manufacturer provide drug free of charge to participants in double-blind study of drug for 12 months after study was completed as agreed to in contract did not violate doctrine of primary jurisdiction by taking decision away from Food and Drug Administration (FDA) with respect effectiveness of drug; FDA's determination of efficacy did not have to precede injunction requiring one year of drug be provided free of charge to participants who subjected themselves to double-blind study. Dahl v. HEM Pharmaceuticals Corp., C.A.9 (Nev.) 1993, 7 F.3d 1399.

Determination that new drug application was "approved" in December of 1981 when manufacturer was informed of approval, even though the approval was granted with the understanding that remaining issues concerning final printed labeling be resolved, was not arbitrary and capricious, so that drug was not entitled to period of nonpatent exclusivity under the Hatch-Waxman Amendments. Mead Johnson Pharmaceutical Group, Mead Johnson & Co. v. Bowen, 1988, 838 F.2d 1332, 267 U.S.App.D.C. 382.

Position of Food and Drug Administration that it could approve new drug application prior to submission of final labeling was reasonable interpretation of statute where statute only required submission of proposed labeling and FDA regulation stated that approval would ordinarily follow submission of final labeling. Norwich Eaton Pharmaceuticals, Inc. v. Bowen, C.A.6 (Ohio) 1987, 808 F.2d 486, certiorari denied 108 S.Ct. 68, 484 U.S. 816, 98 L.Ed.2d 32.

In determining effectiveness of drugs, Commissioner of Food and Drug Administration is not required to defer to conclusions of experts that studies submitted by drug companies are adequate and well-controlled and prove effectiveness of drugs under consideration; both validity of methodology used in particular studies and ultimate question of effectiveness are issues for Commissioner to determine. Warner-Lambert Co. v. Heckler, C.A.3, 1986, 787 F.2d 147.

With respect to application for clearance to market a new animal drug, when Food and Drug Administration proceeds by way of ad hoc articulation of safety standards, it is incumbent upon it to give applicant notice of those standards and of manner in which the data before it failed to meet them and that notice must be given in timely fashion to put manufacturer in position to dispute Administration's interpretation of the safety criteria, object to Administration's critique of submitted studies, and conduct and proffer new studies meeting newly articulated requirements, and, should applicant then identify a material issue of fact, Administration must hold hearing. American Cyanamid Co. v. Food and Drug Administration, 1979, 606 F.2d 1307, 196 U.S.App.D.C. 400.

Recommendations of the National Academy of Sciences-National Research Council as to effectiveness of a new drug are advisory in nature. Holland Rantos Co., Inc. v. U.S. Dept. of Health, Ed. and Welfare, 1978, 587 F.2d 1173, 190 U.S.App.D.C. 276.

Food and Drug Administration's disregard, without reasons, of recommendation of study group of the National Academy of Sciences-National Research Council that new drug be

considered effective for treatment of vaginitis did not constitute sufficient ground to set aside final order denying new drug application where refusal to accept panel's rating of effectiveness was essentially judgment that applicant had not yet offered substantial evidence of drug's effectiveness and should be put to its proof and where subsequent events vindicated such judgment in that application was unable to produce necessary adequate and well-controlled studies of drug's effectiveness. Holland Rantos Co., Inc. v. U.S. Dept. of Health, Ed. and Welfare, 1978, 587 F.2d 1173, 190 U.S.App.D.C. 276.

Action of Federal Trade Commission in ordering operations of weight loss clinics to state in their advertisements that one of the drugs being used was a new drug which had not been determined to be effective for obesity did not impermissibly encroach upon the confidential relationship between a physician and a patient; the FTC order did not affect the right of a physician to prescribe or administer the drug for his or her patients but merely prevented the weight loss clinics from advertising their clinics and weight reduction program in a way which failed to disclose that the Food and Drug Administration had not approved the drug for such use. Simeon Management Corp. v. F.T.C., C.A.9, 1978, 579 F.2d 1137.

A new drug may not be introduced into interstate commerce unless an application has been filed with and approved by the Food and Drug Administration; the FDA may not approve a new drug application unless it finds that there is substantial evidence that the drug is effective for the labeled use. Simeon Management Corp. v. F.T.C., C.A.9, 1978, 579 F.2d 1137.

Under this subchapter, ultimate determination of safety of a drug is not a matter given to the courts, but one to be determined by the Food and Drug Administration upon submission of a new drug application. U.S. v. 1,048,000 Capsules, More or Less, "Afrodex", C.A.Tex.1974, 494 F.2d 1158.

Order of Commissioner of Food and Drugs withdrawing approval of line of drugs for interstate marketing was not supported by adequate findings and conclusions, where order merely tracked language of this section, stating in conclusory terms that there was lack of substantial evidence that the drugs were effective, and did not disclose evidence upon which the Commissioner based his judgment. USV Pharmaceutical Corp. v. Secretary of Health, Ed. and Welfare, 1972, 466 F.2d 455, 151 U.S.App.D.C. 284.

Where Commissioner of Food and Drugs had failed to name hearing examiner in response to drug manufacturer's demand and delayed more than two months in responding to manufacturer's request, filed two years later, for a stay pending decision in manufacturer's action for declaratory judgment that its drugs were not new drugs, Commissioner's precipitous summary withdrawal of approval of previously granted new drug applications were arbitrary. USV Pharmaceutical Corp. v. Secretary of Health, Ed. and Welfare, 1972, 466 F.2d 455, 151 U.S.App.D.C. 284.

Issue of whether drug is actually safe and effective is for the Food and Drug Administration. USV Pharmaceutical Corp. v. Secretary of Health, Ed. and Welfare, 1972, 466 F.2d 455, 151 U.S.App.D.C. 284.

Commissioner of Food and Drugs has jurisdiction, in proceeding to determine whether lack of effectiveness as claimed makes a drug unmarketable, to decide the threshold question whether the product in controversy is a "new drug," and if the administrative agency takes jurisdiction, the same jurisdictional issue is present for judicial review on direct appeal from the administrative decision. Ciba Corp. v. Richardson, C.A.N.J.1972, 463 F.2d 225, affirmed 93 S.Ct. 2495, 412 U.S. 640, 37 L.Ed.2d 230.

In light of Food and Drug Administration's function of protecting public health and safety, "paper new drug application policy" which allows approval of duplicate new drug application without examination of raw data when verification of prior studies has been accomplished through scrutiny of scientific community and which is supported by argument that likelihood of fraud or bias existing after years of published studies subject to verification through scrutiny of publishing journals and general scientific community, potential for testing and duplication, and experience of drug's performance once it has been on market, becomes vastly diminished, is valid. Upjohn Mfg. Co. v. Schweiker, D.C.Mich.1981, 520 F.Supp. 58, affirmed 681 F.2d 480.

Determination of actual safety and effectiveness of drug product is committed to Food and Drug Administration due to its superior access to technical expertise. U.S. v. Articles of Drug . . . HORMONIN, D.C.N.J.1980, 498 F.Supp. 424, affirmed 672 F.2d 902, 904.

Determination of whether product constituted a "new drug" requiring filing and approval of a new drug application was within the primary jurisdiction of the Food and Drug Administration, precluding district court review until final agency action and exhaustion of administrative remedies. IMS Ltd. v. Califano, D.C.Cal.1977, 453 F.Supp. 157.

Since the Federal Drug Administration has failed to act in contemplation of what Congress intended in this section, the Administration and Department of Health, Education and Welfare would be found to have in fact disapproved the use of laetrile for treating cancer, and the district court, for want of action on the part of the agencies, had jurisdiction of class action brought by cancer victims and their spouses seeking an order directing the Administration to desist from precluding the administration of laetrile to patients in the United States suffering from cancer. Rutherford v. U.S., D.C.Okl.1975, 399 F.Supp. 1208, affirmed and remanded on other grounds 542 F.2d 1137, on remand 424 F.Supp. 105.

Whether drugs are "new" or "old" requires determination by the Food and Drug Administration as to whether they are generally recognized, among qualified experts, as safe and effective for their intended use. National Ethical Pharmaceutical Ass'n v. Weinberger, D.C.S.C. 1973, 365 F.Supp. 735, affirmed 503 F.2d 1051.

15. —— Judicial

In cases where there has been no formal administrative determination of jurisdictional issue whether drug product is a "new drug" subject to provisions of this chapter district court might well stay its hand, awaiting appropriate administrative determination of this threshold jurisdictional question; however, where there is an administrative determination, whether it be explicit or implicit in the withdrawal of a new drug application, the tactic of "reserving" the threshold jurisdictional question for later judicial determination is not tolerable. CIBA Corp. v. Weinberger, N.J.1973, 93 S.Ct. 2495, 412 U.S. 640, 37 L.Ed.2d 230.

Action by pharmaceutical trade association and one of its member companies seeking judicial review of Food and Drug Administration's regulation of certain drugs which were treated as "new drugs," and seeking a judgment declaring that those drugs were not "new drugs," was properly dismissed on the ground that the matter lay within the primary jurisdiction of the Food and Drug Administration, that judicial review was available only after a formal administrative ruling, and that, in respect to the prayer for declaratory relief, a sound exercise of discretion required the court to refuse to take jurisdiction. National Ethical Pharmaceutical Ass'n v. Weinberger, C.A.S.C.1974, 503 F.2d 1051.

Determination of Court of Appeals reviewing decision of Commissioner of Food and Drugs that a drug is a "new drug" within meaning of this section providing for exclusion of new drugs from market unless proven effective as claimed is reviewable by the Supreme Court, and it is not appropriate that a district court entertain a separate suit by the loser in the administrative proceeding for a redetermination of the same question. Ciba Corp. v. Richardson, C.A.N.J. 1972, 463 F.2d 225, affirmed 93 S.Ct. 2495, 412 U.S. 640, 37 L.Ed.2d 230.

The Food and Drug Administration had primary jurisdiction to determine whether each drug named in applicants' complaint was "new drug" and, following such administrative determination, applicants would then be entitled to seek judicial review. National Ethical Pharmaceutical Ass'n v. Weinberger, D.C.S.C.1973, 365 F.Supp. 735, affirmed 503 F.2d 1051.

Determination by Food and Drug Administration that a product is "new drug" or a "me-too" drug is reviewable. National Ethical Pharmaceutical Ass'n v. Weinberger, D.C.S.C.1973, 365 F.Supp. 735, affirmed 503 F.2d 1051.

15a. —— Timeliness

Writ of mandamus would not issue to compel Food and Drug Administration to expedite processing of application for approval of generic drug, following expiration of statutory period during which decision was to be made; while judicial intervention might benefit applicant, there would be corresponding harm to other applicants whose processing would be further delayed. In re Barr Laboratories, Inc., 1991, 930 F.2d 72, 289 U.S.App.D.C. 187, certiorari denied 112 S.Ct. 297, 298, 116 L.Ed.2d 241.

16. Withdrawal of approval

Under this chapter as originally enacted, which empowers the Food and Drug Administration to withdraw approval of a new drug application whenever new evidence comes to light suggesting that the drug has become unsafe, whether or not the drug was generally recognized as safe in the interim, a new drug application remains effective unless it is suspended. Weinberger v. Hynson, Westcott and Dunning, Inc., Va.1973, 93 S.Ct. 2469, 412 U.S. 609, 37 L.Ed.2d 207.

Substantial evidence supported determination of Commissioner of Food and Drug Administration that use of concomitant medication flawed clinical study of oral proteolytic enzymes and that other studies were in violation of regulatory criteria such that withdrawal of approval was appropriate. Warner-Lambert Co. v. Heckler, C.A.3, 1986, 787 F.2d 147.

Manufacturer was not prejudiced by nine-year delay between request for hearing before Food and Drug Administration on hair and scalp products and Food and Drug Administration's withdrawal of approval, where the delay enabled him to continue marketing the products and where the deaths of doctors who conducted studies did not prejudice defendant in that the truth of their views was not the issue but whether the studies on their face complied with Food and Drug Administration guidelines. Brandenfels v. Heckler, C.A.9, 1983, 716 F.2d 553.

Manufacturers of drug were entitled to notice of specific grounds on which the Food and Drug Administration proposed to withdraw approval of the drug's new drug application and to an opportunity to submit evidence which would entitle them to a hearing before an order of withdrawal could be validly issued. Sterling Drug Inc. v. Weinberger, C.A.2, 1974, 503 F.2d 675.

If court finds that Food and Drug Administration's order withdrawing drug from market identified defects which conclusively rendered each piece of evidence submitted in support of drug's efficacy as being inadequate or uncontrolled in light of permit regulations, court must affirm order. Cooper Laboratories, Inc. v. Commissioner, Federal Food and Drug Administration, 1974, 501 F.2d 772, 163 U.S.App.D.C. 212.

Standard of review to be applied to order of the Food and Drug Administration denying an evidentiary hearing on effectiveness of drug previously approved for marketing solely on demonstration that it was safe for its intended use is whether deficiencies found in the studies submitted by manufacturer of the drug conclusively render the studies inadequate. E. R. Squibb & Sons, Inc. v. Weinberger, C.A.3, 1973, 483 F.2d 1382.

Satisfactory adjudication of appeal from denial by the Food and Drug Administration of evidentiary hearing on effectiveness of drug which had been previously approved on the basis of safety only mandated that a meaningful comparison be made by the FDA between the study submitted in the instant case and study held sufficient by the Supreme Court, and also mandated amplification and clarification in light of highly esoteric and scientific terms employed in the information before the court. E. R. Squibb & Sons, Inc. v. Weinberger, C.A.3, 1973, 483 F.2d 1382.

Action of Food and Drug Administration (FDA) in rescinding its approval of manufacturer's application to make and sell new drug, on ground that approval had been issued through

inadvertent mistake, was not so clearly ultra vires as to justify disregard of exclusive jurisdiction of Court of Appeals and intervention by district court; even if right vested, manufacturer was not deprived of factual hearing to prove its qualifications to make and sell drug, and postdenial hearing met due process requirements. American Therapeutics, Inc. v. Sullivan, D.D.C.1990, 755 F.Supp. 1.

Proposed withdrawal of approval of new drug applications in effect for drug is not a final order and is not ordinarily reviewable in district court. Sterling Drug, Inc. v. Weinberger, D.C.N.Y. 1974, 384 F.Supp. 557, affirmed 509 F.2d 1236.

Secretary of Health, Education, and Welfare must, under this section and section 357 of this title governing withdrawal of antibiotic and nonantibiotic drugs, upon finding of lack of substantial evidence that the drugs have effect they are represented to have under conditions of use prescribed, recommended or suggested in labeling, begin procedures to withdraw a drug when he concludes that there is no substantial evidence of efficacy rather than thereafter granting manufacturers time to bolster record regarding the drug's effectiveness. American Public Health Ass'n v. Veneman, D.C.D.C.1972, 349 F.Supp. 1311.

Invocation of emergency procedure to immediately suspend drugs which present an imminent hazard to the public health is matter which is peculiarly one of judgment. American Public Health Ass'n v. Veneman, D.C.D.C.1972, 349 F.Supp. 1311.

16a. Insurance

Notwithstanding provisions in health insurance policy providing that policy was to be interpreted in accordance with laws of District of Columbia where laetrile was illegal, insured, who was terminally ill, who received laetrile treatments in Oklahoma under specific authority under an order of United States district court and who complied with policy's requirements with regard to establishing her claim, was entitled to have laetrile treatments paid for by insurer as covered medical expenses. Wilson v. Travelers Ins. Co., Okl.1980, 605 P.2d 1327.

17. Hearing

Food and Drug Administration's so-called administrative summary judgment procedure, whereby it will not provide a formal hearing on proposed withdrawal of an effective new drug application because of lack of substantial evidence of efficacy of drug when it is apparent at threshold that applicant has not tendered any evidence which on its face meets statutory standards as particularized by regulations, is valid. Weinberger v. Hynson, Westcott and Dunning, Inc., Va.1973, 93 S.Ct. 2469, 412 U.S. 609, 37 L.Ed.2d 207.

This section and regulations issued thereunder, which express well-established principles of scientific investigation, in their reduction of "substantial evidence" standard to detailed guidelines for protection of public, make Food and Drug Administration's so-called administrative summary judgment procedure, whereby the FDA will not provide a formal hearing on proposed withdrawal of effective new drug application because of lack of substantial evidence of efficacy of drug when it is apparent at threshold that applicant has not tendered any evidence which on its face meets statutory standards as particularized by regulations, appropriate. Weinberger v. Hynson, Westcott and Dunning, Inc., Va.1973, 93 S.Ct. 2469, 412 U.S. 609, 37 L.Ed.2d 207.

Due process does not demand a hearing on proposed withdrawal of an effective new drug application because of lack of substantial evidence of efficacy of drug when it appears conclusively from applicant's pleadings that it cannot succeed. Weinberger v. Hynson, Westcott and Dunning, Inc., Va.1973, 93 S.Ct. 2469, 412 U.S. 609, 37 L.Ed.2d 207.

Food and Drug Administration's denial of adjudicatory hearing on application for clearance to market a new animal drug will be upheld if Administration identifies at least one conclusive deficiency in each of tests proffered, but if studies adopting all reasonably applicable methods of showing drug's safety have not been conclusively demonstrated to be inadequate, Administration must hold a hearing. American Cyanamid Co. v. Food and Drug Administration, 1979, 606 F.2d 1307, 196 U.S.App.D.C. 400.

Food and Drug Administration would have valid ground for denying hearing on application for clearance to market a new animal drug if Administration's interpretation and application of statutory safety standards are unimpeachable. American Cyanamid Co. v. Food and Drug Administration, 1979, 606 F.2d 1307, 196 U.S.App. D.C. 400.

Only if drug manufacturer has had fair opportunity to dispute newly articulated safety standards of Food and Drug Administration and to resubmit compliant tests, or if original tests conclusively failed to meet general statutory prerequisites, may Food and Drug Administration deny hearing on basis of methodology of research relied upon by manufacturer. American Cyanamid Co. v. Food and Drug Administration, 1979, 606 F.2d 1307, 196 U.S.App.D.C. 400.

Under this chapter, it is contemplated that a new drug will be approved or disapproved on the basis of scientific tests contained in the new drug application; the hearing offers an opportunity to test the strength and credibility of this material. Edison Pharmaceutical Co., Inc. v. Food and Drug Admin., Dept. of Health, Ed. and Welfare, 1979, 600 F.2d 831, 195 U.S.App. D.C. 17.

Though a new drug applicant may present testimony or evidence at the hearing to show that the studies and data submitted with the new drug application in fact constitute the adequate tests and substantial evidence necessary for new drug approval, the applicant cannot submit new studies at the hearing to be considered in the first instance by the administrative law judge; to do so would effectively shield an applicant's data from the initial scrutiny of staff experts. Edison Pharmaceutical Co., Inc. v. Food and Drug Admin., Dept. of Health, Ed. and Welfare, 1979, 600 F.2d 831, 195 U.S.App. D.C. 17.

On hearing to determine threshold issue of safety of double-blind tests for new drug, it was

appropriate to require Commissioner, as an exception to usual case, whichever way he decides threshold issue, to hold a full evidentiary hearing on "all" relevant issues relating to approvability of new drug application, where drug manufacturer had first filed new drug application over six years prior thereto and in the interim its application had been denied on three separate occasions without an opportunity for hearing despite direction to contrary from court. Edison Pharmaceutical Co., Inc. v. Food and Drug Administration, Dept. of Health, Ed. and Welfare, 1975, 513 F.2d 1063, 16 U.S.App.D.C. 278, rehearing denied 517 F.2d 164, 170 U.S.App. D.C. 350.

The Food and Drug Administration may withdraw a drug from the market without a hearing when, and only when, it appears conclusively from the applicants "pleadings" that the new drug application cannot succeed. Sterling Drug Inc. v. Weinberger, C.A.2, 1974, 503 F.2d 675.

Word "applicant" or "respondent" in subsec. (g) of this section refers only to holders of new-drug applications; thus, said subsection did not require Secretary personally to notify drug manufacturers which produced anorectic drugs containing amphetamines and which did not hold new-drug applications covering combination amphetamine products of hearing regarding Secretary's withdrawal of approval of such applications. North American Pharmacal, Inc. v. Department of Health, Ed. and Welfare, C.A.8, 1973, 491 F.2d 546.

Publication in Federal Register of notice of hearing regarding the withdrawal of approval of new-drug applications covering combination amphetamine products gave manufacturers, which produced anorectic drugs containing amphetamines and which did not hold new-drug applications covering combination amphetamine products, sufficient opportunity to be heard; and failure personally to notify each manufacturer of hearing did not deprive them of due process. North American Pharmacal, Inc. v. Department of Health, Ed. and Welfare, C.A.8, 1973, 491 F.2d 546.

Petitioner was not entitled to hearing before Commissioner on question of whether or not its product constituted new animal drug within meaning of this section. Agri-Tech, Inc. v. Richardson, C.A.8, 1973, 482 F.2d 1148.

Opportunity to be heard administratively is not prerequisite to prosecution for introduction of a "new drug" into interstate commerce without approval of a new drug application. Durovic v. Richardson, C.A.Ill.1973, 479 F.2d 242, certiorari denied 94 S.Ct. 232, 414 U.S. 944, 38 L.Ed.2d 168, rehearing denied 94 S.Ct. 611, 414 U.S. 1088, 38 L.Ed.2d 494.

Where drug manufacturer's applications for marketing a line of drugs had been approved pursuant to prior law but Commissioner of Food and Drugs proposed, without a hearing, to withdraw that approval on basis of a new standard and new information, together with evidence available when approval was originally granted, it was incumbent upon Commissioner, before calling upon manufacturer for additional evidence establishing a right to a hearing, to state facts and reasons showing at least prima facie that the evidence before him raised no material issue of fact which would justify a hearing. U.S.V. v. Pharmaceutical Corp. v. Secretary of Health, Ed. and Welfare, 1972, 466 F.2d 455, 151 U.S.App.D.C. 284.

In circumstance in which the Food and Drug Administration publishes in Federal Register the required notice to drug manufacturers of opportunity for hearing and proposed withdrawal of drugs from market and manufacturers then fail to avail themselves of opportunity for the hearing within required 30 days, withdrawal of drugs from market is required by this section governing withdrawal of drugs and is purely a ministerial duty, and failure to withdraw constitutes agency action unlawfully withheld. American Public Health Ass'n. v. Veneman, D.C.D.C. 1972, 349 F.Supp. 1311.

Hearing on withdrawal of a new drug application is to be scheduled as soon as practicable after request by drug manufacturers for such a hearing; and, while some agency discretion is conferred in scheduling the hearing, interminable delay is not contemplated. American Public Health Ass'n. v. Veneman, D.C.D.C.1972, 349 F.Supp. 1311.

17a. Jurisdiction

Jurisdictional question whether a drug product is a "new drug," which is defined in section 321 of this title as a drug not generally recognized among experts is effective as well as safe for its intended uses, involves a determination of technical and scientific questions by experts, and agency is therefore appropriately the arm of government to make threshold determination of issue of coverage. CIBA Corp. v. Weinberger, N.J.1973, 93 S.Ct. 2495, 412 U.S. 640, 37 L.Ed.2d 230.

Food and Drug Administration has jurisdiction in an administrative proceeding on proposed withdrawal of an effective new drug application because of lack of substantial evidence of efficacy to determine jurisdictional question whether a drug product is a "new drug" within this chapter which defines a new drug as a drug not generally recognized among experts as effective as well as safe for its intended uses. CIBA Corp. v. Weinberger, N.J.1973, 93 S.Ct. 2495, 412 U.S. 640, 37 L.Ed.2d 230.

Food and Drug Administration has jurisdiction to decide "new drug" status of product and district court may refer new drug issue to Food and Drug Administration for resolution, but court may exercise its concurrent jurisdiction to adjudicate status of product. Premo Pharmaceutical Laboratories, Inc. v. U.S., C.A.N.Y.1980, 629 F.2d 795.

Limited "new drug" issue was sufficiently clear to warrant district court's exercise of its subject-matter jurisdiction, especially where to refer issue to Food and Drug Administration at the late date would be wasteful and duplicative. Premo Pharmaceutical Laboratories, Inc. v. U.S., C.A.N.Y.1980, 629 F.2d 795.

Decision of Commissioner that Laetrile is a "new drug" subject to premarketing approval under this chapter was properly within Food and Drug Administration's primary jurisdiction. Carnohan v. U.S., C.A.Cal.1980, 616 F.2d 1120.

Initial determination of whether drug is new animal drug is within jurisdiction of Commis-

sioner, and he may summarily deny hearing on issue whether drug is generally "recognized" and therefore exempt from withdrawal provisions if he finds there is no "substantial evidence" raising issue of fact. Agri-Tech, Inc. v. Richardson, C.A.8, 1978, 482 F.2d 1148.

Since Congress has created primary jurisdiction in Food and Drug Administration to determine in first instance safety and efficacy of new drug with such administrative determinations subject to review in appropriate court of appeals, as a jurisdictional matter district courts have no role to play in determining whether a new drug should be approved by Food and Drug Administration. Hanson v. U.S., D.C.Minn.1976, 417 F.Supp. 30, affirmed 540 F.2d 947.

Under section 1337 of Title 28 giving the district courts original jurisdiction of any civil action or proceeding arising under any act of Congress regulating commerce, the district court had jurisdiction of class action brought against the United States and the Secretary of Health, Education and Welfare by cancer victims, and their spouses, seeking an order directing the Federal Drug Administration to desist from precluding the administration of laetrile to patients in the United States suffering from cancer, as the prohibiting language of this section stems from and has to do with commerce powers of the United States, and as plaintiffs were being precluded from transporting laetrile in commerce. Rutherford v. U.S., D.C.Okl.1975, 399 F.Supp. 1208, affirmed and remanded on other grounds 542 F.2d 1137, on remand 424 F.Supp. 105.

18. Persons entitled to bring suit

Drug company met "zone of interests" test for prudential standing to bring action to prevent Food and Drug Administration (FDA) from approving generic versions of Intal Nebulizer Solution (cromolyn) without requiring specific testing, as Congress intended Hatch-Waxman Amendments which govern FDA's approval of applications for generic versions of pioneer drugs to benefit pioneer drug manufacturers. Fisons Corp. v. Shalala, D.D.C.1994, 860 F.Supp. 859.

Claim of AIDS (Acquired Immunodeficiency Syndrome) sufferer that drug manufacturer and university acted illegally when they terminated investigation into use of drug Ampligen as treatment for the disease and ceased providing him with the drug as part of their clinical studies did not arise under the Federal Food, Drug, and Cosmetic Act so as to give court jurisdiction over his claim as the civil action arising under an act of Congress regulating commerce. DeVito v. HEM, Inc., M.D.Pa.1988, 705 F.Supp. 1076.

Drug manufacturer which marketed drug under trademark and which filed pioneer new drug application for that drug had standing to file action challenging Food and Drug Administration's approval of new drug application to British manufacturer and distributor of drug called "ibuprofen" on its claim of competitive market position and its claim that trade secret data and information contained in its pioneer new drug application was made subject to public disclosure due to approval of challenged new drug application. Upjohn Mfg. Co. v. Schweiker, D.C.Mich.1981, 520 F.Supp. 58, affirmed 681 F.2d 480.

Threat of injury to plaintiffs, whose claim was not that they would in fact consume unsafe or ineffective drugs, but that they were being subjected to risk to their health on account of marketing of Category III drugs, was both real and immediate and, hence, was sufficient to give plaintiffs standing in suit for declaratory and injunctive relief against regulations of Food and Drug Administration governing the over-the-counter drug market. Cutler v. Kennedy, D.C.D.C.1979, 475 F.Supp. 838.

Action wherein plaintiff consumers challenged regulations adopted by Food and Drug Administration for policing the nation's over-the-counter drug market met the ripeness requirement in that the issue whether the regulations were consistent with the statutory scheme pursuant to which they were promulgated was fit for judicial resolution and both litigants would suffer a hardship from further delay in resolving that issue. Cutler v. Kennedy, D.C.D.C.1979, 475 F.Supp. 838.

Where individual and corporate defendant had actual notice that Food and Drug Administration considered subject drugs "new drugs" and knew that there was no effective new drug application permitting sale of subject drugs, defendants were not entitled to claim that this section prohibiting sale of new drugs without approval of new drug application by FDA was unconstitutionally vague and could not support a conviction. U.S. v. Marcen Laboratories, Inc., D.C.N.Y.1976, 416 F.Supp. 453, affirmed 556 F.2d 562.

As the named plaintiff, a cancer victim, and those similarly situated were wholly without means or resources to comply with provisions of this section pertaining to filing an application with the Secretary of Health, Education and Welfare for approval to introduce a new drug into interstate commerce, the named plaintiff and those similarly situated, in being thus denied freedom of choice for treatment by the drug laetrile to alleviate or cure their cancer, were deprived of life, liberty or property without due process of law. Rutherford v. U.S., D.C.Okl.1975, 399 F.Supp. 1208, affirmed and remanded on other grounds 542 F.2d 1137, on remand 424 F.Supp. 105.

Consumer organizations were without standing to institute suit against drug companies on behalf of themselves, their members and all other purchasers of certain allegedly ineffective drugs to recover money spent by purchasers of such drugs and to obtain punitive damages where such organizations had not purchased any of drugs involved and had not themselves been injured in fact, and where individualized proof would be necessary to establish each particular purchase and resulting damages incurred by each member and individual damage claims would be governed by common law of each state in which drug sales took place. Consumer Federation of America v. Upjohn Co., D.C.App.1975, 346 A.2d 725.

18a. Discretion of court

Trial court did not abuse its discretion in dismissing, on forum non conveniens grounds, suit brought by individual against drug company, on behalf of himself and other purchasers of allegedly ineffective drugs to recover money spent in purchase of such drugs and to obtain punitive damages. Consumer Federation of America v. Upjohn Co., D.C.App.1975, 346 A.2d 725.

19. Res judicata

Doctrine of res judicata did not preclude Federal Food and Drug Administration from proceeding to withdraw approval of drug on theory that drug had not been proved effective as single active component drug, though administration had previously determined that drug had not been shown to be effective as fixed combination drug. Sterling Drug Inc. v. Weinberger, C.A.N.Y.1975, 509 F.2d 1236.

20. Estoppel

Drug manufacturer could be collaterally estopped from litigating, in seizure proceeding, whether Fiorinal with codeine was "new drug" that could not be marketed without Food and Drug Administration (FDA) approval, in view of determination in prior seizure proceeding concerning related drugs that differed only in amount of codeine they contained; amounts of codeine in drugs was immaterial to new drug determination, factual and legal issues in proceedings were almost identical, findings of other court were necessary to outcome of prior proceeding, and manufacturer had full and fair opportunity to litigate in other proceeding. U.S. v. Sandoz Pharmaceuticals Corp., C.A.6 (Ohio) 1990, 894 F.2d 825, certiorari denied 111 S.Ct. 45, 498 U.S. 810, 112 L.Ed.2d 21.

Prior litigation between consumers of over-the-counter drugs and Food and Drug Administration in which it was determined that consumers had standing to challenge Food and Drug Administration's regulations, which went unappealed by Food and Drug Administration, precluded Food and Drug Administration from attempting to assert that consumers had no standing to challenge rule implementing Food, Drug, and Cosmetic Act, under doctrine of collateral estoppel, in absence of evidence of change in controlling facts sufficient to justify exception to collateral estoppel principles. Cutler v. Hayes, 1987, 818 F.2d 879, 260 U.S.App.D.C. 230.

Since Food and Drug Administration had no authority to approve marketing of drug product without new drug application, Government was not estopped from asserting that that drug product and related product were "new drugs" under section 321 of this title. U.S. v. Articles of Drug . . . HORMONIN, D.C.N.J.1980, 498 F.Supp. 424, affirmed 672 F.2d 902, 904.

United States was not estopped from bringing an enforcement proceeding to prevent further shipment of drug X—Otag Plus in interstate commerce without first obtaining an approved new drug application or abbreviated new drug application despite claim that, because of refusal of Food and Drug Administration to follow its own regulations, abbreviated new drug application submitted by manufacturer for X—Otag Plus was rejected. U.S. v. X—Otag Plus Tablets, D.C.Colo.1977, 441 F.Supp. 105, affirmed in part, remanded in part, on other grounds 602 F.2d 1387.

Food and Drug Administration could not ban use of laetrile under grandfather clause if in fact laetrile had been used prior to the cutoff date in treatment of cancer and without ill effect, it was not necessary that the drug be shown to have been effective in treatment of cancer. Rutherford v. U.S., D.C.Okl.1977, 429 F.Supp. 506.

21. Burden of proof

Proponents of laetrile did not conduct the research and laboratory testing required under prevailing agency procedures and by this chapter, thus, they did not meet their burden to fulfill premarketing requirements. Rutherford v. U.S., C.A.Okl.1980, 616 F.2d 455, certiorari denied 101 S.Ct. 336, 449 U.S. 937, 66 L.Ed.2d 160.

Where Federal Trade Commission sought an order requiring weight loss clinics to disclose in their advertisements the fact that one of the drugs being used in the program was a new drug which had not been determined by the Food and Drug Administration to be effective for obesity, FTC did not have the burden of proving that the weight loss clinics' program was unsafe or ineffective. Simeon Management Corp. v. F.T.C., C.A.9, 1978, 579 F.2d 1137.

Those who seek to market a drug or food additive in interstate commerce have some burden of proving the safety and, for drugs, the effectiveness of their product. U.S. v. Articles of Food and Drug Consisting of Coli-Trol 80, F4C–60 Feed Grade, Entrol-S Medicated, Entrol-P, C.A.Ga.1975, 518 F.2d 743.

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Burden is on sponsor of new drug to demonstrate its safety and effectiveness. Edison Pharmaceutical Co., Inc. v. Food and Drug Administration, Dept. of Health, Ed. and Welfare, 1975, 513 F.2d 1063, 168 U.S.App.D.C. 273, rehearing denied 517 F.2d 164, 170 U.S.App.D.C. 350.

Drug manufacturers must carry burden of showing by substantial evidence the claimed efficacy and safety of drugs. North American Pharmacal, Inc. v. Department of Health, Ed. and Welfare, C.A.8, 1978, 491 F.2d 546.

Physicians and patients challenging, by way of petition for preliminary injunction, decision of Secretary suspending new drug applications for phenformin hydrochloride on ground that drug posed an "imminent hazard" had burden of demonstrating substantial likelihood that decision was a clear error of judgment and that he failed to articulate any rational connection between facts submitted to him and choice he made. Forsham v. Califano, D.C.D.C.1977, 442 F.Supp. 203.

22. Evidence

"Substantial evidence," as used in this section, which directs the Food and Drug Administration to refuse approval of a new drug application or to withdraw any prior approval if substantial evidence that the drug is effective for its intend-

ed use is lacking, means adequate and well-controlled investigations from which experts may conclude that the drug will have the claimed effect. CIBA Corp. v. Weinberger, N.J. 1973, 93 S.Ct. 2495, 412 U.S. 640, 37 L.Ed.2d 230.

Phrase "lack of substantial evidence," in this section which directs Food and Drug Administration to refuse approval of a new drug application and to withdraw any prior approval if substantial evidence that drug is effective for its intended use is lacking, is not applicable only to proof of actual effectiveness of drugs that fall within definition of a new drug; hurdle of "general recognition" of effectiveness requires at least substantial evidence of effectiveness for approval of a new drug application. Weinberger v. Hynson, Westcott and Dunning, Inc., Va.1973, 93 S.Ct. 2469, 412 U.S. 609, 37 L.Ed.2d 207.

Evidence submitted by drug manufacturer with respect to efficacy of drug for use in treatment of premature labor and habitual abortion, including a list of literature references, a copy of an unpublished study, and a representative sample testimonial letter on behalf of the drug, was sufficient to warrant a hearing on proposed withdrawal of effective new drug application because of lack of substantial evidence of efficacy of the drug. Weinberger v. Hynson, Westcott and Dunning, Inc., Va.1973, 93 S.Ct. 2469, 412 U.S. 609, 37 L.Ed.2d 207.

To prevail at a Food and Drug Administration hearing on proposed withdrawal of an effective new drug application because of lack of substantial evidence of efficacy, applicant must furnish evidence stemming from adequate and well-controlled investigations. Weinberger v. Hynson, Westcott and Dunning, Inc., Va.1973, 93 S.Ct. 2469, 412 U.S. 609, 37 L.Ed.2d 207.

Drug manufacturer's attempt to replace evidence of controlled investigation with testimony relating to personal experiences or clinical impressions arising from use of proposed new drug was inconsistent with this chapter as well as with accompanying regulations and explicit Supreme Court precedent. Edison Pharmaceutical Co., Inc. v. Food and Drug Admin., Dept. of Health, Ed. and Welfare, 1979, 600 F.2d 831, 195 U.S.App.D.C. 17.

Substantial evidence including the testimony of three expert witnesses supported decision of the Commissioner that both animal studies and clinical testing offered by drug manufacturer in support of new drug application were insufficient and failed to demonstrate the safety of the new drug. Edison Pharmaceutical Co., Inc. v. Food and Drug Admin., Dept. of Health, Ed. and Welfare, 1979, 600 F.2d 831, 195 U.S.App. D.C. 17.

A drug can be generally recognized as effective only if the expert consensus is based upon substantial evidence that the drug is effective for the labeled use; anecdotal evidence, such as testimonials by satisfied patients or statements by doctors that, based on their experience, they believe the drug is effective do not constitute adequate and well-controlled investigations and cannot provide substantial evidence of effectiveness. Simeon Management Corp. v. F.T.C., C.A.9, 1978, 579 F.2d 1137.

Substantial evidence of effectiveness is a necessary but not a sufficient condition for approval of a new drug application. Edison Pharmaceutical Co., Inc. v. Food and Drug Administration, 1975, 517 F.2d 164, 170 U.S.App.D.C. 350.

Meaning of label is relevant to general recognition of safety of alleged new drug. U.S. v. 1,048,000 Capsules, More of Less, "Afrodex," C.A.Tex.1974, 494 F.2d 1158.

Evidence supported order of Food and Drug Administration withdrawing approval of new-drug applications covering combination amphetamine products. North American Pharmacal, Inc. v. Department of Health, Ed. and Welfare, C.A.8, 1978, 491 F.2d 546.

Evidence warranted submission to jury of issue of whether "Aralen" (chloroquine phosphate) was sold for use in the treatment of lupus erythematosus without adequate testing to determine possible harmful side effects. Hoffman v. Sterling Drug, Inc., C.A.Pa.1973, 485 F.2d 132, on remand 374 F.Supp. 850.

The "substantial evidence" standard as set out in this section and regulation with respect to showing required by manufacturers of drugs is directed only to question of efficacy, and a different standard applies where question of safety arises, and such different standard should be articulated by the Food and Drug Administration. E. R. Squibb & Sons, Inc. v. Weinberger, C.A.3, 1973, 483 F.2d 1382.

Evidence that drug was, prior to Oct. 9, 1962, effective date of amendments to provisions of this chapter, prescribed and enthusiastically endorsed by a few physicians in one city and sold to no more than 150 to 200 doctors in two or three neighboring states was insufficient to establish that the drug was generally recognized as safe on the date in question, and thus drug was not entitled to "grandfather clause" exemption from present requirement of this chapter that drug not be shipped in interstate commerce without prior approval of a new drug application unless it is generally recognized as both safe and effective. U.S. v. An Article of Drug * * * "Bentex Ulcerine", C.A.Tex.1972, 469 F.2d 875, certiorari denied 93 S.Ct. 2772, 412 U.S. 938, 37 L.Ed.2d 397.

Decision of Commissioner of Food and Drugs relating to marketing order entered after a hearing will be upheld and sustained by any substantial evidence, but in determining whether Commissioner acted within limits of discretion on procedural question of whether hearing is to be allowed, test is whether there is any genuine and substantial evidence that supports position of applicant. Hynson, Westcott & Dunning, Inc. v. Richardson, C.A.4 1972, 461 F.2d 215, modified on other grounds 93 S.Ct. 2469, 412 U.S. 609, 37 L.Ed.2d 207.

Evidence in proceeding to withdraw approval of drug supported finding that manufacturer's studies of effect of drug, which was designed to reduce incidence of certain attacks of vertigo, were not sufficiently adequate and well controlled as to constitute substantial evidence of claims for efficacy. Unimed, Inc. v. Richardson, 1972, 458 F.2d 787, 147 U.S.App.D.C. 368.

Substantial evidence of safety and effectiveness of alleged new drug can be shown only by

adequate and well-controlled studies of product itself or by adequate and well-controlled studies which concern another drug with same active ingredients and which demonstrate bioequivalence of product and other drug. U.S. v. Undetermined Quantities of an Article of Drug ... (Anucort HC Suppositories), D.N.J.1987, 709 F.Supp. 511, affirmed 857 F.2d 1464, 1466, certiorari denied 109 S.Ct. 864, 488 U.S. 1040, 102 L.Ed.2d 988.

Even if substantial evidence to support general recognition of safety and effectiveness of a combination drug exists concerning the individual components of the drug, there must also be substantial evidence of the safety and efficacy of the combination of the generally recognized components in order for the combination drug to transcend "new drug" status. U.S. v. Articles of Drugs . . . HORMONIN, D.C.N.J.1980, 498 F.Supp. 424, affirmed 672 F.2d 902, 904.

Plaintiffs, who sought to establish their standing as consumers to challenge regulations adopted by the Food and Drug Administration with respect to policing the nation's over-the-counter drug market, were not required, through independent research, to monitor the Federal Register or similar means to keep abreast of precisely which of the thousands of the over-the-counter drug products contained conditions classifying Category III since such efforts would not alleviate the injury to their statutory interests any more than would decision to forgo the use of the drugs altogether. Cutler v. Kennedy, D.C.D.C.1979, 475 F.Supp. 838.

Fact that much of the raw data used by Bureau of Drugs in arriving at its conclusion that drug posed an imminent hazard had been available for some length of time did not preclude use of data in finding imminent hazard where magnitude of drug's risk was determined only after extensive reevaluation of data following hearing. Forsham v. Califano, D.C.D.C. 1977, 442 F.Supp. 203.

Even though testimony of general practitioners as to safety or efficacy of drugs may be less than compelling, court will not reject all clinical impressions by general practitioners in suit to condemn misbranded drug. U.S. v. 1,048,000 Capsules, More or Less, D.C.Tex.1972, 347 F.Supp. 768, affirmed 494 F.2d 1158.

Evidence in suit to condemn allegedly misbranded drugs was insufficient to meet claimant's burden of proving, as bearing on right to benefit of grandfather clause exemption from showing of effectiveness, that on October 9, 1962 the drug was generally recognized among qualified experts as safe for use under the conditions prescribed, recommended or suggested in the labeling as of that date. U.S. v. 1,048,000 Capsules, More or Less, D.C.Tex.1972, 347 F.Supp. 768, affirmed 494 F.2d 1158.

22a. Admissibility of evidence

At hearing on new drug application, administrative law judge properly excluded testimonial evidence which the drug manufacturer offered to demonstrate the efficacy of the new drug; personal testimonials simply did not meet the exacting standard of evidence required by this chapter and regulations. Edison Pharmaceutical Co., Inc. v. Food and Drug Admin., Dept. of Health, Ed. and Welfare, 1979, 600 F.2d 831, 195 U.S.App.D.C. 17.

At hearing on new drug application, administrative law judge correctly excluded evidence of tests that were not submitted with the new drug application where the drug manufacturer had failed to invoke the regulation which provides a procedure for filing new studies. Edison Pharmaceutical Co., Inc. v. Food and Drug Admin., Dept. of Health, Ed. and Welfare, 1979, 600 F.2d 831, 195 U.S.App.D.C. 17.

At hearing on new drug application, administrative law judge properly excluded as irrelevant evidence concerning different treatment which the Administration allegedly gave to another drug. Edison Pharmaceutical Co., Inc. v. Food and Drug Admin., Dept. of Health, Ed. and Welfare, 1979, 600 F.2d 831, 195 U.S.App.D.C. 17.

24. Questions of fact

Factual question as to whether double-blind tests for new drug were too dangerous to perform was a sufficiently material fact in dispute to require an evidentiary hearing on drug manufacturer's new drug application before Commissioner could issue a final order. Edison Pharmaceutical Co. Inc. v. Food and Drug Administration, Dept. of Health, Ed. and Welfare, 1975, 513 F.2d 1063, 168 U.S.App.D.C. 273, rehearing denied 517 F.2d 164, 170 U.S.App.D.C. 350.

Whether Federal Food and Drug Administration had new information which would justify withdrawal of approval of new drug application in effect for prescription drug was factual determination to be made first by the Administration. Sterling Drug Inc. v. Weinberger, C.A.N.Y.1975, 509 F.2d 1236.

Affidavits stating that particular disease that drug was marketed as treatment for was hard to diagnose, ran variable course, and caused pain did not create factual question requiring Food and Drug Administration to conduct hearing as to whether testimonials of experienced physicians, rather than controlled studies, should be recognized as substantial evidence of drug's efficacy. Cooper Laboratories, Inc. v. Commissioner, Federal Food and Drug Administration, 1974, 501 F.2d 772, 163 U.S.App.D.C. 212.

Whether drug manufacturers violated this section by not submitting new drug application to Food and Drug Administration for "Aralen," their trade name for chloroquine phosphate, when the drug was offered for use in the treatment of lupus erythematosus was question for jury in user's action against manufacturers for loss of vision as result of using the drug. Hoffman v. Sterling Drug, Inc., C.A.Pa.1973, 485 F.2d 132, on remand 374 F.Supp. 850.

Whether manufacturers' alleged violation of this section in the introduction of "Aralen" (chloroquine phosphate) without new drug statement for use in the treatment of lupus erythematosus was proximate cause of the user's loss of vision from use of the drug was question for the jury. Hoffman v. Sterling Drug, Inc., C.A.Pa.1973, 485 F.2d 132, on remand 374 F.Supp. 850.

25. Injunction

Corporation which acquired title to new drug application was not in contempt of order enjoin-

ing previous holder of application from infringing plaintiff's drug patents; plaintiff failed to show that corporation, which acquired title to application and which was not a party to patent infringement case, was an instrumentality of previous holder designed to evade injunction or acted in concert or in participation with original defendants in patent infringement action, and new drug application was not equivalent to product addressed and did not authorize anyone to make, use or sell drug. Eli Lilly and Co. v. Premo Pharmaceutical Laboratories, Inc., C.A.Fed. (N.J.) 1988, 843 F.2d 1378.

Where court's recall order did not address particular violation of this chapter from which injury might be presumed, an independent showing of irreparable harm was required to warrant issuance of such order. U.S. v. Spectro Foods Corp., C.A.N.J.1976, 544 F.2d 1175.

Questions as to whether laetrile was marketed on October 9, 1962, as a cancer drug and was then generally recognized as safe, or whether it was recognized or used as a cancer drug under the same conditions of present use during the period when the Food and Drugs Act of 1906 [Act June 30, 1906, Ch. 3915, 34 Stat. 768] was in effect, and thus question of whether laetrile is exempt as a new drug under this section were sufficiently substantial, difficult and doubtful to support grant of preliminary injunction against interference with cancer patient's personal use of the drug. Rutherford v. U.S., C.A.Okl.1976, 542 F.2d 1137, on remand 424 F.Supp. 105.

District court did not abuse its discretion in refusing to enjoin United States authorities from interfering with distribution of specified vitamin which had not been approved for distribution by the Food and Drug Administration, in absence of showing by distributors that there was substantial probability of success with respect to their claim that such vitamin was not a substance subject to control within meaning of this chapter. Hanson v. U.S., C.A.Minn.1976, 540 F.2d 947.

Pharmaceutical company was not entitled to injunctive relief prohibiting Food and Drug Administration from granting approval of generic copies of drug product Desyrel, trazadone HCL within ten-year period of nonpatent marketing exclusivity provided by 1984 amendments to the Federal Food, Drug, and Cosmetic Act; there was no substantial likelihood that pharmaceutical company could demonstrate that letter of December 24, 1981, which stated that drug "is approved" and which approval would except drug from ten-year period of nonpatent marketing exclusivity, was not approval letter, pharmaceutical company did not demonstrate existence of imminent injury in connection with disclosure of safety and effectiveness data, and pharmaceutical company failed to demonstrate that granting of injunctive relief would not significantly harm other interested parties. Mead Johnson Pharmaceutical Group v. Bowen, D.D.C.1986, 655 F.Supp. 53, affirmed 838 F.2d. 1332, 267 U.S.App.D.C. 382.

Absent showing that probable injury to drug manufacturer without preliminary injunction outweighed harm to Food and Drug Administration and competitor with preliminary injunction or showing of likelihood of success on merits, antibiotic drug manufacturer was not entitled to preliminary injunction to compel Food and Drug Administration to withhold approval of competitor's application to market generic version of manufacturer's new antibiotic drug; public interest was best served by allowing agency to interpret its own regulations and to operate unimpeded by courts in such matter. Glaxo, Inc. v. Heckler, D.C.N.C.1985, 623 F.Supp. 69.

Even if placement of an over-the-counter drug in Category III, absent grandfather status or coverage by a new drug application, was tantamount to a finding of illegality under this chapter, it was not necessary to issue an injunction requiring the commissioner to take the drugs off the over-the-counter market, but only necessary to issue an injunction prohibiting the commissioner from implementing the offensive aspects of the subject regulations. Cutler v. Kennedy, D.C.D.C.1979, 475 F.Supp. 838.

Litigation by Food and Drug Administration of new drug status of two products manufactured by plaintiff in pending condemnation actions would not be preliminarily enjoined given serious question as to correctness of dictum in Lannett decision permitting a generic or "me-too" drug to be marketed without premarketing approval if its therapeutically active ingredients are identical to a recognized drug both chemically and quantitatively. Pharmadyne Laboratories, Inc. v. Kennedy, D.C.N.J.1979, 466 F.Supp. 100, affirmed 596 F.2d 568.

Plaintiff who was dying from cancer of the pancreas and who sought to enjoin the Food and Drug Administration from interfering with importation or interstate transportation of Laetrile for purposes of his own consumption raised right of privacy issue sufficiently serious to be fair grounds for litigation, warranting preliminary injunction. Rizzo v. U.S., D.C.N.Y.1977, 432 F.Supp. 356.

Plaintiff who was dying from cancer and who sought to enjoin Food and Drug Administration from preventing importation or interstate transportation of Laetrile for purposes of his own consumption raised due process question in regard to requirement of filing and prosecution of a "new drug" application of sufficient seriousness to make it fair grounds for litigation, warranting preliminary injunction. Rizzo v. U.S., D.C.N.Y.1977, 432 F.Supp. 356.

Balance of equities tipped decidedly in favor of granting temporary injunction to plaintiff, a cancer patient, who sought to enjoin Food and Drug Administration from preventing importation or interstate transportation of Laetrile for purposes of his own consumption and plaintiff sufficiently demonstrated possibility of irreparable injury by death. Rizzo v. U.S., D.C.N.Y. 1977, 432 F.Supp. 356.

Since plaintiff class, all terminally ill cancer patients, was in danger of suffering irreparable injury if relief in form of allowing such patients who wished to import laetrile for use was postponed or denied and the potential loss to the Food and Drug Administration from granting of relief was slight and record disclosed indications that laetrile was exempt from new drug classification under grandfather clause, court would grant temporary injunction to permit class to import and use laetrile while the Food and Drug

Administration developed proper administrative record to support its claim that laetrile was a new drug. Rutherford v. U.S., D.C.Okl.1977, 429 F.Supp. 506.

In cancer patient's action for preliminary injunction to restrain government or its agents from barring patient's importation of Laetrile solely for his personal use, plaintiff failed to demonstrate substantial probability of success with respect to his claim that Laetrile was not "new drug" within meaning of this section prohibiting importation of such drug until approval of new drug application by Food and Drug Administration. Gadler v. U.S., D.C.Minn.1977, 425 F.Supp. 244.

Proper procedure for manufacturers and distributors of prescription drug involved in proceeding to withdraw approval of new drug applications was to raise defense of res judicata in the administrative proceedings and then have the agency determination on that issue, should it be contrary to their claim, reviewed on appeal to court of appeals from whatever adverse final decision the FDA might make with respect to withdrawal proceedings and manufacturers and distributors were not entitled to circumvent the administrative channels by seeking to enjoin the proceeding. Sterling Drug, Inc. v. Weinberger, D.C.N.Y.1974, 384 F.Supp. 557, affirmed 509 F.2d 1236.

26. Record

Food and Drug Administration must produce an administrative record to support its determination that laetrile is a new drug; FDA must present substantial evidence to support the proposition that laetrile is not generally recognized among qualified experts as safe and effective and that its use is not grandfathered in. Rutherford v. U.S., C.A.Okl.1976, 542 F.2d 1137, on remand 424 F.Supp. 105.

Record established that studies whereby 50 patients with herpes zoster were treated with drug while six received a placebo but without method of selecting patients to insure that subjects were suitable for purposes of study, without subjects being designed in such way as to minimize bias, and without comparability of pertinent variables being assured, and study whereby 34 patients with herpes zoster were treated with drug and ten with injections of Vitamin B_{12}, were not "well-controlled" and were properly rejected by Food and Drug Administration as proof of efficacy of drug. Cooper Laboratories, Inc. v. Commissioner, Federal Food and Drug Administration, 1974, 501 F.2d 772, 163 U.S.App.D.C. 212.

Exclusion from administrative record of documents generated in course of Food and Drug Administration's compliance and enforcement activities did not preclude meaningful public comment on or judicial review of Administration's "current good manufacturing practice" regulations in view of their general, nontechnical nature, especially as administrative record did include descriptive summaries of the Administration's enforcement activities and most of the actual documents were available for public inspection either in the Administration's files or through requests under Freedom of Information Act, section 552 of Title 5. National Association of Pharmaceutical Manufacturers v. Department of Health and Human Services, D.C.N.Y.1984, 586 F.Supp. 740.

Record was inadequate to support finding that Food and Drug Administration abused its discretion by failing to exercise authority to immediately suspend drugs which present an imminent hazard to the public health. American Public Health Ass'n. v. Veneman, D.C.D.C.1972, 349 F.Supp. 1311.

27. Summary judgment

Study which compared new drug's efficacy against that of drug known to be effective and which observed that rate of remission for known drug was 56.5% and that for new drug was 27.6% and thus did not show new drug to be as effective as active control did not produce evidence of new drug's efficacy and thus did not meet Food and Drug Administration's regulatory standards for adequate and well-controlled investigations so as to preclude summary judgment order denying new drug application. Holland-Rantos Co., Inc. v. U.S. Dept. of Health, Ed. and Welfare, 1978, 587 F.2d 1173, 190 U.S.App.D.C. 276.

Food and Drug Administration's endorsement of Dexedrine as effective for short term management of obesity provided prima facie support for drug manufacturer's use of Dexedrine as active control in testing efficacy of new drug to be used in the control of obesity, precluding summary judgment order denying new drug application on ground that clinical trials testing drug's efficacy were deficient under FDA regulation requiring that study provide comparison of results of treatment or diagnosis with a control in such a fashion as to permit quantitative evaluation. Smithkline Corp. v. Food and Drug Administration, 1978, 587 F.2d 1107, 190 U.S.App.D.C. 210.

This section granting applicant's right to due notice and opportunity for hearing prior to withdrawal of approval to market new drugs in interstate commerce does not preclude use of summary judgment procedure by Food and Drug Administration in appropriate circumstances, but it does restrict application of that procedure to cases in which no material factual issue is presented and a hearing would be a hollow formality. USV Pharmaceutical Corp. v. Secretary of Health, Ed. and Welfare, 1972, 466 F.2d 455, 151 U.S.App.D.C. 284.

Manufacturer of hemorrhoidal suppositories with hydrocortisone acetate was not entitled to discovery of specific instances in which Food and Drug Administration approved drug based on extrapolation, in that studies of approved drug could not be extrapolated to newly marketed product simply on basis that new product contained same active ingredient as approved drug. U.S. v. Undetermined Quantities of an Article of Drug ... (Anucort HC Suppositories), D.N.J.1987, 709 F.Supp. 511, affirmed 857 F.2d 1464, 1466, certiorari denied 109 S.Ct. 864, 488 U.S. 1040, 102 L.Ed.2d 988.

In action brought against Secretary by physicians and patients who sought to preliminarily enjoin Secretary from implementing order suspending new drug applications for phenformin hydrochloride on ground that drug posed an

Secretary was precluded by existence of issues of material fact. Forsham v. Califano, D.C.D.C. 1977, 442 F.Supp. 203.

28. Review

While a Food and Drug Administration order denying a new drug application or withdrawing one is reviewable by the Court of Appeals under this section, an order declaring a "new drug" status is reviewable under the Administrative Procedure Act, sections 551 et seq. and 701 et seq. of Title 5, by the district court. Weinberger v. Bentex Pharmaceuticals, Inc., S.C. 1973, 93 S.Ct. 2488, 412 U.S. 645, 37 L.Ed.2d 235.

Declaratory order of Food and Drug Administration that a drug is a "new drug" so as to require an effective new drug application before drug may be introduced into commerce is not reviewable in the Court of Appeals under subsec. (h) of this section, but is reviewable by the district court under Administrative Procedure Act, sections 551 et seq. and 701 et seq. of Title 5. Weinberger v. Hynson, Westcott and Dunning, Inc., Va.1973, 93 S.Ct. 2469, 412 U.S. 609, 37 L.Ed.2d 235.

In reviewing an order of the Commissioner denying a hearing on proposed withdrawal of an effective new drug application because of lack of substantial evidence of efficacy of the drug, a Court of Appeals must determine whether the Commissioner's findings accurately reflect study in question and if they do, whether the deficiencies he finds conclusively render the study inadequate or uncontrolled in light of the pertinent regulations. Weinberger v. Hynson, Westcott and Dunning, Inc., Va.1973, 93 S.Ct. 2469, 412 U.S. 609, 37 L.Ed.2d 235.

Deference owed to political branches in military matters did not preclude judicial review of Food and Drug Administration (FDA) regulation permitting Defense Department to use unapproved, investigational drugs on military personnel, without service member's informed consent, in certain combat-related situations. Doe v. Sullivan, C.A.D.C.1991, 938 F.2d 1370.

District court could not reconsider the issue of drug's lack of effectiveness for alleviation of pain, and had no jurisdiction to reopen the case, where Court of Appeals had previously affirmed district court's affirmance of finding by the Food and Drug Administration with respect to the drug's lack of effectiveness. Rutherford v. U.S., C.A.10 (Okl.) 1986, 806 F.2d 1455.

Action of Food and Drug Administration in withdrawing new drug application for muco-evacuant "Alevaire" on ground that it was not effective as a "fixed combination drug" was arbitrary and invalid where there was no mention of that theory as ground for proposed withdrawal in the notice of opportunity for hearing and the manufacturers were never given a meaningful opportunity to submit studies or data to contravene that theory. Sterling Drug Inc. v. Weinberger, C.A.2, 1974, 503 F.2d 675.

Where the nature of the Food and Drug Administration Interim Index and the basis on which listings thereon are made were not before the court of appeals and were not explored on appeal from Administration's orders which withdrew approval of new drug applications for muco-evacuant drug "Alevaire," the court of appeals would deny manufacturers' motion to require the Administration to remove a listing of "Alevaire" as "ineffective" from the Administration's Interim Index. Sterling Drug Inc. v. Weinberger, C.A.2, 1974, 503 F.2d 675.

Issue of whether anorectic drugs containing amphetamines were "grandfathered" by 1962 amendments to this chapter was initially a matter for determination of the Food and Drug Administration, subject to review in district court pursuant to the Administrative Procedure Act, sections 551 et seq. and 701 et seq. of Title 5, and could not be determined by the Court of Appeals in action by manufacturers of such drugs to set aside order of Administration withdrawing approval of new-drug applications covering combination amphetamine products. North American Pharmacal, Inc. v. Department of Health, Ed. and Welfare, C.A.8, 1973, 491 F.2d 548.

Court of Appeals did not lack jurisdiction to review merits of petition by manufacturers of anorectic drugs containing amphetamines to set aside order of Food and Drug Administration withdrawing approval of new-drug applications covering combination amphetamine products because manufacturers were not holders of such applications but manufactured drugs which were identical, similar or related to drugs covered by another manufacturer's new drug application. North American Pharmacal, Inc. v. Department of Health, Ed. and Welfare, C.A.8, 1973, 491 F.2d 546.

In suit for damages and injunctive relief based on alleged conspiracy by defendants to keep plaintiffs' drug off interstate market by influencing the Administration to deny fair consideration of new drug applications, district court should not be inhibited from considering conclusions reached by the Administration with respect to safety and efficacy of drug for interstate sale in light of whatever showing plaintiffs make of the existence of a conspiracy, unfairness, or conflict of interests on part of defendants. Israel v. Baxter Laboratories, Inc., 1972, 466 F.2d 272, 151 U.S.App.D.C. 101.

District court's review of decision of Secretary to suspend phenformin hydrochloride as an imminently hazardous drug was limited to determination of whether Secretary's decision was arbitrary and capricious, an abuse of discretion, or otherwise not in accordance with the law. Forsham v. Califano, D.C.D.C.1977, 442 F.Supp. 203.

Any error made by Food and Drug Administration in its consideration of a new drug application or an abbreviated new drug application for drug X—Otag Plus manufactured by defendant was not for consideration of district court in enforcement proceeding brought by United States, but was for consideration of court of appeals after a final agency determination on status of drug. U.S. v. X—Otag Plus Tablets, D.C.Colo.1977, 441 F.Supp. 105, affirmed in part, remanded in part on other grounds 602 F.2d 1387.

Whether FDA had "new information" justifying withdrawal of approval of new drug application in effect for prescription drug was factual determination which should first be made by FDA and, only after that determination was made and it became clear on what specific information FDA relied for its conclusion, could court determine whether data used constituted new information. Sterling Drug, Inc. v. Weinberger, D.C.N.Y.1974, 384 F.Supp. 557, affirmed 509 F.2d 1236.

Complaint seeking determination as to whether drug was a "new drug" was an inappropriate vehicle to determine issues of case as, if plaintiffs were to seek judicial review of any Food and Drug Administration order, complaint would have to be withdrawn and petition for review substituted. Carolina Brown, Inc. v. Weinberger, D.C.S.C.1973, 365 F.Supp. 310.

28a. Standards of review

The Food and Drug Administration's denial of claimant's request for relabeling of medical device was an informal adjudicatory process, as to which Administration was not required to conduct an "on the record" hearing to produce record that was basis of action, the basic requirement for substantial evidence review, and thus, decision to deny relabeling was subject to review under the arbitrary and capricious standard contained in 5 U.S.C.A. § 706(2)(A). U.S. v. An Article of Device ... Diapulse, C.A.7 (Ill.) 1985, 768 F.2d 826.

29. Declaratory judgment

Where order of Commissioner on Food and Drugs withdrawing drug manufacturer's new drug applications had not become final prior to district court assuming jurisdiction of manufacturer's suit for declaratory judgment that its drugs were exempt from efficacy requirements, and in fact the Court of Appeals had reversed the Commissioner's decision and proceedings on remand were pending before the Commission, manufacturer was not barred from proceeding in the district court. USV Pharmaceutical Corp. v. Weinberger, Va.1973, 93 S.Ct. 2498, 412 U.S. 640, 37 L.Ed.2d 230.

Drug manufacturer, who had opportunity to litigate jurisdictional question whether drug product was a "new drug" before Food and Drug Administration and to raise issue on appeal to a court of appeals to review withdrawal order, could not relitigate the issue in a separate proceeding for a declaratory judgment. CIBA Corp. v. Weinberger, N.J.1973, 93 S.Ct. 2495, 412 U.S. 640, 37 L.Ed.2d 230.

Plaintiffs who were in commercial business of selling laetrile, who did not need drug, and who did not allege that they were unable to afford new drug application procedures, were not entitled to relief in their action for declaratory judgment that laetrile is a food and is not a new drug and for order decreeing that no agency of United States has right to interfere with importation and distribution of laetrile on theory that it is unconstitutional to deny consumer of laetrile opportunity to obtain it because consumer cannot afford costly procedures required for new drug application. Hanson v. U.S., D.C.Minn.1976, 417 F.Supp. 30, affirmed 540 F.2d 947.

Where issue of whether drug is "new drug" was matter within the primary jurisdiction of the Food and Drug Administration and judicial review would be available following the administrative determination, the district court, in exercise of its sound discretion under Declaratory Judgment Act, section 2201 et seq. of Title 28, would refuse to take jurisdiction of action for declaration that particular drugs were not "new drug." National Ethical Pharmaceutical Ass'n v. Weinberger, D.C.S.C.1973, 365 F.Supp. 735, affirmed 503 F.2d 1051.

30. Prescription drugs

Prescription drugs on market are subject to efficacy requirements of this chapter. USV Pharmaceutical Corp. v. Weinberger, Va.1973, 93 S.Ct. 2498, 412 U.S. 640, 37 L.Ed.2d 230.

Manufacturer of pioneer antibiotic drug was not entitled to protection of amendment to Federal Food, Drug and Cosmetic Act preventing any manufacturer of prescription pharmaceutical drugs from marketing generic version of drug for five years from date of pioneer drug's approval, where drug had not been submitted and approved pursuant to referenced section and had been approved pursuant to another section and only thereafter exempted and subsequently regulated under governing statute. Glaxo, Inc. v. Bowen, E.D.N.C.1986, 640 F.Supp. 933.

31. Drugs administered by physicians

Whether or not endocrine drug was a "new drug," operators of weight reduction clinics were not required to seek Food and Drug Administration approval for use of the drug in treatments administered by licensed physicians. F.T.C. v. Simeon Management Corp., D.C.Cal.1975, 391 F.Supp. 697, affirmed 532 F.2d 708.

The Food and Drug Administration does not have jurisdiction to regulate the administration of a drug by a physician. F.T.C. v. Simeon Management Corp., D.C.Cal.1975, 391 F.Supp. 697, affirmed 532 F.2d 708.

32. Notes of approval

Where Food and Drug Administration had issued and published in the Federal Register a new "Notice of Opportunity for Hearing" on proposal withdrawing approval of New Drug Applications for "Alevaire," a muco-evacuant drug, and the notice made specific reference to Court of Appeals decision which permitted the notice, the Administration would not be required to publish notice of reinstatement of approval of the new drug applications in the Federal Register. Sterling Drug Inc. v. Weinberger, C.A.2, 1974, 503 F.2d 675.

32a. Opinion letters

Issuance of opinion letter stating that particular drug product would not require clearance under "new drug" procedure was beyond statutory authority of Food and Drug Administration, which had no legal authority to permit marketing of the product without new drug application approved for safety and efficacy. U.S. v. Articles of Drug . . . HORMONIN, D.C.N.J.1980, 498 F.Supp. 424, affirmed 672 F.2d 902, 904.

33. Remedy

This section which provides that court may order additional evidence to be taken and to be adduced upon hearing in such manner and upon such terms as to court may seem proper and that Commissioner may modify findings as to

facts by reason of additional evidence gives court broad authority to fashion a remedy capable of balancing fairness to new drug applicant against public's right to expeditious enforcement of this chapter. Smithkline Corp v. Food and Drug Administration, 1978, 587 F.2d 1107, 190 U.S.App.D.C. 210.

Creation of federal common-law damages remedy under this chapter was not necessary to enforcement of claims asserted in individual's suit against drug companies to recover damages arising out of purchase of allegedly ineffective drugs, since cause of action in question was of kind traditionally governed by state law. Consumer Federation of America v. Upjohn Co., D.C.App.1975, 346 A.2d 725.

84. Remand

Where trial before district court should not have occurred, and its record was part of administrative record on remand solely for information it contained and as a matter of administrative convenience, the Food and Drug Administration, in proceeding on claimant's request for relabeling of medical devices, was not bound by findings of the district court, and fact that trial procedure took place did not transform the Administration's decision-making process into adjudicatory hearing. U.S. v. An Article of Device ... Diapulse, C.A.7 (Ill.) 1985, 768 F.2d 826.

There was no error in refusing to remand to the Food and Drug Administration for development of an administrative record in support of Food and Drug Administration's contention that drug was a new drug requiring approval of a new drug application, where the Administration had only instituted condemnation proceedings against a certain quantity of the drug and injunction proceedings against a single drug manufacturer, so that its action was not in the nature of a declaratory order, and where determination that the drug was a "new drug" for purposes of condemnation and injunction proceedings was made by the district court following trial. U.S. v. X—Otag Plus Tablets, C.A.Colo.1979, 602 F.2d 1387.

If Food and Drug Administration has not developed adequate administrative record to permit determination whether laetrile is properly classified as a new drug, appropriate procedure for district court is to remand the case to the FDA for proceedings adequate to develop the record; such proceedings should give laetrile proponents an opportunity to express their views. Rutherford v. U.S., C.A.Okl.1976, 542 F.2d 1187, on remand 424 F.Supp. 106.

85. Investigatory drugs

Food and Drug Administration (FDA) had authority, under statute regulating new drug investigations, to impose recordkeeping requirements on clinical investigators of new drugs, in light of dangers incumbent in receipt of false data. U.S. v. Garfinkel, C.A.8 (Minn.) 1994, 29 F.3d 451.

Food and Drug Administration (FDA) regulation permitting Defense Department to use unapproved, investigational drugs on military personnel, without service member's informed consent, in certain combat-related situations, was within FDA's rule-making authority under Food, Drug, and Cosmetic Act, which provided for use of unimproved investigational drugs only on the informed consent of human subjects affected "except where [the experts administering the drug] deem [the human subject's consent] not feasible." Doe v. Sullivan, C.A.D.C.1991, 938 F.2d 1370.

86. Labeling information

Plaintiffs could not recover from name brand manufacturer for death of their daughter who died as result of ingesting generic equivalent of drug on theory that negligent misrepresentations on generic drug's label were merely copied, as permitted by federal law, from name brand manufacturer's label; manufacturer of generic drug was responsible for accuracy of labels placed on its products and name brand manufacturer's statements regarding its drug could not serve as basis for liability for injuries caused by another manufacturer's drug. Foster v. American Home Products Corp., C.A.4 (Md.) 1994, 29 F.3d 165.

§ 356. Certification of drugs containing insulin

(a) The Secretary, pursuant to regulations promulgated by him, shall provide for the certification of batches of drugs composed wholly or partly of insulin. A batch of any such drug shall be certified if such drug has such characteristics of identity and such batch has such characteristics of strength, quality, and purity, as the Secretary prescribes in such regulations as necessary to adequately insure safety and efficacy of use, but shall not otherwise be certified. Prior to the effective date of such regulations the Secretary, in lieu of certification, shall issue a release for any batch which, in his judgment, may be released without risk as to the safety and efficacy of its use. Such release shall prescribe the date of its expiration and other conditions under which it shall cease to be effective as to such batch and as to portions thereof.

[See main volume for text of (b) and (c)]

(As amended June 16, 1992, Pub.L. 102–300, § 6(b)(2), 106 Stat. 240; Aug. 13, 1993, Pub.L. 103–80, § 3(o), 107 Stat. 777.)

HISTORICAL AND STATUTORY NOTES

1992 Amendments

1 and Pub.L. 96–88 and Pub.L. 102–300, the amendment resulted in no change in text.

1992 Amendments

Subsec. (a). Pub.L. 102–300, § 6(b)(2), struck out "of Health, Education, and Welfare" following "The Secretary".

Change of Name

The Department of Health, Education, and Welfare was redesignated the Department of Health and Human Services, and the Secretary of Health, Education, and Welfare or any other official of the Department of Health, Education and Welfare was redesignated the Secretary or official, as appropriate, of Health and Human Services, with any reference to the Department of Health, Education, and Welfare, the Secretary of Health, Education, and Welfare, or any official of the Department of Health, Education, and Welfare, in any law, rule, regulation, certificate, directive, instruction, or other official paper in force on the effective date of Pub.L. 96–88, as prescribed by section 601 of Pub.L. 96–88, Title VI, Oct. 17, 1979, 93 Stat. 696, set out as a note under section 3401 of Title 20, Education, deemed to refer and apply to the Department of Health and Human Services or the Secretary of Health and Human Services, respectively, except to the extent such reference is to a function or office transferred to the Secretary of Education or the Department of Education under Pub.L. 96–88, Title III, §§ 301 to 307, Oct. 17, 1979, 93 Stat. 677 to 681. See section 3441 to 3447 and 3508 of Title 20.

Federal Policy Regarding the Export of Banned or Significantly Restricted Substances

For provisions relating to the applicability of the term "banned or significantly restricted substance", as defined, and the Federal policy regarding the export of banned or significantly restricted substances, see section 1–101 of Ex. Ord. No. 12264, Jan. 15, 1981, 46 F.R. 4659, set out as a note under section 2403 of Title 50, Appendix, War and National Defense.

CODE OF FEDERAL REGULATIONS

Drugs composed wholly or partly of insulin, see 21 CFR 429.3.

§ 357. Certification of drugs containing penicillin, streptomycin, chlortetracycline, chloramphenicol, bacitracin or any other antibiotic drug

(a) Regulations prescribed by Secretary; release prior to certification; "antibiotic drug" defined

The Secretary, pursuant to regulations promulgated by him, shall provide for the certification of batches of drugs (except drugs for use in animals other than man) composed wholly or partly of any kind of penicillin, streptomycin, chlortetracycline, chloramphenicol, bacitracin, or any other antibiotic drug, or any derivative thereof. A batch of any such drug shall be certified if such drug has such characteristics of identity and such batch has such characteristics of strength, quality, and purity, as the Secretary prescribes in such regulations as necessary to adequately insure safety and efficacy of use, but shall not otherwise be certified. Prior to the effective date of such regulations the Secretary, in lieu of certification, shall issue a release for any batch which, in his judgment, may be released without risk as to the safety and efficacy of its use. Such release shall prescribe the date of its expiration and other conditions under which it shall cease to be effective as to such batch and as to portions thereof. For purposes of this section and of section 352(*l*) of this title, the term "antibiotic drug" means any drug intended for use by man containing any quantity of any chemical substance which is produced by a microorganism and which has the capacity to inhibit or destroy microorganisms in dilute solution (including the chemically synthesized equivalent of any such substance).

[See main volume for text of (b) to (d)]

(e) Exempted new drugs subject to section 355 of this title; request for certification of exempted drug; determination of compliance with sections 351(b) and 352(g) of this title

No drug which is subject to this section shall be deemed to be subject to any provision of section 355 of this title except a new drug exempted from the requirements of this section and of section 352(*l*) of this title pursuant to regulations promulgated by the Secretary. For purposes of section 355 of this title, the initial request for certification, as thereafter duly amended, pursuant to this section, of a new drug so exempted shall be considered a part of the application filed pursuant to section 355(b) of this title with

960 and 961 of this title] shall take effect 120 days after the enactment of this Act [Nov. 18, 1988]."

Change of Name. "Secretary of Health and Human Services" was substituted for "Secretary of Health, Education, and Welfare" on authority of Pub.L. 96–88, Title V, § 509, Oct. 17, 1979, 93 Stat. 695, which is classified to section 3508 of Title 20, U.S.C.A., Education.

Regulations by Attorney General. Section 1903 of Pub.L. 101–647 provided that:

"(a) **Abuse potential.**—The Attorney General, upon the recommendation of the Secretary of Health and Human Services, may, by regulation, exempt any compound, mixture, or preparation containing a substance in paragraph (41) of section 102 of the Controlled Substances Act [par. (41) of this section] (as added by section 2 of this Act [sic]) from the application of all or any part of the Controlled Substances Act [21 U.S.C.A. § 801 et seq.] if, because of its concentration, preparation, mixture or delivery system, it has no significant potential for abuse.

"(b) **Drugs for treatment of rare diseases.**—If the Attorney General finds that a drug listed in paragraph (41) of section 102 of the Controlled Substances Act (as added by section 2 of this Act [sic]) is—

"(1) approved by the Food and Drug Administration as an accepted treatment for a rare disease or condition, as defined in section 526 of the Federal Food, Drug, and Cosmetic Act (21 U.S.C. 360bb) [21 U.S.C.A. § 360bb]; and

"(2) does not have a significant potential for abuse, the Attorney General may exempt such drug from any production regulations otherwise issued under the Controlled Substances Act [21 U.S.C.A. § 801 et seq.] as may be necessary to ensure adequate supplies of such drug for medical purposes.

"(c) **Date of issuance of regulations.**—The Attorney General shall issue regulations implementing this section not later than 45 days after the date of enactment of this Act [Nov. 29, 1990], except that the regulations required under section 3(a) [sic] shall be issued not later than 180 days after the date of enactment of this Act [Nov. 29, 1990]."

Promulgation of Regulations for Administration of Amendment by Alcohol Abuse, Drug Abuse, and Mental Health Amendments of 1984; Inclusion of Findings in Report. Section 301(b) of Pub.L. 98–509, Oct. 19, 1984, 98 Stat. 2364, provided that: "The Secretary of Health and Human Services shall, within ninety days of the date of the enactment of this Act [Oct. 19, 1984], promulgate regulations for the administration of section 102(28) of the Controlled Substances Act as amended by subsection (a) [probably par. 29 of this section] and shall include in the first report submitted under section 505(b) of the Public Health Service Act [section 290aa–4 of Title 42, The Public Health and Welfare] after the expiration of such ninety days the findings of the Secretary with respect to the effect of the amendment made by subsection (a) [amending par. (29) of this section]."

Code of Federal Regulations

Controlled drugs, warnings, see 21 CFR 290.5 et seq.

Treatment of narcotic addicts, see 21 CFR 291.501 et seq.

§ 803. Repealed. Pub.L. 95–137, § 1(b), Oct. 18, 1977, 91 Stat. 1169.

PART B—AUTHORITY TO CONTROL; STANDARDS AND SCHEDULES

§ 811. Authority and criteria for classification of substances

Rules and regulations of Attorney General; hearing

(a) The Attorney General shall apply the provisions of this subchapter to the controlled substances listed in the schedules established by section 812 of this title and to any other drug or other substance added to such schedules under this subchapter. Except as provided in subsections (d) and (e) of this section, the Attorney General may by rule—

(1) add to such a schedule or transfer between such schedules any drug or other substance if he—

(A) finds that such drug or other substance has a potential for abuse, and

(B) makes with respect to such drug or other substance the findings prescribed by subsection (b) of section 812 of this title for the schedule in which such drug is to be placed; or

(2) remove any drug or other substance from the schedules if he finds that the drug or other substance does not meet the requirements for inclusion in any schedule.

Rules of the Attorney General under this subsection shall be made on the record after opportunity for a hearing pursuant to the rulemaking procedures prescribed by subchapter II of chapter 5 of Title 5. Proceedings for the issuance, amendment, or repeal of such rules may be initiated by the Attorney General (1) on his own motion, (2) at the request of the Secretary, or (3) on the petition of any interested party.

Evaluation of drugs and other substances

(b) The Attorney General shall, before initiating proceedings under subsection (a) of this section to control a drug or other substance or to remove a drug or other substance entirely from the schedules, and after gathering the necessary data, request from the Secretary a scientific and medical evaluation, and his recommendations, as to whether such drug or other substance should be so controlled or removed as a controlled substance. In making such evaluation and recommendations, the Secretary shall consider the factors listed in paragraphs (2), (3), (6), (7), and (8) of subsection (c) of this section and any scientific or medical considerations involved in paragraphs (1), (4), and (5) of such subsection. The recommendations of the Secretary shall include recommendations with respect to the appropriate schedule, if any, under which such drug or other substance should be

listed. The evaluation and the recommendations of the Secretary shall be made in writing and submitted to the Attorney General within a reasonable time. The recommendations of the Secretary to the Attorney General shall be binding on the Attorney General as to such scientific and medical matters, and if the Secretary recommends that a drug or other substance not be controlled, the Attorney General shall not control the drug or other substance. If the Attorney General determines that these facts and all other relevant data constitute substantial evidence of potential for abuse such as to warrant control or substantial evidence that the drug or other substance should be removed entirely from the schedules, he shall initiate proceedings for control or removal, as the case may be, under subsection (a) of this section.

Factors determinative of control or removal from schedules

(c) In making any finding under subsection (a) of this section or under subsection (b) of section 812 of this title, the Attorney General shall consider the following factors with respect to each drug or other substance proposed to be controlled or removed from the schedules:

(1) Its actual or relative potential for abuse.

(2) Scientific evidence of its pharmacological effect, if known.

(3) The state of current scientific knowledge regarding the drug or other substance.

(4) Its history and current pattern of abuse.

(5) The scope, duration, and significance of abuse.

(6) What, if any, risk there is to the public health.

(7) Its psychic or physiological dependence liability.

(8) Whether the substance is an immediate precursor of a substance already controlled under this subchapter.

International treaties, conventions, and protocols requiring control; procedures respecting changes in drug schedules of Convention on Psychotropic Substances

(d)(1) If control is required by United States obligations under international treaties, conventions, or protocols in effect on October 27, 1970, the Attorney General shall issue an order controlling such drug under the schedule he deems most appropriate to carry out such obligations, without regard to the findings required by subsection (a) of this section or section 812(b) of this title and without regard to the procedures prescribed by subsections (a) and (b) of this section.

(2)(A) Whenever the Secretary of State receives notification from the Secretary-General of the United Nations that information has been transmitted by or to the World Health Organization, pursuant to article 2 of the Convention on Psychotropic Substances, which may justify adding a drug or other substance to one of the schedules of the Convention, transferring a drug or substance from one schedule to another, or deleting it from the schedules, the Secretary of State shall immediately transmit the notice to the Secretary of Health and Human Services who shall publish it in the Federal Register and provide opportunity to interested persons to submit to him comments respecting the scientific and medical evaluations which he is to prepare respecting such drug or substance. The Secretary of Health and Human Services shall prepare for transmission through the Secretary of State to the World Health Organization such medical and scientific evaluations as may be appropriate regarding the possible action that could be proposed by the World Health Organization respecting the drug or substance with respect to which a notice was transmitted under this subparagraph.

(B) Whenever the Secretary of State receives information that the Commission on Narcotic Drugs of the United Nations proposes to decide whether to add a drug or other substance to one of the schedules of the Convention, transfer a drug or substance from one schedule to another, or delete it from the schedules, the Secretary of State shall transmit timely notice to the Secretary of Health and Human Services of such information who shall publish a summary of such information in the Federal Register and provide opportunity to interested persons to submit to him comments respecting the recommendation which he is to furnish, pursuant to this subparagraph, respecting such proposal. The Secretary of Health and Human Services shall evaluate the proposal and furnish a recommendation to the Secretary of State which shall be binding on the representative of the United States in discussions and negotiations relating to the proposal.

(3) When the United States receives notification of a scheduling decision pursuant to article 2 of the Convention on Psychotropic Substances that a drug or other substance has been added or transferred to a schedule specified in the notification or receives notification (referred to in this subsection as a "schedule notice") that existing legal controls applicable under this subchapter to a drug or substance and the controls required by the Federal Food, Drug, and Cosmetic Act do not meet the requirements of the schedule of the Convention in which such drug or substance has been placed, the Secretary of Health and Human Services, after consultation with the Attorney General, shall first determine whether existing legal controls under this subchapter applicable to the drug or substance and th
Federal Food, Drug, an
requirements of the sched
tion or schedule notice a
action:

(A) If such requirem
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controls.

(B) If such requirer
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the Secretary shall r
General that he initiat
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section.

(C) If such require
existing controls and
Human Services does
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fication, the Secretary

(i) if he deems
necessary to protect
recommended to th
initiate proceedings
substance pursuant
this section, to ap

(ii) request the S
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Secretary-General

(iii) request the
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(iv) in the case
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drug or substance
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schedule notice.

(4)(A) If the Attor
consultation with the S

drug or substance and the controls required by the Federal Food, Drug, and Cosmetic Act, meet the requirements of the schedule specified in the notification or schedule notice and shall take the following action:

(A) If such requirements are met by such existing controls but the Secretary of Health and Human Services nonetheless believes that more stringent controls should be applied to the drug or substance, the Secretary shall recommend to the Attorney General that he initiate proceedings for scheduling the drug or substance, pursuant to subsections (a) and (b) of this section, to apply to such controls.

(B) If such requirements are not met by such existing controls and the Secretary of Health and Human Services concurs in the scheduling decision or schedule notice transmitted by the notification, the Secretary shall recommend to the Attorney General that he initiate proceedings for scheduling the drug or substance under the appropriate schedule pursuant to subsections (a) and (b) of this section.

(C) If such requirements are not met by such existing controls and the Secretary of Health and Human Services does not concur in the scheduling decision or schedule notice transmitted by the notification, the Secretary shall—

(i) if he deems that additional controls are necessary to protect the public health and safety, recommended to the Attorney General that he initiate proceedings for scheduling the drug or substance pursuant to subsections (a) and (b) of this section, to apply such additional controls;

(ii) request the Secretary of State to transmit a notice of qualified acceptance, within the period specified in the Convention, pursuant to paragraph 7 of article 2 of the Convention, to the Secretary-General of the United Nations;

(iii) request the Secretary of State to transmit a notice of qualified acceptance as prescribed in clause (ii) and request the Secretary of State to ask for a review by the Economic and Social Council of the United Nations, in accordance with paragraph 8 of article 2 of the Convention, of the scheduling decision; or

(iv) in the case of a schedule notice, request the Secretary of State to take appropriate action under the Convention to initiate proceedings to remove the drug or substance from the schedules under the Convention or to transfer the drug or substance to a schedule under the Convention different from the one specified in the schedule notice.

(4)(A) If the Attorney General determines, after consultation with the Secretary of Health and Human Services, that proceedings initiated under recommendations made under paragraph (B) or (C)(i) of paragraph (3) will not be completed within the time period required by paragraph 7 of article 2 of the Convention, the Attorney General, after consultation with the Secretary and after providing interested persons opportunity to submit comments respecting the requirements of the temporary order to be issued under this sentence, shall issue a temporary order controlling the drug or substance under schedule IV or V, whichever is most appropriate to carry out the minimum United States obligations under paragraph 7 of article 2 of the Convention. As a part of such order, the Attorney General shall, after consultation with the Secretary, except such drug or substance from the application of any provision of part C of this subchapter which he finds is not required to carry out the United States obligations under paragraph 7 of article 2 of the Convention. In the case of proceedings initiated under subparagraph (B) of paragraph (3), the Attorney General, concurrently with the issuance of such order, shall request the Secretary of State to transmit a notice of qualified acceptance to the Secretary-General of the United Nations pursuant to paragraph 7 of article 2 of the Convention. A temporary order issued under this subparagraph controlling a drug or other substance subject to proceedings initiated under subsections (a) and (b) of this section shall expire upon the effective date of the application to the drug or substance of the controls resulting from such proceedings.

(B) After a notice of qualified acceptance of a scheduling decision with respect to a drug or other substance is transmitted to the Secretary-General of the United Nations in accordance with clause (ii) or (iii) of paragraph (3)(C) or after a request has been made under clause (iv) of such paragraph with respect to a drug or substance described in a schedule notice, the Attorney General, after consultation with the Secretary of Health and Human Services and after providing interested persons opportunity to submit comments respecting the requirements of the order to be issued under this sentence, shall issue an order controlling the drug or substance under schedule IV or V, whichever is most appropriate to carry out the minimum United States obligations under paragraph 7 of article 2 of the Convention in the case of a drug or substance for which a notice of qualified acceptance was transmitted or whichever the Attorney General determines is appropriate in the case of a drug or substance described in a schedule notice. As a part of such order, the Attorney General shall, after consultation with the Secretary, except such drug or substance from the application of any provision of part C of this subchapter which he finds is not required to carry out the United States obligations under paragraph 7 of article 2 of the Convention. If,

as a result of a review under paragraph 8 of article 2 of the Convention of the scheduling decision with respect to which a notice of qualified acceptance was transmitted in accordance with clause (ii) or (iii) of paragraph (3)(C)—

(i) the decision is reversed, and

(ii) the drug or substance subject to such decision is not required to be controlled under schedule IV or V to carry out the minimum United States obligations under paragraph 7 of article 2 of the Convention,

the order issued under this subparagraph with respect to such drug or substance shall expire upon receipt by the United States of the review decision. If, as a result of action taken pursuant to action initiated under a request transmitted under clause (iv) of paragraph (3)(C), the drug or substance with respect to which such action was taken is not required to be controlled under schedule IV or V, the order issued under this paragraph with respect to such drug or substance shall expire upon receipt by the United States of a notice of the action taken with respect to such drug or substance under the Convention.

(C) An order issued under subparagraph (A) or (B) may be issued without regard to the findings required by subsection (a) of this section or by section 812(b) of this title and without regard to the procedures prescribed by subsection (a) or (b) of this section.

(5) Nothing in the amendments made by the Psychotropic Substances Act of 1978 or the regulations or orders promulgated thereunder shall be construed to preclude requests by the Secretary of Health and Human Services or the Attorney General through the Secretary of State, pursuant to article 2 or other applicable provisions of the Convention, for review of scheduling decisions under such Convention, based on new or additional information.

Immediate precursors

(e) The Attorney General may, without regard to the findings required by subsection (a) of this section or section 812(b) of this title and without regard to the procedures prescribed by subsections (a) and (b) of this section, place an immediate precursor in the same schedule in which the controlled substance of which it is an immediate precursor is placed or in any other schedule with a higher numerical designation. If the Attorney General designates a substance as an immediate precursor and places it in a schedule, other substances shall not be placed in a schedule solely because they are its precursors.

Abuse potential

(f) If, at the time a new-drug application is submitted to the Secretary for any drug having a stimulant, depressant, or hallucinogenic effect on the central nervous system, it appears that such drug has an abuse potential, such information shall be forwarded by the Secretary to the Attorney General.

Non-narcotic substances sold over the counter without prescription; dextromethorphan

(g)(1) The Attorney General shall by regulation exclude any non-narcotic substance from a schedule if such substance may, under the Federal Food, Drug, and Cosmetic Act, be lawfully sold over the counter without a prescription.

(2) Dextromethorphan shall not be deemed to be included in any schedule by reason of enactment of this subchapter unless controlled after October 27, 1970 pursuant to the foregoing provisions of this section.

(3) The Attorney General may, by regulation, exempt any compound, mixture, or preparation containing a controlled substance from the application of all or any part of this subchapter if he finds such compound, mixture, or preparation meets the requirements of one of the following categories:

(A) A mixture, or preparation containing a non-narcotic controlled substance, which mixture or preparation is approved for prescription use, and which contains one or more other active ingredients which are not listed in any schedule and which are included therein in such combinations, quantity, proportion, or concentration as to vitiate the potential for abuse.

(B) A compound, mixture, or preparation which contains any controlled substance, which is not for administration to a human being or animal, and which is packaged in such form or concentration, or with adulterants or denaturants, so that as packaged it does not present any significant potential for abuse.

Temporary scheduling to avoid imminent hazards to public safety

(h)(1) If the Attorney General finds that the scheduling of a substance in schedule I on a temporary basis is necessary to avoid an imminent hazard to the public safety, he may, by order and without regard to the requirements of subsection (b) of this section relating to the Secretary of Health and Human Services, schedule such substance in schedule I if the substance is not listed in any other schedule in section 812 of this title or if no exemption or approval is in effect for the substance under section 355 of this title. Such an order may not be issued before the expiration of thirty days from—

(A) the date of the publication by the Attorney General of a notice in the Federal Register of the intention to issue such order and the grounds upon which such order is to be issued, and

(B) the date the Attorney General has transmitted the notice required by paragraph (4).

(2) The scheduling of a substance under this subsection shall expire at the end of one year from the date of the issuance of the order scheduling such substance, except that the Attorney General may, during the pendency of proceedings under subsection (a)(1) of this section with respect to the substance, extend the temporary scheduling for up to six months.

(3) When issuing an order under paragraph (1), the Attorney General shall be required to consider, with respect to the finding of an imminent hazard to the public safety, only those factors set forth in paragraphs (4), (5), and (6) of subsection (c) of this section, including actual abuse, diversion from legitimate channels, and clandestine importation, manufacture, or distribution.

(4) The Attorney General shall transmit notice of an order proposed to be issued under paragraph (1) to the Secretary of Health and Human Services. In issuing an order under paragraph (1), the Attorney General shall take into consideration any comments submitted by the Secretary in response to a notice transmitted pursuant to this paragraph.

(5) An order issued under paragraph (1) with respect to a substance shall be vacated upon the conclusion of a subsequent rulemaking proceeding initiated under subsection (a) of this section with respect to such substance.

(6) An order issued under paragraph (1) is not subject to judicial review.

(Pub.L. 91–513, Title II, § 201, Oct. 27, 1970, 84 Stat. 1245; Pub.L. 95–633, Title I, § 102(a), Nov. 10, 1978, 92 Stat. 3769; Pub.L. 96–88, Title V, § 509, Oct. 17, 1979, 93 Stat. 695; Pub.L. 98–473, Title II, §§ 508, 509(a), Oct. 12, 1984, 98 Stat. 2071, 2072.)

Editorial Notes

References in Text. The Federal Food, Drug, and Cosmetic Act, referred to in subsecs. (d)(3) and (g)(1), is Act June 25, 1938, c. 675, 52 Stat. 1040, as amended, which is classified generally to chapter 9 (section 301 et seq.) of Title 21, U.S.C.A., Food and Drugs.

Schedules IV and V, referred to in subsec. (d)(4)(A), (B), are set out in section 812(c) of this title.

The Psychotropic Substances Act of 1978, referred to in subsec. (d)(5), is Pub.L. 95–633, Nov. 11, 1978, 92 Stat. 3768, which enacted sections 801a, 830, and 852 of Title 21, U.S.C.A., Food and Drugs, amended this section and sections 352, 802, 812, 823, 827, 841 to 843, 872, 881, 952, 953, and 965 of Title 21 and section 242a of Title 42, U.S.C.A., The Public Health and Welfare, and enacted provisions set out as notes under sections 801, 801a, 812, and 830 of Title 21.

Change of Name. "Secretary of Health and Human Services" was substituted for "Secretary of Health, Education, and Welfare" on authority of Pub.L. 96–88, Title V, § 509, Oct. 17, 1979, 93 Stat. 695, which is classified to section 3508 of Title 20, U.S.C.A., Education.

Code of Federal Regulations

Administrative functions, practices, and procedures, see 21 CFR 1316.01 et seq.

Debarment and suspension, drug-free workplace, grants, see 21 CFR 1404.100 et seq.

Drug abuse prevention, audiovisual education, see 34 CFR 763.1 et seq.

Drug-free schools and campuses, see 34 CFR 86.1 et seq.

Mandatory declassification review program, see 21 CFR 1402.1 et seq.

Schedules, see 21 CFR 1308.01 et seq. and Table.

Uniform administrative requirements, grants and cooperative agreements, see 21 CFR 1403.1 et seq.

§ 812. Schedules of controlled substances

Establishment

(a) There are established five schedules of controlled substances, to be known as schedules I, II, III, IV, and V. Such schedules shall initially consist of the substances listed in this section. The schedules established by this section shall be updated and republished on a semiannual basis during the two-year period beginning one year after October 27, 1970 and shall be updated and republished on an annual basis thereafter.

Placement on schedules; findings required

(b) Except where control is required by United States obligations under an international treaty, convention, or protocol, in effect on October 27, 1970, and except in the case of an immediate precursor, a drug or other substance may not be placed in any schedule unless the findings required for such schedule are made with respect to such drug or other substance. The findings required for each of the schedules are as follows:

(1) Schedule I.—

(A) The drug or other substance has a high potential for abuse.

(B) The drug or other substance has no currently accepted medical use in treatment in the United States.

(C) There is a lack of accepted safety for use of the drug or other substance under medical supervision.

(2) Schedule II.—

(A) The drug or other substance has a high potential for abuse.

Q & A

Rohypnol

- What is this drug?
- Hmm. Where is it made?
- How is it getting in the country?
- What does Schedule IV mean?
- How can a drug's schedule be changed?

EXECUTIVE OFFICE OF THE PRESIDENT
OFFICE OF NATIONAL DRUG CONTROL POLICY
Washington, D.C. 20503

January 23, 1996

MEMORANDUM TO ELENA KAGAN
DENNIS BURKE

FROM: EDWARD H. JURITH EHJ

RE: ROHYPNOL

I have further reviewed the law and legislative history surrounding 21 USC 811(h)(1) and the specific argument that the disjunctive nature of the statute would permit the Attorney General to place flunitrazepam (rohypnol) in Schedule 1 on an emergency basis. I ask that you consider the following case law and interpretations in deciding whether we can recommend using the emergency authority in this instance.

First, a plain reading of the statute yields the conclusion that the AG could not temporarily schedule a substance if it was already in Schedules II-V or if it was subject to an IND or NDA under section 355 granted by FDA. Moreover the statute in issue talks in terms of the "scheduling" of a drug. What is being proposed is a "rescheduling" of an previously scheduled drug. Using 811 in this manner would do disruption to the entire CSA scheduling scheme.

Second, can the AG temporarily place a drug in schedule I if it is not subject to a pending IND or NDA, even though it is listed in schedule IV? If that is correct, the converse would also be true -- the AG could place an FDA approved drug in schedule 1 if it is not already scheduled. I believe case law. logic, and the legislative history of the statute argue against this conclusion.

In Grinspoon v. DEA, 828 F.2d 881 (1st Cir, 1987), the court in reviewing the provisions of the emergency scheduling authority noted:

> "This provision allows the Attorney General to place certain substances into schedule I on a temporary basis without regard to the regular scheduling criteria and procedures if such emergency scheduling is 'necessary to avoid an imminent hazard to public safety.' 21 USC 811(h)(1). This amendment to the CSA, however, expressly states that the Attorney

> General's authority to schedule substances in this expedited manner does not apply where an "exemption or approval is in effect for the substances under section 355 of this title", i.e., where the FDA has permitted the substances to be marketed in interstate commerce."

Substances listed in schedules II-V in Section 812 all share the criteria of having a currently accepted medical use in treatment. Grinspoon specifically rejected the notion that a substance must have FDA approval or exemption to have a currently accepted medical use. Thereafter, DEA adopted a five criteria test which would allow it to conclude a medically useful drug not marketed in the United States has a "currently accepted medical use" under the Controlled Substances Act. The test is as follows; the drug's chemistry must be known and reproducible; there must be adequate safety studies, there must be adequate and well controlled studies proving efficacy, acceptance by qualified experts is required, and the scientific evidence must be widely available.

This five criteria test is set forth at 57 Fed. Reg, 10499-10508, March 26, 1992. In this notice DEA, specifically reference the fact that when the Controlled Substances Act was enacted, drugs with medical uses but without approved NDA's, were placed by Congress in Schedules II, III, IV and V. Citing Grinspoon, the notice states that "NDA approval is not the only method by which drugs can achieve Federal recognition as having medical uses" (at page 10504).

Thus, under Grinspoon, if a substance is listed in schedule II - V under section 812 (regardless of whether it has an exemption or approval under section 355) it has an accepted medical use, or if a substance is subject to an approval or exemption under section 355, the AG may not list the substance in schedule I on an emergency basis.

Legislative History

Addressing concerns of medical treatment House Report 98-835 states:

> The Subcommittee believed that these concerns raised significant questions about the impact an emergency scheduling authority would have on the manufacture and distribution of drugs that are currently used in medical treatment. In examining the particular substance for which the scheduling action was most necessary, the Subcommittee concluded that limiting the authority only to substances that have no currently accepted medical use in treatment addressed both the legitimate

> concerns of those in the health care industry and the principal danger to the public health.

The stated congressional intent was to limit the effect of 811(h) to substances that have no currently accepted medical use in treatment.

In essence, being listed in schedules II-V, indicates that a substance has an accepted medical use, as do drugs having an FDA approval or exemption under section 355. Congress did not intend that medically useful drugs be subject to emergency scheduling in schedule I -- which the CSA reserves for substances that have no currently accepted medical uses.

Practical Application

Moreover, the practical use of the emergency authority has been limited to drugs which fall outside the current schedules or lack NDA or IND status under section 355. As the attached list illustrates, it has been directed at fentanyl and other "designer drug" analogs which have a high potential for abuse. This is not the case with medications that have been approved for medical use and otherwise scheduled.

Conclusion

Based on the above analysis, I do not believe we can utilize the emergency scheduling authority to "reschedule" rohypnol in Schedule I

I suggest we explore the following alternatives:

1. Formal rescheduling of rohypnol to schedule II or III. This will ensure tighter controls over the drug from an administrative point of view.

2. Propose legislation that enhances Federal penalties for use of a controlled substance in connection with a sexual assault.

ing held to determine whether the Food and Drug Administration acted rationally in requiring that preparations of vitamins A and D in excess of specified dosages be restricted to prescription sale and be labeled accordingly, for cross-examination by those opposing the actions taken by the Food and Drug Administration. National Nutritional Foods Ass'n v. Mathews, D.C.N.Y.1976, 418 F.Supp. 394.

§ 355. New drugs

(a) Necessity of effective approval of application

No person shall introduce or deliver for introduction into interstate commerce any new drug, unless an approval of an application filed pursuant to subsection (b) or (j) of this section is effective with respect to such drug.

(b) Filing application; contents

(1) Any person may file with the Secretary an application with respect to any drug subject to the provisions of subsection (a) of this section. Such person shall submit to the Secretary as a part of the application (A) full reports of investigations which have been made to show whether or not such drug is safe for use and whether such drug is effective in use; (B) a full list of the articles used as components of such drug; (C) a full statement of the composition of such drug; (D) a full description of the methods used in, and the facilities and controls used for, the manufacture, processing, and packing of such drug; (E) such samples of such drug and of the articles used as components thereof as the Secretary may require; and (F) specimens of the labeling proposed to be used for such drug. The applicant shall file with the application the patent number and the expiration date of any patent which claims the drug for which the applicant submitted the application or which claims a method of using such drug and with respect to which a claim of patent infringement could reasonably be asserted if a person not licensed by the owner engaged in the manufacture, use, or sale of the drug. If an application is filed under this subsection for a drug and a patent which claims such drug or a method of using such drug is issued after the filing date but before approval of the application, the applicant shall amend the application to include the information required by the preceding sentence. Upon approval of the application, the Secretary shall publish information submitted under the two preceding sentences.

(2) An application submitted under paragraph (1) for a drug for which the investigations described in clause (A) of such paragraph and relied upon by the applicant for approval of the application were not conducted by or for the applicant and for which the applicant has not obtained a right of reference or use from the person by or for whom the investigations were conducted shall also include—

(A) a certification, in the opinion of the applicant and to the best of his knowledge, with respect to each patent which claims the drug for which such investigations were conducted or which claims a use for such drug for which the applicant is seeking approval under this subsection and for which information is required to be filed under paragraph (1) or subsection (c) of this section—

(i) that such patent information has not been filed,

(ii) that such patent has expired,

(iii) of the date on which such patent will expire, or

(iv) that such patent is invalid or will not be infringed by the manufacture use, or sale of the new drug for which the application is submitted; and

(B) if with respect to the drug for which investigations described in paragraph (1)(A) were conducted information was filed under paragraph (1) or subsection (c) of this section for a method of use patent which does not claim a use for which the applicant is seeking approval under this subsection, a statement that the method of use patent does not claim such a use.

(3)(A) An applicant who makes a certification described in paragraph (2)(A)(iv) shall include in the application a statement that the applicant will give the notice required by subparagraph (B) to—

(i) each owner of the patent which is the subject of the certification or the representative of such owner designated to receive such notice, and

(ii) the holder of the approved application under subsection (b) of this section for the drug which is claimed by the patent or a use of which is claimed by the patent or the representative of such holder designated to receive such notice.

(B) The notice referred to in subparagraph (A) shall state that an application has been submitted under this subsection for the drug with respect to which the certification is made to obtain approval to engage in the commercial manufacture, use, or sale of the drug before the expiration of the patent referred to in the certification. Such notice shall include a detailed statement of the factual and legal basis of the applicant's opinion that the patent is not valid or will not be infringed.

(C) If an application is amended to include a certification described in paragraph (2)(A)(iv), the notice required by subparagraph (B) shall be given when the amended application is submitted.

(c) Period for approval of application; period for, notice, and expedition of hearing; period for issuance of order

(1) Within one hundred and eighty days after the filing of an application under subsection (b) of this section, or such additional period as may be agreed upon by the Secretary and the applicant, the Secretary shall either—

(A) Approve the application if he then finds that none of the grounds for denying approval specified in subsection (d) of this section applies, or

(B) Give the applicant notice of an opportunity for a hearing before the Secretary under subsection (d) of this section on the question whether such application is approvable. If the applicant elects to accept the opportunity for hearing by written request within thirty days after such notice, such hearing shall commence not more than ninety days after the expiration of such thirty days unless the Secretary and the applicant otherwise agree. Any such hearing shall thereafter be conducted on an expedited basis and the Secretary's order thereon shall be issued within ninety days after the date fixed by the Secretary for filing final briefs.

(2) If the patent information described in subsection (b) of this section could not be filed with the submission of an application under subsection (b) of this section because the application was filed before the patent information was required under subsection (b) of this section or a patent was issued after the application was approved under such subsection, the holder of an approved application shall file with the Secretary the patent number and the expiration date of any patent which claims the drug for which the application was submitted or which claims a method of using such drug and with respect to which a claim of patent infringement could reasonably be asserted if a person not licensed by the owner engaged in the manufacture, use, or sale of the drug. If the holder of an approved application could not file patent information under subsection (b) of this section because it was not required at the time the application was approved, the holder shall file such information under this subsection not later than thirty days after September 24, 1984, and if the holder of an approved application could not file patent information under subsection (b) of this section because no patent had been issued when an application was filed or approved, the holder shall file such information under this subsection not later than thirty days after the date the patent involved is issued. Upon the submission of patent information under this subsection, the Secretary shall publish it.

(3) The approval of an application filed under subsection (b) of this section which contains a certification required by paragraph (2) of such subsection shall be made effective on the last applicable date determined under the following:

(A) If the applicant only made a certification described in clause (i) or (ii) of subsection (b)(2)(A) of this section or in both such clauses, the approval may be made effective immediately.

(B) If the applicant made a certification described in clause (iii) of subsection (b)(2)(A) of this section, the approval may be made effective on the date certified under clause (iii).

(C) If the applicant made a certification described in clause (iv) of subsection (b)(2)(A) of this section, the approval shall be made effective immediately unless an action is brought for infringement of a patent which is the subject of the certification before the expiration of forty-five days from the date the notice provided under paragraph (3)(B) is received. If such an action is brought before the expiration of such days, the approval may be made effective upon the expiration of the thirty-month period beginning on the date of the receipt of the notice provided under paragraph (3)(B) or such shorter or longer period as the court may order because either party to the action failed to reasonably cooperate in expediting the action, except that—

(i) if before the expiration of such period the cour
is invalid or not infringed, the approval may be ma
the court decision,

(ii) if before the expiration of such period the cou
has been infringed, the approval may be made effe
court orders under section 271(e)(4)(A) of Title 35,

(iii) if before the expiration of such period the c
injunction prohibiting the applicant from engaging ir
ture or sale of the drug until the court decides the is
infringement and if the court decides that such
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In such an action, each of the parties shall reasonably c
action. Until the expiration of forty-five days from the d
paragraph (3)(B) is received, no action may be brought
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under such section 2201 shall be brought in the judicial d
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(D)(i) If an application (other than an abbreviated new
ted under subsection (b) of this section for a drug, no a
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application under subsection (b) of this section, was ap
beginning January 1, 1982, and ending on September 24
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described in clause (A) of subsection (b)(1) of this sectic
applicant for approval of the application were not conduc
and for which the applicant has not obtained a right of
person by or for whom the investigations were condu
expiration of ten years from the date of the approval of
approved under subsection (b) of this section.

(ii) If an application submitted under subsection (b) of
active ingredient (including any ester or salt of the activ
been approved in any other application under subsect
approved after September 24, 1984, no application whi
which the subsection (b) application was submitted and f
described in clause (A) of subsection (b)(1) of this sectic
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subsection (b) of this section before the expiration of five
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application may be submitted under subsection (b) of thi
tion of four years from the date of the approval of the sub
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(iv) of subsection (b)(2)(A) of this section. The approval
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patent infringement is commenced during the one-year pe
months after the date of the approval of the subsection
month period referred to in subparagraph (C) shall be ex
time (if any) which is required for seven and one-half ye
the date of approval of the subsection (b) application.

(iii) If an application submitted under subsection (b)
which includes an active ingredient (including any est
ingredient) that has been approved in another applicatio
tion (b) of this section, is approved after September 24, 19
contains reports of new clinical investigations (other th
essential to the approval of the application and conduc
applicant, the Secretary may not make the approval of
under subsection (b) of this section for the conditions of ap
approved subsection (b) application effective before the
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the patent referred to in the certification. Such notice
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will not be infringed.

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notice of an opportunity for a hearing before the Secre-
of this section on the question whether such application is
nt elects to accept the opportunity for hearing by written
after such notice, such hearing shall commence not more
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of forty-five days from the date the notice provided under
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on the date of the receipt of the notice provided under
shorter or longer period as the court may order because
failed to reasonably cooperate in expediting the action.

(i) if before the expiration of such period the court decides that such patent is invalid or not infringed, the approval may be made effective on the date of the court decision,

(ii) if before the expiration of such period the court decides that such patent has been infringed, the approval may be made effective on such date as the court orders under section 271(e)(4)(A) of Title 35, or

(iii) if before the expiration of such period the court grants a preliminary injunction prohibiting the applicant from engaging in the commercial manufacture or sale of the drug until the court decides the issues of patent validity and infringement and if the court decides that such patent is invalid or not infringed, the approval shall be made effective on the date of such court decision.

In such an action, each of the parties shall reasonably cooperate in expediting the action. Until the expiration of forty-five days from the date the notice made under paragraph (3)(B) is received, no action may be brought under section 2201 of Title 28 for a declaratory judgment with respect to the patent. Any action brought under such section 2201 shall be brought in the judicial district where the defendant has its principal place of business or a regular and established place of business.

(D)(i) If an application (other than an abbreviated new drug application) submitted under subsection (b) of this section for a drug, no active ingredient (including any ester or salt of the active ingredient) of which has been approved in any other application under subsection (b) of this section, was approved during the period beginning January 1, 1982, and ending on September 24, 1984, the Secretary may not make the approval of another application for a drug for which the investigations described in clause (A) of subsection (b)(1) of this section and relied upon by the applicant for approval of the application were not conducted by or for the applicant and for which the applicant has not obtained a right of reference or use from the person by or for whom the investigations were conducted effective before the expiration of ten years from the date of the approval of the application previously approved under subsection (b) of this section.

(ii) If an application submitted under subsection (b) of this section for a drug, no active ingredient (including any ester or salt of the active ingredient) of which has been approved in any other application under subsection (b) of this section, is approved after September 24, 1984, no application which refers to the drug for which the subsection (b) application was submitted and for which the investigations described in clause (A) of subsection (b)(1) of this section and relied upon by the applicant for approval of the application were not conducted by or for the applicant and for which the applicant has not obtained a right of reference or use from the person by or for whom the investigations were conducted may be submitted under subsection (b) of this section before the expiration of five years from the date of the approval of the application under subsection (b) of this section, except that such an application may be submitted under subsection (b) of this section after the expiration of four years from the date of the approval of the subsection (b) application if it contains a certification of patent invalidity or noninfringement described in clause (iv) of subsection (b)(2)(A) of this section. The approval of such an application shall be made effective in accordance with this paragraph except that, if an action for patent infringement is commenced during the one-year period beginning forty-eight months after the date of the approval of the subsection (b) application, the thirty-month period referred to in subparagraph (C) shall be extended by such amount of time (if any) which is required for seven and one-half years to have elapsed from the date of approval of the subsection (b) application.

(iii) If an application submitted under subsection (b) of this section for a drug, which includes an active ingredient (including any ester or salt of the active ingredient) that has been approved in another application approved under subsection (b) of this section, is approved after September 24, 1984, and if such application contains reports of new clinical investigations (other than bioavailability studies) essential to the approval of the application and conducted or sponsored by the applicant, the Secretary may not make the approval of an application submitted under subsection (b) of this section for the conditions of approval of such drug in the approved subsection (b) application effective before the expiration of three years from the date of the approval of the application under subsection (b) of this section if the investigations described in clause (A) of subsection (b)(1) of this section and relied upon by the applicant for approval of the application were not conducted by

or for the applicant and if the applicant has not obtained a right of reference or use from the person by or for whom the investigations were conducted.

(iv) If a supplement to an application approved under subsection (b) of this section is approved after September 24, 1984, and the supplement contains reports of new clinical investigations (other than bioavailability studies) essential to the approval of the supplement and conducted or sponsored by the person submitting the supplement, the Secretary may not make the approval of an application submitted under subsection (b) of this section for a change approved in the supplement effective before the expiration of three years from the date of the approval of the supplement under subsection (b) of this section if the investigations described in clause (A) of subsection (b)(1) of this section and relied upon by the applicant for approval of the application were not conducted by or for the applicant and if the applicant has not obtained a right of reference or use from the person by or for whom the investigations were conducted.

(v) If an application (or supplement to an application) submitted under subsection (b) of this section for a drug, which includes an active ingredient (including any ester or salt of the active ingredient) that has been approved in another application under subsection (b) of this section, was approved during the period beginning January 1, 1982, and ending on September 24, 1984, the Secretary may not make the approval of an application submitted under this subsection and for which the investigations described in clause (A) of subsection (b)(1) of this section and relied upon by the applicant for approval of the application were not conducted by or for the applicant and for which the applicant has not obtained a right of reference or use from the person by or for whom the investigations were conducted and which refers to the drug for which the subsection (b) application was submitted effective before the expiration of two years from September 24, 1984.

(d) Grounds for refusing application; approval of application; "substantial evidence" defined

If the Secretary finds, after due notice to the applicant in accordance with subsection (c) of this section and giving him an opportunity for a hearing, in accordance with said subsection, that (1) the investigations, reports of which are required to be submitted to the Secretary pursuant to subsection (b) of this section, do not include adequate tests by all methods reasonably applicable to show whether or not such drug is safe for use under the conditions prescribed, recommended, or suggested in the proposed labeling thereof; (2) the results of such tests show that such drug is unsafe for use under such conditions or do not show that such drug is safe for use under such conditions; (3) the methods used in, and the facilities and controls used for, the manufacture, processing, and packing of such drug are inadequate to preserve its identity, strength, quality, and purity; (4) upon the basis of the information submitted to him as part of the application, or upon the basis of any other information before him with respect to such drug, he has insufficient information to determine whether such drug is safe for use under such conditions; or (5) evaluated on the basis of the information submitted to him as part of the application and any other information before him with respect to such drug, there is a lack of substantial evidence that the drug will have the effect it purports or is represented to have under the conditions of use prescribed, recommended, or suggested in the proposed labeling thereof; or (6) the application failed to contain the patent information prescribed by subsection (b) of this section; or (7) based on a fair evaluation of all material facts, such labeling is false or misleading in any particular; he shall issue an order refusing to approve the application. If, after such notice and opportunity for hearing, the Secretary finds that clauses (1) through (6) do not apply, he shall issue an order approving the application. As used in this subsection and subsection (e) of this section, the term "substantial evidence" means evidence consisting of adequate and well-controlled investigations, including clinical investigations, by experts qualified by scientific training and experience to evaluate the effectiveness of the drug involved, on the basis of which it could fairly and responsibly be concluded by such experts that the drug will have the effect it purports or is represented to have under the conditions of use prescribed, recommended, or suggested in the labeling or proposed labeling thereof.

(e) Withdrawal of approval; grounds; immediate suspension upon finding imminent hazard to public health

The Secretary shall, after due notice and opportunity for hearing to the applicant, withdraw approval of an application with respect to any drug under this section if the Secretary finds (1) that clinical or other experience, tests, or other scientific data show that such drug is unsafe for use under the conditions of use upon the basis of which the

application was approved; (2) that new evider
such application or not available to the Se
approved, or tests by new methods, or te
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that there is an imminent hazard to the public
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to the applicant, withdraw the approval of an a
or (j) of this section with respect to any drug u
that the applicant has failed to establish a sys
has repeatedly or deliberately failed to main
reports, in accordance with a regulation or ord
to comply with the notice requirements of sect
has refused to permit access to, or copying or v
paragraph (2) of such subsection; or (2) that on
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methods used in, or the facilities and controls u
packing of such drug are inadequate to assu
quality, and purity and were not made adequate
written notice from the Secretary specifying the
basis of new information before him, evaluated
when the application was approved, the labeling
of all material facts, is false or misleading in an
a reasonable time after receipt of written no
matter complained of. Any order under this
which it is based.

[See main volume for

(j) Abbreviated new drug applications

(1) Any person may file with the Secreta
approval of a new drug.

(2)(A) An abbreviated application for a new

(i) information to show that the conditio
suggested in the labeling proposed for the n
for a drug listed under paragraph (6) (herei
"listed drug");

(ii)(I) if the listed drug referred to in cl
information to show that the active ingredie
the listed drug;

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(III) if the listed drug referred to in
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(A) of subsection (b)(1) of this section and relied
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pproval of application; "substantial evidence" defined

tice to the applicant in accordance with subsection
opportunity for a hearing, in accordance with said
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(b) of this section, do not include adequate tests by
show whether or not such drug is safe for use
ommended, or suggested in the proposed labeling
show that such drug is unsafe for use under such
drug is safe for use under such conditions; (3) the
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nation before him with respect to such drug, he has
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ation before him with respect to such drug, there is
the drug will have the effect it purports or is
tions of use prescribed, recommended, or suggested
or (6) the application failed to contain the patent
n (b) of this section; or (7) based on a fair evaluation
false or misleading in any particular; he shall issue
plication. If, after such notice and opportunity for
auses (1) through (6) do not apply, he shall issue an
s used in this subsection and subsection (e) of this
ice" means evidence consisting of adequate and well-
clinical investigations, by experts qualified by scienti-
uate the effectiveness of the drug involved, on the
sponsibly be concluded by such experts that the drug
is represented to have under the conditions of use
ested in the labeling or proposed labeling thereof.

immediate suspension upon finding imminent hazard to

notice and opportunity for hearing to the applicant,
n with respect to any drug under this section if the
other experience, tests, or other scientific data show
nder the conditions of use upon the basis of which the

application was approved; (2) that new evidence of clinical experience, not contained in such application or not available to the Secretary until after such application was approved, or tests by new methods, or tests by methods not deemed reasonably applicable when such application was approved, evaluated together with the evidence available to the Secretary when the application was approved, shows that such drug is not shown to be safe for use under the conditions of use upon the basis of which the application was approved; or (3) on the basis of new information before him with respect to such drug, evaluated together with the evidence available to him when the application was approved, that there is a lack of substantial evidence that the drug will have the effect it purports or is represented to have under the conditions of use prescribed, recommended, or suggested in the labeling thereof; or (4) the patent information prescribed by subsection (c) of this section was not filed within thirty days after the receipt of written notice from the Secretary specifying the failure to file such information; or (5) that the at the application contains any untrue statement of a material fact: *Provided*, That if the Secretary (or in his absence the officer acting as Secretary) finds that there is an imminent hazard to the public health, he may suspend the approval of such application immediately, and give the applicant prompt notice of his action and afford the applicant the opportunity for an expedited hearing under this subsection; but the authority conferred by this proviso to suspend the approval of an application shall not be delegated. The Secretary may also, after due notice and opportunity for hearing to the applicant, withdraw the approval of an application submitted under subsection (b) or (j) of this section with respect to any drug under this section if the Secretary finds (1) that the applicant has failed to establish a system for maintaining required records, or has repeatedly or deliberately failed to maintain such records or to make required reports, in accordance with a regulation or order under subsection (k) of this section or to comply with the notice requirements of section 360(k)(2) of this title, or the applicant has refused to permit access to, or copying or verification of, such records as required by paragraph (2) of such subsection; or (2) that on the basis of new information before him, evaluated together with the evidence before him when the application was approved, the methods used in, or the facilities and controls used for, the manufacture, processing, and packing of such drug are inadequate to assure and preserve its identity, strength, quality, and purity and were not made adequate within a reasonable time after receipt of written notice from the Secretary specifying the matter complained of; or (3) that on the basis of new information before him, evaluated together with the evidence before him when the application was approved, the labeling of such drug, based on a fair evaluation of all material facts, is false or misleading in any particular and was not corrected within a reasonable time after receipt of written notice from the Secretary specifying the matter complained of. Any order under this subsection shall state the findings upon which it is based.

[See main volume for text of (f) to (i)]

(j) Abbreviated new drug applications

(1) Any person may file with the Secretary an abbreviated application for the approval of a new drug.

(2)(A) An abbreviated application for a new drug shall contain—

(i) information to show that the conditions of use prescribed, recommended, or suggested in the labeling proposed for the new drug have been previously approved for a drug listed under paragraph (6) (hereinafter in this subsection referred to as a "listed drug");

(ii)(I) if the listed drug referred to in clause (i) has only one active ingredient, information to show that the active ingredient of the new drug is the same as that of the listed drug;

(II) if the listed drug referred to in clause (i) has more than one active ingredient, information to show that the active ingredients of the new drug are the same as those of the listed drug, or

(III) if the listed drug referred to in clause (i) has more than one active ingredient and if one of the active ingredients of the new drug is different and the application is filed pursuant to the approval of a petition filed under subparagraph (C), information to show that the other active ingredients of the new drug are the same as the active ingredients of the listed drug, information to show that the different active ingredient is an active ingredient of a listed drug or of a drug which does not meet the requirements of section 321(p) of this title, and such other

information respecting the different active ingredient with respect to which the petition was filed as the Secretary may require;

(iii) information to show that the route of administration, the dosage form, and the strength of the new drug are the same as those of the listed drug referred to in clause (i) or, if the route of administration, the dosage form, or the strength of the new drug is different and the application is filed pursuant to the approval of a petition filed under subparagraph (C), such information respecting the route of administration, dosage form, or strength with respect to which the petition was filed as the Secretary may require;

(iv) information to show that the new drug is bioequivalent to the listed drug referred to in clause (i), except that if the application is filed pursuant to the approval of a petition filed under subparagraph (C), information to show that the active ingredients of the new drug are of the same pharmacological or therapeutic class as those of the listed drug referred to in clause (i) and the new drug can be expected to have the same therapeutic effect as the listed drug when administered to patients for a condition of use referred to in clause (i);

(v) information to show that the labeling proposed for the new drug is the same as the labeling approved for the listed drug referred to in clause (i) except for changes required because of differences approved under a petition filed under subparagraph (C) or because the new drug and the listed drug are produced or distributed by different manufacturers;

(vi) the items specified in clauses (B) through (F) of subsection (b)(1) of this section;

(vii) a certification, in the opinion of the applicant and to the best of his knowledge, with respect to each patent which claims the listed drug referred to in clause (i) or which claims a use for such listed drug for which the applicant is seeking approval under this subsection and for which information is required to be filed under subsection (b) or (c) of this section—

(I) that such patent information has not been filed,

(II) that such patent has expired,

(III) of the date on which such patent will expire, or

(IV) that such patent is invalid or will not be infringed by the manufacture, use, or sale of the new drug for which the application is submitted; and

(viii) if with respect to the listed drug referred to in clause (i) information was filed under subsection (b) or (c) of this section for a method of use patent which does not claim a use for which the applicant is seeking approval under this subsection, a statement that the method of use patent does not claim such a use.

The Secretary may not require that an abbreviated application contain information in addition to that required by clauses (i) through (viii).

(B)(i) An applicant who makes a certification described in subparagraph (A)(vii)(IV) shall include in the application a statement that the applicant will give the notice required by clause (ii) to—

(I) each owner of the patent which is the subject of the certification or the representative of such owner designated to receive such notice, and

(II) the holder of the approved application under subsection (b) of this section for the drug which is claimed by the patent or a use of which is claimed by the patent or the representative of such holder designated to receive such notice.

(ii) The notice referred to in clause (i) shall state that an application, which contains data from bioavailability or bioequivalence studies, has been submitted under this subsection for the drug with respect to which the certification is made to obtain approval to engage in the commercial manufacture, use, or sale of such drug before the expiration of the patent referred to in the certification. Such notice shall include a detailed statement of the factual and legal basis of the applicant's opinion that the patent is not valid or will not be infringed.

(iii) If an application is amended to include a certification described in subparagraph (A)(vii)(IV), the notice required by clause (ii) shall be given when the amended application is submitted.

(C) If a person wants to submit an abbreviated application for a new drug which has a different active ingredient or whose route of administration, dosage form, or strength differ from that of a listed drug, such person shall submit a petition to the Secretary

seeking permission to file such an application.
prove a petition submitted under this subparagr
petition is submitted. The Secretary shall appro
finds—

(i) that investigations must be conducted
the drug or of any of its active ingredients,
form, or strength which differ from the liste

(ii) that any drug with a different activ
evaluated for approval as safe and effective o
to be submitted in an abbreviated applicatio

(3) Subject to paragraph (4), the Secretary sh
unless the Secretary finds—

(A) the methods used in, or the facilities a
processing, and packing of the drug are i
identity, strength, quality, and purity;

(B) information submitted with the applic
the proposed conditions of use have been p
referred to in the application;

(C)(i) if the listed drug has only one ac
with the application is insufficient to show th
that of the listed drug;

(ii) if the listed drug has more than one a
with the application is insufficient to show th
as the active ingredients of the listed drug,

(iii) if the listed drug has more than one
is for a drug which has an active ingre
information submitted with the application i

(I) that the other active ingredients a
the listed drug, or

(II) that the different active ingredi
drug or a drug which does not meet the
title,

or no petition to file an application for
was approved under paragraph (2)(C);

(D)(i) if the application is for a drug whos
or strength of the drug is the same as the r
strength of the listed drug referred to in th
the application is insufficient to show that th
or strength is the same as that of the listed

(ii) if the application is for a drug whose r
strength of the drug is different from that
application, no petition to file an application f
administration, dosage form, or strength w

(E) if the application was filed pursuant
paragraph (2)(C), the application did not co
Secretary respecting the active ingredient, r
strength which is not the same;

(F) information submitted in the applicatio
is bioequivalent to the listed drug referred to
was filed pursuant to a petition approved
submitted in the application is insufficient to
new drug are of the same pharmacological or
drug referred to in paragraph (2)(A)(i) and
have the same therapeutic effect as the liste
for a condition of use referred to in such pa

(G) information submitted in the applica
labeling proposed for the drug is the same
drug referred to in the application except fo
ences approved under a petition filed under
and the listed drug are produced or dist

rent active ingredient with respect to which the
ry may require;

the route of administration, the dosage form, and
the same as those of the listed drug referred to in
inistration, the dosage form, or the strength of the
application is filed pursuant to the approval of a
ph (C), such information respecting the route of
trength with respect to which the petition was filed

the new drug is bioequivalent to the listed drug
t that if the application is filed pursuant to the
r subparagraph (C), information to show that the
ug are of the same pharmacological or therapeutic
referred to in clause (i) and the new drug can be
peutic effect as the listed drug when administered
e referred to in clause (i);

he labeling proposed for the new drug is the same
e listed drug referred to in clause (i) except for
ifferences approved under a petition filed under
ie new drug and the listed drug are produced or
turers;

uses (B) through (F) of subsection (b)(1) of this

pinion of the applicant and to the best of his
patent which claims the listed drug referred to in
e for such listed drug for which the applicant is
section and for which information is required to be
of this section—

mation has not been filed,

expired,

h such patent will expire, or

nvalid or will not be infringed by the manufacture,
rug for which the application is submitted; and

sted drug referred to in clause (i) information was
of this section for a method of use patent which
ch the applicant is seeking approval under this
method of use patent does not claim such a use.

an abbreviated application contain information in
(i) through (viii).

certification described in subparagraph (A)(vii)(IV)
statement that the applicant will give the notice

t which is the subject of the certification or the
signated to receive such notice, and

d application under subsection (b) of this section for
e patent or a use of which is claimed by the patent
older designated to receive such notice.

se (i) shall state that an application, which contains
ivalence studies, has been submitted under this
to which the certification is made to obtain approval
ture, use, or sale of such drug before the expiration
ertification. Such notice shall include a detailed
sis of the applicant's opinion that the patent is not

to include a certification described in subparagraph
y clause (ii) shall be given when the amended

n abbreviated application for a new drug which has
se route of administration, dosage form, or strength
ich person shall submit a petition to the Secretary

seeking permission to file such an application. The Secretary shall approve or disapprove a petition submitted under this subparagraph within ninety days of the date the petition is submitted. The Secretary shall approve such a petition unless the Secretary finds—

(i) that investigations must be conducted to show the safety and effectiveness of the drug or of any of its active ingredients, the route of administration, the dosage form, or strength which differ from the listed drug; or

(ii) that any drug with a different active ingredient may not be adequately evaluated for approval as safe and effective on the basis of the information required to be submitted in an abbreviated application.

(3) Subject to paragraph (4), the Secretary shall approve an application for a drug unless the Secretary finds—

(A) the methods used in, or the facilities and controls used for, the manufacture, processing, and packing of the drug are inadequate to assure and preserve its identity, strength, quality, and purity;

(B) information submitted with the application is insufficient to show that each of the proposed conditions of use have been previously approved for the listed drug referred to in the application;

(C)(i) if the listed drug has only one active ingredient, information submitted with the application is insufficient to show that the active ingredient is the same as that of the listed drug;

(ii) if the listed drug has more than one active ingredient, information submitted with the application is insufficient to show that the active ingredients are the same as the active ingredients of the listed drug, or

(iii) if the listed drug has more than one active ingredient and if the application is for a drug which has an active ingredient different from the listed drug, information submitted with the application is insufficient to show—

(I) that the other active ingredients are the same as the active ingredients of the listed drug, or

(II) that the different active ingredient is an active ingredient of a listed drug or a drug which does not meet the requirements of section 321(p) of this title,

or no petition to file an application for the drug with the different ingredient was approved under paragraph (2)(C);

(D)(i) if the application is for a drug whose route of administration, dosage form, or strength of the drug is the same as the route of administration, dosage form, or strength of the listed drug referred to in the application, information submitted in the application is insufficient to show that the route of administration, dosage form, or strength is the same as that of the listed drug, or

(ii) if the application is for a drug whose route of administration, dosage form, or strength of the drug is different from that of the listed drug referred to in the application, no petition to file an application for the drug with the different route of administration, dosage form, or strength was approved under paragraph (2)(C);

(E) if the application was filed pursuant to the approval of a petition under paragraph (2)(C), the application did not contain the information required by the Secretary respecting the active ingredient, route of administration, dosage form, or strength which is not the same;

(F) information submitted in the application is insufficient to show that the drug is bioequivalent to the listed drug referred to in the application or, if the application was filed pursuant to a petition approved under paragraph (2)(C), information submitted in the application is insufficient to show that the active ingredients of the new drug are of the same pharmacological or therapeutic class as those of the listed drug referred to in paragraph (2)(A)(i) and that the new drug can be expected to have the same therapeutic effect as the listed drug when administered to patients for a condition of use referred to in such paragraph;

(G) information submitted in the application is insufficient to show that the labeling proposed for the drug is the same as the labeling approved for the listed drug referred to in the application except for changes required because of differences approved under a petition filed under paragraph (2)(C) or because the drug and the listed drug are produced or distributed by different manufacturers;

(H) information submitted in the application or any other information available to the Secretary shows that (i) the inactive ingredients of the drug are unsafe for use under the conditions prescribed, recommended, or suggested in the labeling proposed for the drug, or (ii) the composition of the drug is unsafe under such conditions because of the type or quantity of inactive ingredients included or the manner in which the inactive ingredients are included;

(I) the approval under subsection (c) of this section of the listed drug referred to in the application under this subsection has been withdrawn or suspended for grounds described in the first sentence of subsection (e) of this section, the Secretary has published a notice of opportunity for hearing to withdraw approval of the listed drug under subsection (c) of this section for grounds described in the first sentence of subsection (e) of this section, the approval under this subsection of the listed drug referred to in the application under this subsection has been withdrawn or suspended under paragraph (5), or the Secretary has determined that the listed drug has been withdrawn from sale for safety or effectiveness reasons;

(J) the application does not meet any other requirement of paragraph (2)(A); or

(K) the application contains an untrue statement of material fact.

(4)(A) Within one hundred and eighty days of the initial receipt of an application under paragraph (2) or within such additional period as may be agreed upon by the Secretary and the applicant, the Secretary shall approve or disapprove the application.

(B) The approval of an application submitted under paragraph (2) shall be made effective on the last applicable date determined under the following:

(i) If the applicant only made a certification described in subclause (I) or (II) of paragraph (2)(A)(vii) or in both such subclauses, the approval may be made effective immediately.

(ii) If the applicant made a certification described in subclause (III) of paragraph (2)(A)(vii), the approval may be made effective on the date certified under subclause (III).

(iii) If the applicant made a certification described in subclause (IV) of paragraph (2)(A)(vii), the approval shall be made effective immediately unless an action is brought for infringement of a patent which is the subject of the certification before the expiration of forty-five days from the date the notice provided under paragraph (2)(B)(i) is received. If such an action is brought before the expiration of such days, the approval shall be made effective upon the expiration of the thirty-month period beginning on the date of the receipt of the notice provided under paragraph (2)(B)(i) or such shorter or longer period as the court may order because either party to the action failed to reasonably cooperate in expediting the action, except that—

(I) if before the expiration of such period the court decides that such patent is invalid or not infringed, the approval shall be made effective on the date of the court decision,

(II) if before the expiration of such period the court decides that such patent has been infringed, the approval shall be made effective on such date as the court orders under section 271(e)(4)(A) of Title 35 or

(III) if before the expiration of such period the court grants a preliminary injunction prohibiting the applicant from engaging in the commercial manufacture or sale of the drug until the court decides the issues of patent validity and infringement and if the court decides that such patent is invalid or not infringed, the approval shall be made effective on the date of such court decision.

In such an action, each of the parties shall reasonably cooperate in expediting the action. Until the expiration of forty-five days from the date the notice made under paragraph (2)(B)(i) is received, no action may be brought under section 2201 of Title 28 for a declaratory judgment with respect to the patent. Any action brought under section 2201 shall be brought in the judicial district where the defendant has its principal place of business or a regular and established place of business.

(iv) If the application contains a certification described in subclause (IV) of paragraph (2)(A)(vii) and is for a drug for which a previous application has been submitted under this subsection continuing such a certification, the application shall be made effective not earlier than one hundred and eighty days after—

(I) the date the Secretary receiv
previous application of the first com
previous application, or

(II) the date of a decision of a c
holding the patent which is the subje
infringed,

whichever is earlier.

(C) If the Secretary decides to disapprove a
applicant notice of an opportunity for a hearin
whether such application is approvable. If the
for hearing by written request within thirty c
commence not more than ninety days after th
Secretary and the applicant otherwise agree
conducted on an expedited basis and the Secre
ninety days after the date fixed by the Secre

(D)(i) If an application (other than an abb
under subsection (b) of this section for a drug
or salt of the active ingredient) of which has
under subsection (b) of this section, was appr
1, 1982, and ending on September 24, 1984, th
an application submitted under this subsectio
subsection (b) application was submitted effect
the date of the approval of the applicatio

(ii) If an application submitted under subs
active ingredient (including any ester or salt o
approved in any other application under subse
September 24, 1984, no application may be sub
to the drug for which the subsection (b) applic
of five years from the date of the approval of t
section, except that such an application may be
expiration of four years from the date of the a
it contains a certification of patent invalidity o
(IV) of paragraph (2)(A)(vii). The approva
effective in accordance with subparagraph (
infringement is commenced during the one-y
after the date of the approval of the subsectio
referred to in subparagraph (B)(iii) shall be e
which is required for seven and one-half years
of the subsection (b) application.

(iii) If an application submitted under subs
includes an active ingredient (including any e
has been approved in another application appr
is approved after September 24, 1984, and if
clinical investigations (other than bioavailabilit
application and conducted or sponsored by th
the approval of an application submitted unc
approval of such drug in the subsection (b) ap
three years from the date of the approval of th
section for such drug.

(iv) If a supplement to an application appro
approved after September 24, 1984, and the su
investigations (other than bioavailability stu
supplement and conducted or sponsored by th
Secretary may not make the approval of an ap
for a change approved in the supplement effe
from the date of the approval of the supplem

(v) If an application (or supplement to an a
of this section for a drug, which includes an act
of the active ingredient) that has been approve
(b) of this section, was approved during the
ending on September 24, 1984, the Secreta

ed in the application or any other information available to
i) the inactive ingredients of the drug are unsafe for use
ribed, recommended, or suggested in the labeling pro-
i) the composition of the drug is unsafe under such
type or quantity of inactive ingredients included or the
ive ingredients are included;

ubsection (c) of this section of the listed drug referred to
this subsection has been withdrawn or suspended for
first sentence of subsection (e) of this section, the
notice of opportunity for hearing to withdraw approval of
ction (c) of this section for grounds described in the first
of this section, the approval under this subsection of the
he application under this subsection has been withdrawn
aph (5), or the Secretary has determined that the listed
from sale for safety or effectiveness reasons;

not meet any other requirement of paragraph (2)(A); or

ains an untrue statement of material fact.

and eighty days of the initial receipt of an application
such additional period as may be agreed upon by the
e Secretary shall approve or disapprove the application.

lication submitted under paragraph (2) shall be made
date determined under the following:

made a certification described in subclause (I) or (II) of
both such subclauses, the approval may be made effective

e a certification described in subclause (III) of paragraph
y be made effective on the date certified under subclause

ade a certification described in subclause (IV) of para-
val shall be made effective immediately unless an action
nt of a patent which is the subject of the certification
orty-five days from the date the notice provided under
ved. If such an action is brought before the expiration of
all be made effective upon the expiration of the thirty-
n the date of the receipt of the notice provided under
shorter or longer period as the court may order because
failed to reasonably cooperate in expediting the action.

iration of such period the court decides that such patent
ged, the approval shall be made effective on the date of

piration of such period the court decides that such patent
e approval shall be made effective on such date as the
ction 271(e)(4)(A) of Title 35 or

expiration of such period the court grants a preliminary
the applicant from engaging in the commercial manufac-
g until the court decides the issues of patent validity and
the court decides that such patent is invalid or not
al shall be made effective on the date of such court

h of the parties shall reasonably cooperate in expediting
expiration of forty-five days from the date the notice
h (2)(B)(i) is received, no action may be brought under
28 for a declaratory judgment with respect to the patent.
nder section 2201 shall be brought in the judicial district
has its principal place of business or a regular and
usiness.

contains a certification described in subclause (IV) of
is for a drug for which a previous application has been
ection continuing such a certification, the application shall
lier than one hundred and eighty days after—

(I) the date the Secretary receives notice from the applicant under the previous application of the first commercial marketing of the drug under the previous application, or

(II) the date of a decision of a court in an action described in clause (iii) holding the patent which is the subject of the certification to be invalid or not infringed,

whichever is earlier.

(C) If the Secretary decides to disapprove an application, the Secretary shall give the applicant notice of an opportunity for a hearing before the Secretary on the question of whether such application is approvable. If the applicant elects to accept the opportunity for hearing by written request within thirty days after such notice, such hearing shall commence not more than ninety days after the expiration of such thirty days unless the Secretary and the applicant otherwise agree. Any such hearing shall thereafter be conducted on an expedited basis and the Secretary's order thereon shall be issued within ninety days after the date fixed by the Secretary for filing final briefs.

(D)(i) If an application (other than an abbreviated new drug application) submitted under subsection (b) of this section for a drug, no active ingredient (including any ester or salt of the active ingredient) of which has been approved in any other application under subsection (b) of this section, was approved during the period beginning January 1, 1982, and ending on September 24, 1984, the Secretary may not make the approval of an application submitted under this subsection which refers to the drug for which the subsection (b) application was submitted effective before the expiration of ten years from the date of the approval of the application under subsection (b) of this section.

(ii) If an application submitted under subsection (b) of this section for a drug, no active ingredient (including any ester or salt of the active ingredient) of which has been approved in any other application under subsection (b) of this section, is approved after September 24, 1984, no application may be submitted under this subsection which refers to the drug for which the subsection (b) application was submitted before the expiration of five years from the date of the approval of the application under subsection (b) of this section, except that such an application may be submitted under this subsection after the expiration of four years from the date of the approval of the subsection (b) application if it contains a certification of patent invalidity or noninfringement described in subclause (IV) of paragraph (2)(A)(vii). The approval of such an application shall be made effective in accordance with subparagraph (B) except that, if an action for patent infringement is commenced during the one-year period beginning forty-eight months after the date of the approval of the subsection (b) application, the thirty-month period referred to in subparagraph (B)(iii) shall be extended by such amount of time (if any) which is required for seven and one-half years to have elapsed from the date of approval of the subsection (b) application.

(iii) If an application submitted under subsection (b) of this section for a drug, which includes an active ingredient (including any ester or salt of the active ingredient) that has been approved in another application approved under subsection (b) of this section, is approved after September 24, 1984, and if such application contains reports of new clinical investigations (other than bioavailability studies) essential to the approval of the application and conducted or sponsored by the applicant, the Secretary may not make the approval of an application submitted under this subsection for the conditions of approval of such drug in the subsection (b) application effective before the expiration of three years from the date of the approval of the application under subsection (b) of this section for such drug.

(iv) If a supplement to an application approved under subsection (b) of this section is approved after September 24, 1984, and the supplement contains reports of new clinical investigations (other than bioavailability studies) essential to the approval of the supplement and conducted or sponsored by the person submitting the supplement, the Secretary may not make the approval of an application submitted under this subsection for a change approved in the supplement effective before the expiration of three years from the date of the approval of the supplement under subsection (b) of this section.

(v) If an application (or supplement to an application) submitted under subsection (b) of this section for a drug, which includes an active ingredient (including any ester or salt of the active ingredient) that has been approved in another application under subsection (b) of this section, was approved during the period beginning January 1, 1982, and ending on September 24, 1984, the Secretary may not make the approval of an

application submitted under this subsection which refers to the drug for which the subsection (b) application was submitted or which refers to a change approved in a supplement to the subsection (b) application effective before the expiration of two years from September 24, 1984.

(5) If a drug approved under this subsection refers in its approved application to a drug the approval of which was withdrawn or suspended for grounds described in the first sentence of subsection (e) of this section or was withdrawn or suspended under this paragraph or which, as determined by the Secretary, has been withdrawn from sale for safety or effectiveness reasons, the approval of the drug under this subsection shall be withdrawn or suspended—

(A) for the same period as the withdrawal or suspension under subsection (e) of this section or this paragraph, or

(B) if the listed drug has been withdrawn from sale, for the period of withdrawal from sale or, if earlier, the period ending on the date the Secretary determines that the withdrawal from sale is not for safety or effectiveness reasons.

(6)(A)(i) Within sixty days of September 24, 1984, the Secretary shall publish and make available to the public—

(I) a list in alphabetical order of the official and proprietary name of each drug which has been approved for safety and effectiveness under subsection (c) of this section before September 24, 1984;

(II) the date of approval if the drug is approved after 1981 and the number of the application which was approved; and

(III) whether in vitro or in vivo bioequivalence studies, or both such studies, are required for applications filed under this subsection which will refer to the drug published.

(ii) Every thirty days after the publication of the first list under clause (i) the Secretary shall revise the list to include each drug which has been approved for safety and effectiveness under subsection (c) of this section or approved under this subsection during the thirty-day period.

(iii) When patent information submitted under subsection (b) or (c) of this section respecting a drug included on the list is to be published by the Secretary, the Secretary shall, in revisions made under clause (ii), include such information for such drug.

(B) A drug approved for safety and effectiveness under subsection (c) of this section or approved under this subsection shall, for purposes of this subsection, be considered to have been published under subparagraph (A) on the date of its approval or September 24, 1984, whichever is later.

(C) If the approval of a drug was withdrawn or suspended for grounds described in the first sentence of subsection (e) of this section or was withdrawn or suspended under paragraph (5) or if the Secretary determines that a drug has been withdrawn from sale for safety or effectiveness reasons, it may not be published in the list under subparagraph (A) or, if the withdrawal or suspension occurred after its publication in such list, it shall be immediately removed from such list—

(i) for the same period as the withdrawal or suspension under subsection (e) of this section or paragraph (5), or

(ii) if the listed drug has been withdrawn from sale, for the period of withdrawal from sale or, if earlier, the period ending on the date the Secretary determines that the withdrawal from sale is not for safety or effectiveness reasons.

A notice of the removal shall be published in the Federal Register.

(7) For purposes of this subsection:

(A) The term "bioavailability" means the rate and extent to which the active ingredient or therapeutic ingredient is absorbed from a drug and becomes available at the site of drug action.

(B) A drug shall be considered to be bioequivalent to a listed drug if—

(i) the rate and extent of absorption of the drug do not show a significant difference from the rate and extent of absorption of the listed drug when administered at the same molar dose of the therapeutic ingredient under similar experimental conditions in either a single dose or multiple doses; or

(ii) the extent of absorp
difference from the extent of
at the same molar dose of th
tal conditions in either a sing
the listed drug in the rate of a
its proposed labeling, is not e
concentrations on chronic use
drug.

(8) The Secretary shall, with res
subsection, maintain a record of—

(A) the name of the applicant,

(B) the name of the drug cove

(C) the name of each person
application was assigned and the

(D) the name of each person
application was assigned and the

The information the Secretary is requi
to an application submitted under thi
after the approval of such application.

(k) **Records and reports; required infor**

(1) In the case of any drug for
subsection (b) or (j) of this section is i
such records, and make such report
experience and other data or inform
applicant with respect to such drug, a
order with respect to such applicatio
records and reports are necessary in
facilitate a determination, whether the
of this section. Regulations and o
subsection (i) of this section shall ha
medical profession and the interests o
deems it to be appropriate, for the ex
such regulations or orders are applic
obtained by the Secretary.

(2) Every person required under th
charge or custody thereof, shall, upon
the Secretary, permit such officer or e
and copy and verify such records.

(l) **Public disclosure of safety and effect**

Safety and effectiveness data anc
application under subsection (b) of thi
been disclosed to the public shall be r
extraordinary circumstances are show

(1) if no work is being or will

(2) if the Secretary has determ
legal appeals have been exhauste

(3) if approval of the applicatio
and all legal appeals have been e

(4) if the Secretary has dete

(5) upon the effective date of t
tion (j) of this section which refe
approval of an application under
drug could be made effective if s

section which refers to the drug for which the
itted or which refers to a change approved in a
ication effective before the expiration of two years

subsection refers in its approved application to a
drawn or suspended for grounds described in the
section or was withdrawn or suspended under this
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e withdrawal or suspension under subsection (e) of
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n withdrawn from sale, for the period of withdrawal
d ending on the date the Secretary determines that
for safety or effectiveness reasons.

tember 24, 1984, the Secretary shall publish and

of the official and proprietary name of each drug
fety and effectiveness under subsection (c) of this
84;

drug is approved after 1981 and the number of the
and

vo bioequivalence studies, or both such studies, are
nder this subsection which will refer to the drug

publication of the first list under clause (i) the
lude each drug which has been approved for safety
c) of this section or approved under this subsection

bmitted under subsection (b) or (c) of this section
t is to be published by the Secretary, the Secretary
use (ii), include such information for such drug.

nd effectiveness under subsection (c) of this section
all, for purposes of this subsection, be considered to
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s withdrawn or suspended for grounds described in
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and extent of absorption of the listed drug when
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ditions in either a single dose or multiple doses; or

(ii) the extent of absorption of the drug does not show a significant difference from the extent of absorption of the listed drug when administered at the same molar dose of the therapeutic ingredient under similar experimental conditions in either a single dose or multiple doses and the difference from the listed drug in the rate of absorption of the drug is intentional, is reflected in its proposed labeling, is not essential to the attainment of effective body drug concentrations on chronic use, and is considered medically insignificant for the drug.

(8) The Secretary shall, with respect to each application submitted under this subsection, maintain a record of—

(A) the name of the applicant,

(B) the name of the drug covered by the application,

(C) the name of each person to whom the review of the chemistry of the application was assigned and the date of such assignment, and

(D) the name of each person to whom the bioequivalence review for such application was assigned and the date of such assignment.

The information the Secretary is required to maintain under this paragraph with respect to an application submitted under this subsection shall be made available to the public after the approval of such application.

(k) Records and reports; required information; regulations and orders; access to records

(1) In the case of any drug for which an approval of an application filed under subsection (b) or (j) of this section is in effect, the applicant shall establish and maintain such records, and make such reports to the Secretary, of data relating to clinical experience and other data or information, received or otherwise obtained by such applicant with respect to such drug, as the Secretary may by general regulation, or by order with respect to such application, prescribe on the basis of a finding that such records and reports are necessary in order to enable the Secretary to determine, or facilitate a determination, whether there is or may be ground for invoking subsection (e) of this section. Regulations and orders issued under this subsection and under subsection (i) of this section shall have due regard for the professional ethics of the medical profession and the interests of patients and shall provide, where the Secretary deems it to be appropriate, for the examination, upon request, by the persons to whom such regulations or orders are applicable, of similar information received or otherwise obtained by the Secretary.

(2) Every person required under this section to maintain records, and every person in charge or custody thereof, shall, upon request of an officer or employee designated by the Secretary, permit such officer or employee at all reasonable times to have access to and copy and verify such records.

(l) Public disclosure of safety and effectiveness data

Safety and effectiveness data and information which has been submitted in an application under subsection (b) of this section for a drug and which has not previously been disclosed to the public shall be made available to the public, upon request, unless extraordinary circumstances are shown—

(1) if no work is being or will be undertaken to have the application approved,

(2) if the Secretary has determined that the application is not approvable and all legal appeals have been exhausted,

(3) if approval of the application under subsection (c) of this section is withdrawn and all legal appeals have been exhausted,

(4) if the Secretary has determined that such drug is not a new drug, or

(5) upon the effective date of the approval of the first application under subsection (j) of this section which refers to such drug or upon the date upon which the approval of an application under subsection (j) of this section which refers to such drug could be made effective if such an application had been submitted.

(m) "Patent" defined

For purposes of this section, the term "patent" means a patent issued by the Patent and Trademark Office of the Department of Commerce.

(As amended Aug. 16, 1972, Pub.L. 92–387, § 4(d), 86 Stat. 562; Sept. 24, 1984, Pub.L. 98–417, Title I, §§ 101, 102(a)–(b)(5), 103, 104, 98 Stat. 1585, 1592, 1593, 1597; May 13, 1992, Pub.L. 102–282, § 5, 106 Stat. 161; Aug. 13, 1993, Pub.L. 103–80, § 3(n), 107 Stat. 777.)

HISTORICAL AND STATUTORY NOTES

1993 Amendments

Subsec. (j)(6)(A)(ii). Pub.L. 103–80, § 3(n)(1)(A), corrected a typographical error in the original by substituting "Secretary" for "Secretry".

Subsec. (j)(6)(A)(iii). Pub.L. 103–80, § 3(n)(1)(B), inserted a comma after "published by the Secretary".

Subsec. (k)(1). Pub.L. 103–80, § 3(n)(2), struck out ": Provided, however, That regulations" and inserted in lieu thereof a period and "Regulations".

1992 Amendments

Subsec. (j)(8). Pub.L. 102–282, § 5, added par. (8).

1984 Amendment

Subsec. (a). Pub.L. 98–417, § 102(b)(1), added "or (j)" following "pursuant to subsection (b)".

Subsec. (b)(1). Pub.L. 98–417, § 103(a), designated the existing provisions of subsec. (b) as par. (1) thereof and redesignated existing cls. (1) through (6) of par. (1) as so redesignated as cls. (A) through (F) thereof, respectively.

Pub.L. 98–417, § 102(a)(1), added requirement that the applicant file with the application the patent number and the expiration date of any patent which claims the drug for which the applicant submitted the application or which claims a method of using such drug and with respect to which a claim of patent infringement could reasonably be asserted if a person not licensed by the owner engaged in the manufacture, use, or sale of the drug, that the applicant amend the application to include such information if an application is filed under this subsection for a drug and a patent which claims such drug or a method of using such drug is issued after the filing date but before approval of the application, and that, upon approval of the application, the Secretary publish the information submitted.

Subsec. (b)(2), (3). Pub.L. 98–417, § 103(a), added pars. (2) and (3).

Subsec. (c)(1). Pub.L. 98–417, § 102(a)(2), designated the existing provisions of subsec. (c) as par. (1) thereof and in par. (1) as so designated redesignated former pars. (1) and (2) as subpars. (A) and (B), respectively.

Pub.L. 98–417, § 102(b)(2), substituted "subsection (b) of this section" for "this subsection".

Subsec. (c)(2). Pub.L. 98–417, § 102(a)(2), added par. (2).

Subsec. (c)(3). Pub.L. 98–417, § 103(b), added par. (3).

Subsec. (d)(6). Pub.L. 98–417, § 102(a)(3)(A), added cl. (6) relating to the failure of the application to contain the patent information prescribed by subsec. (b) of this section. Former cl. (6) was redesignated (7).

Subsec. (d)(7). Pub.L. 98–417, § 102(a)(3)(A), redesignated former cl. (6) as (7).

Subsec. (e). Pub.L. 98–417, § 102(a)(3)(B), added, in the first sentence covering the grounds for withdrawal of approval by the Secretary, a new cl. (4) relating to the failure to file the patent information prescribed by subsec. (c) of this section within 30 days after the receipt of written notice from the Secretary specifying the failure to file such information, and redesignated the former cl. (4) as (5).

Pub.L. 98–417, § 102(b)(3), inserted, in the provisions of the second sentence preceding cl. (1) of the enumeration of clauses covering the grounds for withdrawal of approval by the Secretary, the phrase "submitted under subsection (b) or (j) of this section" after "withdraw the approval of an application".

Pub.L. 98–417, § 102(b)(4), substituted, in cl. (1) of the second sentence covering the grounds for withdrawal of approval by the Secretary, the phrase "under subsection (k) of this section or to comply with the notice requirements of section 360(k)(2) of this title" for "under subsection (j) of this section or to comply with the notice requirements of section 360(j)(2) of this title".

Subsec. (j). Pub.L. 98–417, § 101, added subsec. (j). Former subsec. (j) was redesignated (k).

Subsec. (k). Pub.L. 98–417, § 101, redesignated former subsec. (j) as (k).

Subsec. (k)(1). Pub.L. 98–417, § 102(b)(5), substituted "under subsection (b) or (j) of this section" for "pursuant to this section".

Subsecs. (*l*), (m). Pub.L. 98–417, § 104, added subsecs. (*l*) and (m).

1972 Amendment

Subsec. (e). Pub.L. 92–387 inserted "or to comply with the notice requirements of section 360(j)(2)" in clause (1) of the second sentence relating to the maintenance of records.

Change of Name

The Department of Health, Education, and Welfare was redesignated the Department of Health and Human Services, and the Secretary of Health, Education, and Welfare or any other official of the Department of Health, Education and Welfare was redesignated the Secretary or official, as appropriate, of Health and Human Services, with any reference to the Department of Health, Education, and Welfare, the Secretary of Health, Education, and Welfare, or any official of the Department of Health, Education, and Welfare, in any law, rule, regulation, certificate, directive, instruction, or other official paper in force on the effective date of Pub.L. 96–88, as prescribed by section 601 of Pub.L.

96–88, Title VI, Oct. 17, 1979, 93 Stat. 69
out as a note under section 3401 of Titl
Education, deemed to refer and apply t
Department of Health and Human Servic
the Secretary of Health and Human Ser
respectively, except to the extent such refer
is to a function or office transferred to
Secretary of Education or the Departmer
Education under Pub.L. 96–88, Title III, §§
to 307, Oct. 17 1979, 93 Stat. 677 to 681.
section 3441 to 3447 and 3508 of Title 20.

Effective Date of 1984 Amendment

Section 105 of Pub.L. 98–417 provided

"(a) The Secretary of Health and Hu
Services shall promulgate, in accordance
the notice and comment requirements of se
553 of title 5, United States Code [section 5
Title 5, Government Organization and Em
ees], such regulations as may be necessary
the administration of section 505 of the Fe
Food, Drug, and Cosmetic Act [this section
amended by sections 101, 102, and 103 of
Act [enacting subsec. (j) of this section
amending subsecs. (a) to (e) and (k)(1) of
section and section 360cc(a) and (b) of this t
within one year of the date of enactment of
Act [Sept. 24, 1984].

"(b) During the period beginning sixty
after the date of the enactment of this Act [S
24, 1984], and ending on the date regulat
promulgated under subsection (a) take ef
abbreviated new drug applications may be
mitted in accordance with the provisions of
tion 314.2 of title 21 of the Code of Fe
Regulations and shall be considered as suit
for any drug which has been approved for sa
and effectiveness under section 505(c) of
Federal Food, Drug, and Cosmetic Act [sul
(c) of this section] before the date of the en

CROS

Patents, extension of patent term, see sec
156 of Title 35, Patents.

FEDERAL PRA

Review of administrative decisions in cour
appeals, see Wright, Miller, Cooper & Gr
man: Jurisdiction § 3941.

WEST'S FEDE

Application for use of new drug, see § 3

CODE OF FE

Formal evidentiary public hearing, see
CFR 12.1 et seq.
New animal drugs, see 21 CFR 510.8.

LAW REVI

A survey of law regarding the liability
manufacturers and sellers of drug products
medical devices. Bryan J. Maedgen and She
Lynn McCall, 18 St. Mary's L.J. 395 (19

Brother can you spare a drug: Should
experimental drug distribution standards
modified in response to the needs of pers
with Aids? 19 Hofstra L.Rev. 191 (1990).

tions for potentially harmful drug without authorization by prescribing physician was immaterial since consistency in verdicts is not necessary. Dugan Drug Stores, Inc. v. U. S., C.A.Tex.1964, 326 F. 2d 835.

§ 354. Repealed. Pub.L. 86–618, Title I, § 103(a) (2), July 12, 1960, 74 Stat. 398

Historical Note

Section, Act June 25, 1938, c. 675, § 504, 52 Stat. 1052, required the Secretary to promulgate regulations for the listing of coal-tar colors for drugs and is covered by section 376 of this title

Effective Date of Repeal. Repeal of section effective, subject to the provisions of section 203 of Pub.L. 86–618, on July 12, 1960, see section 202 of Pub.L. 86–618, set out as a note under section 376 of this title.

§ 355. New drugs—Necessity of effective approval of application

(a) No person shall introduce or deliver for introduction into interstate commerce any new drug, unless an approval of an application filed pursuant to subsection (b) of this section is effective with respect to such drug.

Filing application; contents

(b) Any person may file with the Secretary an application with respect to any drug subject to the provisions of subsection (a) of this section. Such person shall submit to the Secretary as a part of the application (1) full reports of investigations which have been made to show whether or not such drug is safe for use and whether such drug is effective in use; (2) a full list of the articles used as components of such drug; (3) a full statement of the composition of such drug; (4) a full description of the methods used in, and the facilities and controls used for, the manufacture, processing, and packing of such drug; (5) such samples of such drug and of the articles used as components thereof as the Secretary may require; and (6) specimens of the labeling proposed to be used for such drug.

Period for approval of application; period for, notice, and expedition of hearing; period for issuance of order

(c) Within one hundred and eighty days after the filing of an application under this subsection, or such additional period as may be agreed upon by the Secretary and the applicant, the Secretary shall either—

(1) approve the application if he then finds that none of the grounds for denying approval specified in subsection (d) of this section applies, or

(2) give the applicant notice of an opportunity for a hearing before the Secretary under subsection (d) of this section on the question whether such application is approvable. If the applicant elects to accept the opportunity for hearing by written request within thirty days after such notice, such hearing shall commence not more than ninety days after the expiration of such thirty days unless the Secretary and the applicant otherwise agree. Any such hearing shall thereafter be conducted on an expedited basis and the Secretary's order thereon shall be issued within ninety days after the date fixed by the Secretary for filing final briefs.

Grounds for refusing application; approval of application; "substantial evidence" defined

(d) If the Secretary finds, after due notice to the applicant in accordance with subsection (c) of this section and giving him an opportunity for a hearing, in accordance with said subsection, that (1) the investigations, reports of which are required to be submitted to the Secretary pursuant to subsection (b) of this section, do not include adequate tests by all methods reasonably applicable to show whether or not such drug is safe for use under the conditions prescribed, recommended, or suggested in the proposed labeling thereof; (2) the results of such tests show that such drug is unsafe for use under such conditions or do not show that such drug is safe for use under such conditions; (3) the methods used in, and the facilities and controls used for, the manufacture, processing, and packing of such drug are inadequate to preserve its identity, strength, quality, and purity; (4) upon the basis of the information submitted to him as part of the application, or upon the basis of any other information before him with respect to such drug, he has insufficient information to determine whether such drug is safe for use under such conditions; or (5) evaluated on the basis of the information submitted to him as part of the application and any other information before him with respect to such drug, there is a lack of substantial evidence that the drug will have the effect it purports or is represented to have under the conditions of use prescribed, recommended, or suggested in the proposed labeling thereof; or (6) based on a fair evaluation of all material facts, such labeling is false or misleading in any particular; he shall issue an order refusing to approve the application. If, after such notice and opportunity for hearing, the Secretary finds that clauses (1) through (6) do not apply, he shall issue an order approving the application. As used in this subsection and subsection (e) of this section, the term "substantial evidence" means evidence consisting of adequate and well-controlled investigations, including clinical investigations, by experts qualified by scientific training and experience to evaluate the effectiveness of the drug involved, on the basis of which it could fairly and responsibly be concluded by such experts that the drug will have the

effect it purports or is represented to have under the conditions of use prescribed, recommended, or suggested in the labeling or proposed labeling thereof.

Withdrawal of approval; grounds; immediate suspension upon finding imminent hazard to public health

(e) The Secretary shall, after due notice and opportunity for hearing to the applicant, withdraw approval of an application with respect to any drug under this section if the Secretary finds (1) that clinical or other experience, tests, or other scientific data show that such drug is unsafe for use under the conditions of use upon the basis of which the application was approved; (2) that new evidence of clinical experience, not contained in such application or not available to the Secretary until after such application was approved, or tests by new methods, or tests by methods not deemed reasonably applicable when such application was approved, evaluated together with the evidence available to the Secretary when the application was approved, shows that such drug is not shown to be safe for use under the conditions of use upon the basis of which the application was approved; or (3) on the basis of new information before him with respect to such drug, evaluated together with the evidence available to him when the application was approved, that there is a lack of substantial evidence that the drug will have the effect it purports or is represented to have under the conditions of use prescribed, recommended, or suggested in the labeling thereof; or (4) that the application contains any untrue statement of a material fact: *Provided*, That if the Secretary (or in his absence the officer acting as Secretary) finds that there is an imminent hazard to the public health, he may suspend the approval of such application immediately, and give the applicant prompt notice of his action and afford the applicant the opportunity for an expedited hearing under this subsection; but the authority conferred by this proviso to suspend the approval of an application shall not be delegated. The Secretary may also, after due notice and opportunity for hearing to the applicant, withdraw the approval of an application with respect to any drug under this section if the Secretary finds (1) that the applicant has failed to establish a system for maintaining required records, or has repeatedly or deliberately failed to maintain such records or to make required reports, in accordance with a regulation or order under subsection (j) of this section, or the applicant has refused to permit access to, or copying or verification of, such records as required by paragraph (2) of such subsection; or (2) that on the basis of new information before him, evaluated together with the evidence before him when the application was approved, the methods used in, or the facilities and controls used for, the manufacture, processing, and packing of such drug are inadequate to assure and preserve its identity, strength, quality, and purity and were not made adequate within a reasonable

time after receipt of written notice from the Secretary specifying the matter complained of; or (3) that on the basis of new information before him, evaluated together with the evidence before him when the application was approved, the labeling of such drug, based on a fair evaluation of all material facts, is false or misleading in any particular and was not corrected within a reasonable time after receipt of written notice from the Secretary specifying the matter complained of. Any order under this subsection shall state the findings upon which it is based.

Revocation of order refusing, withdrawing or suspending approval of application

(f) Whenever the Secretary finds that the facts so require, he shall revoke any previous order under subsection (d) or (e) of this section refusing, withdrawing, or suspending approval of an application and shall approve such application or reinstate such approval, as may be appropriate.

Service of orders

(g) Orders of the Secretary issued under this section shall be served (1) in person by any officer or employee of the Department designated by the Secretary or (2) by mailing the order by registered mail or by certified mail addressed to the applicant or respondent at his last-known address in the records of the Secretary.

Appeal from order

(h) An appeal may be taken by the applicant from an order of the Secretary refusing or withdrawing approval of an application under this section. Such appeal shall be taken by filing in the United States court of appeals for the circuit wherein such applicant resides or has his principal place of business, or in the United States Court of Appeals for the District of Columbia Circuit, within sixty days after the entry of such order, a written petition praying that the order of the Secretary be set aside. A copy of such petition shall be forthwith transmitted by the clerk of the court to the Secretary, or any officer designated by him for that purpose, and thereupon the Secretary shall certify and file in the court the record upon which the order complained of was entered, as provided in section 2112 of Title 28. Upon the filing of such petition such court shall have exclusive jurisdiction to affirm or set aside such order, except that until the filing of the record the Secretary may modify or set aside his order. No objection to the order of the Secretary shall be considered by the court unless such objection shall have been urged before the Secretary or unless there were reasonable grounds for failure so to do. The finding of the Secretary as to the facts, if supported by substantial evidence, shall be conclusive. If any person shall apply to the court for leave to

adduce additional evidence, and shall show to the satisfaction of the court that such additional evidence is material and that there were reasonable grounds for failure to adduce such evidence in the proceeding before the Secretary, the court may order such additional evidence to be taken before the Secretary and to be adduced upon the hearing in such manner and upon such terms and conditions as to the court may seem proper. The Secretary may modify his findings as to the facts by reason of the additional evidence so taken, and he shall file with the court such modified findings which, if supported by substantial evidence, shall be conclusive, and his recommendation, if any, for the setting aside of the original order. The judgment of the court affirming or setting aside any such order of the Secretary shall be final, subject to review by the Supreme Court of the United States upon certiorari or certification as provided in section 1254 of Title 28. The commencement of proceedings under this subsection shall not, unless specifically ordered by the court to the contrary, operate as a stay of the Secretary's order.

Exemptions of drugs for research; discretionary and mandatory conditions; direct reports to Secretary

(i) The Secretary shall promulgate regulations for exempting from the operation of the foregoing subsections of this section drugs intended solely for investigational use by experts qualified by scientific training and experience to investigate the safety and effectiveness of drugs. Such regulations may, within the discretion of the Secretary, among other conditions relating to the protection of the public health, provide for conditioning such exemption upon—

(1) the submission to the Secretary, before any clinical testing of a new drug is undertaken, of reports, by the manufacturer or the sponsor of the investigation of such drug, of preclinical tests (including tests on animals) of such drug adequate to justify the proposed clinical testing;

(2) the manufacturer or the sponsor of the investigation of a new drug proposed to be distributed to investigators for clinical testing obtaining a signed agreement from each of such investigators that patients to whom the drug is administered will be under his personal supervision, or under the supervision of investigators responsible to him, and that he will not supply such drug to any other investigator, or to clinics, for administration to human beings; and

(3) the establishment and maintenance of such records, and the making of such reports to the Secretary, by the manufacturer or the sponsor of the investigation of such drug, of data (including but not limited to analytical reports by investigators) obtained as the result of such investigational use of such drug, as the Secre-

tary finds will enable him to evaluate the safety and effectiveness of such drug in the event of the filing of an application pursuant to subsection (b) of this section.

Such regulations shall provide that such exemption shall be conditioned upon the manufacturer, or the sponsor of the investigation, requiring that experts using such drugs for investigational purposes certify to such manufacturer or sponsor that they will inform any human beings to whom such drugs, or any controls used in connection therewith, are being administered, or their representatives, that such drugs are being used for investigational purposes and will obtain the consent of such human beings or their representatives, except where they deem it not feasible or, in their professional judgment, contrary to the best interests of such human beings. Nothing in this subsection shall be construed to require any clinical investigator to submit directly to the Secretary reports on the investigational use of drugs.

Records and reports; required information; regulations and orders; access to records

(j) (1) In the case of any drug for which an approval of an application filed pursuant to this section is in effect, the applicant shall establish and maintain such records, and make such reports to the Secretary, of data relating to clinical experience and other data or information, received or otherwise obtained by such applicant with respect to such drug, as the Secretary may by general regulation, or by order with respect to such application, prescribe on the basis of a finding that such records and reports are necessary in order to enable the Secretary to determine, or facilitate a determination, whether there is or may be ground for invoking subsection (e) of this section: *Provided, however*, That regulations and orders issued under this subsection and under subsection (i) of this section shall have due regard for the professional ethics of the medical profession and the interests of patients and shall provide, where the Secretary deems it to be appropriate, for the examination, upon request, by the persons to whom such regulations or orders are applicable, of similar information received or otherwise obtained by the Secretary.

(2) Every person required under this section to maintain records, and every person in charge or custody thereof, shall, upon request of an officer or employee designated by the Secretary, permit such officer or employee at all reasonable times to have access to and copy and verify such records.

June 25, 1938, c. 675, § 505, 52 Stat. 1052; 1940 Reorg.Plan No. IV, § 12, eff. June 30, 1940, 5 F.R. 2422, 54 Stat. 1237; June 25, 1948, c. 646, § 32(b), 62 Stat. 991; May 24, 1949, c. 139, § 127, 63 Stat. 107; 1953 Reorg.Plan No. 1, § 5, eff. Apr. 11, 1953, 18 F.R. 2053, 67 Stat.

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Stat. 1237; June 25, 1948, c.
9, c. 139, § 127, 63 Stat. 107;
1, 1953, 18 F.R. 2053, 67 Stat.

631; June 11, 1960, Pub.L. 86–507, § 1(18), 74 Stat. 201; Oct. 10, 1962, Pub.L. 87–781, Title I, §§ 102(b)–(d), 103(a), (b), 104(a)–(d)(2), 76 Stat. 781–783, 784, 785.

Historical Note

1962 Amendment. Subsec. (a). Pub.L. 87–781, § 104(a), inserted "an approval of" preceding "an application."

Subsec. (b). Pub.L. 87–781, § 102(b), inserted "and whether such drug is effective in use" following "is safe for use."

Subsec. (c). Pub.L. 87–781, § 104(b), substituted provisions requiring the Secretary, within 180 days after filing an application, or such additional period as the Secretary and the applicant agree upon, to either approve the application, if meeting the requirements of subsec. (d) of this section, or give notice of opportunity for hearing on question of whether such application is approvable, and providing that if applicant requests hearing in writing within 30 days, the hearing shall begin within 90 days after expiration of said 30 days, unless the Secretary and applicant agree otherwise, that such hearing shall be expedited, and that the Secretary's order shall be issued within 90 days after date for filing final briefs, for provisions which had an application become effective on the sixtieth day after filing thereof unless prior thereto the Secretary postponed the date by written notice to such time, but not more than 180 days after filing, as the Secretary deemed necessary to study and investigate the application.

Subsec. (d). Pub.L. 87–781, § 102(c), inserted references to subsec. (e), added cls. (5) and (6), provided that if after notice and opportunity for hearing, the Secretary finds that cls. (1)–(6) do not apply, he shall approve the application, and defined "substantial evidence" as used in this subsection and subsec. (e) of this section.

Subsec. (e). Pub.L. 87–781, § 102(d) amended subsection generally, and among other changes, directed the Secretary to withdraw approval of an application if by tests, other scientific data or experience, or new evidence of clinical experience not contained in the application or available at the time of its approval, the drug is shown to be unsafe, or on the basis of new information, there is shown a lack of substantial evidence that the drug has the effect it is represented to have, and provided that if the Secretary, or acting Secretary, finds there is an imminent hazard to public health, he may suspend approval immediately, notify the applicant, and give him opportunity for an expedited hearing, that the Secretary may withdraw approval if the applicant fails to establish a system for maintaining required records, or has repeatedly or deliberately failed to maintain records and make reports, or has refused access to, or copying or verification of such records, or if the Secretary finds on new evidence that the methods, facilities and controls in the manufacturing, processing, and packing are inadequate to assure and preserve the drugs' identity, strength, quality and purity, and were not made adequate within a reasonable time after receipt of written notice thereof, or finds on new evidence, that the labeling is false or misleading and was not corrected within a reasonable time after receipt of written notice thereof.

Subsec. (f). Pub.L. 87–781, § 104(c), substituted provisions requiring the Secretary to revoke any previous order under subsecs. (d) or (e) of this section refusing, withdrawing, or suspending approval of an application and to approve such application or reinstate such approval, for provisions which required him to revoke an order refusing effectiveness to an application.

Subsec. (h). Pub.L. 87–781, § 104(d)(1), (2), inserted "as provided in section 2112 of Title 28", and "except that until the filing of the record the Secretary may modify or set aside his order", substituted "or withdrawing approval of an application under this section" for "to permit the application to become effective, or suspending the effectiveness of the application", "United States court of appeals for the circuit" for "district court of the United States within any district", "Court of Appeals for the District of Columbia Circuit" for "District Court for the District of Columbia", "transmitted by the clerk of the court to" for "served upon", and "by the Supreme Court of the United States upon

take its meaning from the statute that is being amended—ERISA. And ERISA, for whatever reason, defines the word "employer" only for subchapter I.[1] Defining its meaning for subchapter III is up to the courts. *Cf. Robinson v. C.I.R.*, 805 F.2d 38, 40 (1st Cir.1986).[2]

[3] This conclusion brings us back to what the Trustee is really asking us to do: to define the word "employer" to include controlling shareholders and officers. We decline, for the following reasons.

First, as mentioned before, the principle of limited liability for corporate debts is longstanding enough and important enough to be considered a background norm, against which Congress may act of course, but which is controlling in the absence of such action. *See Connors v. P & M Coal Co.*, 801 F.2d at 1376. In deciding whether Congress has acted to expand liability "federal courts will look closely at the purpose of the federal statute to determine whether the statute places importance on the corporate form...." *Town of Brookline v. Gorsuch*, 667 F.2d 215, 221 (1st Cir.1981) (citations omitted). The MPPAA does not on its face indicate any intention to treat corporate debts for withdrawal liability different from any other corporate debts. The way that one could have expected Congress to make such an intention felt was through a definition of the word "employer." Yet Congress did not define the word in the MPPAA. Nor did Congress provide an applicable definition in ERISA.

Furthermore, the purposes of the MPPAA, as described in the legislative history of that act, would not be served by an extension of personal liability for corporate withdrawal payments. The Act represents a balance between efforts to protect existing pension plan beneficiaries through a short term strategy of imposing burdens on current employer contributors and through a long term strategy of encouraging new employers to contribute to multi-employer pension funds. *See* H.R. No. 96-869, 96th Cong., 2d Sess., *reprinted in* 1980 U.S.Code Cong. & Admin.News at 2918, 2919-20, 2935. Imposing personal liability for withdrawal payments would hurt that long term strategy by discouraging controlling individuals from directing their corporations to participate in multi-employer pension funds.

Withdrawal liability under the MPPAA is quite different than payroll taxes under the Social Security Act and minimum wage payments under the Fair Labor Standards Act, two corporate debts for which controlling shareholders and officers can be held liable. *See Donovan v. Agnew*, 712 F.2d at 1511; *United States v. McMullen*, 516 F.2d 917, 920 (7th Cir.1975) (26 U.S.C. § 7512 imposes liability for payroll taxes on person with control over corporations affairs). Payroll taxes and minimum wage payments are liabilities which a corporation can choose to pay or not pay. A decision to forgo paying payroll taxes or wages is a conscious decision to prefer some creditors over the government or the corporation's employees. Corporations do not have the same control over withdrawal liability payments, especially in the context in which shareholder and officer liability is most likely to be relevant: bankruptcy. Withdrawal liability is not assessed until an employer "withdraws" from the pension plan, by ceasing to do business for instance. If the liabilities of the employer corporation exceed its assets, which is the likely condition when a pension fund seeks to recover against officers or shareholders personally, the corporation will enter into bankruptcy proceedings, thereby losing control over which creditors receive payments.

Given the control corporations have over payroll taxes and wages, personal liability for those debts should rarely have actually assessed. The *threat* of personal liability should be enough to induce the individuals who control corporations to prefer the IRS and employee creditors over other creditors in times of financial difficulty. If not, the individuals controlling the corporation accept a known risk. Personal liability for withdrawal payments, on the other hand, cannot be similarly avoided. This personal liability may well force corporations to more extreme efforts to avoid bankruptcy, but any benefit is likely to be marginal, since controlling shareholders can be expected to attempt to avoid bankruptcy generally, in the hope of obtaining some return on their investment. Rather than a rarely exercised threat that induces a desired behavior, personal liability for withdrawal payments would be a routine accompaniment to corporate bankruptcy proceedings. This personal liability would discourage controlling shareholders and officers from directing their corporations to contribute to multi-employer pension plans, thereby making it less likely that their employees will receive pension benefits. In the long run, personal liability would hurt even those employees who are already beneficiaries of multi-employer pension plans, because the vitality of those plans depends on new employers contributing to them. *See* House Report, 1980 U.S.Code Cong. & Admin. News at 2919-20, 2935.

The decision of the district court is *affirmed*.

1. In *Nachman Corp. v. Pension Benefit Guar. Corp.*, 446 U.S. 359, 370 n. 14, 100 S.Ct. 1723, 1731 n. 14, 64 L.Ed.2d 354 (1980), the Supreme Court noted that Congress made some Title I (subchapter I in the Code) definitions applicable to Title IV (part of subchapter III in the Code), *see, e.g.*, 29 U.S.C. § 1321(a)(1). "This specific incorporation suggests that Title I definitions do not apply elsewhere in the Act of their own force...." *Id.*

2. We do not reach the question whether the subchapter I definition includes controlling officers or shareholders, a question which has occasioned considerable litigation, and difference of opinion. *Compare, e.g., Solomon v. Klein*, 770 F.2d 352, 354 (3d Cir.1985) (controlling shareholder and officer not an "employer") *with, e.g., Mass. State Carpenters Pension Fund v. Atlantic Diving Co., Inc.*, 635 F.Supp. 9, 13-14 (D.Mass. 1984) (controlling shareholder or officer may be "employer"). We reserve this question for a case in which it makes a difference in the outcome.

Lester GRINSPOON, M.D., Petitioner,

v.

DRUG ENFORCEMENT ADMINISTRATION, Respondent.

No. 86-2007.

United States Court of Appeals, First Circuit.

Heard March 3, 1987.

Decided Sept. 18, 1987.

Administrative Drug Enforcement Administration issued final rule placing 3, 4-methylenedioxymethamphetamine into Schedule I of Controlled Substances Act. Researcher on therapeutic use of substance petitioned for review. The Court of Appeals, Coffin, Circuit Judge, held that: (1) absence of FDA interstate marketing approval was not conclusive evidence that substance had no currently accepted medical use or lacked accepted safety for use under medical supervision; (2) there was sufficient evidence to support finding that substance had high potential for abuse; and (3) administrator was not required to consider evidence that placement of substance into Schedule I would strongly discourage medical research on substance.

Rule vacated and remanded.

1. Drugs and Narcotics ⇐46

Absence of interstate marketing approval of substance by Federal Drug Administration is not conclusive evidence that substance has no currently accepted medical use and lacks accepted safety for use under medical supervision for purposes of determining whether substance should be placed in Schedule I under Controlled Substances Act. Comprehensive Drug Abuse Prevention and Control Act of 1970, § 202(b)(1), as amended, 21 U.S.C.A. § 812(b)(1).

2. Drugs and Narcotics ⇐46

Finding that 3, 4-methylenedioxymethamphetamine had "high" potential for

abuse was not arbitrary and capricious, where administrator of Drug Enforcement Administration considered close structural and pharmacological similarity between substance and other substances which had already been found to have high potential for abuse and placed in Schedule I, as well as studies which suggested that substance was related in its effect to Schedule I and II substances. Comprehensive Drug Abuse Prevention and Control Act of 1970, § 202(b)(1), as amended, 21 U.S.C.A. § 812(b)(1).

3. Drugs and Narcotics ⇐46

Alleged failure of administrator of Drug Enforcement Administration to consider impact of determination to place substance on Schedule I upon legitimate scientific research was not improper. Comprehensive Drug Abuse Prevention and Control Act of 1970, § 202(b)(1), as amended, 21 U.S.C.A. § 812(b)(1).

4. Administrative Law and Procedure ⇐764

Drugs and Narcotics ⇐46

Department of Health and Human Services' adoption of analysis already performed by Drug Enforcement Administration that substance should have been classified in Schedule I without consulting any organization medical professionals or its own panel of experts was harmless error, and did not require rescheduling of substance, where there was substantial evidence to support classification. Comprehensive Drug Abuse Prevention and Control Act of 1970, § 201(b, c), as amended, 21 U.S.C.A. § 811(b, c).

Richard Cotton, Washington, D.C., for petitioner.

Harry S. Harbin, Washington, D.C., with whom William F. Weld, Asst. Atty. Gen., Criminal Div., Boston, Mass., Charles S. Sapho, Chief, Narcotic and Dangerous Drug Section, Dennis F. Hoffman, Chief Counsel, Drug Enforcement Admin., Stephen E. Stone, Associate Chief Counsel, Drug Enforcement Admin., Washington, D.C., and Charlotte A. Johnson, were on brief, for respondent.

Before COFFIN and TORRUELLA, Circuit Judges, and PETTINE,* Senior District Judge.

COFFIN, Circuit Judge.

On November 13, 1986, the Administrator of the Drug Enforcement Administration ("DEA") issued a final rule placing the substance 3,4-methylenedioxymethamphetamine ("MDMA") into Schedule I of the Controlled Substances Act ("CSA"), 21 U.S.C. §§ 811, 812 (1987).[1] 51 Fed.Reg. 36,552 (1986). In reaching this decision, the Administrator found that MDMA met all three of the statutory requirements for classification as a Schedule I substance, namely,

> (A) The drug or other substance has a high potential for abuse.
>
> (B) The drug or other substance has no currently accepted medical use in treatment in the United States.
>
> (C) There is a lack of accepted safety for use of the drug or other substance under medical supervision.

21 U.S.C. § 812(b)(1).

Dr. Lester Grinspoon, a psychiatrist and faculty member of the Harvard Medical School, petitions this court to review the final rule. Dr. Grinspoon seeks to conduct research on the therapeutic use of MDMA and believes that the imposition of Schedule I controls will effectively foreclose such research. He cites four reasons for vacating the Administrator's scheduling determination. The first reason advanced is that the Administrator applied the wrong legal standards for "currently accepted medical use in treatment in the United States" and for "accepted safety for use ... under medical supervision" in 21 U.S.C. § 812(b)(1). The other three reasons contained in Dr. Grinspoon's petition challenge the scheduling determination as arbitrary and capricious because (a) the Administrator's determination that MDMA had a "high" potential for abuse was flawed by his failure to articulate a legal standard and his reliance on insufficient record evidence; (b) the Administrator failed to give adequate weight to the evidence showing that placing MDMA into Schedule I would create a barrier to medical research on the drug; and (c) the rule is based upon incomplete and arbitrary recommendations from the Secretary of Health and Human Services. Petitioner urges this court to remand the case to the DEA with instructions to place the substance MDMA into Schedule III.

Although we are satisfied that these final three claims do not require us to overturn the rule, we believe that Dr. Grinspoon's first claim has considerable merit and requires us to remand the scheduling determination for reconsideration by the Administrator. After describing the administrative history of the rule, we shall consider each of petitioner's claims in turn.

I. *Administrative History.*

In January of 1984, the DEA prepared a document entitled "Schedule I Control Recommendation Under the CSA for 3,4-Methylenedioxymethamphetamine (MDMA)." The control recommendation, which was based upon information compiled from various DEA data sources and scientific and medical literature, considered all three Schedule I criteria listed in section 812(b)(1) and concluded that (1) MDMA has a high potential for abuse; (2) MDMA has no known legitimate medical use for treatment in the United States; and (3) there is a lack of accepted safety for the use of MDMA under medical supervision. Based upon these findings, the DEA recommended that MDMA be placed into Schedule I of the CSA.

In March of 1984, pursuant to the procedures set out in the CSA, 28 U.S.C. 811(b),[2] the Administrator submitted the DEA's control recommendation to the Assistant Secretary for Health of the Department of Health and Human Services ("HHS") for scientific and medical evaluation and for an HHS recommendation as to whether MDMA should be controlled. The HHS evaluation was conducted by Dr. Charles Tocus, Chief of the Drug Abuse Staff of the Food and Drug Administration ("FDA"). Dr. Tocus stated in his affidavit that he searched the FDA files and found no reference to MDMA. Based upon this absence of information in the FDA files and a review of the information contained in the DEA control recommendation carried out by Dr. Tocus, HHS responded by making minor (typographical) corrections in the DEA's eight-factor analysis[3] and concurring in the recommendation that MDMA be placed into Schedule I.

Upon receiving the HHS evaluation and recommendation, the Administrator issued a Notice of Proposed Rulemaking with regard to placing MDMA into Schedule I of the CSA. 49 Fed.Reg. 30,210 (1984). Later, following the receipt of several com-

* Of the District of Rhode Island, sitting by designation.

1. The Act established five categories of substances whose manufacture and distribution are subject to federal control. The Act's initial scheduling of substances can be found in 21 U.S.C. § 811. These listings are subject to amendments and additions pursuant to 21 U.S.C. § 811. Substances placed into Schedule I are subject to the most severe controls and penalties imposed by the Act.

2. 21 U.S.C. § 811(b) provides that

> The Attorney General shall, before initiating proceedings under subsection (a) of this section to control a drug or other substance ..., and after gathering the necessary data, request from the Secretary a scientific and medical evaluation, and his recommendations, as to whether such drug or other substance should be so controlled.

3. Section 811(c) requires the Administrator to consider the following eight factors for each drug proposed to be controlled under the CSA:

> (1) [The drug's] actual or relative potential for abuse.
>
> (2) Scientific evidence of its pharmacological effect, if known.
>
> (3) The state of current scientific knowledge regarding the drug or other substance.
>
> (4) Its history and current pattern of abuse.
>
> (5) The scope, duration, and significance of abuse.
>
> (6) What, if any, risk there is to the public health.
>
> (7) Its psychic or physiological dependence liability.
>
> (8) Whether the substance is an immediate precursor of a substance already controlled under this subchapter.

21 U.S.C. § 811(c).

ments and requests for a hearing, the Administrator referred the matter to an Administrative Law Judge ("ALJ") with instructions to "conduct a hearing for the purpose of receiving factual evidence and expert opinion regarding the proposed scheduling of MDMA." 51 Fed.Reg. 36,-552 (1986). During the course of the hearing, the ALJ heard 33 witnesses and received 95 exhibits into evidence.[4] On May 22, 1986, the ALJ issued a comprehensive opinion finding that MDMA fit none of the three criteria prerequisite to placement in Schedule I. Relying on the hearing testimony of experts in the health care community, the ALJ concluded that MDMA had an accepted medical use for treatment in the United States, 21 U.S.C. § 812(b)(1)(B), and an accepted safety for use under medical supervision, 21 U.S.C. § 812(b)(1)(C). The ALJ also found that the record did not establish that MDMA had a "high" potential for abuse. 21 U.S.C. § 812(b)(1)(A). The ALJ therefore recommended that MDMA be placed into Schedule III of the CSA.

The Administrator, however, declined to accept the reasoning and scheduling recommendation of the ALJ. In his October 13, 1986, decision, the Administrator held that the phrases "currently accepted medical use in treatment in the United States" and "accepted safety for use ... under medical supervision" as used in the CSA, 21 U.S.C. § 812(b)(1), both mean that the FDA has evaluated the substance for safety and approved it for interstate marketing in the United States pursuant to the Federal Food, Drug, and Cosmetic Act of 1938 ("FDCA"), 21 U.S.C. § 355. From these premises, the Administrator reasoned that because the FDA has not approved a new drug application ("NDA") or investigational new drug application ("IND") authorizing interstate marketing of MDMA under the FDCA, MDMA cannot be lawfully marketed and has neither a currently accepted medical use in treatment in the United States nor an accepted safety for use under medical supervision. Finally, the Administrator found that the DEA had sustained its burden of proving that MDMA has a high potential for abuse. The Administrator's final rule, effective November 13, 1986, placed MDMA into Schedule I. Dr. Grinspoon appeals from this final rule under the CSA, 21 U.S.C. § 877.

II. *Accepted Medical Use And Safety Under The CSA.*

We turn first to petitioner's claim that the Administrator erred in interpreting the phrases "accepted medical use in treatment in the United States" and "accepted safety for use ... under medical supervision" in section 812(b)(1) to mean, in essence, "approved for interstate marketing by the FDA under the FDCA." Before embarking on an analysis of that issue, however, we begin by explaining the appropriate standard of review in a case, such as this, where a court must assess an agency's interpretation of a statute it administers.

A. *Standard of Review.*

The Administrator argues correctly that we must review his interpretation of the CSA in light of the guidelines set forth by the Supreme Court in *Chevron U.S.A., Inc. v. Natural Resources Defense Council, Inc.*, 467 U.S. 837, 104 S.Ct. 2778, 81 L.Ed.2d 694 (1984). In *Chevron* the Court explained that a reviewing court must employ a two-step analysis that focuses initially on the intentions of Congress:

> First, always, is the question whether Congress had directly spoken to the precise question at issue. If *the intent of Congress is clear*, that is the end of the matter; for the court, as well as the agency, must give effect to the unambiguously expressed intent of Congress.

Id. at 842–43, 104 S.Ct. at 2781 (emphasis supplied). In the absence of congressional intent, however, the court must proceed to a second inquiry:

> If ... the court determines Congress has not directly addressed the precise question at issue, the court does not simply impose its own construction on the statute, as would be necessary in the absence of an administrative interpretation. Rather, if the statute is silent or ambiguous with respect to the specific issue, the question for the court is whether the agency's answer is based on a *permissible construction of the statute.*

Id. at 843, 104 S.Ct. at 2781–82 (footnote omitted; emphasis supplied).

It is undisputed that Congress has not directly spoken to the question at issue here, namely, the proper means of interpreting the second and third criteria of section 812(b)(1). The absence of express intent, however, does not compel us to proceed to the deferential second step of the *Chevron* scheme. As the Supreme Court indicated in a footnote to its *Chevron* opinion, "[i]f a court, employing traditional tools of statutory construction, ascertains that Congress had an intention on the precise question at issue, that intention is law and must be given effect." *Id.* at 843 n. 9, 104 S.Ct. at 2781 n. 9. Recently the Supreme Court has reaffirmed this proposition, holding in *INS v. Cardoza-Fonseca*, — U.S. —, 107 S.Ct. 1207, 94 L.Ed.2d 434 (1987), that a court faced with a "pure question of statutory interpretation" should rely upon traditional methods of statutory construction in an attempt to determine the intent of Congress. *Id.* 107 S.Ct. at 1221; *International Union, UAW v. Brook*, 816 F.2d 761, 764–65 (D.C.Cir. 1987) (applying "traditional tools" of statutory construction to invalidate agency's interpretation of statutory language as conflicting with intent of Congress).

[1] The Administrator contends that congressional intent favoring his interpretation of the CSA can be gleaned from the language of the statute, its legislative history, and the language and history of subsequent legislative enactments designed to enhance the regulatory system established by the CSA in 1970. In the alternative, he argues that if the intent of Congress is ambiguous, then his construction of the statute is permissible in view of the statutory scheme.[5] Our review of the sources identified by the litigants convinces us that Congress neither expressed nor implied an affirmative intent regarding how the second and third Schedule I criteria should be interpreted. Nevertheless, these same sources—the language and structure of the CSA and FDCA, the legislative history of the CSA, and the subsequent handiwork of Congress in the area of controlled substance regulation—lead us to conclude that the Administrator's construction of subsections (B) and (C) of 21 U.S.C. § 812(b)(1) is contrary to congressional intent.[6]

B. *Statutory Language and Structure.*

The Administrator begins by arguing that the language of the CSA itself is evidence of congressional intent favoring his construction of the statute. His argument is based on the definitions of terms chosen by Congress in drafting the relevant provisions of the CSA. He first cites the definition of the term "United States" as used in "accepted medical use in treatment in the United States." 21 U.S.C. § 812(b)(1)(B). This term is the only portion of the Schedule I criteria that Congress has expressly defined in the CSA, providing that "[t]he term 'United States,' when used in a geographic sense, means *all places* ... subject

4. On July 1, 1985, while the hearing was proceeding, the Administrator placed MDMA into Schedule I of the Controlled Substances Act pursuant to the emergency scheduling provisions of the Act, 21 U.S.C. § 811(h)(1). 50 Fed. Reg. 23,118 (1985). The Administrator determined that this action was necessary to avoid an imminent hazard to the public safety. *Id.*

5. Contrary to the assertions of the Administrator, this is not a situation in which Congress has expressly vested the Administrator with authority to define general statutory criteria by issuing regulations. Were this such a case, such regulations would be controlling unless they were "arbitrary, capricious, or manifestly contrary to the statute." *Chevron*, 467 U.S. at 843–44, 104 S.Ct. at 2782. Here, the CSA expressly delegates to the Attorney General only the authority to make "the *findings* prescribed by subsection (b) of section 812 of this title for the schedule in which [a] drug is to be placed." 21 U.S.C. § 811(a)(1)(B) (emphasis supplied). This explicit delegation of authority to *apply* prescribed statutory criteria is not equivalent to an explicit delegation of authority to *define* those criteria.

6. Our review of the legislative sources below also convinces us that the Administrator's interpretation is unreasonable and would be invalid even under the second prong of the *Chevron* test. *See International Union, UAW v. Brock*, 816 F.2d at 765 n. 6.

to the jurisdiction of the United States." 21 U.S.C. § 802(28) (emphasis supplied). Coupling this statutory definition of "United States" with the dictionary definition of "accepted"—which means "generally approved" or "generally agreed upon"—the Administrator argues that the phrase "*accepted* medical use in treatment in the *United States*," 21 U.S.C. § 812(b)(1)(B), must contemplate an administrative determination that the substance has been "generally approved" for use in treatment in "all places" subject to United States jurisdiction. In other words, FDA interstate marketing approval is necessary to satisfy this criterion because, otherwise, the substance could not be deemed to be "generally approved" *everywhere* in the United States.[7]

We find this argument to be strained and unpersuasive. The CSA's definition of "United States" plainly does not require the conclusion asserted by the Administrator simply because section 802(28) defines "United States" as "*all places* subject to the jurisdiction of the United States." 21 U.S.C. § 802(28) (emphasis supplied). Congress surely intended the reference to "all places" in section 802(28) to delineate the broad jurisdictional scope of the CSA and to clarify that the CSA regulates conduct occurring *any place*, as opposed to *every place*, within the United States. As petitioner aptly notes, a defendant charged with violating the CSA by selling controlled substances in only two states would not have a defense based on section 802(28) if he contended that his activity had not occurred in "all places" subject to United States jurisdiction. We add, moreover, that the Administrator's clever argument conveniently omits any reference to the fact that the pertinent phrase in section 812(b)(1)(B) reads "*in the* United States," (emphasis supplied). We find this language to be further evidence that the Congress did not intend "accepted medical use in treatment in the United States" to require a finding of recognized medical use in every state or, as the Administrator contends, approval for interstate marketing of the substance.

Nor does the dictionary definition of "accepted" offered by the Administrator convince us that Congress intended FDA approval to be the equivalent of the second and third Schedule I criteria. Use of the term "accepted" in sections 812(b)(1)(B) and 812(b)(1)(C) may indicate that Congress intended the medical use or safety of the substance to be "generally agreed upon," but this alone does not inform us as to *who* must generally be in agreement. The Administrator reads "accepted" to mean that *the FDA* must have approved the drug for interstate marketing. Dr. Grinspoon, on the other hand, prefers to interpret "accepted" as meaning that the *medical community* generally agrees that the drug in question has a medical use and can be used safely under medical supervision. Our conclusion is that the term "accepted" does not cure the statute's ambiguity. We are simply unable to extrapolate from the drafters' choice of the word "accepted" and thereby ascertain a general congressional intention favoring the interpretation advanced by the Administrator.

In another argument focusing upon the language of the statute, the Administrator urges us to adopt his interpretation of the CSA because it is entirely consistent with the interpretation of the phrase "accepted medical use in treatment in the United States" employed in the Commissioners' Notes to the Uniform Controlled Substances Act, §§ 203–12, 9 U.L.A. 221–35 (1979) ("Uniform CSA").[8] At first glance, this argument appears to have considerable merit. The Uniform CSA, like its federal counterpart, creates five schedules of controlled substances and, indeed, was modeled on the federal CSA. 9 U.L.A. 187, 188 (1979).[9] But, while we agree that the Uniform CSA offers an interesting comparison, we fail to see how the interpretation of the Uniform CSA offered by the Commissioners has any bearing at all on the intent of Congress, which enacted the federal CSA *prior to* the creation of the Uniform CSA. We can only conclude, therefore, that this argument, despite its facial appeal, has no bearing on the claim that the language of the federal CSA evidences congressional intent to adopt the construction of the statute favored by the Administrator.

While the Administrator's arguments fail to persuade us that Congress affirmatively intended his construction of the CSA, we believe nevertheless that the language and structure of the two relevant statutes, the CSA and the FDCA, are helpful in determining whether the Administrator's interpretation squares with congressional intent. Although, as the District of Columbia Circuit has stated, "[t]he interrelationship between the two Acts [CSA and FDCA] is far from clear," *National Organization for Reform of Marijuana Laws (NORML) v. DEA*, 559 F.2d 735, 750 (D.C. Cir.1977), we are persuaded that this interrelationship precludes the Administrator's reliance on the absence of FDA approval as a substitute for the second and third Schedule I criteria under the CSA.

The CSA clearly provides that a substance may not be placed in Schedule I unless it lacks *both* a "currently accepted medical use in treatment in the United States" *and* "accepted safety for use ... under medical supervision." The FDCA, on the other hand, provides that a substance may fail to obtain FDA interstate marketing approval (or exemption) for any of seven specific reasons. 21 U.S.C. § 355(d)(1)–(7). Although approval may be withheld because the substance lacks both "safety", 21 U.S.C. § 355(d)(2), and "efficacy" for a particular use, 21 U.S.C. § 355(d)(5), it is equally possible for a substance to be disapproved for interstate marketing because it lacks only *one* of these attributes, or because the application fails to contain relevant patent information, 21 U.S.C. § 355(d)(6), or even because the labeling proposed for the drug "is false or misleading in any particular." 21 U.S.C. § 355(d)(7). Thus, we find no necessary linkage between failure to obtain FDA interstate marketing approval and a determination that the substance in question is unsafe *and* has no medical use. Indeed, the FDCA does not even mention the term "medical use." In short, it is plainly possible that a substance may fail to obtain interstate marketing approval even if it has an accepted medical use.

Another possible reason for failure to obtain FDA new drug approval is that the manufacture, distribution, and use of a substance might not involve interstate marketing.[10] Unlike the CSA scheduling restrictions, the FDCA interstate marketing provisions do not apply to drugs manufactured and marketed wholly intrastate. *Compare* 21 U.S.C. § 801(5) *with* 21 U.S.C. § 321(b), 331, 355(a). Thus, it is possible that a substance may have both an accepted medical use and safety for use under medical supervision, even though no one has deemed it necessary to seek approval for interstate marketing. Indeed, as Dr. Grinspoon argues, there is no economic or other incentive to seek interstate marketing approval for a drug like MDMA because it cannot be patented and exploited commercially. The prospect of commercial development, of course, is irrelevant to one

7. The Administrator does not confine this argument to section 812(b)(1)(B), but also states that "*accepted* safety for use ... under medical supervision, 21 U.S.C. § 812(b)(1)(C), is equivalent to FDA approval because, otherwise, the safety of the substance could never be "generally agreed upon."

8. The Commissioners' Notes provide:

> Experimental substances found to have a potential for abuse in early testing will also be included in Schedule I. When those substances are accepted by the Federal Food and Drug Administration as being safe and effective, they will then be considered to have an accepted medical use for treatment in the United States, and thus, will be eligible to be shifted to an appropriate schedule based upon the criteria set out in Sections 205, 207, 209, and 211.

9 U.L.A. at 221.

9. The Uniform CSA was approved for adoption by the states in 1970. To date, 48 states, the District of Columbia, Guam, and the Virgin Islands have adopted the Uniform CSA. 9 U.L.A. Supp. 123–24 (1986).

10. Indeed, Dr. Grinspoon argues that MDMA is a drug that has been legally manufactured and used only within a particular state. Petitioner's brief at 20.

who, like Grinspoon, seeks only to do research.

These considerations tend to indicate that the absence of FDA approval for interstate commerce does not foreclose the possibility that a substance might still possess an accepted medical use or even be considered safe for use under medical supervision. It appears, instead, that blind reliance on the lack of FDA interstate marketing approval could cause a substance to be placed in Schedule I, even though one or two of the three requirements prescribed by Congress for placement of a drug in Schedule I have not been proven. Based solely on the language of the CSA and the FDCA, therefore, we find it unlikely that substituting the lack of FDA interstate marketing approval for the statutory requirements that a substance lack both an "accepted medical use" and "accepted safety for use ... under medical supervision" is consistent with the intent of Congress in enacting the CSA. We turn now to consider whether the legislative history of the CSA confirms or rebuts this tentative conclusion.

C. *Legislative History.*

The Administrator purports to have identified portions of the CSA's legislative history that support his construction of the statutory language. First, he cites a passage from the House Committee Report that states:

> Under Reorganization Plan No. 1 of 1968 [*reprinted in* 1968 U.S.Code Cong. & Ad.News 4734] a Bureau of Narcotics and Dangerous Drugs has been established in the Department of Justice to regulate all these drugs (including legitimate importation, exportation, manufacture, and distribution) to prevent diversion from legitimate channels. Safety and efficacy will continue to be regulated under the Federal Food, Drug, and Cosmetic Act by [HHS].

H.R.Rep. No. 1444, 91st Cong., 2d Sess. (1970), *reprinted in* 1970 U.S.Code Cong. & Ad.News 4566, 4584 (hereinafter cited as "House Committee Report"). From this, the Administrator draws the proposition that "Congress clearly intended that the 'safety and efficacy' of narcotic and dangerous drugs (*e.g.*, whether such drugs are acceptable for medical use and safe for such use) be determined by [HHS] under the [FDCA]." Respondent's Brief at 17–18 (emphasis deleted). The Administrator's conclusion is objectionable, however, because his parenthetical comment—equating a finding of "safety and efficacy" by the FDA with a finding of "accepted medical use" and "accepted safety for use ... under medical supervision"—is totally unsupported by the quoted passage from the House Committee Report. Nowhere does Congress equate "safety and efficacy" under the FDCA with the second and third Schedule I criteria contained in section 812(b)(1). This, indeed, is the point at issue in this litigation, and we are loath to accept such a disingenuous argument.

Second, the Administrator looks to the history underlying the legislative scheduling of the drug alphacetylmethadol in Schedule I for support. With regard to the scheduling of this substance, there is evidence that the Director of the Bureau of Narcotics and Dangerous Drugs represented to Congress that the FDA had not issued an NDA or an IND for alphacetylmethadol, and claimed that this lack of FDA approval settled the issue whether alphacetylmethadol had a "currently accepted medical use." Because Congress eventually did schedule alphacetylmethadol in Schedule I of the CSA, *see* 21 U.S.C. § 812, Schedule I(a)(3), the Administrator contends that it directly approved the statutory interpretation he advances today. We are unpersuaded, however, that this isolated instance—with no indication of express congressional approval or even tacit reliance on the Director's statement—is reason enough to defer to the Administrator's construction of the statute. Indeed, the impermissibility of substituting FDCA standards for CSA scheduling criteria becomes even more apparent when we compare the dearth of support in the legislative history for such an interpretation with the language and history of several subsequent legislative enactments in the controlled substance field.

D. *Subsequent Legislation.*

The Administrator has cited three subsequent legislative enactments as support for his position that Congress has approved his construction of the second and third criteria for Schedule I substances. Our review of these legislative enactments, however, leads us to find that the subsequent legislation tends to weaken, not strengthen, the position espoused by the Administrator in this litigation. We can only conclude, despite the Administrator's claim that Congress has repeatedly approved his construction of the CSA, that Congress has never expressly or implicitly approved an interpretation of section 812(b)(1) that would direct findings of "no currently accepted medical use" and "lack of accepted safety for use ... under medical supervision" whenever a substance lacked FDA interstate marketing approval. Rather, we are persuaded to the contrary that the subsequent enactments by Congress buttress our conclusion that the Administrator's construction of the CSA conflicts with congressional intent. To demonstrate why this is so, we shall review each of the three pieces of subsequently enacted legislation relevant to the current dispute in the paragraphs that follow.

First, in 1984, Congress amended the CSA to include an "emergency scheduling" provision. *See* 21 U.S.C. § 811(h). This provision allows the Attorney General to place certain substances into Schedule I on a temporary basis without regard to the regular scheduling criteria and procedures if such emergency scheduling is "necessary to avoid an imminent hazard to the public safety." 21 U.S.C. § 811(h)(1). This amendment to the CSA, however, expressly states that the Attorney General's authority to schedule substances in this expedited manner does not apply where an "exemption or approval is in effect for the substance under section 355 of this title," [11] *i.e.*, where the FDA has permitted the substance to be marketed in interstate commerce. *Id.* The fact that Congress expressly authorized the Attorney General to use expedited procedures and rely upon the absence of FDA interstate marketing approval, rather than the usual Schedule I criteria, only in temporary emergency situations suggests to us that these shorthand methods are not appropriate in routine (i.e., nonemergency) situations such as the one before us in the instant case. We do not interpret the explicit reference to FDA approval in the "emergency scheduling" provision to mean, as the Administrator would have us believe, that Congress sought to permit blind reliance on FDA standards as a legitimate shortcut in the general run of cases.

Second, Congress amended the CSA again in 1986 when it enacted the Controlled Substance Analogue Enforcement Act, Pub.L. No. 99–570, §§ 1201–04, 100 Stat. 3207 (codified at 21 U.S.C. §§ 802(32)(A), 813). This amendment defines a "controlled substance analogue" as a substance having a chemical structure and effect on the central nervous system substantially similar to that of a Schedule I or II controlled drug. 21 U.S.C. § 802(32)(A). It provides that analogues of Schedule I and II controlled substances shall, to the extent intended for human consumption, be subject to the same controls and penalties as the controlled substances themselves. 21 U.S.C. § 813. As the Administrator points out, the provision expressly excludes from its definition of "controlled substance analogue," and hence from the scope of the amendment's substantive controls pending final scheduling, any substance for which there is an approved new drug application or an exemption for investigational use under section 355 of the FDCA. 21 U.S.C. § 802(32)(B)(ii), (iii). Again, however, we are unpersuaded by the Administrator's argument that explicit permission to rely on FDA standards in the case of analogues evidences congressional approval of his use of this shorthand method in *all* scheduling determinations. We believe instead that the authorization to impose Schedule I controls based on the lack of FDA approval, rather than satisfaction of the scheduling

11. 21 U.S.C. § 355 is the section of the FDCA describing the standards and procedures for FDA interstate marketing approvals and exemptions.

criteria set out in section 812(b)(1), in the unique situation of analogues intended for human consumption constitutes a special, and justifiable, exception to the general procedure mandated by section 812(b)(1). We believe, however, that in other cases involving nonanalogues, or analogues intended for uses other than human consumption, absolute reliance on the absence of FDA approval would be inappropriate and, indeed, contrary to the intent of Congress in enacting the CSA.

Third, in 1984, Congress legislatively placed the drug methaqualone in Schedule I. Despite its reputation as a widely abused substance, methaqualone was universally acknowledged to have an accepted medical use and had been approved for interstate marketing by the FDA. The House Committee Report concerning the scheduling of methaqualone stated:

> the [DEA] does not have authority to impose Schedule I controls on a drug which has been approved by the [FDA] for medical use. The statutory findings required for agency scheduling decisions clearly state that the agency may not, in the absence of Congressional action, subject drugs with a currently accepted medical use in the United States to Schedule I controls.

H.R.Rep. No. 534, 98th Cong., 2d Sess. 4 (1984), *reprinted in* 1984 U.S.Code Cong. & Ad.News 540, 543. The Administrator cites this passage in yet another attempt to demonstrate congressional approval of his position that a substance cannot have an accepted medical use unless the FDA has already approved it for interstate marketing. In fact, however, the actions of Congress with respect to methaqualone demonstrate at most the converse of this proposition: that FDA approval precludes scheduling of a substance in Schedule I. In other words, the methaqualone legislation demonstrates Congress' belief that FDA approval is sufficient to establish the existence of an accepted medical use, but not that the lack of FDA approval—the issue in this case—necessarily negates the possibility that the substance in question has an accepted medical use and is safe for use under medical supervision. We therefore do not find the methaqualone legislation to be persuasive authority for the proposition that the Administrator's interpretation of section 812(b)(1) is consistent with congressional intent.

E. *Need For A Meaningful Hearing.*

We believe there is yet one additional policy reason, no doubt related to some of the other factors already discussed, for rejecting the construction of the CSA advanced by the Administrator as contrary to congressional intent. Under the statutory scheme set up by Congress, the Attorney General may not schedule a substance under the CSA without first obtaining the recommendation of the FDA, through its parent agency, HHS, 21 U.S.C. § 811(b), and providing an "opportunity for a hearing pursuant to the rulemaking procedures prescribed by [the Administrative Procedure Act]." 21 U.S.C. § 811(a). It is plain, therefore, that while Congress intended the recommendation of HHS to have significant weight in the decisionmaking process, it also intended that there be an opportunity for a meaningful hearing *after* receipt of the HHS report. It would surely be anomalous if the FDA's recommendation, based solely on the absence of approval for interstate marketing, sufficed to determine the ultimate conclusion prior to the hearing.

If we were to accept the Administrator's construction of section 812(b)(1) in this case, the opportunity for a meaningful hearing would be lost, and satisfaction of the "accepted medical use" and "accepted safety" criteria would turn solely on the existence of FDA approval for interstate marketing. A hearing on issues of the sort required by the statute—Does the substance have an accepted medical use in treatment in the United States? Is the substance safe for use under medical supervision?—would be reduced to an empty formality and, for participants like Dr. Grinspoon, would amount to an exercise in futility. We hesitate to interpret the CSA in a manner that would cause its important provision requiring a administrative hearing to be meaningless as to two of the three requirements for scheduling a substance in Schedule I. We believe instead that, for the hearing opportunity to be a significant one on these issues, the agency must remain flexible enough to weigh and consider claims raised at the administrative hearing to the effect that a substance has an accepted use and is accepted as safe even though it is not approved for distribution in interstate commerce.

The importance of a meaningful hearing prior to scheduling can best be appreciated when one considers those situations for which Congress has permitted the Administrator to regulate substances in the absence of a hearing. Neither the emergency scheduling provision, 21 U.S.C. § 811(h), nor the provision for treatment of controlled substance analogues, 21 U.S.C. § 813, requires the Administrator to hold a hearing prior to taking regulatory action. Congress crafted both of these sections to serve as stop-gap measures to be employed pending a final scheduling determination by the DEA, following a full evidentiary hearing, for the substance in question. Significantly, it is only in these provisions for *temporary* controls pending final scheduling that Congress has emphasized the absence of FDA interstate marketing approval, 21 U.S.C. § 811(h)(1) (emergency scheduling provision); 21 U.S.C. § 802(32)(B)(ii), (iii) (controlled substance analogue act). In the case of emergency scheduling, it appears that Congress has already done the balancing and determined that the risk of ongoing abuse amounting to an "imminent hazard to the public safety" justifies temporary scheduling without a hearing in the absence of FDA approval. Likewise in the latter case, Congress has responded to the need for expedited investigation and prosecution of "clandestine chemists who develop subtle chemical variations of controlled substances (called analogues or 'designer drugs') for illicit distribution and use," H.R.Rep. No. 848, 99th Cong., 2d Sess., pt. 1, 2 (1986), and permitted Schedule I controls to take effect without first requiring a hearing so long as FDA approval is lacking. Thus, in both "emergency" situations for which Congress has seen fit to place particular weight on the absence of FDA interstate marketing approval, it has also determined that a hearing procedure is unwarranted. Clearly, this is not the case in the general administrative scheduling proceedings and the hearing requirement should be given full effect rather than being shortcircuited by blind reliance on the absence of FDA approval.

F. *Conclusion.*

For the reasons listed above, we conclude that the Administrator erroneously applied an interpretation of the "accepted medical use in treatment in the United States" and "accepted safety for use ... under medical supervision" criteria of section 812(b)(1) that directly conflicts with congressional intent. We therefore vacate the Administrator's determination that MDMA should be placed in Schedule I of the CSA and remand the rule for further consideration by the DEA. On remand, the Administrator will not be permitted to treat the absence of FDA interstate marketing approval as conclusive evidence that MDMA has no currently accepted medical use and lacks accepted safety for use under medical supervision.

Petitioner Grinspoon has offered his own theory concerning the type of inquiry the Administrator must make under the statute. He urges us to adopt a standard for the second and third criteria that is based upon the opinion of members of the medical community. He contends that Congress drafted the CSA with this type of standard in mind. To support this contention, Grinspoon cites the testimony of two representatives of the Bureau of Narcotics and Dangerous Drugs ("BNDD"), DEA's predecessor agency, during legislative consideration of Pub.L. No. 91-513, the Comprehensive Drug Abuse Prevention and Control Act of 1970. Michael R. Sonnenreich, Deputy Chief Counsel of the BNDD, testified that drugs in Schedule I would "have no medical use as determined by the medical community," and that "the medical community" would decide "whether or not the drug has [a] medical use...." Hearings on Drug Abuse Control Amendments Before

the Subcomm. on Public Health and Welfare of the House Comm. on Interstate and Foreign Commerce, 91st Cong., 2d Sess. 696, 718 (1970) ("House Hearings"). Likewise, John Ingersoll, Director of the BNDD, testified that substances placed in Schedule I would be those drugs that "the medical profession has already determined to have no legitimate medical use in the United States." House Hearings at 678.

While we acknowledge that the statements by the BNDD witnesses before the House Subcommittee tend to support Dr. Grinspoon's position, we do not believe they are entitled to much weight as indicia of congressional intent in fashioning the "accepted medical use" and "accepted safety for use ... under medical supervision" criteria. *See McCaughn v. Hershey Chocolate Co.*, 283 U.S. 488, 493-94, 51 S.Ct. 510, 512, 75 L.Ed. 1183 (1931) ("statements ... made to committees of Congress ... are without weight in the interpretation of a statute"). This is especially true where, as here, there is no indication whatsoever in either the legislative history or the history of any subsequent amendments that Congress concurred with the views expressed by the witnesses. In short, we do not find Grinspoon's evidence to be persuasive on the issue of affirmative congressional intent to have certain members of the medical community determine whether a substance has an "accepted medical use in treatment in the United States" or "accepted safety for use ... under medical supervision.".

The nature of our review further constrains us from requiring the Administrator to adopt Dr. Grinspoon's proposed construction of section 812(b)(1). Although we find that the Administrator's present interpretation of the second and third Schedule I criteria contravenes congressional intent, we are unable to ascertain with any certainty what Congress intended to be the proper interpretation of subsections (B) and (C). In other words, while we are satisfied that Congress intended to preclude reliance on the absence of FDA approval in assessing whether a substance has an "accepted medical use" and "accepted safety for use ... under medical supervision," we have found nothing to indicate how Congress affirmatively intended these two ambiguous statutory phrases to be construed and applied. It appears to us that Congress has implicitly delegated to the Administrator the authority to interpret these portions of the CSA, and we must therefore refrain from imposing our own statutory interpretation upon the agency. *Chevron*, 467 U.S. at 843, 104 S.Ct. at 2781. Hence, to avoid unduly infringing upon the Administrator's legitimate discretion to develop a legally acceptable standard—i.e., one that does not conflict with the intentions of Congress, and makes sense in light of the statutory language, the legislative history, and the purposes of the entire legislative scheme—we remand the rule to the Administrator for reconsideration and for further proceedings not inconsistent with this opinion.

III. *Challenges Based on "Arbitrary and Capricious" Standard.*

Although a remand is necessary due to our above holding, we nonetheless feel compelled to address the other issues raised in Dr. Grinspoon's petition because they are likely to arise again when the Administrator reconsiders the rule.

A. *"High" Potential For Abuse.*

In addition to the "accepted medical use" and "accepted safety" criteria discussed above, the CSA also requires substances identified for placement in Schedule I to have a "high potential for abuse." 21 U.S.C. § 812(b)(1)(A). Dr. Grinspoon contends that the Administrator's placement of MDMA in Schedule I is arbitrary and capricious because the Administrator failed to articulate a legal standard for assessing MDMA's potential for abuse and because the evidence in the record is insufficient to support a finding that MDMA has a "high" potential for abuse. While conceding that MDMA has some potential for abuse, and therefore should be scheduled under the CSA, Dr. Grinspoon insists that the Administrator has not proved, as he must for a Schedule I substance, that MDMA's potential for abuse is high.

1. *Legal Standard.*

The CSA provides no definition of the phrase "high potential for abuse," but both parties agree that the legislative history of the statute provides guidance in this regard. Specifically, the report of the House Committee on Interstate and Foreign Commerce accompanying the bill that eventually became the CSA sets forth four alternative legal standards for determining when a substance possesses a "potential for abuse." Borrowing from regulations promulgated under the FDCA, the House Committee Report provides that the Administrator may determine a substance has potential for abuse if:

> (1) There is evidence that individuals are taking the drug or drugs containing such a substance in amounts sufficient to create a hazard to their health or to the safety of other individuals or of the community; *or*
>
> (2) There is significant diversion of the drug or drugs containing such a substance from legitimate drug channels; *or*
>
> (3) Individuals are taking the drug or drugs containing such a substance on their own initiative rather than on the basis of medical advice from a practitioner licensed by law to administer such drugs in the course of his professional practice; *or*
>
> (4) The drug or drugs containing such a substance are new drugs so related in their action to a drug or drugs already listed as having a potential for abuse to make it likely that the drug will have the same potentiality for abuse as such drugs, thus making it reasonable to assume that there may be significant diversions from legitimate channels, significant use contrary to or without medical advice, or that it has a substantial capability of creating hazards to the health of the user or to the safety of the community.

House Committee Report, *supra*, at 4601. The Committee Report goes on to state that "potential for abuse" exists only when there is "a substantial potential for the occurrence of significant diversions from legitimate channels, significant use by individuals contrary to professional advice, or substantial capability of creating hazards to the health of the user or the safety of the community." House Committee Report, *supra*, at 4602.

The Administrator argues that he applied the standards expressly approved by Congress, but Dr. Grinspoon complains that the Administrator articulated no standard for showing that MDMA had a *relative* potential for abuse sufficient to warrant placement in Schedule I. As Grinspoon notes, the passage from the legislative history quoted above provides guidance only as to the minimum needed to show *any* potential for abuse, in other words, enough to justify a level of CSA control as low as placement in Schedule V. It offers no guidance for assessing whether a substance should be subject to Schedule I controls, the strictest imposed under the CSA, which require a "high" potential for abuse. For this, argues Grinspoon, the Administrator must prove that MDMA has a high potential for abuse *relative* to other scheduled substances and must base its proof on existing levels of actual abuse "on the streets."

[2] While we acknowledge that the Administrator's final rule is silent with respect to the legal standard required for a finding of "high" potential for abuse, we do not find the Administrator's action to be arbitrary and capricious. The fourth standard contained in the segment of the Committee Report quoted above makes it quite clear that the Administrator can permissibly reach a conclusion regarding a substance's level of potential for abuse by comparing the substance to drugs already scheduled under the CSA. Here the Administrator has done just that, offering several findings concerning the evidence of close structural and pharmacological similarity between MDMA and other substances, such as MDA,[12] which already

12. "MDA" is 3,4-methylenedioxyamphetamine and, like MDMA, belongs to a class of compounds known as phenethylamines or, more narrowly defined, phenylisopropylamines or amphetamines.

have been found to have a high potential for abuse and have been placed in Schedule I or II. 51 Fed.Reg. 36,555–57 (1986). The Administrator also cited animal studies, human behavioral studies, and a survey of MDMA users which suggest that MDMA is related in its effects to Schedule I and II substances such as LSD, cocaine, mescaline, and MDA.[13] We believe this approach to ascertaining MDMA's potential for abuse is entirely consistent with the statutory scheme developed by Congress and therefore hold that the Administrator's method is not arbitrary and capricious.[14] The question remains, of course, whether the evidence collected by the Administrator is sufficient to justify his conclusion that MDMA has a high potential for abuse. Since Dr. Grinspoon has also challenged this aspect of the scheduling determination as arbitrary and capricious, we turn next to a discussion of this issue.

2. *Substantial Evidence.*

In reviewing the Administrator's conclusion regarding MDMA's potential for abuse, we must determine whether it is based on "substantial evidence," a term the Supreme Court has defined as " 'such relevant evidence as a reasonable mind might accept as adequate to support a conclusion.' " *American Textile Manufacturers Institute, Inc. v. Donovan*, 452 U.S. 490, 522–23, 101 S.Ct. 2478, 2497, 69 L.Ed.2d 185 (1981) (quoting *Universal Camera Corp. v. NLRB*, 340 U.S. 474, 477, 71 S.Ct. 456, 459, 95 L.Ed. 456 (1951)). The Court has further explained this lenient standard of review, stating that " 'the possibility of drawing two inconsistent conclusions from the evidence does not prevent an administrative agency's findings from being supported by substantial evidence.' " *Id.* (quoting *Consolo v. Federal Maritime Commission*, 383 U.S. 607, 620, 86 S.Ct. 1018, 1026, 16 L.Ed.2d 131 (1966)). In other words, "[e]ven if reasonable minds could also go the other way, we must uphold the [agency] if its ultimate finding is supported by substantial evidence in the record as a whole." *NLRB v. J.K. Electronics, Inc.*, 592 F.2d 5, 7 (1st Cir.1979).

The question before us, therefore, is whether there is substantial evidence in the administrative record to support the Administrator's determination that MDMA is "so related in [its] action to a drug or drugs already listed as having a [high] potential for abuse" that it is likely MDMA "will have the same potentiality for abuse as such drugs." House Committee Report, *supra*, at 4601. In support of his conclusion, the Administrator made 46 numbered findings related to MDMA's similarity to other drugs with a high potential for abuse. These findings were based on scientific evidence concerning the chemical structural similarity between MDMA and other Schedule I and II drugs; the similar pharmacological effects of MDMA and these other drugs; animal drug discrimination studies; animal self-administration studies; and recent studies of the neurotoxic effects of MDMA and related drugs on rats. Based on this evidence, the Administrator found, among other things, that (1) MDMA is the N-methyl analogue of MDA and retains the psychomimetic properties of MDA; (2) MDMA produces pharmacological effects in common with both central nervous system ("CNS") stimulants like amphetamine and hallucinogens like MDA in animals; (3) MDMA and MDA produce the same spectrum of pharmacological effects in mice, dogs, and monkeys when observed during toxicity studies; (4) MDMA, like MDA, amphetamine, and methamphetamine, produces neurotoxic effects when administered to animals; (5) MDMA and MDA may both produce the same neurotoxic effects to serotonergic nerves in humans; (6) in drug discrimination tests, rats trained to recognize amphetamine also recognized MDA and MDMA, and rats trained to recognize MDA also recognized MDMA; (7) based on recent tests involving human subjects, MDMA can be described as maintaining the same potency as MDA, but exhibiting subtle differences in the qualitative nature of the intoxication.

Dr. Grinspoon, in an item-by-item analysis contained in the proposed findings of fact and conclusions of law he submitted to the DEA, calls into question many of the Administrator's findings concerning MDMA's similarity to other drugs with a high potential for abuse. For instance, Grinspoon agrees that MDMA is a member of a family of psychoactive drugs, but disputes the validity of the inference drawn from the similarity by the Administrator. According to Grinspoon, "chemical similarity is not necessarily a good guide to the actual effects of a compound in the human body." Petitioner's Brief at 37. Grinspoon notes that of the 28 known phenethylamines, 17 were not scheduled under the CSA as late as December 1983. Even a subsequent review of these 17 substances by the World Health Organization's Expert Committee on Drug Dependence resulted in a recommendation that only nine of the substances be scheduled by member nations. Eight were thought harmless enough to remain unscheduled.[15] Also, referring to the Administrator's finding that MDMA, like MDA and amphetamine, is a central nervous system stimulant, Grinspoon asserts that this evidence of pharmacological similarity proves nothing. Several other substances also fit this description, including caffeine and six of the eight phenethylamines that are neither currently controlled nor recommended for control by WHO. Based on this, Grinspoon concludes that the mere fact that a substance is a CNS stimulant does not necessarily imply that it has a high potential for abuse.

In addition, Dr. Grinspoon (1) attacks the Administrator's other findings concerning MDMA's LD–50 rating[16] as being irrele-

13. The Administrator also considered that the United Nations Commission on Narcotic Drugs has placed MDMA in Schedule I of the Convention on Psychotropic Substances and that MDMA occupies the same schedule in the Canadian Food and Drug Act as MDA and LSD. 51 Fed.Reg. 36,559 (1986).

14. In addition to the evidence comparing MDMA to other substances with a high potential for abuse, the Administrator also considered evidence related to the "actual" abuse of MDMA and made several findings in this regard. *See* 51 Fed.Reg. 36,557–36,558 (1986). These findings reveal, among other things, that: (1) between 1972 and April 1985, DEA laboratories identified 41 exhibits of MDMA, consisting of 60,000 dosage units; (2) from July 1985, when MDMA was temporarily placed in Schedule I pursuant to the Administrator's emergency scheduling powers, up to the time that the final rule was promulgated, 14 MDMA exhibits, consisting of 35,000 dosage units, had been identified by DEA laboratories; (3) DEA has encountered five laboratories capable of clandestinely producing kilogram quantities of MDMA; (4) the estimate of one DEA witness is that street distribution of MDMA has increased from 10,000 dosage units in 1978 to 30,000 dosage units *per month* in 1985; (5) according to Dr. Grinspoon himself, MDMA is being taken by a growing number of people, particularly students and young professionals, in a casual and recreational manner; and (6) MDMA is reported to have been associated with two overdose deaths.

Dr. Grinspoon attacks these findings of actual abuse, focusing on the need to assess the *relative* level of actual abuse and stressing what he perceives as the current low level of MDMA abuse "on the streets." For example, Grinspoon notes in his brief that the statistics above concerning the 41 evidentiary exhibits identified as MDMA during the period 1972–1985 are insignificant when one considers that MDMA accounted for only one ten-thousandth of all DEA exhibits compiled during this period. Likewise, the five laboratories with the potential to manufacture MDMA account for only a minute fraction of the 2400 laboratories seized by the DEA from 1972–1983. Furthermore, Grinspoon challenges the finding that MDMA has been associated with overdose deaths as "seriously suspect."

While we appreciate Dr. Grinspoon's point that MDMA abuse is low relative to other drugs that seem to be more popular "on the street," we do not believe that this fact precludes the Administrator from finding that MDMA has a high *potential* for abuse. Grinspoon's argument overlooks the importance of the term "potential" in section 812(b)(1)(A) and runs contrary to the explicit intent of Congress that the Administrator "not be required to wait until a number of lives have been destroyed or substantial problems have already arisen before designating a drug as subject to the controls of the bill." House Committee Report, *supra*, at 4602. So long as the Administrator can marshal substantial evidence to demonstrate that MDMA is sufficiently similar to scheduled drugs with a "high potential for abuse," we will sustain his determination regardless of existing levels of actual abuse.

15. These eight are clobenzorex, fenbutrazate, furfenorex, morazone, para-oxyamphetamine, 4–bromo–2,5–dimethoxyphenethylamine, N,N–dimethylamphetamine, and N–ethyl–3,4–methylenedioxyamphetamine.

16. "LD–50" signifies the dose of a given drug that will kill 50% of the animals treated with that dose.

vant to the "potential for abuse" inquiry; (2) discounts the importance of findings that MDMA is neurotoxic when administered to rats; (3) questions the relevancy of the findings related to animal drug discrimination studies; and (4) asserts that the Administrator has incorrectly interpreted the results of two animal self-administration studies. We have reviewed Dr. Grinspoon's item-by-item analysis closely, but find no basis sufficient to overturn the Administrator's decision. Grinspoon's reinterpretation of the scientific evidence before the agency surely demonstrates that the available evidence does not inexorably lead to a conclusion that MDMA is similar to drugs possessing a high potential for abuse. But, faced with such uncertainty, we must defer to the conclusion reached by the Administrator, even if we may have favored Dr. Grinspoon's approach had we studied the evidence in a *de novo* fashion. In reaching this conclusion, we follow the well-established maxim that "[w]here the agency presents scientifically respectable evidence which the petitioner can continually dispute with rival, and we will assume, equally respectable evidence, the court must not second-guess the particular way the agency chooses to weigh the conflicting evidence or resolve the dispute." *Asarco, Inc. v. OSHA*, 746 F.2d 483, 490 (9th Cir.1984) (quoting *United Steelworkers of America v. Marshall*, 647 F.2d 1189, 1263 (D.C.Cir.1980), *cert. denied*, 453 U.S. 913, 101 S.Ct. 3148, 69 L.Ed.2d 997 (1981)). We find this maxim to have particular force in a case such as this because, as one court has explained, "[a]ppellate courts have neither the expertise nor the resources to evaluate complex scientific claims." *Thompson Medical Co. v. FTC*, 791 F.2d 189, 196 (D.C.Cir.1986), *cert. denied*, — U.S. —, 107 S.Ct. 1289, 94 L.Ed.2d 146 (1987).

B. *Impact Of Scheduling On Research.*

Dr. Grinspoon also takes issue with the Administrator's alleged failure to consider evidence tending to show that placement of MDMA in Schedule I would strongly discourage medical research on the drug. Grinspoon contends that failure to consider the impact of a scheduling decision on legitimate research amounts to arbitrary and capricious action on the part of the Administrator because he did not weigh all relevant factors in making his decision. *Motor Vehicle Manufacturers Association v. State Farm Mutual Insurance Co.*, 463 U.S. 29, 42–43, 103 S.Ct. 2856, 2866, 77 L.Ed.2d 443 (1983). To buttress his contention, Grinspoon recites a litany of legal, administrative, and practical obstacles that hinder researchers seeking to conduct experiments with Schedule I drugs. These obstacles include mandatory FDA approval of research involving Schedule I substances, 21 C.F.R. § 1301.42(a)–(c); mandatory special registration with the DEA, 21 C.F.R. §§ 1301.33, 1301.42; mandatory reporting and security procedures beyond those required for drugs placed in Schedules II through V; unavoidable bureaucratic delays; and other adverse impacts due to the grave concern caused by a substance's placement in Schedule I, such as difficulty in obtaining volunteers for clinical studies and, for academic researchers, difficulty in securing approval from institutional review boards.

[3] Again, we do not doubt that Dr. Grinspoon has correctly identified several ways in which the placement of MDMA in Schedule I will impede his research and the efforts of other researchers interested in exploring the possibility of clinical uses for MDMA. We must conclude, nevertheless, that the existence of such hurdles does not render the Administrator's scheduling decision arbitrary and capricious. First, it is simply untrue that the Administrator failed to consider the impact on medical research that would be caused by a decision to place MDMA in Schedule I. In the final rule, the Administrator states explicitly that he "read with interest the comments from various parties in the record concerning the effect placement of MDMA into Schedule I would have on legitimate research into the substance." 51 Fed.Reg. 36,559 (1986). After several paragraphs discussing the contours of the additional Schedule I controls, the Administrator concludes that "those who wish to conduct research with MDMA have available avenues by which to pursue such research." *Id.*

Second, and more importantly, Dr. Grinspoon has identified nothing in the CSA, its legislative history, or its implementing regulations that can be read to require the Administrator to consider the impact of a scheduling determination upon legitimate scientific research. From our review of the CSA, we can only conclude that Congress has already weighed the costs and benefits of legitimate research on dangerous drugs and has determined, in a categorical manner, that if the three Schedule I criteria are satisfied, *see* 21 U.S.C. § 812(b)(1), then the substance should be subject to Schedule I controls even if this action will create administrative and other burdens for researchers. Here there is no dispute that the Administrator *considered* all of the section 812(b)(1) criteria in arriving at his final rule, so we are left with a situation in which there can be no complaint that the Administrator failed to consider any relevant factor.

C. *Reliance Upon HHS Evaluation And Recommendation.*

Dr. Grinspoon's final dissatisfaction with the final rule is the Administrator's alleged reliance on the conclusions recommended by HHS on the criteria enumerated in section 812(b)(1). Grinspoon argues that the determination by the Secretary of HHS was arbitrary and capricious and not in accordance with law, and that all relevant scientific and medical evidence was not before the Secretary at the time of the determination. The record, in fact, reveals that HHS performed in a less than admirable fashion in making its recommendation to the Administrator. The record indicates that HHS failed to look beyond its own files upon receiving the Administrator's section 811(b) request for a scientific and medical evaluation; neglected to consult any organization of medical professionals or even the FDA's own panel of experts, the Drug Abuse Advisory Committee; and simply rubber-stamped the Administrator's conclusion by adopting the section 811(c) eight-factor analysis already performed by the DEA. There is also evidence that FDA analysts failed to forward a letter received from the National Institute of Drug Abuse, which stated that the evidence cited by the DEA did not support the existence of abuse potential in animals, to either the FDA Commissioner or the Assistant Secretary of HHS prior to the issuance of the HHS recommendation to the Administrator.[17]

[4] Despite these alleged procedural shortcomings, we fail to see how the procedure followed by HHS tainted the Administrator's determination. The CSA does not specify the steps to be taken by HHS; it simply requires the Administrator to request from the Secretary of HHS a scientific and medical evaluation. 21 U.S.C. § 811(b). Moreover, the HHS recommendation to schedule a substance is not binding[18] and, indeed, serves to trigger an administrative hearing at which interested persons may introduce evidence to rebut the Secretary's scheduling recommendation. Ultimately, of course, responsibility rests with the Administrator, not HHS, to ensure that the final rule rests on permissible legal standards and substantial evidence. It is true that the Administrator twice mentioned the HHS recommendation in his final rule, once in relation to the "accepted medical use" criterion and once in relation to the "high potential for abuse" criterion. With regard to the first mention, however, we have already determined that this aspect of the case must be remanded and reconsidered because the Administra-

17. Dr. Grinspoon also complains that the Acting Assistant Secretary of Health concluded erroneously that MDMA had a "high" potential for abuse because the recommendation of FDA's Deputy Commissioner described MDMA's potential for abuse as "significant," rather than "high." In light of the fact that the FDA Deputy Commissioner recommended placement of MDMA in Schedule I, we attribute no significance to this semantic argument.

18. According to section 811(b), the HHS recommendation is binding as to "scientific and medical" matters, but not with respect to the appropriate schedule in which to place a particular substance. The exception to this rule is that, "if the Secretary recommends that a drug or other substance *not* be controlled, the Attorney General shall not control the drug or other substance." 21 U.S.C. § 812(b) (emphasis supplied).

tor interpreted the statutory language in a manner that is contrary to the intent of Congress. Because, on remand, the Administrator will not be able to rely on lack of FDA approval to demonstrate the absence of an accepted medical use, we need not discuss any possible reliance on the HHS recommendation regarding the absence of an accepted medical use. With regard to the second mention, we believe that the Administrator's conclusion that MDMA has a high potential for abuse is amply supported by a substantial amount of independent evidence. Because we believe that the Administrator's finding with regard to MDMA's potential for abuse is justified even in the absence of the HHS recommendation to place MDMA in Schedule I, we hold that any reliance on the HHS evaluation by the Administrator constitutes, at most, harmless error.

For the foregoing reasons, the rule is vacated and remanded to the Administrator for further proceedings consistent with this opinion.

Aaron J. FURMAN, Martin J. Joel, Jr., Alvin Katz, Francis P. Maglio, Harvey Sheid, Everard M.C. Stamm and Robert C. Stamm, Plaintiffs,

Martin J. Joel, Jr., Harvey Sheid, Everard M.C. Stamm and Robert C. Stamm, Plaintiffs-Appellants,

v.

John CIRRITO, Harold S. Coleman, John A. Miller, Francis G. Rea, Peter M. Toczek and A.J. Yorke, Defendants-Appellees.

No. 18, Docket 86-7283.

United States Court of Appeals, Second Circuit.

Argued Oct. 20, 1986.

Decided Sept. 1, 1987.

Minority general partners of partnership brought civil claim against majority owners of partnership pursuant to RICO statute. The United States District Court for the Southern District of New York, Irving Ben Cooper, J., 578 F.Supp. 1535, dismissed action for failure to state claim, and appeal was taken. The Court of Appeals, 741 F.2d 524, affirmed. On petition for writ of certiorari, the United States Supreme Court, 105 S.Ct. 3550, vacated. Following vacation, 779 F.2d 36, and on remand, the district court concluded that complaint failed to allege any continuity of activity and dismissed RICO cause of action, and appeal was again taken. The Court of Appeals, Van Graafeiland, Circuit Judge, held that: (1) sale of partnership assets did not constitute wrongdoing to support RICO action; (2) majority partners were not guilty of any criminal conduct based on alleged failure to promptly inform minority partners that they would be required to sign written contract with purchasing partnership; and (3) even if minority partners spelled out some form of criminal fraud on part of majority partners, they failed to allege pattern of racketeering activity conducted in affairs of "enterprise."

Affirmed.

George C. Pratt, Circuit Judge, filed dissenting opinion.

1. Partnership ⇐70, 97

Rights and obligations of partners, as between themselves, are fixed by terms of partnership agreement; even terms which permit self-dealing by partner will be enforced.

2. Commerce ⇐82.72

Allegations by minority shareholders of partnership to effect that majority members committed mail fraud in selling assets of partnership was frivolous, and thus could not support action brought pursuant to RICO statute; partnership agreement gave absolute and sole discretion to majority members to sell partnership assets, and further, allegation that principal of another brokerage firm was "prepared to negotiate" purchase of partnership at higher price was inadequate to establish that other firm made offer to purchase. 18 U.S. C.A. §§ 1961–1968.

3. Commerce ⇐82.72

Allegations by minority partners that their signatures on written contract for sale of partnership assets were coerced by criminal conduct on part of majority partners and that minority partners were "forced to accept employment" on unfavorable terms was too conclusory to support charge of criminal wrongdoing in order to maintain action under RICO statute; each partner had right to negotiate on his or her behalf whether, and on what terms, he or she was willing to become associated with purchasing partnership, and even if minority partners lacked sufficient sophistication to know that they could not be bonded over to purchasing partnership without their consent, they made no allegation of anything that prevented them from refusing to sign contract unless they received more favorable treatment. 18 U.S.C.A. §§ 1961–1968.

4. Commerce ⇐82.72

Assuming that minority general partners' complaint spelled out some form of criminal fraud on part of majority partners in selling partnership assets, complaint failed to allege pattern of racketeering activity conducted in affairs of "enterprise" to enable minority partners to maintain RICO action; at time allegedly wrongful acts occurred, majority partners were not functioning as continuing unit in ongoing organization, as they were acting solely on their own to prevent alleged enterprise from being ongoing, continuing unit through sale of partnership. 18 U.S.C.A. §§ 1961–1968.

Seymour Shainswit, New York City (Cooper Cohen Singer Ecker & Shainswit and Steven E. Levitsky, New York City, of counsel), for plaintiffs-appellants.

Max Gitter, New York City (Paul, Weiss, Rifkind, Wharton & Garrison and Dorothy E. Roberts, New York City, of counsel), for defendants-appellees.

Before VAN GRAAFEILAND, NEWMAN and PRATT, Circuit Judges.

VAN GRAAFEILAND, Circuit Judge:

This is an appeal from an order of the United States District Court for the Southern District of New York (Cooper, J.) granting appellees' motion under Fed.R. Civ.P. 12(b)(1) and (6) to dismiss appellants' complaint, and from the judgment entered pursuant thereto. For the reasons that follow, we affirm.

Appellants' complaint states three causes of action, two that are state law claims of partnership fraud and breach of fiduciary duty and a third grounded on the Racketeer Influenced and Corrupt Organizations Act (RICO), 18 U.S.C. §§ 1961–68. It twice has been dismissed by the district court. The first dismissal was based on appellants' failure to allege a separate, distinct racketeering enterprise injury. 578 F.Supp. 1535 (S.D.N.Y.1984). This Court's affirmance of that decision, 741 F.2d 524, was vacated by the Supreme Court, 473 U.S. 922, 105 S.Ct. 3550, 87 L.Ed.2d 672 (1985), on the basis of its holdings in *Sedima, S.P.R.L. v. Imrex Co.*, 473 U.S. 479, 105 S.Ct. 3275, 87 L.Ed.2d 346 (1985), and *American Nat'l Bank & Trust Co. v. Haroco, Inc.*, 473 U.S. 606, 105 S.Ct. 3291, 87 L.Ed.2d 437 (1985) (per curiam). Following remand to the district court, appellees moved to dismiss for failure to allege a "pattern of racketeering activity", 18 U.S.C. § 1962(c), or, in the alternative, to compel arbitration pursuant to the Federal Arbitration Act, 9 U.S.C. §§ 1–14. Relying on *Sedima, supra*, 473 U.S. at 496 n. 14, 105 S.Ct. at 3285 n. 14; *id.* at 527–28, 105 S.Ct. at 3289–90 (Powell, J., dissenting), and cases that followed, the district court held that racketeering activity must be continuous and related in order to constitute a pattern and must be ongoing or occur in more than one criminal episode. Although the district court felt that appellees' alleged acts were related, it concluded that the complaint failed to allege any continuity of activity, and dismissed the RICO cause of action. The district court held

Tariff Act of 1930. On February 4, 1992, the Commission scheduled a public hearing in connection therewith for March 26, 1992. On March 17, 1992, the Commission received notice of withdrawal from the only scheduled witness for the hearing scheduled for March 26, 1992. Therefore, the public hearing in connection with this investigation (scheduled to be held beginning at 9:30 a.m. on March 26, 1992, at the U.S. International Trade Commission Building, 500 E Street, SW., Washington DC), is cancelled.

EFFECTIVE DATE: March 20, 1992.

FOR FURTHER INFORMATION CONTACT: Edward Carroll (202-205-1819), Office of Public Affairs, U.S. International Trade Commission. Hearing impaired persons can obtain information on this study by contacting the Commission's TDD terminal on (202-205-1810).

By order of the Commission

Dated: March 24, 1992.

Kenneth R. Mason,

Secretary.

[FR Doc. 92-7160 Filed 3-25-92; 8:45 am]

BILLING CODE 7020-02-M

INTERSTATE COMMERCE COMMISSION

[Finance Docket No. 32016]

Sioux & Western Railroad Co.—Construction Exemption—Charles County, Mo; Notice

AGENCY: Interstate Commerce Commission.

ACTION: Notice of exemption.

SUMMARY: Pursuant to 49 U.S.C. 10505, the Interstate Commerce Commission conditionally exempts from the prior approval requirements of 49 U.S.C. 10901 the construction by the Sioux & Western Railroad Company of approximately 2 miles of rail line between the Sioux Plant and a Union Pacific Railroad Company line in Charles County, MO.

DATES: The exemption will not become effective until the environmental process is completed. At that time, the Commission will issue a further decision addressing the environmental matters and establishing an effective date for the exemption, if appropriate. Petitions to reopen must be filed by April 15, 1992.

ADDRESSES: Send pleadings referring to Finance Docket No. 32016 to:

(1) Office of the Secretary, Case Control Branch, Interstate Commerce Commission, Washington, DC 20423.

(2) Petitioner's representative: John R. Molm, Esquire, Troutman, Sanders, Lockerman and Ashmore, 1400 Candler Building, 127 Peachtree Street, NE., Atlanta, GA 30303.

FOR FURTHER INFORMATION CONTACT: Joseph H. Dettmar, (202) 927-5660. (TDD for hearing impaired: (202) 927-5712.

SUPPLEMENTARY INFORMATION: Additional information is contained in the Commission's decision. To purchase a copy of the full decision, write to, call, or pick up in person from: Dynamic Concepts, Inc., room 2229, Interstate Commerce Commission Building, Washington, DC 20423. Telephone: (202) 289-4357/4359. (Assistance for the hearing impaired is available through TDD services (202) 927-5721.)

Decided: March 11, 1992.

By the Commission, Chairman Philbin, Vice Chairman McDonald, Commissioners Simmons, Phillips, and Emmett.

Sidney L. Strickland, Jr.,

Secretary.

[FR Doc. 92-7017 Filed 3-25-92; 8:45 am]

BILLING CODE 7035-01-M

DEPARTMENT OF JUSTICE

Drug Enforcement Administration

[Docket No. 86-22]

Marijuana Scheduling Petition; Denial of Petition; Remand

AGENCY: Drug Enforcement Administration, Justice.

ACTION: Final order.

SUMMARY: This is a final order of the Administrator of the Drug Enforcement Administration (DEA) concluding the plant material marijuana has no currently accepted medical use and denying the petition of the National Organization for Reform of Marijuana Laws (NORML) to reschedule marijuana from Schedule I to Schedule II of the Controlled Substances Act.

EFFECTIVE DATE: March 26, 1992.

FOR FURTHER INFORMATION CONTACT: Office of Congressional and Public Affairs, 202-307-7363.

SUPPLEMENTARY INFORMATION:

Background

On December 21, 1989, the former Administrator of DEA, following rulemaking on the record, which included a hearing before an administrative law judge, issued a final order concluding the plant material marijuana has no currently accepted medical use, and denying the petition of NORML to reschedule marijuana from Schedule I to Schedule II of the Controlled Substances Act. 54 FR 63767. On April 26, 1991, the United States Court of Appeals for the District of Columbia Circuit remanded the matter to the Administrator for clarification of DEA's interpretation of the term "currently accepted medical use in treatment in the United States." *Alliance for Cannabis Therapeutics* v. *DEA*, 930 F.2d 936.

Following a review of the entire record in this matter, and a comprehensive re-examination of the relevant statutory standard, I conclude that marijuana has no currently accepted medical use and must remain in Schedule I. Further hearings are unnecessary since the record is extraordinarily complete, all parties had ample opportunity and wide latitude to present evidence and to brief all relevant issues, and the narrow question on remand centers exclusively on this Agency's legal interpretation of a statutorily-created standard.

Summary of the Decision

Does the marijuana plant have any currently accepted medical use in treatment in the United States, within the meaning of the Federal Controlled Substances Act, 21 U.S.C. 801, *et seq.*? Put simply, is marijuana good medicine for illnesses we all fear, such as multiple sclerosis (MS), glaucoma and cancer?

The answer might seem obvious based simply on common sense. Smoking causes lung cancer and other deadly diseases. Americans take their medicines in pills, solutions, sprays, shots, drops, creams and sometimes as suppositories, but never by smoking. No medicine prescribed for us today is smoked.

With a little homework, one can learn that marijuana has been rejected as medicine by the American Medical Association, the National Multiple Sclerosis Society, the American Glaucoma Society, the American Academy of Ophthalmology, the American Cancer Society. Not one American health association accepts marijuana as medicine.

For the last half century, drug evaluation experts at the United States Food and Drug Administration (FDA) have been responsible for protecting Americans from unsafe and ineffective new medicines. Relying on the same scientific standards used to judge all other drugs, FDA experts repeatedly have rejected marijuana for medical use.

Yet claims persist that marijuana has medical value. Are these claims true? What are the facts?

Between 1987 and 1988, DEA and NORML, under the guidance of an administrative law judge, collected relevant information on this subject. Stacked together it stands nearly five feet high. Is there reliable scientific evidence that marijuana is medically

effective. If it has medical value, do its benefits outweight its risks? What do America's top medical and scientific experts say? Would they prescribe it for their patients, their families, their friends?

As the current Administrator of Drug Enforcement, and as a former United States District Judge, I have made a detailed review of the evidence in this record to find the answers.

There are significant short-term side effects and long-term risks linked to smoking marijuana. Marijuana is likely to be more cancer-causing than tobacco; damages brain cells; causes lung problems, such as bronchitis and emphysema; may weaken the body's antibacterial defenses in the lungs; lowers overall blood pressure, which could adversely affect the supply of blood to the head; causes sudden drops in blood pressure (orthostatic hypotension), rapid heart beat (tachycardia), and heart palpitations; suppresses luteinizing hormone secretion in women, which affects the production of progesterone, an important female hormone; causes anxiety and panic in some users because of its mind-altering effects; produces dizziness, trouble with thinking, trougle with concentrating, fatigue, and sleepiness; and impairs motor skills.

As a plant, marijuana can contain bacteria capable of causing serious infections in humans, such as salmonella enteritidis, Klebsiella pneumoniae, group D Streptoccoccus and pathogenic aspergillus.

Several of these risk stand out. The immune systems of cancer patients are weakened by radiation and chemotherapy, leaving them susceptible to infection. If they experiment with marijuana to control nausea, they risk weakening their immune systems further and exposing themselves to the infection-causing bacteria in the plant. It is estimated, for example, that at Memorial Sloan-Kettering Cancer Center 60 patients die each year from pathogenic aspergillus infections.

Glaucoma patients face possible blindness caused by very high fluid pressures within their eyes. If they experiment with marijuana to lower their eye fluid pressure, it can cause dramatic drops in their blood pressure and reduce the blood supply to their heads. Glaucoma experts testified this reduced the blood supply to the optic nerves and could speed up, rather than slow down, their loss of eyesight.

MS, glaucoma and cancer patients who have undiagnosed heart problems risk heart palpitations, very rapid heart beats and sudden dramatic drops in blood pressure if they experiment with marijuana. For MS and glaucoma patients who must take medications for the rest of their lives, experimenting with marijuana poses the additional risks of lung cancer, emphysema, bladder cancer and leukemia.

Many risks remain unknown. Marijuana contains over 400 separately identified chemicals. No one knows all the effects of burning these chemicals together and inhaling the burnt mix. Are these risks outweighed by medical benefits?

There are scientific studies showing pure THC (Delta-9-Tetrahydrocannabinol), one of the many chemicals found in marijuana, has some effect in controlling nausea and vomiting. Pure THC is pharmaceutically made in a clean capsule form, called Marinol, and is available for use by the medical community. More information on Marinol can be found in the "Physicians' Desk Reference," available in most libraries.

Since marijuana contains THC, you might think marijuana also would be effective. However, the effect of taking a drug in combination with other chemicals is seldom the same as taking just the pure drug. As already noted, marijuana contains over 400 other chemicals, not just THC. There are no reliable scientific studies that show marijuana to be significantly effective in controlling nausea and vomiting. People refer to the Sallan study as proving marijuana's effectiveness. They are mistaken. The Sallan study involved pure THC, not marijuana. People refer to the Chang study to support marijuana's effectiveness. They also are mistaken. Doctor Chang tested the combination of pure THC and marijuana to treat nausea and vomiting. The preliminary results he got were probably due to the THC, not the marijuana. Because he tested the combination, we cannot tell just what effects can be attributed to marijuana alone. People cite a third study, done by Doctor Levitt, as proof marijuana is effective. They are mistaken. Doctor Levitt compared marijuana to THC in controlling nausea and vomiting, and he concluded that THC was the more effective drug.

A librarian can help locate copies of thes studies should you want to see them for yourself. Sallan, et al., "Antiemetic Effect of Delta-9-Tetrahydrocannibinol in Patients Receiving Cancer Chemotherapy," 293 New England Journal of Medicine 795–797 (1975); Chang, et al., "Delta-9-Tetrahydrocannabinol as an Antiemetic in Cancer Patients Receiving High-Dose Methotrexate," 91 Annals of Internal Medicine 819–824 (1979); Levitt, et al., "Randomized Double Blind Comparison of Delta-9-Tetrahydrocannabinol (THC) and Marijuana As Chemotherapy Antiemetics," (Meeting Abstract) 3 Proceedings of the Annual Meeting of the American Society of Clinical Oncology 91 (1984).

During the 1970's and 1980's, a number of states set up research programs to give marijuana to cancer and glaucoma patients, on the chance it might help. Some people point to these programs as proof of marijuana's usefulness. Unfortunately, all research is not necessarily good scientific research. These state programs failed to follow responsible scientific methods. Patients took marijuana together with their regular medicines, so it is impossible to say whether marijuana helped them. Observations or results were not scientifically measured. Procedures were so poor that much critical research data were lost or never recorded. Although these programs were well-intentioned, they are not scientific proof of anything.

Some people refer to a study by Doctor Thomas Ungerleider as proof marijuana reduced nausea in bone marrow transplant patients. Unfortunately, Doctor Ungerleider neglected to follow responsible scientific methods in his study. Like state programs, it proves nothing. Doctor Ungerleider chose not to publish his study evidently because of its serious weaknesses. He admitted as much when questioned under oath.

Those who say there are reliable scientific studies showing marijuana is an effective drug for teating nausea and vomiting are wrong. No such studies exist.

Our nation's top cancer experts reject marijuana for medical use. Doctor Dr. S. Ettinger, a professor of oncology at the Johns Hopkins University School of Medicine, an author of over 100 scholarly articles on cancer treatment and a nationally respected cancer expert, testified:

> There is no indication that marijuana is effective in treating nausea and vomiting resulting from radiation treatment or other causes. No legitimate studies have been conducted which make such conclusions.

Doctor Richard J. Gralla, a professor of medicine at Cornell University Medical College, an associate attending physician at the Memorial Sloan-Kettering Cancer Center, and an expert in cancer research, testified:

> Most experts would say, and our studies support, that the cannabinoids in general are not very effective against the major cause of nausea and vomiting.

Doctor Gralla added:

I have found that because of the negative side effects and problems associated with marijuana * * * most medical oncologists and researchers have little interest in marijuana for the treatment of nausea and vomiting in their patients.

Doctor John Laszlo, Vice President of Research for the American Cancer Society, an expert who has spent 37 years researching cancer treatments, and who has written a leading textbook on the subject, "Antiemetics and Cancer Chemotherapy," testified there is not enough scientific evidence to justify using marijuana to treat nausea and vomiting. Not one nationally-recognized cancer expert could be found to testify on marijuana's behalf.

To be an effective treatment for glaucoma, a drug must: (i) Lower the pressure within the eye (intraocular pressure), (ii) for prolonged periods of time, and (iii) actually preserve sight (visual fields). Five scientific studies are cited as evidence marijuana is an effective glaucoma treatment. Those who cite these studies are mistaken. These studies tested pure THC, not marijuana. W.D. Purnell and J.M. Gregg, "Delta-9-Tetrahydorcannabinol. Euphoria and Intraocular Pressure in Man," 7 Annals of Ophthalmology 921-923 (1975); M. Perez-Reyes, D. Wagner, M.E. Wall, and K.H. Davis, "Intravenous Administration of Cannabinoids on Intraocular Pressure," The Pharmacology of Marijuana 829-832 (M.C. Braude and S. Szara eds. 1976); J.C. Merritt, S.M. McKinnon, J.R. Armstrong, G. Hatem, and L.A. Reid, "Oral Delta-9-Tetrahydrocannabinol in Hyperogeneous Glaucomas," 12 Annals of Ophthalmology 947 (1980); K. Green and M. Roth, "Ocular Effects of Topical Administration of Delta-9-Tetrahydrocannabinol in Man," 100 Archives of Ophthalmology 265-267 (1982); and W.M. Jay and K. Green, "Multiple-Drop Study of Topically Applied 1% Delta-9-Tetrahydrocannabinol in Human Eyes," 101 Archives of Ophthalmology 591-593 (1983).

Threee studies show very heavy doses of marijuana, taken for short periods of time, can reduce eye pressure. R.S. Hepler, I.M. Frank, and T.J. Ungerleider, "Pupillary Constriction After Marijuana Smoking," 74 American Journal of Ophthalmology 1185-1190 (1972); R.S. Hepler, I.M. Frank, and R. Petrus, "Ocular Effects of Marijuana Smoking," The Pharmacology of Marijuana 815-824 (1976); and J.C. Merritt, W.J. Crawford, P.C. Alexander, A.L. Anduze and S.S. Gelbart, "Effect of Marijuana on Intraocular and Blood Pressure in Glaucoma," 87 Ophthalmology 222-228 (1980).

Unusally large doses or marijuana were needed in these three studies to achieve the desired effect. Heavy marijuana use produces dizziness, trouble with thinking, impaired motor skills, fatigue and sleepiness. The 1976 study by Doctors Hepler, Frank and Petrus emphasized "Our subjects were sometimes too sleepy to permit measurement of intraocular pressures * * * 3 hours after intoxication." If a glaucoma patient were to smoke marijuana 8 to 10 times every day for the rest of his life, would he be alert and energetic enough to live a relatively normal life? Would he develop other diseases? No scientific studies exist to answer these questions. Robert Randall claims to have saved his sight by smoking 8 to 10 marijuana cigarettes every day. Under oath he admits he stays at home most days, follows no daily schedule or routine, and has not held a regular job in over 15 years. He also has avoided having a comprehensive medical examination since 1975.

No scientific studies have shown marijuana can reduce eye pressure over long periods of time.

No scientific studies have shown marijuana can save eyesight.

America's top glaucoma experts reject marijuana as medicine. Doctor Keith Green is a professor of Ophthalmology who serves, or has served, on the editorial boards of eight prestigious eye journals (Ophthalmic Research, Oftalmo Abstracto, Current Eye Research, Experimental Eye Research, Investigative Opthalmology, American Journal of Ophthalmology, Archives of Ophthalmology, and Survey of Ophthalmology). Doctor Green has conducted extensive basic and clinical research using marijuana and THC to treat glaucoma patients. He has authored over 200 books or research articles in ophthalmology and is a highly respected expert on this subject. Doctor Green testified:

There is no scientific evidence * * * that indicates that marijuana is effective in regulating the progression of symptoms associated with glaucoma. * * * It is clear that there is no evidence that marijuana use prevents the progression of visual loss in glaucoma. * * * The quantities of the drug required to reduce intraocular pressure in glaucoma sufferers are large, and would require the inhalation of at least six marijuana cigarettes each day. * * * Smoking is not a desirable form of treatment for many reasons * * * [M]arijuana . . . has little potential future as a glaucoma medication.

Doctor George Spaeth is the Direct of the Glaucoma Service at Wills Ey Hospital in Philadelphia, the largest service in the United States devoted researching and treating glaucoma a to teaching other doctors about this disease. Doctor Spaeth is President o the American Glaucoma Society. He professor of ophthalmology, the edit a scholarly eye journal (Ophthalmic Surgery), and the author of over 200 research articles on glaucoma. He testified:

I have not found any documentary evidence which indicates that a single pa has had his or her natural history of the disease altered by smoking marijuana.

Amputees and victims of MS can suffer from extreme muscle spasms. claimed marijuana is useful in treati spasticity. Three unusually small, inconclusive studies have tried usin pure THC, not marijuana, to treat spasticity. D.J. Petro and C. Ellenber "Treatment of Human Spasticity wi Delta-9-Tetrahydro-cannabinol," 21 Journal of Clinical Pharmacology 41 416S (1981) (included only nine patients). Two of the studies are me abstracts, or short digests, without r detail. Hanigan, Destee & Troung Al B45. Clin. Pharmacol. Ther. 198 (198 (included only five patients), and Sandyk, Cannoe, Stern and Snider Abstr. PP 331, 38 Neurology 342 (198 (included only three patients).

No scientific studies exist which t marijuana to relieve spasticity.

National experts on MS reject marijuana as medicine. Doctor Ken P. Johnson is Chariman of the Department of Neurology at the University of Maryland School of Medicine. He manages that Maryla Center for MS, one of the most acti MS research and treatment centers the United States. He sits on the editorial boards of noted medical journals related to MS (Neurology a Journal of Neuroimmunology). He is author of over 100 scientific and me articles on MS. Doctor Johnson has spent most of his long career researching MS and has diagnosed treated more than 6,000 patients wi MS. Doctor Johnson testified:

At this time, I am not aware of * * * legitimate medical research in which marijuana was used to treat the sympto multiple sclerosis. * * * To conclude th marijuana is therapeutically effective w conducting rigorous testing would be professionally irresponsible.

Doctor Stephen Reingold is Assis Vice President of Research for the National Multiple Sclerosis Society which spends over $7 million each

on MS research. Only the Federal Government spends more. Doctor Reingold testified:

> I could find no actual published research which has used marijuana * * * In the existing research using THC, the results were inconclusive * * * In the absence of any well-designed, well-controlled research * * *, the National Multiple Sclerosis Society * * * does not endorse or advocate its use * * *.

Doctor Donald H. Silberberg is Chairman of the Department of Neurology at the University of Pennsylvania School of Medicine and Chief of the Neurology Service at the Hospital of Pennsylvania. Doctor Silberberg is on the editorial board of Annals of Neurology and is President of the National Medical Advisory Board for the National Multiple Sclerosis Society. He has been actively researching and treating MS for most of his career, has written over 130 medical articles on MS and is Co-Director of a large MS research center at the University of Pennsylvania. Doctor Silberberg testified:

> I have not found any legitimate medical or scientific works which show that marijuana * * * is medically effective in treating multiple sclerosis or spasticity. * * * The long-term treatment of the symptoms of multiple sclerosis through the use of marijuana could be devastating. * * * [T]he use of (marijuana), especially for long-term treatment * * * would be worse than the original disease itself.

The only favorable evidence that could be found by NORML and DEA consists of stories by marijuana users who claim to have been helped by the drug. Scientists call these stories anecdotes. They do not accept them as reliable proofs. The FDA's regulations, for example, provide that in deciding whether a new drug is a safe and effective medicine, "isolated case reports * * * will not be considered." 21 CFR 314.126(e). Why do scientists consider stories from patients and their doctors to be unreliable?

First, sick people are not objective scientific observers, especially when it comes to their own health. We all have heard of the placebo effect. Patients have a tendency to respond to drugs as they believe is expected of them. Imagine how magnified this placebo effect can be when a suffering person experiments on himself, praying for some relief. Many stories no doubt are due to the placebo effect, not to any real medical effects of marijuana.

Second, most of the stories come from people who took marijuana at the same time they took prescription drugs for their symptoms. For example, Robert Randall claims marijuana has saved his sight, yet he has taken standard glaucoma drugs continuously since 1972. There is no objective way to tell from these stories whether it is marijuana that is helpful, or the proven, traditional medicines. Even these users can never know for sure.

Third, any mind-altering drug that produces euphoria can make a sick person think he feels better. Stories from patients who claim marijuana helps them may be the result of the mind-altering effects of the drug, not the results of improvements in their conditions.

Fourth, long-time abusers of marijuana are not immune to illness. Many eventually get cancer, glaucoma, MS and other diseases. People who become dependent on mind-altering drugs tend to rationalize their behavior. They invent excuses, which they can come to believe, to justify their drug dependence. Stories of marijuana's benefits from sick people with a prior history of marijuana abuse may be based on rationalizations caused by drug dependence, not on any medical benefits caused by the drug. Robert Randall, for example, admits under oath to becoming a regular user in 1968, four years before he showed the first signs of, and was diagnosed as having, glaucoma. Since then he has smoked marijuana 8 to 10 times every day.

A century ago many Americans relied on stories to pick their medicines, especially from snake oil salesmen. Thanks to scientific advances and to the passage of the Federal Food, Drug and Cosmetic Act (FDCA) in 1906, 21 U.S.C. 301 *et seq.*, we now rely on rigorous scientific proof to assure the safety and effectiveness of new drugs. Mere stories are not considered an acceptable way to judge whether dangerous drugs should be used as medicines.

There are doctors willing to testify that marijuana has medical uses NORML found over a dozen to testify in this case. We have a natural tendency to believe doctors. We assume their opinions are entitled to respect. But what if a doctor is giving an opinion beyond his professional competence? Evaluating the safety and effectiveness of drugs is a specialized area. Does the doctor have this specialized expertise? Is he familiar with all the published scientific studies? Or is he improperly basing his opinion on mere stories or anecdotal evidence? Does he really know what he is talking about? Does he have a personal motive to exaggerate or lie? Questions like these led the United States Supreme Court, in 1973, to warn about the opinions of doctors concerning the value of drugs as medicine, when not supported by rigorous scientific testing. *Weinberger* v. *Hynson, Etc.*, U.S. 609, 639:

> [I]mpressions or beliefs of physicians, no matter how fervently held, are treacherc

Nearly half the doctors who testif for NORML are psychiatrists. They not specialize in treating or researci cancer, glaucoma or MS. One is a general practitioner who works as a wellness counselor at a health spa. Under oath he admits to using every illegal, mind-altering drug he has ev studied, and he prides himself on recommending drugs that would ne be recommended by medical schoo reputable physicians. Another is a general practitioner who quit practi in 1974. He admits he has not kept u new medical and scientific informa about marijuana for 18 years.

Only one of the doctors called by NORML is a nationally-recognized expert. Doctor John C. Merritt is a board-certified ophthalmologist an researcher who has authored articl the use of marijuana and cannabin to reduce eye pressure. He is in pri practice and sees mostly children v suffer from glaucoma. Doctor Merr testified, "[M]arijuana is a highly effective IOP-lowering drug which be of critical value to some glaucor patients who, without marijuana, v progressively go blind." The last scientific study using marijuana in glaucoma patients, published by D Merritt in 1979, concluded:

> It is because of the frequency and se with which the untoward events occur that marijuana inhalation is not an ide therapeutic modality for glaucoma pati

One year later, in 1980, Doctor M gave the following testimony, unde oath, before the United States Con House Select Committee on Narco Abuse and Control:

> For me to sit here and say that the lo pressure effects occurred repeatedly, d and day out, I have no data, and neithe anyone else, and that is the real crux o matter. When we are talking about trea disease like glaucoma, which is a chron disease, the real issue is, does the man repeatedly lower the intraocular pressu have shown you no * * * studies, and knowledge there is no data to that effe

Doctor Merritt was unable to ex under oath, the contradictory posi he has taken on this subject.

Each of NORML's doctors testifi opinion is based on the published scientific studies. With one excepti none of them could identify under the scientific studies they swore th relied on. Only one had enough knowledge to discuss the scientific technicalities involved. Eventually

one admitted he was basing his opinion on anecdotal evidence, on stories he heard from patients, and on his impressions about the drug.

Sadly, Doctor Ivan Silverberg, an oncologist from San Francisco, exaggerated while on the witness stand. At first he swore "there is voluminous medical research which shows marijuana is effective in easing nausea and vomiting." Pushed on crose-examination to identify this voluminous research, Doctor Silverberg replied, "Well * * *, I'm going to have to back off a little bit from that." How far would Doctor Silverberg back off? Was he aware, at least, of the approximate number of scientific studies that have been done using marijuana to treat nausea? Under oath, he replied, "I would doubt very few. But, no, I'm not."

Beyond doubt, the claims that marijuana is medicine are false, dangerous and cruel.

Sick men, women and children can be fooled by these claims and experiment with the drug. Instead of being helped, they risk serious side effects. If they neglect their regular medicines while trying marijuana, the damage could be irreversible. It is a cruel hoax to offer false hope to desperately ill people.

Those who insist marijuana has medical uses would serve society better by promoting or sponsoring more legitimate scientific research, rather than throwing their time, money and rhetoric into lobbying, public relations campaigns and perennial litigation.

Clarification of Currently Accepted Medical Use

The Controlled Substances Act of 1970 divides the universe of all durgs of abuse into five sets or schedules. Drugs in Schedule I are subject to the most severe controls, because they have a high potential for abuse and no currently accepted medical use in treatment in the United States. 21 U.S.C. 812 (b)(1). Drugs of abuse which have currently accepted medical use in treatment in the United States are placed in Schedules II, III, IV and V. Regrettably, the Controlled Substances Act does not speak directly to what is meant by "currently accepted medical use."

A century before the Controlled Substances Act was enacted, the determination of what drugs to accept as medicine was totally democratic and totally standardless. Each patient and each physician was free to decide for himself, often based on no more than anecdotal evidence. This state of affairs became unsatisfactory to a majority of the American people. In 1906, Congress intervened with the passage of the Food, Drug and Cosmetic Act (FDCA). A shift began away from anecdotal evidence to objectively conducted scientific research, away from uninformed opinions of lay persons and local doctors to expert opinions of specialists trained to evaluate the safety and effectiveness of drugs, and away from totally democratic decision-making to oversight by the Federal Government.

By 1938, Congress had developed detailed Federal statutory criteria under the FDCA to determine whether drugs are acceptable for medical use. Those deemed acceptable can be marketed nationally. Those deemed unacceptable are subject to Federal seizure if marketed interstate. The FDCA is a very complex regulatory scheme not easily summarized. However, it is fair to say that drugs falling into one of four FDCA categories were accepted by Congress for medical use.

First, Congress accepted new drugs which have been approved by FDA's experts as safe and effective for use in treatment, based on substantial scientific evidence. 21 U.S.C. 321(p) and 355 (so-called "NDA-approved drugs").

Second, Congress accepted those drugs "generally recognized, among experts qualified by scientific training and experience to evaluate the safety and effectiveness of drugs, as safe and effective," based on substantial scientific evidence. 21 U.S.C. 321(p) and 355; *Weinberger* v. *Bentex Pharmaceuticals, Inc.*, 412 U.S. 645 (1973). An acronym for this category is "human GRASE drugs" (Generally Recognized As Safe and Effective). These drugs achieve acceptance through rigorous scientific proof, through a past history of widespread use in treatment in the United States, and through recognition by a consensus of drug experts outside the FDA.

Third, Congress accepted for use in veterinary medicine those drugs "generally recognized, among experts qualified by scientific training and experience to evaluate the safety and effectiveness of animal drugs, as safe and effective," based on substantial scientific evidence. 21 U.S.C. 321(w) and 355. An acronym for these is "animal GRASE drugs." They achieve acceptance through rigorous scientific evidence and through recognition by a consensus of drug experts outside the FDA. Unlike human GRASE drugs, animal GRASE drugs need not have a past history of widespread use.

Finally, Congress accepted those drugs marketed prior to 1938 which had been subject to the 1906 provisions of the FDCA, provided these very old drugs retain their exact formulations and are never promoted for new uses. 21 U.S.C. 321(p) and (w). These are politically "grandfathered" drugs. They need not meet modern standards for safety and effectiveness.

A fifth group of drugs was accepted for research use only, not for use in treatment of patients. 21 U.S.C. 355(i) (so-called "IND or approved investigational new drugs").

Drugs intended for medical use and shipped interstate are subject to Feder seizure under the FDCA if they do not within one of the above accepted sets groupings. It seems fair to say that seizable drugs were rejected by Congress for medical uses.

In enacting the Controlled Substanc Act in 1970, could Congress have intended to create a totally new Feder standard for determining whether dru have accepted medical uses? Or did Congress intend to rely on standards i had developed over the prior 64 years under the FDCA? There is nothing in t Controlled Substances Act, its legislative history, or its purposes tha would indicate Congress intended to depart radically from existing Federa law.

Indeed, it seems likely that the core standards developed under the FDCA represent a long-term consensus of expert medical and scientific opinion concerning when a drug should be accepted by anyone as safe and effective for medical use.

Fortunately, there is a way to corroborate what Congress intended. Congress did more than just announc criteria for scheduling drugs of abuse under the Controlled Substances Act. Congress applied those criteria to an initial listing of drugs that it placed in the original five schedules of the Act.

NDA-approved drugs were placed Congress into Schedules II, III, IV an of the Act. For example, pethidine (a known as meperidine) received New Drug Application (NDA) approval in 1942. Congress put it into Schedule II(b)(14). Methamphetamine had an approved NDA. Congress put it into Schedule III(a)(3). I am not aware of drug with an approved NDA that Congress originally put into Schedul

Drugs with medical uses, but witho approved NDA's also were placed b Congress into Schedules II, III, IV an For example, cocaine was put into Schedule II(a)(4). Codeine combinati were put into Schedules III(d)(1) and Morphine combinations were put int Schedule III(d)(8). Phenobarbital wa put into Schedule IV(11). Barbiturate were put into Schedule III(b)(1). Amphetamines were put into Schedu III(a)(1).

The Court of Appeals for the First Circuit was correct when it decided

Grinspoon v. *DEA*, 828 F.2d 881 (1987) that NDA approval is not the only method by which drugs can achieve Federal recognition as having medical uses. Congress put both GRASE drugs and pre-1938-grandfathered drugs into Schedules II, III, IV and V of the CSA.

Drugs recognized under the FDCA for research use only, not for use in treatment, such as alphacetylmethadol and marijuana, were placed by Congress into Schedule I.

Unfortunately, Federal records are not complete enough to do a comprehensive mathematical mapping, tracing every drug in the initial Controlled Substances Act schedules back to its legal status under the FDCA. Nevertheless, determining legislative intent does not require mathematical certainty. Probability based on circumstantial evidence, on samplings, and on inductive reasoning can suffice, especially when there is nowhere else to turn.

The pattern of initial scheduling of drugs in the Controlled Substance Act, viewed in light of the prior legal status of these drugs under the FDCA, convinces me that Congress equated the term "currently accepted medical use in treatment in the United States" as used in the Controlled Substances Act with the core FDCA standards for acceptance of drugs for medical use.

This is not to say that every FDCA requirement for GRASE status, or for NDA approval, is pertinent to scheduling determinations under the Controlled Substances Act. There are differences. But the core FDCA criteria appear to have guided the Congress in the decisions it made concerning the initial scheduling of drugs in the Act.

These same core FDCA criteria served as the basis for an eight-point test used by my predecessor as Administrator to describe drugs with currently accepted medical uses. 54 FR 53783 (December 29, 1989):

1. Scientifically determined and accepted knowledge of its chemistry;
2. The toxicology and pharmacology of the substance in animals;
3. Establishment of its effectiveness in humans through scientifically designed clinical trials;
4. General availability of the substance and information regarding the substance and its use;
5. Recognition of its clinical use in generally accepted pharmacopeia, medical references, jounals or textbooks;
6. Specific indications for the treatment of recognized disorders;
7. Recognition of the use of the substance by organizations or associations of physicians; and
8. Recognition and use of the substance by a substantial segment of the medical practitioners in the United States.

Some uncertainty remains over the precise meaning and application of parts of this test. Therefore, the Court of Appeals for the District of Columbia Circuit remanded these proceedings for a further explanation. In addition to addressing those parts of the test that concerned the Court of Appeals, it would be useful to clarify the entire test, pinpoint its origins, and identify which elements are both necessary and sufficient to establish a prima facie case of currently accepted medical use. This is not an effort to change the substantive law. The statutory meaning of currently accepted medical use remains the same as enacted by Congress in 1970. My purpose simply is to clarify this Agency's understanding of the law.

A. The Drug's Chemistry Must Be Known and Reproducible

The ability to recreate a drug in standardized dosages is fundamental to testing that drug and to using it as a medicine. Knowing the composition, properties, methods of production, and methods of analysis of a drug is essential to reproducing it in standardized dosages. To be GRASE or to receive NDA approval, a drug's chemistry must be known and reproducible. See *e.g.*, 21 CFR 314.50(d)(1) and 314.126(b)(7)(d); *Dorovic* v. *Richardson*, 749 F.2d 242, 251 (7th Cir. 1973). The listing of a drug in a current edition of one of the official compendia normally satisfies this requirement. 21 U.S.C. 321(j); 21 CFR 314.50(d)(1).

The first element of our eight-point test, namely, "scientifically determined and acccepted knowledge of its chemistry," should be clarified to read:

The substance's chemistry must be scientifically established to permit it to be reproduced into dosages which can be standardized. The listing of the substance in a current edition of one of the official compendia, as defined by section 201(j) of the Food, Drug and Cosmetic Act, 21 U.S.C. 321(j), is sufficient generally to meet this requirement.

Acceptance of this knowledge will be discussed elsewhere.

B. There Must Be Adequate Safety Studies

No drug can be considered safe in the abstract. Safety has meaning only when judged against the intended use of the drug, its known effectiveness, its known and potential risks, the severity of the illness to be treated, and the availability of alternative therapies. *Hess & Clark Division of Rhodia, Inc.* v. *FDA*, 495 F.2d 975, 993 (D.C. Cir. 1974). To know the risks, there must be adequate stud all methods reasonably applicabl show the pharmacological and toxicological effects of the drug. 2 314.125(b)(2). This includes anima studies and clinical trials in large numbers of humans. 21 CFR 312.2 studies need not be well-controlle they must be adequate. *Edison Pharmaceuticals Co.* v. *FDA*, 600 837 (D.C. Cir. 1979). Short term (a studies of a drug intended to treat term (chronic) illnesses, such as glaucoma or MS, are clearly inad *United States* v. Naremco, Inc., 55 1138, 1143 (8th Cir. 1977). The sec element of our eight-point test, na "the toxicology and pharmacolog substance in animals," should be clarified as follows:

There must be adequate pharmacol and toxicological studies, done by all methods reasonably applicable, on th of which it could fairly and responsib concluded, by experts qualified by sc training and experience to evaluate t and effectiveness of drugs, that the s is safe for treating a specific, recogni disorder.

It must be emphasized that wh existence of adequate safety test separate analytical question, the ultimate determination of whethe drug is safe for a specific use is n distinct issue. Safety and effectiv are inextricably linked in a risks benefits calculation. A determina that a drug is ineffective is tantar to a determination that it is unsa *United States* v. *Rutherford*, 442 (1970).

The scheduling criteria of the Controlled Substances Act appe treat the lack of medical use and safety as separate consideration rulings of this Agency purported safety as a distinct factor. 53 FR (February 22, 1988). In retrospect inconsistent with scientific realit Safety cannot be treated as a sep analytical question.

C. There Must Be Adequate and Controlled Studies Proving Effic

Since 1962, Congress has proh the FDA to approve an NDA unl applicant submits adequate, wel controlled, well-designed, well-conducted, and well-documente studies, performed by qualified investigators, which prove the ef of a drug for its intended use. 21 355(d); 21 CFR 314.126. Similarly cannot be considered GRASE un is supported by this same quanti quality of scienfitic proof. 21 CFI 314.200(e)(i); *Weinberger* v. *Hyn Etc.*, 412 U.S. 609, 629 (1973).

Studies involving related, but not identical, drugs are irrelevant. *United States* v. *Articles of Food & Drug*, 518 F.2d 743, 747 (5th Cir. 1975). Studies involving the same drug combined with other drugs are irrelevant. *United States* v. *Articles of Drug * * * Promise Toothpaste*, *626 F.2d 584, 570 (7th Cir. 1987). Incomplete studies are insufficient. United States* v. *Articles of Food & Drug, supra.* Uncontrolled studies are insufficient. 21 U.S.C. 355(d); *Cooper Labs* v. *FDA*, 501 F.2d 772, 778 (D.C. Cir. 1974). Statistically insignificant studies are insufficient. 21 CFR 312.21, 314.50(d)(6) and 314.126(b)(7). Poorly designed studies are insufficient. 21 CFR 314.126(b)(2). Poorly conducted studies are insufficient. 21 CFR part 58—Good Laboratory Practices. Poorly documented studies are insufficient. 21 CFR 312.58 and 314.200(e)(4). Studies by investigators who are not qualified, both to conduct and to evaluate them are insufficient. 21 U.S.C. 355(d). Moreover, since scientific reliability requires a double examination with similar results, one valid study is insufficient. There must be two or more valid studies which corroborate each other. See 1 J. O'Reilley "Food and Drug Administration" 13–55 n.12 (1985).

Lay testimonials, impressions of physicians, isolated case studies, random clinical experience, reports so lacking in details they cannot be scientifically evaluated, and all other forms of anecdotal proof are entirely irrelevant. 21 CFR 314.126(e); *Weingerger* v. *Hynson, Etc.*, 412 U.S. 609, 630 (1973).

Element three of our eight-point test, namely, "establishment of its effectiveness in humans through scientifically designed clinical trials," should be restated as:

> There must be adequate, well-controlled, well-designed, well-conducted and well-documented studies, including clinical investigations, by experts qualified by scientific training and experience to evaluate the safety and effectiveness of drugs, on the basis of which it could fairly and responsibly be concluded by such experts that the substance will have the intended effect in treating a specific, recognized disorder.

D. Acceptance by Qualified Experts Is Required

The opinions of lay persons are totally irrelevant to whether a drug is GRASE or meets NDA requirements. The observations and opinions of medical practioners who are not experts in evaluating drugs also are irrelevant to whether a drug is GRASE or meets NDA requirements. *Weinberger* v. *Hynson, Etc.*, 412 U.S. 609, 619 (1973). By explicit requirements in the FDCA since 1938, the only body of opinion that counts is that of experts qualified by scientific training and experience to evaluate the safety and effectiveness of drugs. 21 U.S.C. 321 (p) and (w).

From this, one would conclude that expert acceptance of a drug as safe and effective for its intended use is essential to a drug having a currently accepted medical use under the CSA. How widespread must this expert acceptance be?

To be GRASE, a drug must be "generally recognized" among experts as safe and effective for its intended use. The drug must be known or familiar to the national community of relevant experts. *United States* v. *Articles of Drug * * * Furestrol Vaginal Suppositories*, 294 F. Supp. 1307, 1309 (N.D. Ga. 1968) *aff'd*, 415 F.2d 390 (5th Cir. 1969). To determine if a drug is known to the community of experts, courts have looked to whether there is widely available scientific literature about the drug, *Premo Pharmaceutical Laboratories, Inc.* v. *United States*, 629 F.2d 795, 803 (2d Cir. 1980), whether it is widely taught in medical schools, *Lemmon Pharmaceuticals Co.* v. *Richardson*, 319 F. Sup. 375, 378 (E.D. Pa. 1970), and whether it is widely discussed by experts. *United States* v. *Bentex Ulcerine*, 469 F. 2d 875, 880 (5th Cir. 1972).

The recognition of a drug as GRASE need not be universal. General recognition is sufficient. *United States* v. *41 Cartons * * * Ferro-Lac*, 420 F.2d 1128, 1132 (5th Cir. 1970). The Supreme Court has interpreted this to mean a consensus of experts is familiar with and accepts a drug as safe and effective. *Weinberger* v. *Hynson, Etc.*, 412 U.S. 609, 629 (1973). However, if there is a serious dispute among the experts, a drug cannot be considered GRASE. *United States* v. *An Article of Food * * * Coco Rico*, 752 F.2d 11, 15 (1st Cir. 1985); *Merrit Corp.* v. *Folsom*, 165 F. Supp. 418, 421 (D.D.C. 1958).

During the NDA process, the FDA may reach out to the expert community for its views. 21 CFR 314.103(c)(3). The FDA need not determine that a drug is generally known and accepted by the expert community. Nor must the FDA develop a consensus of opinion among outside experts. The FDA has both the experts and the statutory mandate to resolve conflicts over the safety and efficacy of new drugs. *Weinberger* v. *Bentex Pharmaceuticals, Inc.*, 412 U.S.C 638, 653 (1973).

In drafting the Controlled Substances Act, Congress appears to have accommodated, rather than chosen from these different FDCA standards. Clearly, the Controlled Substances Act does n authorize the Attorney General, nor b delegation the DEA Administrator, to make the ultimate medical and policy decision as to whether a drug should used as medicine. Instead, he is limite to determing whether others accept a drug for medical use. Any other construction would have the efect of reading the word "accepted" out of th statutory standard. Since Congress recognized NDA-approved drugs as having currently accepted medical us without any need for a national consensus of experts, FDA acceptanc of a drug through the NDA process would seem to satisfy the Controlled Substances Act. And, since Congress recognized GRASE drugs as having currently accepted medical uses, without the need for NDA approval, acceptance of a drug by a national consensus of experts also would seem satisfy the Act.

When a drug lacks NDA approval is not accepted by a consensus of experts outside FDA, it cannot be fou by the Attorney General or his deleg to have a currently accepted medical use. To do so would require the Attorney Genral to resolve complex scientific and medical disputes amon experts, to decide the ultimate medic policy question, rather than merely determine whether the drug is accep by others.

Because the recognition of a drug b non-experts is irrelevant to GRASE status, to NDA approval, and to currently accepted medical use unde the Controlled Substances Act, point seven and eight of our eight-point tes should be combined and restated as follows:

> The drug has a New Drug Application (NDA) approved by the Food and Drug Administration pursuant to the Food, Dru and Cosmetic Act, 21 U.S.C. 355. Or, a consensus of the national community of experts, qualified by scientific training a experience to evaluate the safety and effectiveness of drugs, accepts the safety effectiveness of the substance for use in treating a specific, recognized disorder. A material conflict of opinion among exper precludes a finding of consensus.

This restatement also incorporates component of part one of our eight-p test concerning "accepted knowledg its chemistry."

E. The Scientific Evidence Must Be Widely Available

Nothing in the FDCA, nor in FDA regulations, requires that scientific evidence supporting an NDA be published. This stems from the fact a consensus of experts outside FDA

not required for NDA approval. In contrast, most courts have held that a drug cannot be considered GRASE unless the supporting scientific evidence appears in the published scientific and medical literature. Without published studies, it would be difficult for the community of experts outside FDA to develop an informed acceptance of a drug for medical use. *Cooper Labs Inc. v. FDA*, 501 F.2d 772, 786 (D.C. Cir. 1974).

Point four of the eight-point test focuses, in part, on the "general availability of information regarding the substance and its use." This should be clarified to read:

> In the absence of NDA approval, information concerning the chemistry, pharmacology, toxicology and effectiveness of the substance must be reported, published, or otherwise widely available, in sufficient detail to permit experts, qualified by scientific training and experience to evaluate the safety and effectiveness of drugs, to fairly and responsibly conclude the substance is safe and effective for use in treating a specific, recognized disorder.

F. General Availability of a Drug Is Irrelevant

The second component of point four of the eight—point test involves the "general availability of the substance" for use in treatment. The second component of point eight focuses on "use of the substance by a substantial segment of the medical practitioners in the United States." These elements justifiably concerned the Court of Appeals, leading to the remand in this case.

Under the FDCA, a human GRASE drug must have a material history of past use in treatment in the United States. 21 U.S.C. 321(p)(2) (which has "* * * otherwise than in such investigations, been used to a material extent or a material time); *Weinberger v. Hynson, Etc.*, 412 U.S. 609, 631 (1973). Rigorous scientific proofs and current unanimous acceptance by the medical and scientific community are not enough for a human drug to be GRASE. *Tri-Bio Labs, Inc. v. United States*, 836 F.2d 135, 142 n.8 (3d Cir. 1987). The general availability of a drug for use in treatment is a factor courts have considered to determine if a human drug is GRASE.

In contrast, a drug can achieve current acceptance for human medical use through the NDA process without a past history of use in treatment. Also, animal drugs can become accepted as GRASE without any past history of medical use. Given this conflict in FDCA standards, which did Congress choose when drafting the CSA?

As the Court of Appeals points out, requiring a material history of past use in treatment before recognizing a drug as having a currently accepted medical use, would permanently freeze all Schedule I drugs into Schedule I. 930 F.2d at 940. Clearly, Congress did not intend this result. Moreover, the use of the word "currently" before the term "accepted medical use" would indicate Congress rejected the human GRASE requirement of past material use in treatment. I conclude that the general availability of a drug is irrelevant to whether it has a currently accepted medical use in treatment within the meaning of the Controlled Substances Act.

G. Recognition in Generally Accepted Texts Is Irrelevant

Point five of the eight-point test deals with "recognition of its clinical use in generally accepted pharmacopeia, medical references, journals or textbooks." The listing of a drug in an official compendium is sufficient to show its chemistry is scientifically established. This appears in my clarification to point one. The requirement that information concerning the chemistry, pharmacology, toxicology and effectiveness of the substance be reported, published or otherwise widely available, is explained adequately in revised point four. To the extent the scheduling of a drug directly influences its recognition in publications, this element is subject to the same criticism identified by the Court of Appeals concerning point four. Therefore, this should not be treated as a distinct requirement.

H. Specific, Recognized Disorders Are the Referent

It is impossible to judge the safety and effectiveness of a drug except in relation to a specific intended use. A drug cannot obtain NDA approval or GRASE status except in relation to the treatment of a specific, recognized disorder. This is an essential aspect of whether a drug has currently accepted medical use. Rather than standing alone, this requirement will be more clearly understood by incorporating it into the other critical elements.

To summarize, the five necessary elements of a drug with currently accepted medical use in treatment in the United States are:

(i) The Drug's Chemistry Must Be Known and Reproducible

The substance's chemistry must be scientifically established to permit it to be reproduced into dosages which can be standardized. The listing of the substance in a current edition of one of the official compendia, as defined by section 20 Food, Drug and Cosmetic Act, 21 U.S 321(j), is sufficient generally to meet requirement.

(ii) There Must Be Adequate Safety

There must be adequate pharmac and toxicological studies done by ali reasonably applicable on the basis o it could fairly and responsibly be co by experts qualified by scientific tra experience to evaluate the safety an effectiveness of drugs, that the subst safe for treating a specific, recognize disorder.

(iii) There Must Be Adequate and W Controlled Studies Proving Efficacy

There must be adequate, well-con well-designed, well-conducted and v documented studies, including clinic investigations, by experts qualified b scientific training and experience to the safety and effectiveness of drugs basis of which it could fairly and res be concluded by such experts, that t substance will have its intended eff treating a specific, recognized disor

(iv) The Drug Must Be Accepted by Experts

The drug must have a New Drug Application (NDA) approved by the Drug Administration, pursuant to th Drug and Cosmetic Act, 21 U.S.C. 35 consensus of the national communit experts, qualified by scientific train experience to evaluate the safety an effectiveness of drugs, must accept th and effectiveness of the substance o treating a specific, recognized disor material conflict of opinion among e precludes a finding of consensus.

(v) The Scientific Evidence Must Be Available

In the absence of NDA approval, information concerning the chemistr pharmacology, toxicology and effec of the substance must be reported, p or otherwise widely available in su detail to permit experts, qualified b scientific training and experience to the safety and effectiveness of drug and responsibly conclude the substa safe and effective for use in treating specific, recognized disorder.

Together these five elements constitute prima facie evidence drug has currently accepted me in treatment in the United State interest of total clarity, let me er those proofs that are irrelevant determination of currently acce medical use, and that will not b considered by the Administrato

(i) Isolated case reports;

(ii) Clinical impressions of practit

(iii) Opinions of persons not quali scientific training and experience to the safety and effectiveness of the s at issue;

(iv) Studies or reports so lacking as to preclude responsible scientific evaluation;

(v) Studies or reports involving drug substances other than the precise substance at issue:

(vi) Studies or reports involving the substance at issue combined with other drug substances:

(vii) Studies conducted by persons not qualified by scientific training and experience to evaluate the safety and effectivness of the substance at issue:

(viii) Opinions of experts based entirely on unrevealed or unspecified information:

(ix) Opinions of experts based entirely on theoretical evaluations of safety or effectiveness.

Bad Medicine By Any Standard

My predecessor as DEA Adminstrator developed and relied upon an eight-point test to determine whether marijuana has accepted medical uses. 54 FR 53783 (December 29, 1989):

1. Scientifically determined and accepted knowledge of its chemistry:

2. the toxicology and pharmacology of the substance in animals:

3. Establishment of its effectiveness in humans through scientifically designed clinical trials:

4. General availability of the substance and information regarding the substance and its use:

5. Recognition of its clincial use in generally accepted pharmacopeia, medical references, journals or textbooks:

6. Specific indications for the treatment of recognized disorders:

7. Recognition of the use of the substance by organizations or associations of physicians: and

8. Recognition and use of the substance by a substantial segment of the medical practitioners in the United States.

The Court of Appeals remanded the decision of my predecessor for clarification of what role factors (4), (5) and (8) of the initial eight-point test played in his reasoning. For ease of discussion, these factors can be divided as follows:

(4)(a) General availability of the substance * * *.

(4)(b) General availability of * * * information regarding the substance and its use:

(5) Recognition of its clinical use in generally accepted pharmacopeia, medical references, journals or textbooks:

(8)(a) Recognition * * * of the substance by a substantial segment of the medical practitioners in the United States: and

(8)(b) [U]use of the substance by a substantial segment of the medical practitioners in the United States.

I have found no evidence indicating initial factors (4)(a) or (8)(b) played any role in my predecessor's decision. In light of my understanding of the legal standard involved, these factors are irrelevant to whether marijuana has a currently accepted medical use.

My predecessor emphasized the lack of scientific evidence of marijuana's effectiveness, and the limited data available on its risks, as reflected in the published scientific studies. He also emphasized the importance of this data to the conclusions reached by experts concerning the drug. 54 FR 53783. I take this to mean that, under initial factor (4)(b), he believed the information available to experts is insufficient for them responsibly and fairly to conclude the marijuana is safe and effective for use as medicine.

Marijuana is not recognized as medicine in generally accepted pharmacopeia, medical references and textbooks, as noted by my predecessor. 54 FR 53784. I take this to mean, under initial factor (5), that he determined that marijuana's chemistry is neither known, nor reproducible, as evidenced by its absence from the official pharmacopeia. Finally, my predecessor concluded, under initial factor (8)(a), that the vast majority of physicians does not accept marijuana as having medical use. 54 FR 53784. Along the way, he found that highly respected oncologists and antiemetic researchers reject marijuana for use in controlling nausea and vomiting. 54 FR 53777, that experts experienced in researching glaucoma medications reject marijuana for use in treating glaucoma. 54 FR 53779, and that noted neurologists who specialize in treating and conducting research in spasticity reject marijuana for use by MS patients. 54 FR 53780. I take this to mean my predecessor found no national consensus of qualified experts accepts marijuana's value as medicine.

Certainly I cannot know my predecessor's unstated reasoning. However, I have reviewed the entire record *de novo*, and I am convinced that his application of the initial eight-point test to this record correctly resulted in the conclusion that marijuana has no currently accepted medical use in treatment in the United States. Therefore, I adopt in their entirety the findings of facts and conclusions of law reached by the former Administrator in his final order of December 21, 1989, 54 FR 53767.

Pursuant to the remand of the Court of Appeals, I have condensed and clarified the initial standard into a five-point test. My application of the refined, five-point test to this record is set out briefly below.

First, marijuana's chemistry is neither fully known, nor reproducible. Thus far, over 400 different chemicals have been identified in the plant. The proportions and concentrations differ from plant to plant, depending on growing conditions, age of the plant, harvesting and storage factors. THC levels can vary from less than 0.2% to over 10%. It is not known how smoking or burning the plant material affects the composition of these chemicals. It is not possible t reproduce the drug in dosages whi can be considered standardized by currently accepted scientific criter Marijuana is not recognized in any current edition of the official comp 21 U.S.C. 321(j).

Second, adequate safety studies not been done. All reasonably applicable pharmacological and toxicological studies have not been carried out. Most of the chronic an studies have been conducted with or intravenous THC, not with mari Pharmacological data on marijuan bioavailability, metabolic pathway pharmacokinetics in inadequate. S in humans are too small and too fe Sophisticated epidemiological stud marijuana use in large populations required, similar to those done for tobacco use. Far too many questio remain unknown for experts fairly responsibly to conclude marijuana safe for any use.

Third, there are no adequate, w controlled scientific studies provin marijuana is effective for anything

Fourth, marijuana is not accepte medical use in treatment by even respectable minority, much less a consensus, of experts trained to ev drugs. The FDA's expert drug eval have rejected marijuana for medic No NDA has been approved by FD marijuana. The testimony of natio recognized experts overwhelmingl rejects marijuana as medicine, compared to the scientifically emp testimony of the psychiatrists, a wellness counselor and general practitioners presented by NORM

Fifth, given my conclusions on p one, two and three, it follows that published scientific evidence is no adequate to permit experts to fair responsibly conclude that marijua safe and effective for use in huma

A failure to meet just one of the points precludes a drug from havi currently accepted medical use. Marijuana fails all five points of t

NORML has argued, unsuccessf that the legal standard for current accepted medical use should be w a respectable minority of physicia accepts the drug. The key to this medical malpractice defense is th minority opinion must be recogniz respectable, as competent, by mer of the profession.

In the absence of reliable evide adequately establishing marijuan chemistry, pharmacology, toxicol and effectiveness, no responsible physician could conclude that ma

is safe and effective for medical use. To quote Doctor Kenneth P. Johnson, Chairman of the Department of Neurology at the University of Maryland, and the author of over 100 scientific and medical articles on MS: "To conclude that marijuana is therapeutically effective without conducting rigorous testing would be professionally irresponsible."

By any modern scientific standard, marijuana is no medicine.

Under the authority vested in the Attorney General by section 201(a) of the Controlled Substances Act, 21 U.S.C. 811(a), and delegated to the Administrator of the Drug Enforcement Administration by regulations of the Department of Justice, 28 CFR 0.100(b), the Administrator hereby orders that marijuana remain in Schedule I as listed in 21 CFR 1308.11(d)(14).

Dated: March 18, 1992.

Robert C. Bonner,

Administrator.

[FR Doc. 92-6774 Filed 3-25-92; 8:45 am]

BILLING CODE 4410-09-M

NUCLEAR REGULATORY COMMISSION

ENVIRONMENTAL PROTECTION AGENCY

Proposed Guidance Document on the Testing of Mixed Radioactive and Hazardous Waste

AGENCIES: Nuclear Regulatory Commission, Environmental Protection Agency.

ACTION: Notice of availability and request for public comment.

SUMMARY: The Nuclear Regulatory Commission (NRC) and the Environmental Protection Agency (EPA) are jointly issuing a proposed guidance document on the testing of mixed radioactive and hazardous waste (mixed waste). This guidance document was developed to assist mixed waste generators in identifying and performing the testing required under the Federal regulations that implement the Resource Conservation and Recovery Act Subtitle C hazardous waste program and to ensure that employee radiation exposures are maintained As Low As Reasonably Achievable (ALARA). The agencies are soliciting comments from interested members of the regulated community, the States, and the public.

Interested individuals may provide the agencies with their comments on the proposed guidance document by forwarding their written comments to the NRC at the address listed in the "ADDRESSES" section. Interested parties may also participate in a public meeting being held to solicit oral comments on the proposed guidance document. Interested individuals will be given an opportunity to speak for fifteen minutes at this meeting. This time allowance may be extended, on request for good cause, if the schedule of speakers permits this extension.

DATES: The agencies will accept written comments until May 26, 1992. Individuals submitting comments after this date cannot be assured that the agencies will be able to afford their comments full consideration in any revisions that may be made to the proposed guidance document.

The public meeting to solicit oral comments on the proposed guidance document will be held on April 14, 1992, from 8:30 a.m. until 4:30 p.m. at the MayBower/Stouffer Hotel, New York Room 1127 Connecticut Avenue NW., Washington, DC 20036, telephone (202) 347-3000.

ADDRESSES: Copies of the proposed guidance document may be obtained by contacting Dominick A. Orlando, NRC Mixed Waste Project Manager, Division of Low-Level Waste Management and Decommissioning, Office of Nuclear Material Safety and Safeguards, U.S. Nuclear Regulatory Commission, Washington, DC 20555, telephone (301) 504-2566.

Written comments on the proposed guidance document should be directed to David L. Meyer, Chief, Regulatory Publications Branch, Division of Freedom of Information and Publications Service, Office of Administration, U.S. Nuclear Regulatory Commission, Washington, DC 20555 or hand delivered to the Commission's offices at 7920 Norfolk Avenue, Bethesda, MD between the hours of 7:45 a.m. and 4:14 p.m. on Federal workdays.

Requests to speak at the public meeting should be submitted, in writing, to EPA. The written request should be addressed to Reid Rosnick, Mixed Waste Coordinator, Permits and State Programs Branch, Office of Solid Waste (OS-342), U.S. Environmental Protection Agency, 401 M Street SW., Washington, DC 20460. Interested speakers should include in the written request a statement identifying the topics to be addressed in their presentations, the names and affiliations of the individual(s) that will speak, and the amount of time the speaker(s) will require. A transcript of the oral proceedings will be included in the record for this action.

FOR FURTHER INFORMATION CONTACT: Dominick A. Orlando, Mixed Waste Project Manager, Division of Low-Level Waste Management and Decommissioning, Office of Nuclear Material Safety and Safeguards, U.S. Nuclear Regulatory Commission, Washington, DC 20555, telephone (301) 504-2566 or: Reid Rosnick, Mixed Waste Coordinator, Permits and State Programs Division, Office of Solid Waste, U.S. Environmental Protection Agency, 401 M Street SW., Washington, DC 20460, telephone (202) 260-4755.

Dated at Rockville, MD this 19th day of March, 1992.

For the U.S. Nuclear Regulatory Commission.

Robert M. Bernero,

Director, Office of Nuclear Material Safety and Safeguards.

For the U.S. Environmental Protection Agency.

Sylvia K. Lowrance,

Director, Office of Solid Waste.

[FR Doc. 92-7031 Filed 3-25-92; 8:45 am]

BILLING CODE 7590-01-M

OFFICE OF MANAGEMENT AND BUDGET

Circular No. A-76: Performance of Commercial Activities; Amendmen

AGENCY: Office of Management and Budget.

ACTION: Issuance of Transmittal Memorandum No. 11, amending OM Circular No. A-76, "Performance of Commercial Activities."

SUMMARY: This notice contains Transmittal No. 11, dated February _____, 1992, to OMB Circular No. A "Performance of Commercial Activities."

This Transmittal Memorandum updates the Federal pay raise assumptions and inflation factors u for computing the Government's in-house personnel and non-pay cost increases for Fiscal Years 1992 thro 1997. The Federal pay raise assump and the non-pay category rates are contained in the President's Budget Fiscal Year 1993. The factors conta in OMB Circular No. A-76, Transm Memorandum No. 10, dated Februa 1991, are outdated.

The revision does not require an agency to (1) create or maintain a duplicate control/monitoring/repor system or (2) adopt any additional controls, not presently in complian with Federal Acquisition Regulatio (FAR).

FOR FURTHER INFORMATION CONTAC Mr. David Childs, Federal Services Branch, General Management Divi

DEPARTMENT OF JUSTICE

Drug Enforcement Administration

21 CFR Part 1308

Schedules of Controlled Substances; Temporary Placement of Bromazepam, Camazepam, Clobazam, Clotiazepam, Cloxazolam, Delorazepam, Estazolam, Ethyl Loflazepate, Fludiazepam, Flunitrazepam, Haloxazolam, Ketazolam, Loprazolam, Lormetazepam, Medazepam, Nimetazepam, Nitrazepam, Nordiazepam, Oxazolam, Pinazepam, and Tetrazepam into Schedule IV

AGENCY: Drug Enforcement Administration, Justice.

ACTION: Finale rule.

SUMMARY: This final rule is issued by the Administrator of the Drug Enforcement Administration to temporarily place twenty-one (21) benzodiazepine substances into Schedule IV of the Controlled Substances Act (CSA) (21 U.S.A. 801 *et seq.*). The 21 benzodiazepine substances are bromazepam, camazepam, clobazam, clotiazepam, cloxazolam, delorazepam, estazolam, ethyl loflazepate, fludiazepam, flunitrazepam, haloxazolam, ketazolam, loprazolam, lormetazepam, medazepam, nimetazepam, nitrazepam, nordiazepam, oxazolam, pinazepam, and tetrazepam. This temporary scheduling action is required in order for the United States to discharge its obligations under the Convention on Psychotropic Substances, 1971. The effects of this rule will be to require that the manufacture, distribution, dispensing, security, registration, record keeping, reporting, inventory, exportation and importation of each of the 21 benzodiazepines are subject to controls for Schedule IV substances. The temporary scheduling order for each substance shall remain in effect until the process of permanent scheduling, pursuant to sections 201 (a) and (b) (21 U.S.C. 811 (a) and (b)) of the CSA, is completed.

EFFECTIVE DATE: November 5, 1984.

FOR FURTHER INFORMATION CONTACT: Howard McClain, Jr., Chief, Drug Control Section, Drug Enforcement Administration, Washington, DC 20537, Telephone: (202) 633–1366.

SUPPLEMENTARY INFORMATION:

List of Subjects in 21 CFR Part 1308

Administrative practice and procedure, Drug traffic control, Narcotics, Prescription drugs.

By notice of March 29, 1984, the Secretary-General of the United Nations advised the Secretary of State of the United States that the Commission on Narcotic Drugs (CND) has decided that the above 21 benzodiazepine substances be added to Schedule IV of the Convention on Psychotropic Substances, 1971.

In a letter dated May 1, 1984, the Assistant Secretary for Health, on behalf of the Secretary of the Department of Health and Human Services (DHHS), advised the Administrator of the Drug Enforcement Administration that the 21 benzodiazepines be controlled in CSA Schedule IV, using authority provided by sections 201(d)(3)(B) and 201(d)(4) (A) and (C) of the CSA. This allows for the issuance of a temporary order controlling a substance in Schedule IV or V, depending upon whichever is most appropriate to carry out the minimum United States obligations, within the time period required by paragraph 7 of article 2 of the Convention, that is, within 180 days after the date of the CND communication. The findings pursuant to sections 201 (a), (b) and 202(b) which concern an assessment of the abuse potential for each of the 21 benzodiazepines are neither established nor required for this temporary scheduling order.

On Wednesday, August 1, 1984, a notice was published in the Federal Register (49 FR 30748–9) proposing to temporarily place the 21 benzodiazepines into Schedule IV of the CSA. By this action, the United States would be in compliance with the drug control treaty, the Convention on Psychotropic Substances, 1971. All interested persons were given until August 31, 1984 to submit any comments or objections regarding the proposal. No comments or objections were received in response to the proposal nor were there any requests for a hearing.

Therefore, under the authority vested in the Attorney General by section 201(d)(4) (A) and (C) of the CSA (21 U.S.C. 811(d)(4) (A) and (C)) and delegated to the Administrator of the Drug Enforcement Administration by regulations of the Department of Justice (28 CFR Part 0.100), the Administrator hereby orders that paragraph (c) of § 1308.14 be amended by revising the list of controlled substances to read as follows:

§ 1308.14 Schedule IV.

* * * * *

(c) * * *

(1) Alprazolam	2882
(2) Barbital	2145
(3) Bromazepam	2748
(4) Camazepam	2749
(5) Chloral betaine	3480
(6) Chloral hydrate	2465
(7) Chlordiazepoxide	2744
(8) Clobazam	2751
(9) Clonazepam	2737
(10) Clorazepate	2768
(11) Clotiazepam	2752
(12) Cloxazolam	2753
(13) Delorazepam	2754
(14) Diazepam	2765
(15) Estazolam	2756
(16) Ethchlorvynol	2540
(17) Ethinamate	2545
(18) Ethyl loflazepate	2758
(19) Fludiazepam	2759
(20) Flunitrazepam	2763

(21) Flurazepam	2767
(22) Halazepam	2762
(23) Haloxazolam	2771
(24) Ketazolam	2772
(25) Loprazolam	2773
(26) Lorazepam	2885
(27) Lormetazepam	2774
(28) Mebutamate	2800
(29) Medazepam	2836
(30) Meprobamate	2820
(31) Methohexital	2264
(32) Methylphenobarbital (mephobarbital)	2250
(33) Nimetazepam	2837
(34) Nitrazepam	2834
(35) Nordiazepam	2838
(36) Oxazepam	2835
(37) Oxazolam	2839
(38) Paraldehyde	2585
(39) Petrichloral	2591
(40) Phenobarbital	2285
(41) Pinazepam	2883
(42) Prazepam	2764
(43) Temazepam	2925
(44) Tetrazepam	2886
(45) Triazolam	2887

. . . . .

Effective Dates for applicable regulations:

All regulations applicable to each of the 21 benzodiazepines as temporarily controlled substances in Schedule IV of the CSA are effective on November 5, 1984, except as otherwise provided below:

1. *Registration.* Any person who manufactures, distributes, imports or exports any of the 21 benzodiazepines or who engages in research or conducts instructional activities, must apply for registration by November 5, 1984, to conduct such activities in accordance with Parts 1301 and 1311 of Title 21 of the Code of Federal Regulations.

2. *Security.* Each of the 21 benzodiazepines must be manufactured, distributed and stored in accordance with §§ 1301.71–1301.76 of Title 21 of the Code of Federal Regulations.

3. *Labeling and Packaging.* All labels and labeling for commercial containers of each of the 21 benzodiazepines must comply with the requirements of §§ 1302.03–1302.05 and 1302.06 of Title 21 of the Code of Federal Regulations by February 4, 1985.

4. *Inventory.* Every registrant required to keep records who possesses any quantity of any of the 21 benzodiazepines must take inventories pursuant to §§ 1304.11–1304.19 of Title 21 of the Code of Federal Regulations, of all stocks of these substances on hand.

5. *Records and Reports.* All registrants required to keep records and submit reports pursuant to Part 1304 of Title 21 of the Code of Federal Regulations shall do so regarding each of the 21 benzodiazepines.

6. *Prescriptions.* None of the 21 benzodiazepines can be prescribed since none have attained accepted medical use in treatment status in the United States, as would be indicated by approval of a new drug application by the Foods and Drug Administration.

7. *Importation and Exportations.* All importation and exportation of each of the 21 benzodiazepines shall be in compliance with Part 1312 of Title 21 of the Code of Federal Regulations.

8. *Criminal Liability.* The Administrator, Drug Enforcement Administration, hereby orders that any activity with respect to each of the 21 benzodiazepines not authorized by, or in violation of, the Controlled Substances Act or the Controlled Substances Import and Export Act, conducted after (November 5, 1984) shall be unlawful, except that any person who is not now registered to handles each benzodiazepine but who is entitled to registration under such Acts may continue to conduct normal business or professional practice with any of the 21 benzodiazepines between the date on which this rule is published and the date which the person obtains or is denied registration provided that the application for such registration is submitted on or before November 5, 1984.

Pursuant to 5 U.S.C. 605(b), the Administrator certifies that the placement of the 21 benzodiazepines into Schedule IV of the CSA will have no impact upon small businesses or other entities whose interests must be considered under the Regulatory Flexibility Act (Pub. L. 96-354). This action involves the initial control of substances with no legitimate medical use in the United States and must be carried out in order to fulfill United States international treaty obligations, in any event.

In accordance with the provisions of 21 U.S.C. 811(d), this scheduling action is a formal rulemaking that is required by United States obligations under international convention, that is, the Convention on Psychotropic Substances, 1971. Such formal proceedings are conducted pursuant to the provisions of 5 U.S.C. 556 and 557, and as such, have been exempted from the consultation requirements of Executive Order 12991 (46 FR 13193).

Dated: October 1, 1984.

Francis M. Mullen, Jr.,

Administrator, Drug Enforcement Administration.

[FR Doc. 84-[illegible] Filed 10-4-84; 8:45 am]

BILLING CODE 4410-09-M

98TH CONGRESS
2d Session
HOUSE OF REPRESENTATIVES
REPT. 98-835
Part 1

DANGEROUS DRUG DIVERSION CONTROL ACT OF 1984

JUNE 12, 1984.—Ordered to be printed

Mr. HUGHES, from the Committee on the Judiciary, submitted the following

REPORT

[To accompany H.R. 5656 which on May 15, 1984, was referred jointly to the Committee on the Judiciary and the Committee on Energy and Commerce]

[Including cost estimate of the Congressional Budget Office]

The Committee on the Judiciary, to whom was referred the bill (H.R. 5656) to amend the Controlled Substances Act to strengthen the authority to prevent diversion of controlled substances, and for other purposes, having considered the same, report favorably thereon with an amendment and recommend that the bill as amended do pass.

The amendment is as follows:

Strike out all after the enacting clause and insert in lieu thereof the following:

That (a) this Act may be cited as the "Dangerous Drug Diversion Control Act of 1984".

(b) Whenever in sections 2 through 14 an amendment or repeal is expressed in terms of an amendment to, or repeal of, a section or other provision, the reference shall be considered to be made to a section or other provision of the Controlled Substances Act, and whenever in sections 15 through 21 an amendment or repeal is expressed in terms of an amendment to, or repeal of, a section or other provision, the reference shall be considered to be made to a section or other provision of the Controlled Substances Import and Export Act.

SEC. 2. (a) Section 102 (21 U.S.C. 802) is amended by redesignating paragraphs (14) through (29) as paragraphs (15) through (30), respectively, and by adding after paragraph (13) the following:

"(14) The term 'isomer' means the optical isomer, except as used in schedule I(c) and schedule II(a)(4). As used in schedule I(c), the term 'isomer' means the optical, positional, or geometric isomer. As used in schedule II(a)(4), the term 'isomer' means the optical or geometric isomer.".

(b) Paragraph (17) (as so redesignated) of section 102 is amended to read as follows:

"(17) The term 'narcotic drug' means any of the following whether produced directly or indirectly by extraction from substances of vegetable origin, or independ-

The Subcommittee felt that these concerns were meritorious and narrowed the scope fo the factor to apply to "such other conduct which may threaten the public health and safety." This change satisfactorily responds to those concerns.

Seizing drugs of an out-of-business registrant

The American Pharmaceutical Association and the American Veterinary Medical Association expressed concern that a minimum 90-day period before the Attorney General could destroy the controlled substances sealed or seized from an out-of-business registrant provided for in H.R. 4698 was too short. The Subcommittee took these meritorious concerns into consideration in revising section 8 by lengthening the period of time and adding certain protective procedures.

Emergency scheduling

The proposal for emergency scheduling was subject to extensive comment and concern by the American Medical Association, the American Pharmaceutical Association, the American Veterinary Medical Association and the Pharmaceutical Manufacturers Association. All of these concerns were based on a perception that drugs currently used in medical treatment might be subject to temporary control by the Attorney General who would take into consideration principally law enforcement issues. Consequently, several witnesses urged that the bill permit emergency scheduling only if there were affirmative concurrence of the Secretary of Health and Human Services. Indeed, it appeared that the Administration had this understanding of its proposal in view of the testimony of the Department of Health and Human Services.

The Subcommittee believed that these concerns raised significant questions about the impact an emergency scheduling authority would have on the manufacture and distribution of drugs that are currently used in medical treatment. In examining the particular substances for which the scheduling action was most necessary, the Subcommittee concluded that limiting the authority only to substances that have no currently accepted medical use in treatment addressed both the legitimate concerns of those in the health care industry and the principal danger to the public health.

Registration of importers and exporters

The original version to these amendments (H.R. 4698) included two sections (sections 19 and 21) that were designed to eliminate the cross-references from the Controlled Substances Import and Export Act (section 1008 (a) and (c)) (21 U.S.C. 958 (a) and (c)) to the Controlled Substances Act (section 303(a) and (d) (21 U.S.C. 823 (a) and (d)) with respect to the registration criteria for importers and exporters.

At full Committee markup of the Subcommittee's reported bill, those sections were deleted because by eliminating language that related to the manufacture of drugs, they created the appearance of a change in policy although no policy change was intended.

The current law is settled, and does not need to be revised to resolve any ambiguity. The Administration and the affected parties

urged that the current law be retained. The Committee agreed and struck out those two sections.

Hearing on application for registration to import Schedule I and II substances

The Administration had urged that section 1008(h) (21 U.S.C. 958(h)) be amended to eliminate a right for registered bulk manufacturers to intervene in the application of a party to become an importer of Schedule I or II substances. A recent proceeding under this section lasted for several years and involved a commitment of several thousand hours of DEA staff time. The Administration suggested that the hearing did not substantially contribute to the determination of the legal and factual issues involved.

The Committee believes that the opportunity for public hearings in these matters are important and should be retained. The questions of additional registration often involves economic questions concerning the adequacy of competitive conditions for which expert testimony can be valuable. Therefore, the Committee deleted that portion of section 22 of the Subcommittee's reported bill which would have eliminated the right to a public hearing. This action retains current law.

The Committee, however, wants to express its concern that these hearings not be permitted to be used for purposes of unreasonable delay in the consideration of meritorious applications for registration. The Committee urges that these matters be resolved expeditiously.

Section-by-Section Analysis

Section 1. Short Title: The Dangerous Drug Diversion Control Act of 1984.

Section 2. (a) The term "isomer" is defined to eliminate the potential ambiguity regarding different types of isomers used in the definitions of various controlled substances.

(b) The term "narcotic drug" is redefined for added clarity with respect to the derivatives of opium and opiates and the derivatives of coca leaves, including cocaine and ecgonine. Newly included in the term are "poppy straw", and "concentrate of poppy straw", major narcotic raw materials that are imported into the United States.

(c) Schedule II(A)(4) is amended to explicitly include as a derivative of coca leaves cocaine and ecgonine and their salts, isomers, derivatives and salts of isomers and derivatives. Coupled with the definition of the term "isomer", as used in this paragraph of Schedule II. defenses to prosecutions under the Act with respect to cocaine will be precluded from raising what has been called the "isomer defense."

Section 3. This section creates a new procedure for scheduling substances on an expedited and temporary basis which have no currently accepted medical use in treatment in the United States when they are found by the Attorney General to pose an imminent hazard to the public health.

This new procedure is intended by the Committee to apply to what has been called "designer drugs", new chemical analogs or

variations of existing controlled substances, or other new substances, which have a psychedelic, stimulant or depressant effect, and have a high potential for abuse.

Examples of such drugs include PCE and PHP which have been clandestinely developed and manufactured to imitate the effects of the controlled psychedelic drug, PCP. Other substances, fentanyl analogs, have been developed and marketed illicitly as "synthetic heroin". In other cases, substances which have been known to chemists for some time, are "discovered" by illicit drug researchers to have psychedelic effects. The substance, MPPP, is an example, which is similar to the schedule II drug, meperidine (Demerol). In 1982, illicitly manufactured MPPP was sold in California. It was contaminated in the course of its improper manufacture with a related toxic chemical, MPTP, which caused Parkinson's disease-like symptoms in the users. Over 140 cases of MPTP induced Parkinson's Disease symptoms have been confirmed. The MPPP/MPTP incident appears to have been single incident. However, the ability to establish controls on MPPP, if its production for drug abuse were to be encountered more often, would be important to protect the public health and to prosecute those who wantonly risk the public health.

Section 3 of the bill adds a new subsection (h) to the section relating to scheduling.

Paragraph (1) provides that the Attorney General by order may schedule a substance in Schedule I without regard to the requirement of 21 U.S.C 811(b) relating to the Secretary of Health and Human Services if the scheduling is necessary to avoid an imminent hazard to the public safety.

The order may only be issued after 30 days have elapsed from the date of publication of a notice of intention to issue such a order in the Federal Register along with the grounds upon which such an order is to be issued. The order may only be issued after 30 days have elapsed from the date the Attorney General transmits notice of the proposed order to the Secretary of Health and Human Services. The two 30-days periods may be concurrent.

Paragraph (2) provides that the scheduling shall expire at the end of 1 year from the issuance of the order. However, if a rulemaking proceeding to schedule the substance has been initiated pursuant to section 201(a)(1) (21 U.S.C. 811(a)(1)), the Attorney General may extend the temporary scheduling for up to 6 months.

Paragraph (3) provides that the Attorney General in finding that a substance poses an imminent hazard to the public safety shall consider three factors in paragraphs (4), (5) and (6) of section 201(c):

The substance's "history and current pattern of abuse"; "The scope, duration and significance of abuse"; "What, if any, risk there is to the public health"; and include in the consideration actual abuse, diversion from legitimate channels, and clandestine importation, manufacture, or distribution.

Paragraph (4) provides that the Attorney General transmit to the Secretary of Health and Human Services notice of the order to schedule a substance that he proposes to issue. The Attorney General is directed to take into consideration any comments submitted by the Secretary in response to the transmitted notice. The Attorney General's authority to issue a temporary scheduling order is

List of Substances placed in "Temporary Scheduling to Avoid Imminent Hazards to Public Safety" Pursuant to 21 U.S.C. 811(h)

Methcathinone	Sch I
Aminorex	Sch I
Alpha-Ethyltryptamine	Sch I
4-bromo-2,5-dimethoxyphenethylamine	Sch I
Thenylfentanyl	Sch I
Benzylfentanyl	Sch I
N,N-Dimethylamphetamine	Sch I
4-Methylaminorex	Sch I
Beta-Hydroxy-3-methylfentanyl	Sch I
Acetyl-alpha-methylfentanyl	Sch I
Alpha-methylthiofentanyl	Sch I
Beta-hydroxyfentanyl	Sch I
3-methylthiofentanyl	Sch I
Thiofentanyl	Sch I
3,4-methylenedioxy-N-ethylamphetamine	Sch I
N-hydroxy-3,4-methylenedioxyampetamine	Sch I
Para-fluorofentanyl	Sch I
N-ethyl MDA	Sch I
N-hydroxy MDA	Sch I
3,4-methylenedioxymethamphetamine	Sch I
3-methylfentanyl	Sch I
1-methyl-4-phenyl-4-propionoxypiperidine (MPPP)	Sch I
1-(2-phenethyl)-4-phenyl-4-acetoxypiperidine (PEPAP)	Sch I

Rohypnol Talking Points

- Chemical name
    - flunitrazepam
        - The drug is a benzodiazepine, the same class as valium
            - The pill is 10 times strong than valium
            - The pill is round, flat, and the size of an antacid. The word "roche" (pronunced "RO-shay") with an encircled 2 are embosed on the tablet.
    - given as sleep aid or for the sedation of psychotics; in Latin American countries, it is used as a sediation for patients undergoing surgery
- Slang terms
    - "roofies, "poor man's Quaalude, "ruffies", "roach", "forget pill", "Mexican valium", "Date rape drug"
- Side effects
    - hallucinations
    - respiratory problems
    - sleep disturbances
    - anexity
    - amensia
    - reduces inhibitions
    - combined with alcohol, the pills have an added depressant effect
        - Some men have been known to give this drug to women in an alcoholic drink so he can sexually dominate her after the pill takes effect and she will not recall the incident
- Dangerous pill since October, 1990
    - Always classified as illegal in US

- Produced in US by Roche, an American-Swiss pharmaceuticals company
    - Shipped to oversees markets
    - Usually re-enters US through traditional heorin and cocaine routes
- Who uses the pill
    - teenagers
        - very cheap
            - price ranges from $.50 to $3 per pill
            - does not cause nausea or easily detectable in UAs
            - Kids get drunk quickly and it lasts longer
            - Easily available in all-night dance clubs, schools
    - gangs
        - used as part of initiation rites
        - used in gang rapings, which can also be part of an initiation rite
    - heroin addicts
        - enhances sedating effects of lower-purity heroin
    - cocaine addicts
        - use it ot parachute down from a binge
        - these two substances were found in grunge singer body, Curt Corbain, blood samples after a suicide attempt in Europe
            - Substance has caused two deaths in Texas
                - used primarily in the South

January 10, 1996

Presidential Memorandum on the drug, Rohypnol

Proposed Action

President signs a Memorandum to the Attorney General to schedule Rohypnol as a Schedule I substance (subjecting it to the strongest possible restrictions under the law) under the Drug Abuse and Prevention Control Act.

Purpose

This drug is widely used by adolescents, the one age segment in which drug use is increasing. Senator Biden recently wrote a report on youth drug use, which addresses the use of this drug and he is proposing legislation to increase the restrictions on this drug. This Presidential Memorandum will show action and leadership -- that he is willing to address the growing youth drug use problem head-on, do all within his power to curb its use, and not wait for the legislative process to accomplish a goal that he can implement immediately.

Background

Rohypnol is a drug that has recently hit the youth scene and has quickly become popular. It was first documented in the U.S. in June 1993 by the National Institute on Drug Abuse. Its use incredibly pervasive in South Florida and its use by teenager has now been reported in 30 States.

Rohypnol is classified as a depressant, and as such, it can be fatal if combined with alcohol. Although it is marketed legally in many countries around the world, it has no legal use in the United States. Where Rohypnol is available legally, it is primarily used as sedative/hypnotic to treat insomnia and for some anastethetic procedures.

Rohypnol has been widely reported as used for date rape. In fact, in many areas and in a number of newspaper accounts, Rohypnol has been referred to as a "date rapte drug."

The most famous example of Rohypnol overdose made the news when Kurt Cobain, lead singer of the rock band Nirvana, attempted suicide with a near fatal mixture of champagne and Rohypnol (Cobain was more successful the next time when he used a shotgun).

Biden -- what does his bill actually say?

What does changing to Schedule I really mean?

Do we the authority to only do it temporarily?

What are the steps that need to occur to schedule it "temporarily"?

Who manufactures this drug and where?

How many DEA busts have occurred in Florida and other States w/ regards to this drug?

DRAFT

ROHYPNOL - STATEMENT OF THE PROBLEM

The abuse of Rohypnol (flunitrazepam), a Schedule IV controlled substance, was first documented in June 1993. At that time, Rohypnol was only seen in South Florida; since then, according to DEA reports, use of the drug has spread throughout the South and investigative cases have now been reported in 32 states and Puerto Rico. It is a drug that is often abused by our nation's youth and is often associated with date rape.

Rohypnol has been described as 10 times as potent as diazepam (Valium) on a weight basis. Rohypnol slows psychomotor performance and induces amnesia, muscle relaxation and sleep. Its use may lead to the development of physical and psychic dependence.

Rohypnol is marketed extensively worldwide but is not manufactured or available for medical use in the United States. DEA reports that Rohypnol is being publicized on the Internet with advice being given how to import into the U.S.

The importation of Rohypnol as well as other prescription medication, is generally allowed regardless of citizenship or residency. The Code of Federal Regulations, 21 CFR 1311.27 allows an individual to import prescription drugs in his possession which he has lawfully obtained for his personal medical use or for administration to an animal accompanying him, providing the following conditions are met:

(a) The controlled substance is in the original container in which it was dispensed to the individual; and

(b) The individual makes a declaration to an appropriate official of the U.S. Customs Service stating:

(1) That the controlled substance is possessed for his personal use, or for an animal accompanying him; and

(2) The trade or chemical name and the symbol designating the schedule of the controlled substance if it appears on the container label, or, if such name does not appear on the label, the name and address of the pharmacy or practitioner who dispensed the substance and the prescription number, if any.

U.S. Customs allows individuals to enter the drug at ports of entry when crossing into the U.S. when proper documentation, per 1311.27, is presented. FDA regulations permit individuals a 3 month supply for "personal use". DEA reports that many individuals are abusing this regulation by acquiring a three month supply daily in Mexico and then stock pile the drug in the United States.

The Rohypnol problem is further enhanced in that a traveller may properly declare at the port, but if later stopped in the U.S., the drugs may be seized by state authorities and the violator is subject to arrest. This is occurring in the State of Texas.

For a prescription to be valid in the State of Texas it must have been issued by a doctor licensed and registered in Texas, or in another state if the doctor has a current Drug Enforcement Administration registration number and can legally prescribe controlled substances in that state. A prescription issued for a controlled substance by a doctor in Mexico is NOT VALID in Texas unless the doctor meets the above criteria. U.S. Customs does not enforce this state law.

U.S. Customs has seized over the past ----------
quantities of the drug Rohypnol at U.S. Customs mail facilities. Regulations do not allow the mailing of the drug; it must accompany the individual when entering the United States.

In South Florida, the drug is arriving primarily from Colombia via international mail services or commercial airlines with overnight mail appearing to be the preferred method of importation.

Although the previous drug czar, Mr. Lee Brown, in December 1995, stated that this is a not a national problem, Federal, State and Local law enforcement agencies believe it is and that abuse of Rohypnol is likely to increase.

CUSTOMS ACTION PLAN TO ADDRESS THE ROHYPNOL PROBLEM:

OBJECTIVE: Prohibit or restrict entry of prescription drugs into the United States. In partnership with other law enforcement agencies and with local communities, decrease the number of crimes related to prescription drug abuse.

SHORT TERM:

A series of enforcement initiatives and enhancements designed to increase Customs enforcement efforts, thereby increasing the amounts of prescription drugs voluntarily surrendered to Customs and/or seized by local law enforcement agencies. Obtain or force compliance by the travelling public and thereby reduce the abuse problem.

1) A letter from the President to Justice and Treasury is anticipated advising agencies of the level of abuse of the prescription drug Rohypnol. This letter most likely will advise that Treasury and Justice agencies should become proactive in addressing this problem. Customs should be proactive and write a letter (see attached) to DEA Administrator Constantine urging both agencies to work together to change regulations regarding the entry of prescription drugs into the United States.

Tasking: Commissioner's office

Start Date: February 22, 1996

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2) Seek cooperation with FDA. Do FDA regulations override DEA regulations? Can they be easily changed?

Tasking: Office of Field Operations, Office of Investigations

Start Date: February 22, 1996

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3) A letter should be written from U.S. Customs to Texas Department of Public Safety (DPS) advising DPS of Customs requirements to allow prescription drugs into the U.S, based on 21 USC 1311.27. This puts U.S. Customs on record with Texas DPS as recognizing the problem exists and what we can and will attempt to do about it.

Tasking: Office of Investigations, Office of Field Operations

Start Date: February 1996

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4) Commissioner Weise should seek ONDCP support to recognize this as a national problem.

Comment: In December 1995 was quoted as stating that this was not a national problem. Dr. Brown opposed - General McCaffrey may support

Tasking: Commissioner's office

Start Date: February 1996

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6) Posting of flyers (see Del Rio example). Generic poster in English and Spanish on reverse side. This flyer would be posted at all POE's on the Southwest border and in Customs offices nationwide.

Tasking: Office of Field Operations, Office of Investigations

Start Date: February 1996

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7) Media blitz per Port Director, Laredo suggestion. Work with local news stations, radio and newspapers along with other law enforcement agencies (ONDCP/State(s)/DEA/USC/FDA) to publicize increased efforts in enforcing the importation and unlawful distribution of prescription drugs

Question: ONDCP Funding?

Tasking: CMC (Public Affairs), Port Directors, Office of Investigations

Start Date: February 1996

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8) Seek cooperation with local law enforcement agencies in those states where it is against that State's law to bring prescription drugs into that state. Post a state law enforcement officer in Customs secondary.

Question: Legal? For all prescriptions?

Tasking: Office of Field Operations, Office of Investigations, Chief Counsel

Start Date: February 1996

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9) Initiate outreach efforts with local schools and the community. This would be a state/federal partnership.

Tasking: Office of Investigations
Start Date: March 1, 1996

10) Commissioner Weise to release a statement to the press regarding increased Customs efforts in partnership with other law enforcement agencies

Tasking: Commissioner's office

Start Date: March 1, 1996

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11) Explore changes to Customs policy/authority to enforce state law. Can we enforce State law? Do we want to enforce State law? Can we use discretion? (Example: Allow for the Elderly/AIDS patient/Cancer, etc).

Tasking: Office of Field Operations, Office of Investigations, Chief Counsel

Start Date: March 1996

LONG TERM:

Seek legislative change to the Controlled Substance Schedules for prescription drugs and/or in regulations regarding the importation of personal use quantities by residents/non-residents. Obtain compliance by the American public and thereby reduce the drug abuse problem nationally. Assist in a community policing effort to decrease crimes related to prescription drug abuse.

1) Support DEA's efforts to reschedule prescription drugs as a Schedule I drug.

Comment: A change from Schedule IV to Schedule I is not likely to happen, however, DEA has stated they will begin this process.

Tasking: Office of Investigations, Office of Field Operations
DEA

Start Date: February 13, 1996 - Continuing

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2) Seek Congressional support (Kiki De la Garza/Kasselbaum) for changes in law or regulations.

Comment: Kasselbaum has asked for FDA reform.

Tasking: Office of Congressional Affairs, Office of Field Operations, Office of Investigations, DEA and FDA

Start Date: March 1, 1996 - continuing

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3) Seek Change in 21 CFR 1311.27 and Customs regulations as follows:

- Limit quantities to a 30 day supply per declaration, instead of the current 90 day allowance for controlled substances in general

- Limit the exemption for entry of controlled substances for personal use to the standard "once in a 30 day" period which is currently in effect for the $400 personal exemption (19 CFR 148.36).

- requirement for a 48 hour stay abroad to be eligible for the $400 personal exemption should be required for the exemption for entry of controlled substances for personal use, except in specifically defined cases (19 CFR 148.35 9a))

- Require a written declaration for each entry of controlled substances for personal use (19CFR 148.13).

- If not successful in placing prescription drugs in Schedule I, then seek a change in regulations allowing only non-residents to import prescription drugs for personal use. U.S. citizens would not be allowed to import for personal use unless a prescription can be obtained from a U.S. medical doctor.

- In partnership with FDA enforce FDA labelling requirements in that if prescription drugs do not contain the following required information, entry will be denied:

- description, indications of usage, contraindications, warnings, adverse, reactions, drug abuse and dependence, (if a controlled substance must so indicate), overdosage, dosage and administration. The physician's name and prescription number must appear on the container.

Comment: Downside: AIDS/ELDERLY/Cancer/Financial considerations
Enforceable? - Would involve seeking cooperation from other countries

Tasking: Office of Field Operations, Office of Investigations in partnership with other agencies

Start Date: February 22, 1996 - continuing

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5) Through NAFTA negotiations, require Mexico to have their physicians log prescription dispensed and require identification to fill all prescriptions. Require that Mexican FDA police physicians and pharmacies to ensure that they are not allowing an individual to acquire more than a 3 month supply over a 3 month period.

Comment: Realistic? NAFTA issues?

Tasking: Office of Field Operations (NAFTA Task Force)
Office of Investigations, Foreign Operations

Start Date: March 1996 - continuing

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6) Customs Attache to work closely with Mexican authorities to make known the prescription drug abuse problem in the United States and how Mexican authorities can work with the United States in stopping the problem

Tasking: Customs Attache, Mexico

Start Date: March 1996 - continuing

TEST

Begin February 26, 1996 media blitz, posting of flyers, outreach and stationing of local law enforcement officers at ports of entry in the southwest border ports of Laredo, Del Rio, McAllen, Brownsville, El Paso. Evaluate after 90 days.

Measure effectiveness

Our effectiveness will be measured by:

1. The extent of cooperation by Mexican authorities

2. The extent of cooperation by U.S. law enforcement agencies, federal, state and local and Congressional members

3. The extent of cooperation with the local communities

4. Subsequent changes in monitoring dispensing of prescription drugs by Mexican authorities.

5. A change in the Controlled Substance Schedules, placing prescription drugs in Schedule I. REALISTIC? Not likely.

6. A change in regulations which would allow a 30 day supply of prescription drugs for non residents, NONE for U.S. residents unless a prescription can be obtained from a U.S. doctor.

7. A change in policy which would allow Customs to enforce state laws regarding prescription drugs

8. Changes in Customs policy - requiring a written CF 6059-B

9. Monitor seizure statistics and crime statistics. Is there a decrease in crime related to prescription drug abuse. Are seizures going down as the community is educated regarding abuse of the drug Rohypnol and other prescription drugs.

DEPARTMENT OF THE TREASURY

U.S. CUSTOMS SERVICE

DEL RIO, TEXAS

NOTICE

EVEN THOUGH A RETURNING UNITED STATES RESIDENT DECLARES MEDICATIONS CONTAINING CONTROLLED SUBSTANCES TO U. S. CUSTOMS AND CUSTOMS ALLOWS THE IMPORTATION, POSSESSION OF CERTAIN CONTROLLED SUBSTANCES IN THE STATE OF TEXAS MAY BE ILLEGAL.

UNDER TEXAS LAW FOR A PRESCRIPTION CONTAINING CERTAIN CONTROLLED SUBSTANCES TO BE VALID IT MUST HAVE BEEN ISSUED BY A DOCTOR LICENSED AND REGISTERED IN TEXAS, OR IN ANOTHER STATE IF THE DOCTOR HAS A CURRENT DRUG ENFORCEMENT ADMINISTRATION NUMBER AND CAN LEGALLY PRESCRIBE CONTROLLED SUBSTANCES IN THAT STATE. A PRESCRIPTION ISSUED FOR A CONTROLLED SUBSTANCE BY A DOCTOR IN MEXICO IS NOT VALID IN TEXAS UNLESS THE DOCTOR MEETS THE ABOVE CRITERIA.

QUESTIONS SHOULD BE DIRECTED TO A TEXAS DEPARTMENT OF PUBLIC SAFETY OFFICER.

PORT DIRECTOR OF CUSTOMS
DEL RIO, TEXAS
(210) 703-2012

DRAFT

The Honorable Thomas A. Constantine
Administrator
Drug Enforcement Administration
Washington, D.C. 20537

Dear Mr. Constantine:

The U.S. Customs Service and the Drug Enforcement Administration have each independently identified an issue which must be jointly addressed by our two agencies. Specifically, I am referring to the practice of importing, under the guise of for "personal use", small amounts of prescription medicines. Our respective agencies have identified the drug "Rohypnol" as one such drug, and others, which are being imported into the United States (U.S.) through our various ports of entry, most notably along the Southwest border. Rohypnol is not sold in the U.S., and has become a drug of abuse in Florida, Texas and in numerous other U.S. localities.

I have been informed that a joint USC/DEA meeting was held on February 13, 1996 at your headquarters to discuss this problem. It appears the basis for allowing "personal use" quantities of prescription drugs into the U.S. is derived from Chapter 21 Code of Federal Regulations, Section 1311.27. This regulation, combined with Food and Drug Administration guidelines which define personal use as a 90 day supply, is enabling those individuals who are so inclined to abuse the system. To make matters worse, certain States, such as Texas, prohibit possession of prescribed drugs which do not conform to State regulations, which are legally imported through Customs under 21 CFR 1311.27.

My staff is exploring alternatives within the Customs Regulations which would enable U.S. Customs to intercept these types of prescription drugs. However, unlike alcohol, there are no provisions to enforce state controls on other controlled substances. At this time, there does not appear to be any basis within the Customs Regulations to prevent abuses and importations utilizing this "loophole" in the Federal regulations. I am aware that it is no small undertaking, but it appears the only permanent solution to preventing abuses of prescription medicines is to rewrite 21 CFR 1311.27.

It is refreshing to see that our two agencies continue to undertake joint strategies and initiatives to address common problems.

Please call upon me if I or the Customs Service can be of assistance in helping you garner support for effecting the necessary changes to the Federal Regulations. We must continue to closely coordinate this matter, as the Customs Service must insure that any changes to 21 CFR 1311.27 are enforceable at our ports of entry.

Sincerely,

George J. Weise
Commissioner

E X E C U T I V E O F F I C E O F T H E P R E S I D E N T

22-Feb-1996 06:17pm

TO: BURKE_D

FROM: Mark Kleiman Crim.Just. 495

SUBJECT: Re: Conference

Dennis:

Rescheduling Rohypnol is probably only a partial solution. You might want to talk to Susan and get her thoughts. In any case, there's lots of prevention stuff to do, and methamphetamine is a much bigger problem, possibly a very big one indeed. In my previous I forgot to mention methcathinone, which is still a third problem. BOTEC could put together a pretty good emerging-drugs issues-and-options paper by conference time if we got going right away; one option would be to have CASA pay for it and BOTEC do it as a contractor for them.

Aside from coerced-abstinence stuff (establishing coerced abstinence as a national policy, requiring states to make measurements and do plans as a condition of getting their crime and drugs money, creating legislation to make it a reality in federal probation and pretrial) I'm a little thin on legislative ideas.

1. Resources (people and research money) for ONDCP. This should be easy.

2. Restore some of the CSAT (treatment) demonstration-program money, some of the HUD drug-elimination money, some of the DoEd drug-free schools and communities money, with a requirement that ONDCP evaluate these programs and report to Congress in eighteen months about what's worth doing and what isn't.

Argument: it's silly not to do something about these problems; if the money isn't currently being used right, let ONDCP sort it out. Maybe the Education money should be converted back from block grants, which have been abused, to categorical grants-in-aid, so Riley can make people spend it for the right stuff. But I think the HUD money has been well spent.

3. Authorize/require NIDA to conduct studies on drug trafficking, drug markets, and all aspects of drug abuse control including enforcement. Authorize/require CSAP to mount programs on preventing dealing as well as drug abuse.

I know all of this is boring. I'll try to come up with something interesting.

Mark