Withdrawal/Redaction Sheet
Clinton Library

DOCUMENT NO. AND TYPE	SUBJECT/TITLE	DATE	RESTRICTION
001. note	re: FDA Reform [partial] (1 page)	07/12/1996	b(6)

COLLECTION:

Clinton Presidential Records
Domestic Policy Council
Elizabeth Drye
OA/Box Number: 10452

FOLDER TITLE:

FDA Reform 1996 [2]

2014-0046-S
rc1402

RESTRICTION CODES

Presidential Records Act - [44 U.S.C. 2204(a)]

P1 National Security Classified Information [(a)(1) of the PRA]
P2 Relating to the appointment to Federal office [(a)(2) of the PRA]
P3 Release would violate a Federal statute [(a)(3) of the PRA]
P4 Release would disclose trade secrets or confidential commercial or financial information [(a)(4) of the PRA]
P5 Release would disclose confidential advice between the President and his advisors, or between such advisors [a)(5) of the PRA]
P6 Release would constitute a clearly unwarranted invasion of personal privacy [(a)(6) of the PRA]

C. Closed in accordance with restrictions contained in donor's deed of gift.
PRM. Personal record misfile defined in accordance with 44 U.S.C. 2201(3).
RR. Document will be reviewed upon request.

Freedom of Information Act - [5 U.S.C. 552(b)]

b(1) National security classified information [(b)(1) of the FOIA]
b(2) Release would disclose internal personnel rules and practices of an agency [(b)(2) of the FOIA]
b(3) Release would violate a Federal statute [(b)(3) of the FOIA]
b(4) Release would disclose trade secrets or confidential or financial information [(b)(4) of the FOIA]
b(6) Release would constitute a clearly unwarranted invasion of personal privacy [(b)(6) of the FOIA]
b(7) Release would disclose information compiled for law enforcement purposes [(b)(7) of the FOIA]
b(8) Release would disclose information concerning the regulation of financial institutions [(b)(8) of the FOIA]
b(9) Release would disclose geological or geophysical information concerning wells [(b)(9) of the FOIA]

The New York Times

Forget bookmarks. Build your library.
CLICK HERE TO CREATE YOUR CUSTOM START PAGE.

April 1, 1996

Creation of Food Safety Panel Criticized

Related Articles

- Political Points: A Guide to Web Resources
- Politics Index

By MARIAN BURROS

A little-noted amendment to the farm bill approved by the Congress last week is causing an uproar among consumer groups and even some producers of meat and poultry. But the framers of the amendment, Republican staff members of the House Agriculture Committee, say they cannot understand what all the furor is about.

The amendment creates a Safe Meat and Poultry Inspection Panel, with broad powers to review the decisions by the Department of Agriculture's Food Safety and Inspection Service on such matters as inspection procedures, food safety standards and practices in meat and poultry plants as well as work rules and labor relations.

Backers say the review panel would improve food safety by requiring more scientists to be involved in the decisions. Opponents say the panel's mandate will be too comprehensive. "We would grind to a halt," said Mike Taylor, acting under secretary for food safety and inspection services. "An incredible array of almost all the decisions we make would be put through this committee."

The creation of the panel comes at a time when the Agriculture Department is about to replace the current system of visual inspections of meat and poultry with a more scientific approach that includes microbial testing and performance standards.

While the industry does not agree with all provisions of the new system, called Hazard Analysis Critical Control Point, most in the industry are eager for it to begin.

Faced with an avalanche of reports of tainted meat and poultry that have caused thousands of cases of illness and hundreds of deaths each year, the industry sees the new system as a way to improve the public's perception of its products. The reports of the spread of what is known as mad cow disease in Britain have heightened their interest.

Carol Tucker Foreman, assistant secretary of agriculture for food and consumer services in the Carter administration who now works as a consultant on food issues, said the amendment was being treated as though it were an honest contribution to the safety process, but "it is not."

"It's intention," Mrs. Foreman said, "is to stop the implementation of performance standards and microbial testing."

The department's scientific methods seem to be under attack, she said, adding, "Some members of Congress didn't like USDA's science about harmful bacteria, so they are going to set up a panel to try to get the science they do like."

William O'Conner, the policy director of the House Agriculture Committee, which added the amendment, said the panel was "not designed to slow down the process" and was only advisory.

Besides, O'Conner said, "the HACCP rule is purported to be science-based, but it seemed clear that some of the regulatory decisions have no scientific validity. The regulations should never have gotten to this stage."

O'Conner said the review panel was necessary because the inspection service devised its new system without consulting its existing advisory panel, the National Advisory Committee for Microbiological Criteria for Meat and Poultry.

Taylor said, however, that was not true and provided documentation of the committee's meetings. "HACCP is based on the recommendations of that committee," he said.

At the largest producer of beef and pork in the world, IBP of Dakota City, Neb., officials say they have serious concerns about the review panel.

"It adds another layer of bureaucracy and potentially would delay innovations aimed at enhancing food safety regulations," said Gary Mickelson, an IBP spokesman.

The amendment would require the secretary of agriculture to submit formal regulations and informal directives to the review panel and respond in writing in the Federal Register to any panel report. The secretary would then have to allow an additional 90 days for public comment. If the secretary ignored a panel report, Mrs. Foreman said, the Agriculture Department could face a reduction in appropriations.

This system would make speedy decisions impossible, Taylor said. It would also hamper actions like the agency's recent directive to the beef industry for increased surveillance of cattle before slaughter because of an increase in what is known as mad cow disease in Britain and concern about a possible human form of the disease.

"We're dealing with an emergency situation," Taylor said. "With the panel in place, instead of being able to issue directions we'd be subject to the panel review process."

Unlike outside advisory panels at other agencies that are convened at the discretion of the agency head, the Agriculture review panel would decide which Food Safety and Inspection Service decisions it wanted to examine. In addition, it could meet in secret.

"Outside scientists can be quite useful," Taylor said, "but I don't know of any other advisory panel that decides how a department does business."

The amendment would also require the Agriculture Department to pay the travel and per diem costs for the seven-member panel out of the existing budget at a time when the inspection service is seeking additional money to run its food safety program. At least five of the panel members would have to be food, meat and poultry scientists.

"Why would you create a panel for a human health program and require that a majority of them be experts on animal health?" Mrs. Foreman asked.

Taylor said: "The provisions of the amendment are so poorly thought through that it has given food, meat and poultry scientists a charge that is so broad it is beyond their expertise. It is severe overkill."

Among the decisions the panel could examine under the amendment are work rules and labor relations, but O'Conner said the panel would not be involved in such work rules as whether plant workers could have "two or three bathroom visits."

The amendment was added to the farm bill at the House-Senate conference, an occasional way of passing controversial legislation without attracting attention or opposition.

"An ordinary bill becomes law by holding hearings," Mrs. Foreman said, "but there were no hearings. Now it is a typical congressional mess because they decided they wanted to slip something in under the cover of night. We're going to end up in court for years."

O'Conner disagreed. "I don't consider that much of a criticism," he said.

President Clinton is expected to sign the bill, but a senior administrative official said: "The administration has serious concerns about the effect the amendment would have in delaying modernization of food safety inspection."

The New York Times

April 1, 1996

Critic Calls Anti-Smoking Drive Off Course

By BARNABY J. FEDER

CHICAGO -- Everyone from President Clinton to tobacco companies is preaching these days that teen-agers should be kept from smoking, and that has some anti-tobacco advocates worried.

"The anti-tobacco movement has careened off on this narrow path because they know it's noncontroversial," said Stanton Glantz, a cardiology professor at the University of California in San Francisco. "But it's probably counterproductive. A kid-centered program is doomed to fail."

Glantz fears the focus on trying to stop the 3 million teen-agers under the age of 18 who become smokers each year is diverting too much attention from the nation's 40 million adult smokers. He argues that any letup in the pressure on adult smokers to quit or at least cut back will end up reinforcing the industry's message that smoking is a pleasure to be enjoyed by adults.

The result: naturally rebellious teen-agers will be seduced into becoming the tobacco companies' next generation of customers at the same time the industry is claiming public relations credit for saying "kids shouldn't smoke."

Glantz's views, which were spelled out in a recent editorial published by the American Journal of Public Health, angered some anti-tobacco advocates.

Many were even more upset when he attacked plans announced last month by the Robert Wood Johnson Foundation and other groups to finance a new clearinghouse called the National Center for Tobacco-Free Kids, calling it "a total waste of money."

The bigger danger as they see it is that Glantz is sowing doubt and sapping momentum among groups that need all the unity they can get to battle the $45 billion tobacco industry.

"You don't need to have someone saying you should focus on something else just when you are about to achieve some of your goals," said Bill Godshall, who is head of SmokeFree Pennsylvania, in Pittsburgh, and a firm believer that a direct attack on teen-age access to cigarettes could have a big impact.

The squabbling among the anti-smoking forces has been largely confined to private conversations and E-mail on Scarcnet, an electronic bulletin board used by anti-tobacco groups.

But it underscores the diversity among anti-tobacco groups and experts that often undercuts their efforts to counter the money and lobbying skills of the tobacco companies.

The divisiveness showed up this year in Kentucky when the state passed a law aimed at reducing teen-age smoking, with the support of the tobacco industry, retailers and tobacco growers. The law included penalties for teen-age smokers and money for inspections of retail establishments.

The bill was endorsed by the Kentucky Medical Association on the grounds, as an association spokesman put it, "It was the best you could expect from a tobacco state."

Other members of the state's coalition of anti-tobacco groups were furious at the Kentucky Medical Association. They thought group's endorsement undercut their chances, however remote, of forcing the Legislature to turn out a stronger law, such as one that would ban cigarette vending machines.

"The argument over the focus on kids is fairly new but there is always a split of one kind or another," said Phillip Wilbur, a spokesman for the Advocacy Institute, a Washington lobbying group.

The most common disputes, like those in Kentucky, are over tactics and which changes to emphasize. But tobacco critics are also at odds over fundamental goals.

Although many health experts see cigarettes as socially tolerable for adults if smoking is more strictly regulated, like alcohol, others active in the anti-tobacco effort want total prohibition.

"There are some real zealots," said Dr. Kenneth Warner of the Michigan School of Public Health, who favors toleration. "They're a minority but they are vocal and visible."

The tobacco companies, which typically refer to critics as the "anti-tobacco industry," maintain that prohibition is the goal of all of their important critics, whether stated openly or not.

Walker Merryman, the chief spokesman for the Tobacco Institute, the Washington-based trade group, said, "If someone in the industry came to me and said we have to open a dialogue with these people, I don't know who I'd speak with."

The toughest question for tobacco critics may be one that is rarely openly discussed: Should they encourage tobacco companies to produce and market safer cigarettes? Some health experts argue that such products would be beneficial to society because 46 million Americans are addicted smokers. Others say that such products would make it harder to combat smoking.

So far, the tobacco critics have been spared an all-out civil war because no company has successfully introduced an obviously safer product. The closest test came in 1988 when R.J. Reynolds Tobacco Co. tried to market a smokeless cigarette called Premier.

The company and most tobacco critics presumed it was healthier because of low-tar levels and virtually no secondhand exposure to smoke, although Reynolds refrained from making any explicit health claims.

A few industry critics expressed interest in the potential benefits, but they were drowned out by attacks on the company. As it turned out, though, there was little chance for debate because Premier was quickly pulled from the market after being rejected by smokers.

"There was only one politically correct side in the tobacco-control movement when Premier came out," Warner said. "I don't think that would be true now."

For now, there is plenty to disagree over concerning teen-age smoking, an issue ushered onto center stage by Congress' passage in 1992 of the Synar Amendment. That measure, named after former Rep. Mike Synar, D-Okla., required states to clamp down on teen-age access to cigarettes or lose federal grants for programs to fight drugs.

Final regulations spelling out how states should prove they were complying were published in February. By then, however, the spotlight had shifted to the Food and Drug Administration's proposal to attack teen-age smoking with nationwide restrictions on the sale, distribution and marketing of cigarettes.

Glantz and some supporters argue that preoccupation with the FDA rule and other so-called youth-access measures has made it easier for the industry to divert broad, aggressive anti-tobacco advertising campaigns in states like California and Massachusetts toward less effective youth-oriented advertising.

Glantz says the switch is at least partly to blame for a slowing in the decline of adult smoking and a rise in teen-age smoking in California.

The same preoccupation, he said, diverted the attention of most tobacco control groups from the Occupational Safety and Health Administration's proposal for a nationwide ban on smoking in public workplaces. Restrictions exist in many municipalities, including New York City. They are cited by Glantz as a means of reducing the number of smoking workers by 25 percent (others say evidence of the impact of these measures is mixed) and cutting second-hand exposure.

The outlook is now bleak for the OSHA proposal. While most tobacco-control groups kept their attention on the Food

and Drug Administration, the tobacco industry managed to get the ban proposed by OSHA merged into a far broader group of proposed regulations, which are now stalled by widespread criticism.

"When you reframe the goal from a smoke-free society to not wanting kids to smoke, it really narrows what you can do about issues like second-hand smoke," said Robin Hobart, associate director of Americans for Non-Smoker Rights in Berkeley, Calif.

But others say the focus on youth can help draw attention to the whole range of tobacco control issues.

"One of the ways you get adults concerned is by focusing on kids," said Dr. David Burns of the University of California at San Diego. "There's a lot more people involved in smoking control in 1996 than in 1993 because we have a theme that a lot of people can identify with."

Copyright 1996 The New York Times Company

FDA Reform 3/22/96 —
FDA D

Jerry Klepner
Jerry Mande
Diane
Bill Schultz
Tracy
Sally
Mike Fitzpatrick
Chris Jennings

- Wed. night met w/ Hill staff — trying to get better understanding w/staff.
- Put in what FDA's proposed fix would be.—
- Gave them marked up bill. —

Kassebaum — Mikulski, Dodd, Welstone, Kennedy — agreed to meet with
- to have further discussions about bipartisan fix to her bill

---

(1) Devices — # of ways — companies can make changes w/out coming to us
"Device changes which affect safety"

(2) "efficacy std." — drugs & device
# of ways...
↳ Device area — change defn. of std

1/3 of devices never come to FDA
98% go through 510(k) — "as good as

(3) Deadlines w/out resources — how that interferes w/ PDUFA....

Industry will say more if Democrats are unified
Members are mtg. Monday...

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

19-Mar-1996 06:38pm

TO: Elizabeth E. Drye

FROM: Jeremy D. Benami
Domestic Policy Council

SUBJECT: Schall letter

Thoughts on the Schall response:

Dear Ellen:

Thank you so much for your letter and for your offer to pull together some leaders of non-profits to meet with the President. I am sorry it has taken me a little while to get back to you.

I am very interested in continuing the dialogue on how best to involve the President and the Administration in the consideration of the role of non-profits in these turbulent times. There are some discussions going on among White House staff on this very topic, and I will certainly keep your offer in mind as these proceed. Also, if we decide to sponsor a meeting here in Washington, I may be back in touch with you for ideas regarding possible attendees and the agenda.

Once again, I enjoyed my visit in New York immensely and I appreciate your offer of assistance.

Sincerely,

File I:\dpc\data\schall.ltr

Denver Is Proving Fertile Ground For Theme of Million Man March

By JAMES BROOKE

DENVER, March 24 — After a 3-year-old boy was killed in a drive-by shooting in December, 100 black men fanned out through a black neighborhood here. They knocked on doors until leads resulted in three arrests several days later.

After rival gangs firebombed four houses in the same northeast Denver neighborhood in January, more than 1,000 men turned out for a five-hour protest rally, the All Black Men Conference. The firebombings stopped.

It has been nearly six months since the Million Man March, the gathering of hundreds of thousands of black men in October in Washington organized by the Nation of Islam and its leader, Louis Farrakhan. Far from fading away, the march's messages of moral renewal and personal responsibility have found particularly fertile ground among the 100,000 blacks in the Denver area, the largest such community in the Rocky Mountain West. Denver's black neighborhoods seem changed by the event, in ways tangible and intangible.

"Men are getting more involved on their blocks; traditionally, it was only the women," said Alvertis Simmons, who is organizing a local follow-up rally to the Million Man March to be held here next month.

Recalling his efforts to set up anti-crime groups three years ago, he said: "Before, there were hardly any men in the neighborhood watch groups. Last week, I heard of a black man setting up one on his block."

The march has inspired a similar level of activity in other black neighborhoods around the nation. From New York to Los Angeles, black men are becoming more involved.

At Northeast High School in Kansas City, Mo., for example, several dozen are volunteering as tutors, counselors and cafeteria monitors in a program to provide a positive male image for teen-agers. In Chicago, a similar mentor program has attracted about 100 black men, many of whom took part in the Washington march in October. And in Detroit and Los Angeles, agencies that help

Continued on Page A12, Column 1

Continued from Page A1

in the adoption of black children are reporting a surge of interest.

About 350 communities now have Million Man March organizing committees, said Benjamin F. Chavis Jr., national director of the Million Man March Organizing Committee, which is based in Washington.

In Atlanta, he said, march organizers have registered 28,000 people to vote and have directed a campaign that increased deposits in black-owned banks by $2 million, Mr. Chavis said in a telephone interview.

He said Denver was "typical of what is happening in numerous areas around the country."

In political discourse here, there has been an overwhelming shift to the march's themes. Prominent blacks as diverse as Jamal Muhammad, a local Nation of Islam minister, and Joe Rogers, a Republican lawyer who became the first black to run for Congress in Colorado, both emphasize responsibility.

"Our youths are killing each other," Mr. Muhammad told a rapt audience at a predominantly black high school here last month. "You can't blame that on the white man. You better take responsibility, black man."

Mr. Rogers sounded a similar theme in a recent interview. "We have to go forward to a basic set of values: hard work, family responsibility, social responsibility," he said. "There is a movement taking place in northeast Denver that says, 'It's time to wake up.'"

In Denver, there is no white political power structure to blame. Instead, there is a nascent black business class to emulate.

Although blacks account for only 5 percent of the two million people who live in the Denver metropolitan area, the city's Mayor, Wellington E. Webb, is black, as is the president of the school board, Aaron Gray.

Hardly ghettos, Denver's black neighborhoods include low-rise housing projects, working-class bungalows and suburban ranch homes. Bolstering a black middle class, there are about 4,000 black-owned businesses in greater Denver.

"Denver has so many good things going for it — we've elected a black Mayor and re-elected a black Mayor," said the Rev. James Peters, pastor of the New Hope Baptist Church. "The gangs are not representative of black people in Denver. You've had retired people from the military, working two jobs and buying nice homes here."

But, as the 63-year-old pastor spoke one recent Saturday, police officers stationed in his vestibule handed out basketball tickets to men who turned in handguns, no questions asked.

"Denver's like a comfort zone," warned Mr. Muhammad, who was sent here last year from Los Angeles by Mr. Farrakhan. "A lot of black people, and a lot of white people, come here to get away from urban problems."

But he noted that the Crips and the Bloods, two national street gangs, had recruited here and warned that "Denver could end up like L.A."

Two-thirds of the area's homicides have occurred in Denver's urban core even though it has only a fifth of the greater metropolitan area's population. But the surge in youth violence was driven home this winter when the Denver Fire Department announced that there were 51 firebombings in the city in 1995, up from 39 the previous year.

Of the firebombings, 13 are believed to be gang-related. Arrests were made in only one of the 13 cases. More than two-thirds of the firebombings occurred in the last six months of 1995.

"Getting leads from the community is like pulling teeth," Lieut. Joe Sarconi, chief of the department's Arson Bureau, said in an interview. "The community is terribly intimidated by these gang members."

Although no one has been killed in the firebombings, Lieutenant Sarconi said that was only a matter of luck. "These are more indiscriminate than drive-by shootings," he said. "The potential to kill groups of people is greater."

In early January, the local Million Man March organizing committee decided to hold the black men's conference at the Macedonia Baptist Church. Four firebombings in the previous two weeks served to swell the crowd when the conference was held on Jan. 27.

"We expected only 400 people," recalled Mr. Simmons, executive director of the organizing committee. "We had 1,100 people inside — and 200 people trying to get in."

Mr. Simmons, a former mayoral aide for gang liaison, recalled the angry words inside the packed church. "We gave them an edict," he said, referring to the gangs. "We will help you get a job, but our babies' lives are not negotiable."

Everyone agrees on what happened afterward. Gang-related firebombings stopped in Denver's black neighborhoods.

Not everyone agrees on why.

"We had a task force out — the gangs felt the pressure on the street," Police Chief David Michaud said in an interview. The anti-arson task force conducted hundreds of interviews and arrested two teenagers. They were charged with the Jan. 25 bombing, a fire that caused $25,000 in damage, leaving a family with five children homeless.

Community leaders argued that public pressure had curbed the gangs.

Mr. Simmons, who received telephoned death threats from the gangs before the conference, said, "I want them to have in the back of their minds, 'If I firebomb that house the neighbors will see me and put me away for 30 years.'"

Next month, Denver's rally for "people of color" will keep pressure on the gangs, predicted Chet Whye Jr., the local director of the National Rainbow Coalition, which is helping oragnize the rally.

"There is a different attitude now that people are coming out," said Mr. Whye, who moved here from Baltimore 10 years ago. "The atmosphere has sparked some people to make real changes in their lives."

THE NEW YORK TIMES
MONDAY, MARCH 25, 1996

Gaynor — May be some ideas for fatherhood initiative here. CHC
cc: Eliz

From One Serbian Militia Chief, A Trail of Plunder and Slaughter

By CHRIS HEDGES

A1

VISEGRAD, Bosnia and Herzegovina, March 21 — For the thousands of Muslims who fled from this town in eastern Bosnia, and for the Serbs who remained, the war has bound this generation and the next to a Serbian militia leader named Milan Lukic.

Witnesses and survivors say Mr. Lukic, 29, killed scores of Muslims in this region from 1992 to 1995. He has not been indicted by the United Nations' war crimes tribunal in The Hague, and the Serbs in Visegrad say they do not know his whereabouts.

Beyond Visegrad, his name and story are largely unknown. But detailed accounts collected over the last two weeks from witnesses, many of them now dispersed around Bosnia, provide a picture of slaughter, pillage and abuse condoned by the local authorities and Serbian commanders from Belgrade.

Mr. Lukic (pronounced LOO-kich) is emblematic of dozens of Serbian militia leaders who rose to prominence in the war in Bosnia, who used the call for an ethnically pure Serbian state to drive tens of thousands of Muslim families from their homes and kill thousands of others.

The legacy he and others left — of hatred, loss and pain — is something no peace agreement seems likely to erase. It helps explain why Muslims, Croats and Serbs refuse to return to homes controlled by other ethnic groups, as called for in the peace agreement reached last year in Dayton, Ohio. And it fuels the yearning for vengeance that could in time unleash another conflict.

"Every child from Visegrad, even those too young to remember, knows the name Milan Lukic," said Mehmet Prtkovic, the leader of the displaced Muslims from Visegrad who now lives in the isolated Muslim enclave of Gorazde. "Our community will never forget. We will never allow our children to forget."

In Visegrad there is a graceful 400-year-old bridge, hewn of large off-white stones, that spans the emerald-green waters of the Drina River. The Nobel laureate Ivo Andric centered his novel "The Bridge on

Continued on Page A8, Column 1

Continued from Page A1

the Drina" around the pumice structure, which he could see from his window as a boy.

The book chronicles, over 350 years, the turbulent and often violent history of Visegrad and Bosnia. And as the novel points out, the bridge has served as a kind of public theater in times of war and upheaval. Brigands and criminals were once impaled and executed on its stone flanks. Mr. Andric wrote in the book, "In all tales about personal, family or public events, the words 'on the bridge' could always be heard."

A Long History Of Major Killers

The steep wooded hillsides that plunge to the river have for centuries also produced killers of appalling magnitude. Mr. Lukic, along with his group of some 15 well-armed companions, was the latest, according to more than two dozen survivors and witnesses. According to their accounts, he too used the bridge as a prop to extinguish a Muslim community that had been here for centuries.

Of the 14,500 Muslims who lived in Visegrad before the war, 3,000 are now missing or dead. The others are scattered around Bosnia, many living in poverty in overcrowded rooms. Most shudder when they speak of this bridge. And even the Serbs in the town speak of what happened in hushed and enigmatic sentences.

"I read again Ivo Andric's novel during the war," said Boshko Polic, 68, the retired principle of the Ivo Andric High School, now taken over by Serbian families displaced from Sarajevo. "I would look up from the pages and see what he was describing around me."

In April 1992, when the conflict between the Bosnian Serbs and Muslims began, Mr. Lukic returned from Serbia to his hometown. He gathered together a group of men, including his brother Milos, his cousin Sredoje and a waiter, Mitar Vasiljevic. Mr. Lukic, who often went barefoot, named the group the Wolves. He set about pillaging and looting Muslim homes, witnesses said.

The Uzice Corps, the Yugoslav Army unit that moved into Visegrad and eventually turned their weapons over to the Bosnian Serbs, did nothing to intervene, survivors said.

The plunder quickly turned to killing. On May 18 Mr. Lukic burst into Dzemo Zukic's home and shot his wife, Bakha, in the back, according to neighbors who saw the shooting. He drove the terrified husband away in the family car, a red Volkswagen Passat. Mr. Zukic was never seen again. But the car became a harbinger of death.

"The sight of the Passat sent terror into our hearts," said Hajdra Karahodsic, whose husband was taken away by Mr. Lukic and who now lives in Gorazde. "We all prayed that it would not stop in front of our homes."

Survivors said the killings quickly became frenzied and common. On one occasion, witnesses said, Mr. Lukic tied a man with a rope to his car and dragged him through the streets until he died.

They said that on at least two occasions, Mr. Lukic herded large groups of Muslims into houses and set the buildings on fire. Zahra Turjacanin, her face and arms badly marred by the flames, escaped from one burning house on June 27 and raced screaming through the streets. Townspeople said she was the only survivor of 71 people inside. She now lives in France.

"We watched all these things," said Fadila Mujakic, 46, who now lives in Gorazde. "But when we saw poor Zahra yelling in terror and pain, we knew Visegrad had descended into some kind of hell. I gathered my family, and we snuck out that same night."

Captured Serb Testifies on Lukic

On Aug. 5, 1994, a United Nations policeman, Sgt. T. Cameron, interviewed a captured Serbian soldier from Visegrad, and gathered the only known Serbian testimony of Mr. Lukic's actions.

The soldier, Milomir Obradovic, told how fleeing Muslims were hauled off buses, lined up and shot by Mr. Lukic and his companions. He identified the sites of two mass graves, but neither have yet been investigated. He said Mr. Lukic and his followers raped young girls held captive at the Vilina Vlas spa outside Visegrad. And he said Jasna Ahmedspahic, a young woman, jumped to her death from a window of the spa after being raped for four days.

But in a move that probably meant death for Mr. Obradovic, he was released in a prisoner exchange. He has since disappeared.

Mr. Lukic, witnesses said, began to drive his captives to the center of the bridge. Women and men said they had turned their heads as Mr. Lukic and his men taunted their victims, who were made to stand on the walls of the bridge, before pushing them into the water and opening fire with automatic weapons.

Muslims in Visegrad were desperate to leave. But the city officials refused to give them papers to leave until they had stripped them of their property and wealth.

On June 7, 1992, Hasan Ajanovic was picked up with five friends and driven to the river by Mr. Lukic and two other men, including Mr. Vasiljevic, the former waiter. One of the victims, Meho Djafic, had worked for 20 years in the Panos restaurant with Mr. Vasiljevic.

"Lukic told us to wade out into the water," he said, interviewed by telephone from a Western European country that he asked not be identified. "I did not hear the first shot, I suspect because Lukic's gun had a silencer. But I heard the screams and then the other shots. Meho's body fell on top of me. I lay with my face in the sand until night. I swam across the river and escaped. The water stank of death."

Killings were occurring each day.

On the afternoon of July 19, 1992, Milos Lukic kicked down the door where Hasena Muharemovic lived with her sister, mother, invalid father and two small girls, Mrs. Muharemovic said. Her husband had been abducted and had disappeared two weeks earlier. She swept up Nermina, 6, and her older girl and hid.

Mother and Sister Are Shot on Bridge

But her mother, Ramiza, and her sister, Asima, were driven to the center of the bridge. Mrs. Muharemovic crept from her hiding place and saw her mother and sister sitting astride the wall.

"Milan Lukic and his brother shot them in the stomach," she said. "When they fell in the water, the men leaned over and laughed."

That night she huddled in an abandoned house with her daughters. At dawn she went to see her father.

"My father told me to take the girls and run away, that if we stayed we would all be killed," she said. "I cannot go, he said. I will stay until they come for me. 'Nermina,' he said to my daughter, 'come kiss your grandfather goodbye for the last time.' Then we fled."

The mother and two girls were picked up by Serbs and taken for two months to a house with six other women, Mrs. Muharemovic said. But she would not talk about the experience.

In September the mother and her daughters where sent to work on a farm with dozens of other captives.

"Lukic would come to stuff pieces of pork in our mouths," she said. (Pork is forbidden under Islamic dietary rules.) "He beat people with metal rods and took many away."

In October 1995 Mrs. Muharemovic and her daughters were freed in a prisoner exchange.

The killings here, witnesses said, filled the waters of the river with bloated and mangled bodies.

Mesud Cocalic lived about 12 miles down river from Visegrad in the village of Slap, which did not fall to the Serbs until last summer. He said he and a group of neighbors had buried 180 bodies they had retrieved from the water. The men identified 82 of the bodies and wrote out detailed descriptions of the others.

"The bodies were often slashed with knife marks and were black and blue," he said. "The young women were wrapped in blankets that were tied at each end. These female corpses were always naked. We buried several children, including two boys 18 months old. We found one man crucified to the back of a door. Once we picked up a garbage bag filled with 12 human heads."

By the autumn, with Visegrad nearly emptied of Muslims, the killings subsided but did not end.

Those who survived the Serbian capture in July 1995 of the United Nations "safe areas" of Srebrenica and Zepa say they saw Mr. Lukic with the Bosnian Serb troops. Mr. Lukic, they said, took away 65 Visegrad natives who had moved to the United Nations "protected" enclaves.

Capture, Killing, Then a Coca-Cola

Jasmin Kulovac, a young Muslim fighter from Zepa who now lives in Sarajevo, tried to escape from Žepa through the woods toward Montenegro after the enclave was captured in July. But he was arrested with eight companions on Aug. 4 by the Serbian police along the border near Zemlica.

The Serbs drove the men to Visegrad and turned them over to Mr. Lukic. Mr. Kulovac said he had seen one companion gunned down along the banks of the Drina and heard shots that he suspects indicated the killing of the others.

"Lukic took me to the middle of Visegrad to have a Coke afterward," he said. "As we sat in the cafe, the other Serbs spat at me. He walked around the town like a god."

Mrs. Muharemovic, who lives in a tiny Sarajevo apartment with her daughters, is gaunt and nervous.

"I do not sleep much," she said. "I am plagued by the same dream. My room is filled with water. I am fighting to get to the surface. I see the bodies of my mother and my sister swirling past me in the current. I burst to the surface."

Her voice went low and hoarse.

"I can always see it above me," she said. "The bridge. The bridge. The bridge."

THE NEW YORK TIMES
MONDAY, MARCH 25, 1996

AMENDMENT NO__________ Calendar No___

Purpose: To reduce overly burdensome, bureaucratic, and unnecessary requirements.

IN THE SENATE OF THE UNITED STATES--104th Cong., 2d Sess.

An Amendment to the amendment offered by Mrs. Kassebaum to S. 1477

To amend the Federal Food, Drug, and Cosmetic Act and Public Health Service Act to improve the regulation of food, drugs, devices, and biological products, and for other purposes.

Referred to the Committee on ____________________________
and ordered to be printed

Ordered to lie on the table and to be printed

AMENDMENTS intended to be proposed by Mr. Kennedy

1 On page xx, strike lines xx-xx and replace with:

2 "(ii) requests for meetings and the scheduling of meetings relating to

3 reviews of protocols and relating to review of applications or submissions

4 (including petitions or notifications) for product approval or clearance;

5 and";

6 On page ~~xx~~ 22, strike lines ~~xx~~ 22 ~~through xx~~ through P. 23, line 5 and replace with:

7 "(2)(A) A clinical investigation of a new drug (including a biological

8 product) may begin thirty days after the date the Secretary receives from

9 the sponsor a notification containing information about the drug and the

10 clinical investigation unless, prior to the thirtieth day, the Secretary

1 informs the sponsor that the investigation may not begin and specifies the

2 basis for the decision. Within an additional twenty days, the Secretary

3 shall specify in writing the deficiencies and the information needed in

4 order for the clinical investigation to commence.

5 On page xx, strike lines xx through xx and replace with:

6 "(3)(A) The Secretary may place a clinical hold on any ongoing

7 clinical investigation if the Secretary determines that such action is

8 necessary for the protection of human subjects or for other reasons set

9 forth by the Secretary in regulations.

10 "(B) If the Secretary places a clinical hold on an ongoing

11 investigation, the Secretary shall immediately advise the sponsor of such

12 investigation in writing of such action, and provide such sponsor an

13 opportunity to confer within ten working days of receipt of such

14 communication to discuss the basis for the clinical hold. Within ten

15 working days of such conference, the Secretary shall provide to the

16 sponsor a written list of conditions for the withdrawal of the clinical hold.

17 Any written request from the sponsor requesting that a clinical hold be

18 withdrawn shall receive a decision in writing and specifying the reasons

19 therefor, within twenty working days of the receipt of the request."

20 On page xx, , strike lines xx through line xx and replace with:

21 "(b) REVIEW BY SCIENTIFIC REVIEW GROUP.--

1 "(1) In General.--The product sponsor or applicant shall have a right
2 to request an evaluation by an appropriate scientific review group
3 established under section 904 of any significant scientific decisions made
4 by the Secretary under this Act. In addition, a product sponsor or
5 applicant shall have a right to request an evaluation by an appropriate
6 scientific review group established under section 904 of any significant
7 scientific issue under this Act appealed by such person under subsection
8 (a) that has been pending before the Secretary, without final resolution, for
9 more than 180 days."

Administration Marries Policy Initiatives to Political Message

CLINTON, From A1

wanted to expand benefits to people exposed to Agent Orange in Vietnam, the White House quickly approved the proposal and Clinton scheduled a speech to announce the move. The real-world impact of these initiatives—a sample of more than a dozen examples so far this year—varies widely.

Six weeks after Clinton unveiled the education tax-credit proposal, for instance, the administration has yet to send a bill to Capitol Hill to implement the idea, and aides say they have yet to make some basic decisions about how the tax credit would work. Even so, Clinton weaves mentions of the plan into almost every campaign speech.

The Agent Orange decision, by contrast, quickly disappeared from view after a round of headlines the day it was announced. The administration offered no precise cost estimates. But medical experts say the decision to compensate every Vietnam veteran who gets prostate cancer could eventually cost the federal government far more than $1 billion, although the big bills won't come due until many years from now as veterans grow older.

The VA made its decision despite a lack of scientific evidence showing anything more than a possible link between Agent Orange exposure and prostate cancer, which more than 10 percent of all males will get regardless of whether they served in Vietnam.

The presidential campaign of former Senate majority leader Robert J. Dole accuses Clinton of politicizing the government and campaigning at taxpayer expense. But White House aides are unapologetic about their determination to merge government policy and campaign message, and claim they are practicing sensible incumbency politics.

Poor coordination between the White House and the reelection campaign contributed significantly to President George Bush's defeat in 1992 by making him vulnerable to the charge that he had no message or philosophy, Clinton aides contend. They are eager not to let Dole benefit the same way they did.

"We are determined to speak with one voice and not have a disconnect," said White House senior adviser George Stephanopoulos.

New examples keep springing forth, sometimes two or three a week.

This spring, with campaign polling showing that people want to get tough on wayward youths, the White House ordered the Justice Department to develop guidelines to be mailed to localities to encourage them to impose night curfews. The Education Department put together a similar manual on how schools can stop truancy.

Last month, the Heath and Human Services Department came up with new rules requiring women to provide more information about who fathered their children before receiving welfare benefits. The move, White House officials said, would help show Clinton as a tough-minded innovator, and help blunt the GOP charge that by vetoing two Republican bills Clinton had reneged on his 1992 promise to "end welfare as we know it."

In March, Clinton announced that Housing and Urban Development Department aid to local housing authorities would be weighted in favor of projects that evict tenants accused of a single crime, even if the tenants have yet to be convicted. HUD and Justice Department officials helped draft the initiative, which a spokesman for the American Civil Liberties Union called "political grandstanding at the expense of the poor."

The next day, Clinton announced that the Food and Drug Administration was streamlining rules to bring anti-cancer drugs to market. Clinton said it was an example of how the administration's "reinventing government" campaign was helping individuals. But it also responded to Republican complaints that the FDA is too slow and bureaucratic.

In April, Clinton answered consumer fears that gasoline prices were rising too high by ordering the Energy Department to sell some of the strategic petroleum reserve. The next day, he answered ranchers' fears that beef prices were falling too low by enlisting the Agriculture Department to speed up school lunch program purchases.

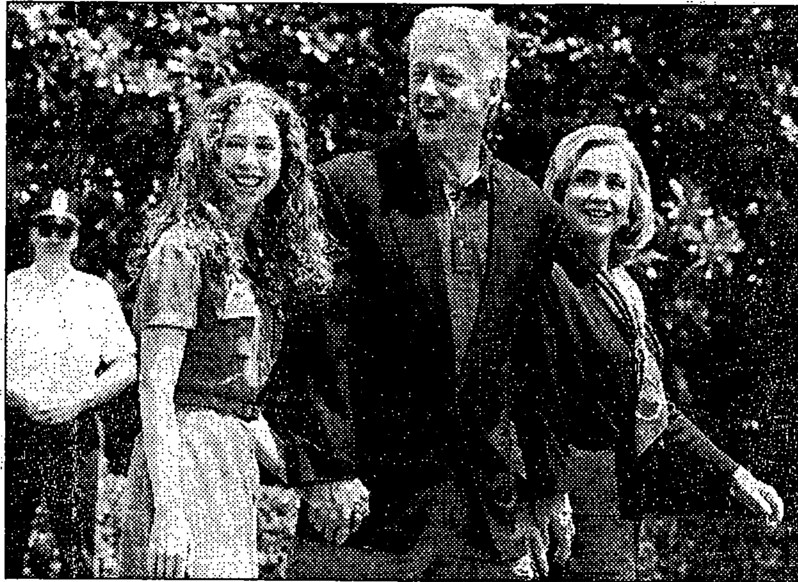
Sometimes, the effort to put Clinton forward with a campaign message of the day involves initiatives that amount to little. Last week's announcement of a program to track guns used in crimes by juveniles was largely a presidential restatment of something the Bureau of Alcohol, Tobacco and Firearms announced more than two years ago.

But sometimes Clinton's pronouncements involve important policy. The Agriculture Department had been working for years on a compromise plan for more rigorous meat inspections. The final announcement was hastened by several days last week, administration officials said, in time for Clinton's weekly radio address, dominating the Sunday papers a week ago.

The relationship between the executive branch and Clinton's political advisers works in both directions. Sometimes the campaign takes advantage of an idea the bureaucracy had been working on. Other times, the political team orders the bureaucracy to work on a proposal that Clinton campaign consultant Dick Morris or some other adviser believes will prove popular.

In the Agent Orange decision last May, Clinton seized upon a policy decision that as a practical matter had already been made. Congress in 1991 passed legislation requiring the government to give the benefit of the doubt to veterans in cases where the scientific evidence is murky about whether Agent Orange causes a particular health problem. A scientific panel found there was "suggestive" but inconclusive evidence of a link between prostate cancer and exposure to the herbicide and recommended the disease be added to a list of others for which Vietnam veterans receive benefits.

Once the panel made its decision, according to interviews with officials at the White House and Department of Veterans Affairs, there was no serious discussion of the considerable costs in



BY RUTH FREMSON—ASSOCIATED PRESS

President Clinton, with daughter Chelsea, left, and wife Hillary, leaves for Camp David. Clinton uses agenda-setting power to "define himself."

PHOTOCOPY
PRESERVATION

future years or any possibility that Clinton might not approve.

Instead, according to officials, there was considerable discussion of how Clinton should announce the decision. Some thought a Memorial Day address would be appropriate, but others thought that would look too political. Clinton made his announcement the day after the holiday, surrounded by veterans.

The education tax credit, by contrast, was conceived at the White House. Clinton, according to an aide, was eager for "a big idea" on education that would help "define what the second term would be about," and had long been intrigued by a Georgia program to subsidize the first two years of college.

The problem was meshing it with the realities of budgeting. Economic adviser Laura D'Andrea Tyson and one of her deputies, Clinton campaign veteran Gene Sperling, supervised a process of extended wrangling among the White House and Departments of Education and Treasury over how big to make the credit, and how to pay for it. Aides said the scope and cost of Clinton's plan was scaled back as it went through the policy process. And some questions, such as whether the tax credit should be paid to the college or to the individual student, are unanswered.

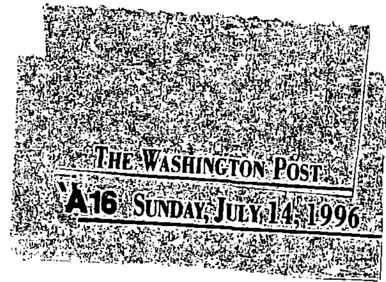
White House press secretary Michael McCurry said Clinton agrees that the tax credit proposal is in part political, but that it is appropriate for a president to offer new policies in an election year to highlight what he would do in a second term.

But Christina Martin, a spokeswoman for Dole, said Clinton is using the powers of incumbency on several fronts to unfair advantage. "Whether it's travel, events staging, 'war rooms' in the White House, or taxpayer funded policy experts being used for Bill Clinton's political gain, it is abusive and wrong," Martin said.

Mary Matalin, a veteran of Bush's campaign, said if Clinton thought the tax credit or other proposals were good ideas, he should have pushed them when Democrats had control of Congress two years ago.

But Martha Joynt Kumar, a Towson State University political scientist, said Clinton is shrewdly using the agenda-setting powers of the presidency. By announcing even a modest proposal, "He can immediately get on the news," and that public exposure gives him a chance "to define himself."

Staff writers Bill McAllister and Rick Weiss contributed to this report.



THE WASHINGTON POST

A16 SUNDAY, JULY 14, 1996

PHOTOCOPY PRESERVATION

Congress May End Funding for Agriculture's Pesticide Testing Program

Associated Press

The Agriculture Department's Pesticide Data Program, created in 1991 to test produce in the wake of the scare over the pesticide Alar in apples, faces possible extinction.

The House passed a spending bill for the Agriculture Department in June that cut out the $11.5 million needed to run the program in 1997. The Senate bill, awaiting final passage, restores the money. Negotiators will have to decide the program's future.

The arguments for ending the program look like those for keeping it.

Farm groups and pesticide makers want it because it shows the food supply has very low levels of pesticides—well below thresholds set by the Environmental Protection Agency.

About 39 percent of the nearly 7,600 samples tested in 1994 had no detectable residues, even though scientists can measure down to the tiniest part. Just under 2 percent of imported produce and just over 1 percent of U.S.-grown produce had residues that would violate standards.

"The data has been our friend," said Dennis Stolte, pesticide specialist with the American Farm Bureau Federation. The American Crop Protection Association, which represents pesticide makers, agreed.

"To the extent this information is valuable in reassuring public confidence in the safety of the food supply, ACPA would be sad to see this program removed from the budget," said Jay J. Vroom, the group's president.

Conversely, the House decided that if pesticide levels were so low, the program wasn't needed. After all, the Food and Drug Administration already enforces pesticide laws, testing 10,000 food samples a year.

The EPA says the data help it do a better job of calculating the health risk from pesticides.

The fruits and vegetables are taken from warehouses and tested after they've been peeled, scrubbed and otherwise prepared for consumption. Without the data, the EPA has to assume that the maximum allowable levels—set for crops ready to harvest rather than eat—are in the food.

The Environmental Protection Agency advises the Agriculture Department on which pesticides to examine. Because of a 1993 report by the National Academy of Scientists, the government has been looking more closely at the special impact of pesticides in the diets of infants and children.

The agency is also beginning the difficult task of looking at total exposure from all pesticides rather than regulating each pesticide as though it were the only one being used. About 36 percent of the samples had traces of more than one pesticide.

Compared with previous years' samples, there were more multiple residues, and 1994 was the first time that as many as 10 residues were found, although only two apples had that many pesticides.

Activist organizations such as the Environmental Working Group also say the program should be kept, especially because of growing concern over exposure to multiple residues.

Although the allowed pesticide levels may be too high by their reckoning, the group says, at least there would be knowledge of the situation.

"With a little bit more refinement, and a little bit harder looking by this program, you could really get a pretty good picture of what pesticides are on these fruits and vegetables when people eat them," said Richard Wiles, the group's pesticide specialist.

PHOTOCOPY PRESERVATION

19 **SEC. 23. ENVIRONMENTAL IMPACT REVIEW.**

20 Chapter VII is amended by adding at the end the

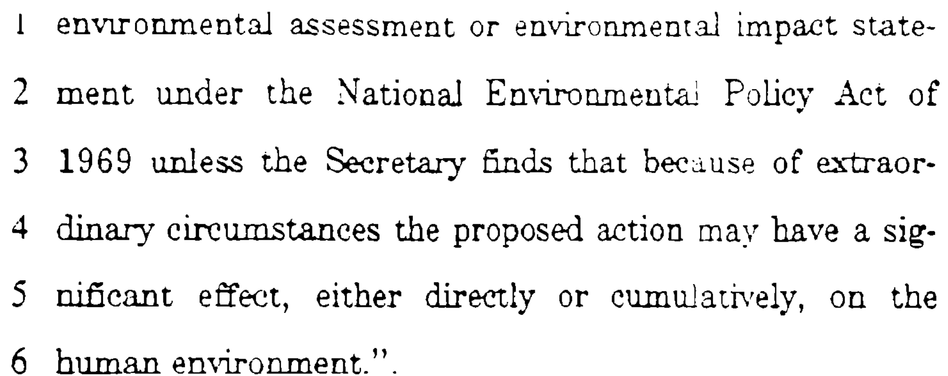
21 following:

22 "SUBCHAPTER D—ENVIRONMENTAL IMPACT REVIEW

23 "**SEC. 741. ENVIRONMENTAL IMPACT REVIEW.**

24 "No action by the Secretary proposed to be taken

25 pursuant to this Act shall require the preparation of an



1 environmental assessment or environmental impact state-

2 ment under the National Environmental Policy Act of

3 1969 unless the Secretary finds that because of extraor-

4 dinary circumstances the proposed action may have a sig-

5 nificant effect, either directly or cumulatively, on the

6 human environment.".

Senate

4 ***SEC. 406. ENVIRONMENTAL IMPACT REVIEW.***

5 *Chapter VII (21 U.S.C. 371 et seq.), as amended by*
6 *section 405, is further amended by adding at the end thereof*
7 *the following new section:*

8 ***"SEC. 745. ENVIRONMENTAL IMPACT REVIEW.***

9 *"Notwithstanding any other provision of law, no ac-*
10 *tion by the Secretary pursuant to this Act shall be subject*
11 *to an environmental assessment, an environmental impact*
12 *statement, or other environmental consideration unless the*
13 *director of the office responsible for the action demonstrates,*
14 *in writing—*

15 *"(1) that there is a reasonable probability that*
16 *the environmental impact of the action is sufficiently*
17 *substantial and within the factors that the Secretary*
18 *is authorized to consider under this Act; and*

19 *"(2) that consideration of the environmental im-*
20 *pact will directly affect the decision on the action.".*

By regulation — proposed rule — they see vastly reduced # of env. analysis

NEPA

4 **SEC. 406. ENVIRONMENTAL IMPACT REVIEW.**

5 *Chapter VII (21 U.S.C. 371 et seq.), as amended by*
6 *section 405, is further amended by adding at the end thereof*
7 *the following new section:*

8 **"SEC. 745. ENVIRONMENTAL IMPACT REVIEW.**

9 *"Notwithstanding any other provision of law, no ac-*
10 *tion by the Secretary pursuant to this Act shall be subject*
11 *to an environmental assessment, an environmental impact*
12 *statement, or other environmental consideration unless the*
13 *director of the office responsible for the action demonstrates,*
14 *in writing—*

15 *"~~(1)~~ that there is a reasonable probability that*
16 *the environmental impact of the action is sufficiently*
17 *substantial* to justify such an assessment, *~~and within the factors that the Secretary~~*
18 *~~is authorized to consider under this Act; and~~*
19 *~~"(2) that consideration of the environmental im-~~*
20 *~~pact will directly affect the decision on the action."~~.*

Shifts burden

burden should why as opposed why.

Possible Senate Substitute

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

02-Aug-1996 10:38am

TO: Jonathan Winer
TO: Sally Katzen
TO: Elizabeth E. Drye
TO: John F. Morrall, III
TO: Michael A. Fitzpatrick

FROM: Daniel J. Chenok
Office of Mgmt and Budget, OIRA

SUBJECT: DELAY OF MARKUP ON FDA REFORM BILLS SEEN AS IMPROVING PROSPE

DELAY OF MARKUP ON FDA REFORM BILLS SEEN AS IMPROVING PROSPECTS FOR
The House Commerce Committee's decision to delay its scheduled markup of Food and Drug Administration reform legislation in favor of continued negotiations with the Clinton administration actually improves the prospects for congressional action, a drug industry source told BNA Aug. 1.
The House Commerce Health and Environment Subcommittee had been expected to consider three FDA reform bills (HR 3199, 3200, 3201) beginning Aug. 1, but announced July 30 that markup would be postponed to allow discussions to proceed through August.
According to the source, both Republican and Democratic staffers have represented the postponement as a positive step, not a reason for disappointment. If the negotiations had broken off for subcommittee markup there would have been more confrontation, rather than less, brought about by amendments being offered on controversial issues, the source said.
It appears that reform bills will be brought to the House floor in September under suspension of the rules, the source added, which means the leadership considers them to be non-controversial and few amendments will be allowed.
Roles Of Bliley, Greenwood
Moreover, the bills currently have approximately 208 cosponsors from both parties, so passage by the House seems assured. The source credited Rep. Jim Greenwood (R-Pa), head of the Republican task force appointed by Commerce Committee Chairman Thomas Bliley Jr. (R-Va), with garnering ``90 percent'' of the cosponsors for the bills.
Greenwood initially took the lead on meeting with FDA Commissioner David Kessler and his staff as well as industry, patient, and medical groups to reach agreement on controversial issues before proceeding to mark up.
Bliley and his staff have moved to the forefront now, however, since Health and Human Services Secretary Donna E. Shalala asked that meetings be held prior to mark up to work out differences between Congress and the administration.
The drug industry source said Bliley wanted one more ``legislative success'' before the end of this congressional session. Bliley's involvement again underscores the probability of the bills will pass in September because

THE WHITE HOUSE

WASHINGTON

Elizabeth,

This was given to Chris by Genentech. He is interested in your views -- they believe it's a sign of movement & hope we can help to push through an acceptable agreement.

—Sandy

DISSEMINATION OF INFORMATION

CURRENT LAW

1) Only when fundamentally consistent with approved label

MACK/FRIST/DODD

1) Only independent journals and texts

2) Only information that is scientifically reliable

3) All information reviewed by FDA for balance

4) Disclaimers

5) Obligation to update by companies

6) Secretary has no authority with respect to cost and cost effectiveness of drug claims

FDA POSITION

1) Dissemination only after a company has filed a supplement

2) Unclear position on other issues

"A THIRD WAY"

1) Limit journals to those approved by the Secretary

2) Create three categories of FDA reviewable documents. Those which relate to:

   a) filed supplemental applications;

   b) those consistent with recommendations of federal health agencies; and

   c) those consistent with medical practice guidelines. These determinations to be made by the Secretary.

3) Limit application of a pending "Guidance document", negotiated rule making, and authority for the FDA to regulate false and misleading claims pending a final rule.

THE WHITE HOUSE

WASHINGTON

August 6, 1996

MEMORANDUM FOR THE PRESIDENT

FROM: Elizabeth Drye, DPC

SUBJECT: Update on FDA Reform Legislation

Many biotechnology, pharmaceutical, and medical device companies would like to see FDA reform legislation pass this year. California biotechnology leaders may raise the issue with you. Senator Kassebaum has moved a bill out of the Labor Committee with some Democratic support. The House Commerce Committee has held hearings on three separate bills addressing FDA's regulation of food, drugs, and medical devices.

As you know, FDA has already made substantial changes under Vice President Gore's National Performance Review to speed drug and device approval times, provide patients earlier access to new drugs for cancer and other life-threatening diseases, and ease regulatory burdens for manufactures. In November of 1995 FDA announced and biotechnology leaders applauded a package of six reforms that help the biotechnology industry. FDA has also proposed a third-party review pilot to test private review of low-risk medical devices.

Democrats have been divided on pending legislation. Senators Dodd, Harkin and Mikulski voted to report Senator Kassebaum's bill out of Committee while noting the need for improvements. Senator Kennedy, however, wrote a scathing op-ed calling the Senate bill a "prescription for disaster." FDA has testified that numerous provisions in both the House and Senate bills undermine safety and efficacy standards.

HHS and FDA staff, in consultation with White House staff, have been working with both House and Senate Committee members and staff toward developing legislation the Administration can support. We have sought to be responsive to industry's concerns while preserving safety and efficacy standards. Key remaining issues include provisions establishing expansive private review of medical devices, unrealistic review deadlines with "hammers" that kick products into private review, and rules governing the distribution of promotional material for "off-label" drug uses (uses for which a drug is not explicitly approved).

We are working to reach agreement on an FDA reform bill that does not undermine safety and efficacy. Given the limited number of legislative days remaining, this Congress is not likely to pass legislation unless Democrats, Republicans, and the Administration achieve consensus soon on outstanding issues.

THE NEW YORK TIMES
FRIDAY, MAY 24, 1996

Senators Offer Bipartisan Plan To Cut Taxes in Washington

By MICHAEL JANOFSKY

WASHINGTON, May 23 — In an effort to reverse years of population and economic decline in the District of Columbia, two Senators said today that they would introduce a bill on Friday that would substantially cut the Federal taxes paid by District residents.

The measure, co-sponsored by Connie Mack, a Florida Republican, and Joseph I. Lieberman, a Connecticut Democrat, is almost identical to a House bill introduced last month by the District's representative, Eleanor Holmes Norton, a Democrat, which she said was the only viable way of saving the city from ruin.

The House and Senate bills would both create a flat Federal income tax rate for District residents of 15 percent, down from as high as 39.6 percent. Standard deductions would rise to $15,000 for single filers, $25,000 for head of household filers and $30,000 for married couples. Those figures were $3,900, $5,750 and $6,550, respectively, last year.

The Senate bill would eliminate capital gains taxes for any business investment in the city, while the House bill would do so only for investments by District residents. The Senate bill would also provide a $5,000 tax credit for first-time home buyers in the District. Ms. Norton's bill has no such incentive.

Describing the tax cuts as "the best way to help" the nation's capital, Mr. Mack said today that he expected both bills to pass this year. And if that happened, Mr. Lieberman said, "I bet you a lot of money President Clinton signs it."

"High taxes are driving people out of the District of Columbia," Mr. Mack said at a news conference, where the Senators were joined by Ms. Norton and Jack Kemp, the Secretary of Housing and Urban Development in the Bush Administration. Mr. Kemp has been a strong supporter of using tax breaks to attract residents and businesses to cities.

The lawmakers and Mr. Kemp said that if the cuts helped Washington's economy, Federal and state tax breaks could be used to resuscitate other urban areas losing population for the same reasons — crime, poor schools and inefficient city services.

It is not clear, however, whether the Clinton Administration supports the idea of Federal tax cuts for District residents or of having the cuts be a model for use across the country. In an interview after Ms. Norton proposed her bill, Alice M. Rivlin, the director of the Office of Management and Budget, said the measure was "more a dramatization of the problem than a real solution."

Also, at a time when Congress and the White House are straining to balance the budget in seven years, the lawmakers said that neither the House nor Senate had analyzed how much the tax cuts would cost the Federal Government.

Mr. Kemp estimated the cuts would cost $700 million to $800 million a year for up to six years.

The proposed tax cuts have become the latest in a series of efforts to restore the District's economy. Congress last year created a financial control board to help the city curb spending. The White House has appointed a task force to work with city agencies to solve problems. And Mayor Marion S. Barry Jr. has begun work on a four-year plan to reduce the size of city government by 25 percent.

But the tax cuts would appear to be the most dramatic of the initiatives.

Stressing the bipartisan nature of their efforts, Mr. Kemp nodded toward Ms. Norton and said: "We've joined together in a bleeding heart issue to save the nation's capital. This is an urgent plea to the White House and leaders of the House and Senate. Do it now. People in this city desperately need urgent action."

Corrections

An article on April 16 about attempts to improve the safety record of the taxi fleet in Nairobi, Kenya, misstated the etymology of the Kiswahili colloquialism for the minivans that make up the bulk of the fleet. Matatu, literally meaning threes, derives from the fare of 30 cents (mateni matatu, or three 10-cent pieces) originally charged by drivers, not from the practice of people banding together to operate the taxis. This correction was delayed for consultation with authorities on Kiswahili.

•

A headline on Wednesday with the continuation of a front-page article about the erosion of consensus among the nation's governors on reshaping the Federal-state health program for the poor referred incorrectly to that program. It is Medicaid, not Medicare.

•

An obituary yesterday about Edward J. Gurney, the former Senator from Florida, misstated Edmund S. Muskie's alma mater. Mr. Muskie, who died in March, was a graduate of Bates College, not Colby College, which was Mr. Gurney's alma mater.

•

An article on Saturday about a resolution by the Association of Justices of the Supreme Court of the State of New York, criticizing Gov. George E. Pataki's proposal to eliminate parole for violent felons, misstated the authorship of the resolution. It was drawn up by the association's executive committee, not by Justice Burton B. Roberts of the Bronx.

•

An obituary on Saturday about Sam Lopata, who designed a number of New York restaurants, gave an incorrect date for the opening of one of them. The restaurant, Joanna, was opened in 1980, not 1978.

•

A Critic's Notebook yesterday about television news reports tied to prime-time shows misidentified the weatherman on WNYW, the Fox-owned station in New York. He is Nick Gregory, not Nick Gomez.

Pataki Outlaws Herbal Stimulant Used by Youths

By CLIFFORD KRAUSS

Gov. George E. Pataki has announced an immediate statewide ban on the sale of so-called Herbal Ecstacy and other herbal products containing the stimulant ephedra, which has been blamed for 15 deaths nationwide.

Typically sold in health food and novelty shops in the form of pills, powders and sodas, the stimulants have become increasingly popular among middle-class youths seeking alternatives to the kick received from illegal drugs. But while the stimulants have been promoted as safe natural-food supplements by about 100 companies, the Food and Drug Administration issued a warning to consumers last month that the stimulants can be dangerous when taken in excess, especially to people with high blood pressure, heart disease and diabetes.

"We're not going to let our kids be exploited for a cheap profit," Governor Pataki said at a news conference in Manhattan yesterday to announce the ban, which state health laws allow him to impose without legislative action. "Obviously the best solution would be a Federal role, but we can't sit back and wait and let our young people die."

The Governor's action came two days after his ally, Senator Alfonse M. D'Amato, introduced legislation to increase Federal controls on ephedra-based products.

Under the Governor's order, the State Health Department has issued a ban on the sale of 20 specific ephedra-based products that are explicitly marketed for people looking for a drug high or that do not include directions on appropriate dosage. Prescription and over-the-counter medications for

Continued on Page B6

Continued From Page B1

allergies, bronchial disorders and asthma that contain ephedra — including Primatene and Sudafed — will not be affected.

Besides Herbal Ecstacy, the products bear such names as Euphoria, Brain Wash and Buzz Tablets.

In a related action, the Commissioner of Agriculture and Markets, Donald R. Davidsen, issued a recall of six carbonated beverages that contain ephedra.

The ban will be enforced by local and state public health officials, who will do spot checks of stores that have sold the products and will investigate complaints. Merchants violating the ban will face fines of $2,000 and prison terms of up to one year.

The state's action does not target possession of ephedra, meaning that there would be little to stop New York residents from buying such herbal products in New Jersey or Connecticut.

But Richard Curtis, an expert on narcotics at John Jay College of Criminal Justice, said he thought Governor Pataki's action would be largely effective in stemming the market. "I can't imagine there will be much of a big black market," he said, "because if you want to go that far, you might as well buy real Ecstasy, the illegal narcotic kind."

Companies can appeal the banning of their products at a hearing in Albany on June 4.

Konstantine Theoharis, the executive media coordinator of Global World Media Corporation, the producer of Herbal Ecstacy, said he thought there was a good chance that the ban on his product could be reversed.

"Politicians and bureaucracies usually overreact," Mr. Theoharis said. "We feel there is tons of misinformation out there and once we have a fair chance to represent ourselves our products will be shown to be harmless and beneficial."

He added, "Our products are an alternative to chemically toxic legal and illegal drugs available to anybody."

Few people in the East Village, a center of ephedra sales in the city, had heard of the ban yesterday, and most sellers and buyers reacted with little emotion.

Armida Barth, owner of Lady in the Moon shop at 111 St. Mark's Place, said that she had stopped selling ephedra products three months ago when she learned of the dangers. "The only reason why I sold it is because I'm against kids using drugs," she said.

Larry Carter, a manager at Love Saves the Day, at 119 Second Avenue, where a sign in the window proclaims "Herbal Ecstacy Sold Here," said, "We're not going to cry if we have to take it off the shelves." But he noted that sales had increased in recent months. In the last nine months, the store's biweekly orders of 10-packs of Herbal Ecstacy pills increased more than three-fold to 860 packages from 150.

While other restrictions have been imposed in Ohio and Florida, the Federal and state governments have for the most part been slow to regulate ephedra because it is considered a safe food supplement when taken according to directions. While technically classified as a natural herb and not a drug, ephedra can induce a euphoric feeling or heart palpitations when taken in excessive doses.

Senator D'Amato, a Republican, Senator Christopher Dodd, Democrat of Connecticut, and Representative Bill Frist, Republican of Tennessee, have introduced legislation that would reclassify as a drug any herb or dietary supplement like ephedra that advertises itself as a euphoria-producing or awareness-heightening product. Such products would then come under stricter regulation by the Federal Drug Administration.

Concern over ephedra intensified last month when a Florida coroner ruled that Peter Schlendorf, a 20-year-old college student from Northport, L.I., had died from taking double the recommended dose of Ultimate Xphoria, one of the 20 products banned yesterday by Mr. Pataki.

Since 1993, according to the F.D.A., about 400 people have reported adverse reactions to ephedra-based products, ranging from dizziness to strokes, and 15 people have died.

In an interview, New York State's Health Commissioner, Barbara A. DeBuono, predicted that many states, including Connecticut and New Jersey, would follow New York's lead. But she said there was no need for a complete ban on ephedra-based products that serve medical functions.

Speaking of several prescription and over-the-counter medications that include ephedra, she said, "There is nothing about the way those products are marketed, advertised or sold that has indicated to us a threat to the public's health, since they are properly labeled and there are appropriate warnings for adverse health affects."

THE NEW YORK TIMES

FRIDAY, MAY 24, 1996

EXECUTIVE OFFICE OF THE PRESIDENT
OFFICE OF MANAGEMENT AND BUDGET
Washington, D.C. 20503-0001

LRM NO: 5218
FILE NO: 1746

SPECIAL

7/29/96

LEGISLATIVE REFERRAL MEMORANDUM

Total Page(s): 6

TO: Legislative Liaison Officer - See Distribution below:

FROM: Janet FORSGREN (for) Assistant Director for Legislative Reference

OMB CONTACT: Robert PELLICCI 395-4871 Legislative Assistant's Line: 395-7362
C=US, A=TELEMAIL, P=GOV+EOP, O=OMB, OU1=LRD, S=PELLICCI, G=ROBERT, I=J
pellicci_r@a1.eop.gov

SUBJECT: HHS Drafting Service RE: HR3199, Drug and Biological Products Reform Act of 1996

DEADLINE: 10:00 a.m. Wednesday, July 31,1996

In accordance with OMB Circular A-19, OMB requests the views of your agency on the above subject before advising on its relationship to the program of the President.

Please advise us if this item will affect direct spending or receipts for purposes of the "Pay-As-You-Go" provisions of Title XIII of the Omnibus Budget Reconciliation Act of 1990.

COMMENTS: The attached language may be added to pending legislation that would reform the operations of the FDA. House Committee markup could occur this week. Please expedite your views on the attached language affecting the regulation of human tissue.

DISTRIBUTION LIST:

AGENCIES: 61-JUSTICE - Andrew Fois - 2025142141
76-National Economic Council - Sonyia Matthews - 2024562174

EOP: Nancy-Ann Min
Chris Jennings
Greg Simon
Jennifer Klein
Elizabeth Drye
Michael Fitzpatrick
Barry Clendenin
Richard Turman
Jim Esquea
Jonathan Winer
Allison Eydt
Elena Kagan
Bob Damus
Janet Forsgren

RESPONSE TO LEGISLATIVE REFERRAL MEMORANDUM

LRM NO: **5218**

FILE NO: **1746**

If your response to this request for views is short (e.g., concur/no comment), we prefer that you respond by e-mail or by faxing us this response sheet.
If the response is short and you prefer to call, please call the branch-wide line shown below (NOT the analyst's line) to leave a message with a legislative assistant.
You may also respond by:
(1) calling the analyst/attorney's direct line (you will be connected to voice mail if the analyst does not answer); or
(2) sending us a memo or letter
Please include the LRM number shown above, and the subject shown below.

TO: Robert PELLICCI 395-4871
Office of Management and Budget
Fax Number: 395-6148
Branch-Wide Line (to reach legislative assistant): 395-7362

FROM: ______________________ (Date)

______________________ (Name)

______________________ (Agency)

______________________ (Telephone)

SUBJECT: HHS Drafting Service RE: HR3199, Drug and Biological Products Reform Act of 1996

The following is the response of our agency to your request for views on the above-captioned subject:

______ Concur

______ No Objection

______ No Comment

______ See proposed edits on pages ______

______ Other: ______________

______ FAX RETURN of ____ pages, attached to this response sheet

REGULATION OF HUMAN TISSUE --

(1) REQUIREMENT -- Part F of Title III of the Public Health Service Act (42 U.S.C. 262 et seq.) is amended by inserting after section 352 the following new section:

"Section 352A. REQUIREMENTS FOR HUMAN TISSUE

(a) IN GENERAL -- Facilities and persons that engage in the recovery, processing, storage, or distribution of human tissue:

(1) shall annually register with the Secretary and provide the Secretary a list of all human tissues that are recovered, processed, stored, or distributed to/from such facility, except that the Secretary may exempt facilities or persons from such requirements on the grounds that they are not necessary to protect the public health;

(2) shall at the time of registration provide a list of all contractors or agents of the tissue establishment who engage in the recovery, processing, storage, or distribution of human tissue; and

(3) shall comply with good tissue practices including, but not limited to, practices that address:

(A) quarantine; recordkeeping; the recovery, processing, storage, and distribution of tissue; validation of manufacturing facilities and equipment; quality control; packaging and labeling; adverse experience reports; complaint files and failure investigations; personnel qualification and training; and tissue tracking procedures to identify tissue from donor to recipient and from recipient to donor; and

(B) donor screening and infectious disease testing.

(4) are subject to inspection by individuals authorized by the Secretary;

(5) shall comply with regulations regarding labeling, advertising, and promotion, which may be promulgated by the Secretary.

(b) REGULATIONS

The Secretary may promulgate regulations for implementation of this section. Such regulations may include provisions for certification of facilities that engage in the recovery, processing, storage, or distribution of human tissue.

(c) FINDING OF INTERSTATE COMMERCE
Congress finds that human tissue that is recovered, processed, distributed, or stored in the United States for medical use is in, or otherwise directly affects, interstate commerce.

(d) DEFINITION –

(1) HUMAN TISSUE – The term "human tissue" means any tissue (an aggregate of similar cells together with their intercellular substance, or acellular integuments that have a particular structure and function) derived from a human body which:

(A) is intended for administration to another human for the diagnosis, cure, mitigation, treatment, or prevention of any condition or disease;

(B) is intended only to replace or repair comparable bodily tissue and does not act through a systemic mechanism;

(C) is recovered, processed, stored, or distributed by methods which do not change tissue function or characteristics or propagate the tissue's cells;

(D) may include the addition of substances that are safe under conditions of intended use and not intended to contribute to or provide a therapeutic effect to the recipient; and

(E) includes demineralized bone, heart valves, and dura mater.

(2) Such term does not include:

(A) human material regulated or classified as a drug, medical device or biological product except as specified in (d)(1)(E) ;

(B) vascularized human organs, such as heart, liver, kidneys, lungs, intestines, or pancreas;

(C) blood, blood products, bone marrow, stem cells, somatic cell therapy, gene therapy, or human milk;

(D) tissue that is combined with a drug, device, biologic, or another tissue; and

(e) TISSUE SPECIFIC REVIEW
For specific human tissue as the Secretary deems appropriate and for which she has

identified a public health concern related to clinical safety or effectiveness, the Secretary may conduct a review of existing data on clinical use, indications, outcomes, safety, and effectiveness of such tissue and may, as part of, or following, such review:

(1) promulgate regulations controlling such tissue including, but not limited to, requirements for special labeling or reclassification (under reclassification subsection) of such tissue; and

(2) set such other limitations as the Secretary may require to protect the public health.

(f) CLASSIFICATION AND RECLASSIFICATION

(1) the Secretary may classify or reclassify a human tissue as a drug, biological product or medical device, if the Secretary determines that such classification or reclassification is needed to protect the public health or, during the tissue specific review of subsection (e), the Secretary determines that premarket study of effectiveness is warranted; and

(2) the Secretary may reclassify a human drug, biological product or medical device as a human tissue, if the Secretary determines that such previous classification is unnecessary to protect the public health.

(g) RECALL, RETENTION, AND DESTRUCTION AUTHORITY --
If the Secretary finds that a facility or human tissue violates any provision in this section or any regulations promulgated thereunder, the Secretary may issue an order that such facility cease distribution of human tissue or that such human tissue be retained, recalled, or destroyed. After receipt of such an order, the person in possession of the human tissue shall not distribute or dispose of the human tissue in any manner except consistent with the provisions of the order. Persons subject to the order who wish to challenge the order, shall, within 5 days of receipt of such order, request an opportunity for an informal hearing to be held within 30 days.

(2) INTERIM REGULATIONS – The requirements set forth in the interim regulations promulgated by the Secretary in December, 1993 shall remain in effect until new regulations that supersede these regulations are in effect.

(3) ADULTERATION PROVISION – Section 501 (21 U.S.C. 351) is amended as follows:

(A) in the first sentence by changing "drug or device" to "drug, device, or human tissue."

(B) by inserting at the end thereof the following new subsection:

"(j) If it is human tissue and it is recovered, processed, stored, or distributed by a facility that does not comply with good tissue practices consistent with section 352(a) of the Public Health Service Act."

(4) MISBRANDING PROVISIONS -- section 502 (21 U.S.C. 352) is amended as follows:

(A) by renaming the section "Misbranded Drugs, Devices, and Human Tissue"

(B) in the first sentence by adding "(a)" before "A drug or device."

(C) by redesignating subsections (a) through (t) as paragraphs (1) through (20).

(D) by adding at the end thereof the following new subsection:

"(b) Human tissue shall be deemed to be misbranded if its labeling is false or misleading in any particular or if its labeling, advertising, or promotion does not comply with regulations promulgated under section 352A(a) (5).

(5) PROHIBITED ACTS. -- Section 301 (21 U.S.C. 331) is amended by inserting the following new subsection:

"(v) The adulteration or misbranding of any human tissue.

(6) SEIZURE. --

(A) Section 304 (a)(2)(D) (21 U.S.C. 334 (a)) is amended by inserting "or human tissue" after "device."

(B) Section 304(d)(1) is amended by deleting the "or" before "cosmetic" and inserting ", or human tissue" after "cosmetic" in the first sentence.

EXECUTIVE OFFICE OF THE PRESIDENT
OFFICE OF MANAGEMENT AND BUDGET
Washington, D.C. 20503-0001

LRM NO: 5218

FILE NO: 1746

SPECIAL

7/29/96

LEGISLATIVE REFERRAL MEMORANDUM

Total Page(s): 6

TO: Legislative Liaison Officer - See Distribution below:

FROM: Janet FORSGREN Janet Forsgren (for) Assistant Director for Legislative Reference

OMB CONTACT: Robert PELLICCI 395-4871 Legislative Assistant's Line: 395-7362
C=US, A=TELEMAIL, P=GOV+EOP, O=OMB, OU1=LRD, S=PELLICCI, G=ROBERT, I=J
pellicci_r@a1.eop.gov

SUBJECT: HHS Drafting Service RE: HR3199, Drug and Biological Products Reform Act of 1996

DEADLINE: 10:00 a.m. Wednesday, July 31,1996

In accordance with OMB Circular A-19, OMB requests the views of your agency on the above subject before advising on its relationship to the program of the President.

Please advise us if this item will affect direct spending or receipts for purposes of the "Pay-As-You-Go" provisions of Title XIII of the Omnibus Budget Reconciliation Act of 1990.

COMMENTS: The attached language may be added to pending legislation that would reform the operations of the FDA. House Committee markup could occur this week. Please expedite your views on the attached language affecting the regulation of human tissue.

DISTRIBUTION LIST:

AGENCIES: 61-JUSTICE - Andrew Fois - 2025142141
76-National Economic Council - Sonyia Matthews - 2024562174

EOP: Nancy-Ann Min
Chris Jennings
Greg Simon
Jennifer Klein
Elizabeth Drye
Michael Fitzpatrick
Barry Clendenin
Richard Turman
Jim Esquea
Jonathan Winer
Allison Eydt
Elena Kagan
Bob Damus
Janet Forsgren

RESPONSE TO LEGISLATIVE REFERRAL MEMORANDUM

LRM NO: **5218**

FILE NO: **1746**

If your response to this request for views is short (e.g., concur/no comment), we prefer that you respond by e-mail or by faxing us this response sheet.
If the response is short and you prefer to call, please call the branch-wide line shown below (NOT the analyst's line) to leave a message with a legislative assistant.
You may also respond by:
(1) calling the analyst/attorney's direct line (you will be connected to voice mail if the analyst does not answer); or
(2) sending us a memo or letter
Please include the LRM number shown above, and the subject shown below.

TO: Robert PELLICCI 395-4871
Office of Management and Budget
Fax Number: 395-6148
Branch-Wide Line (to reach legislative assistant): 395-7362

FROM: ____________________ (Date)

____________________ (Name)

____________________ (Agency)

____________________ (Telephone)

SUBJECT: HHS Drafting Service RE: HR3199, Drug and Biological Products Reform Act of 1996

The following is the response of our agency to your request for views on the above-captioned subject:

_____ Concur

_____ No Objection

_____ No Comment

_____ See proposed edits on pages _________

_____ Other: ____________________

_____ FAX RETURN of ____ pages, attached to this response sheet

REGULATION OF HUMAN TISSUE --

(1) REQUIREMENT -- Part F of Title III of the Public Health Service Act (42 U.S.C. 262 et seq.) is amended by inserting after section 352 the following new section:

"Section 352A. REQUIREMENTS FOR HUMAN TISSUE

(a) IN GENERAL -- Facilities and persons that engage in the recovery, processing, storage, or distribution of human tissue:

(1) shall annually register with the Secretary and provide the Secretary a list of all human tissues that are recovered, processed, stored, or distributed to/from such facility, except that the Secretary may exempt facilities or persons from such requirements on the grounds that they are not necessary to protect the public health;

(2) shall at the time of registration provide a list of all contractors or agents of the tissue establishment who engage in the recovery, processing, storage, or distribution of human tissue; and

(3) shall comply with good tissue practices including, but not limited to, practices that address:

(A) quarantine; recordkeeping; the recovery, processing, storage, and distribution of tissue; validation of manufacturing facilities and equipment; quality control; packaging and labeling; adverse experience reports; complaint files and failure investigations; personnel qualification and training; and tissue tracking procedures to identify tissue from donor to recipient and from recipient to donor; and

(B) donor screening and infectious disease testing.

(4) are subject to inspection by individuals authorized by the Secretary;

(5) shall comply with regulations regarding labeling, advertising, and promotion, which may be promulgated by the Secretary.

(b) REGULATIONS
The Secretary may promulgate regulations for implementation of this section. Such regulations may include provisions for certification of facilities that engage in the recovery, processing, storage, or distribution of human tissue.

(c) FINDING OF INTERSTATE COMMERCE
Congress finds that human tissue that is recovered, processed, distributed, or stored in the United States for medical use is in, or otherwise directly affects, interstate commerce.

(d) DEFINITION --

(1) HUMAN TISSUE -- The term "human tissue" means any tissue (an aggregate of similar cells together with their intercellular substance, or acellular integuments that have a particular structure and function) derived from a human body which:

(A) is intended for administration to another human for the diagnosis, cure, mitigation, treatment, or prevention of any condition or disease;

(B) is intended only to replace or repair comparable bodily tissue and does not act through a systemic mechanism;

(C) is recovered, processed, stored, or distributed by methods which do not change tissue function or characteristics or propagate the tissue's cells;

(D) may include the addition of substances that are safe under conditions of intended use and not intended to contribute to or provide a therapeutic effect to the recipient; and

(E) includes demineralized bone, heart valves, and dura mater.

(2) Such term does not include:

(A) human material regulated or classified as a drug, medical device or biological product except as specified in (d)(1)(E) ;

(B) vascularized human organs, such as heart, liver, kidneys, lungs, intestines, or pancreas;

(C) blood, blood products, bone marrow, stem cells, somatic cell therapy, gene therapy, or human milk;

(D) tissue that is combined with a drug, device, biologic, or another tissue; and

(e) TISSUE SPECIFIC REVIEW
For specific human tissue as the Secretary deems appropriate and for which she has

identified a public health concern related to clinical safety or effectiveness, the Secretary may conduct a review of existing data on clinical use, indications, outcomes, safety, and effectiveness of such tissue and may, as part of, or following, such review:

(1) promulgate regulations controlling such tissue including, but not limited to, requirements for special labeling or reclassification (under reclassification subsection) of such tissue; and

(2) set such other limitations as the Secretary may require to protect the public health.

(f) CLASSIFICATION AND RECLASSIFICATION

(1) the Secretary may classify or reclassify a human tissue as a drug, biological product or medical device, if the Secretary determines that such classification or reclassification is needed to protect the public health or, during the tissue specific review of subsection (e), the Secretary determines that premarket study of effectiveness is warranted; and

(2) the Secretary may reclassify a human drug, biological product or medical device as a human tissue, if the Secretary determines that such previous classification is unnecessary to protect the public health.

(g) RECALL, RETENTION, AND DESTRUCTION AUTHORITY --
If the Secretary finds that a facility or human tissue violates any provision in this section or any regulations promulgated thereunder, the Secretary may issue an order that such facility cease distribution of human tissue or that such human tissue be retained, recalled, or destroyed. After receipt of such an order, the person in possession of the human tissue shall not distribute or dispose of the human tissue in any manner except consistent with the provisions of the order. Persons subject to the order who wish to challenge the order, shall, within 5 days of receipt of such order, request an opportunity for an informal hearing to be held within 30 days.

(2) INTERIM REGULATIONS -- The requirements set forth in the interim regulations promulgated by the Secretary in December, 1993 shall remain in effect until new regulations that supersede these regulations are in effect.

(3) ADULTERATION PROVISION -- Section 501 (21 U.S.C. 351) is amended as follows:

(A) in the first sentence by changing "drug or device" to "drug, device, or human tissue."

(B) by inserting at the end thereof the following new subsection:

"(j) If it is human tissue and it is recovered, processed, stored, or distributed by a facility that does not comply with good tissue practices consistent with section 352(a) of the Public Health Service Act."

(4) MISBRANDING PROVISIONS -- section 502 (21 U.S.C. 352) is amended as follows:

(A) by renaming the section "Misbranded Drugs, Devices, and Human Tissue"

(B) in the first sentence by adding "(a)" before "A drug or device."

(C) by redesignating subsections (a) through (t) as paragraphs (1) through (20).

(D) by adding at the end thereof the following new subsection:

"(b) Human tissue shall be deemed to be misbranded if its labeling is false or misleading in any particular or if its labeling, advertising, or promotion does not comply with regulations promulgated under section 352A(a) (5).

(5) PROHIBITED ACTS. -- Section 301 (21 U.S.C. 331) is amended by inserting the following new subsection:

"(v) The adulteration or misbranding of any human tissue.

(6) SEIZURE. --

(A) Section 304 (a)(2)(D) (21 U.S.C. 334 (a)) is amended by inserting "or human tissue" after "device."

(B) Section 304(d)(1) is amended by deleting the "or" before "cosmetic" and inserting ", or human tissue" after "cosmetic" in the first sentence.

DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Rockville MD 20857

STATEMENT BY

WILLIAM B. SCHULTZ

DEPUTY COMMISSIONER FOR POLICY

FOOD AND DRUG ADMINISTRATION

PUBLIC HEALTH SERVICE

DEPARTMENT OF HEALTH AND HUMAN SERVICES

BEFORE THE

COMMITTEE ON LABOR AND HUMAN RESOURCES

UNITED STATES SENATE

FEBRUARY 22, 1996

FOR RELEASE ONLY UPON DELIVERY

INTRODUCTION

Madam Chairman and Members of the Committee. I appreciate the opportunity to testify on the important issue of promotion of unapproved uses of prescription drugs and medical devices.

My name is William B. Schultz. I am the Deputy Commissioner for Policy at the Food and Drug Administration.

FDA SUPPORTS THE DISSEMINATION OF INFORMATION TO PHYSICIANS

Madam Chairman, I am here today to talk about uses that do not appear in a product's FDA-approved labeling and are not approved by the Agency. Such uses commonly are referred to as "off label," "unapproved," "unlabeled," or "extra-label" uses. The Food and Drug Administration recognizes that, in certain circumstances, off label uses of approved products are appropriate, rational, and accepted medical practice. FDA knows that there are important off label uses of approved drugs. In this context, it is important that physicians have access to accurate information about drugs. But we also know that allowing the promotion of these kinds of uses can have negative public health consequences -- including exposing patients to unnecessary risks and destroying the incentive for companies to conduct the necessary research to demonstrate that products are safe and effective for these uses. Striking the proper balance between the need to regulate the promotion of unapproved uses for drugs and devices and the need for reliable scientific data and

information on unapproved uses of approved products is a difficult and controversial challenge.

FDA'S REGULATORY AUTHORITY

I would like to start today by explaining how, in passing and amending the Federal Food, Drug, and Cosmetic Act (FDC Act), Congress struck that balance and what, as a result of Congressional decisions, FDA can and cannot do with respect to off label uses.

The legislative history of the Federal Food, Drug, and Cosmetic Act indicates that Congress did not intend FDA to interfere with the practice of medicine. Thus, once a drug is approved for marketing, FDA does not generally regulate how, and for what uses, physicians prescribe that drug. A physician may prescribe a drug for uses or in treatment regimens or patient populations that are not listed in the FDA-approved labeling.

Generally, FDA does not prohibit the dissemination of information to health care professionals. Physicians access information about off label uses through compendia, journal articles, continuing medical education programs, symposia, and professional meetings. Physicians also have access to a number of databases that provide information about off label uses. For example, the National Cancer Institute's Physician Data Query (PDQ) system is an excellent source for oncologists to obtain

information about current oncologic therapies. The National Library of Medicine (NLM) offers a Medical Literature Analysis and Retrieval System (MEDLARS), which is a computerized system of databases and databanks pertinent to biomedical research and patient care. NLM currently offers free access to three databases relating to AIDS. FDA does not regulate a physician's access to any of these types of independent off label use information -- no matter how preliminary it may be. In addition, FDA does not prohibit a manufacturer from providing a physician information about off label uses if the physician requests that information. Recently, the Agency announced a proposed change to its policy with respect to the dissemination of reference texts (medical textbooks and compendia). Drug companies may distribute independent reference texts even if they contain certain information about off label uses of approved drugs, as long as the texts do not have a significant focus on an off label use of the manufacturer supporting dissemination of the text. FDA recognizes that all of these sources of information can be very important to good medical practice.

Although the FDC Act does not authorize FDA to regulate the practice of medicine, it specifically directs FDA to regulate the promotion of drugs and devices. Promotional materials are unlawful if they promote an unapproved use for the product; contain claims relating to the dosing, safety or effectiveness of the product that are inconsistent with the approved labeling; or

if they lack a fair and balanced presentation of information, _i.e._, of benefits and risks. Although submission of an article for publication in a journal is not promotional, the use of such an article to sell a drug or device is promotional.

Under current law, if a company wants to promote a use of a drug or device it can do so by submitting an efficacy supplement and getting that use onto the label. As I will explain later in my testimony, getting a use onto the label has benefits beyond being allowed to promote. For example, it ensures reimbursement from third party payors, it helps to get that use included in formularies, and it gives the medical community more complete information about the product. As I will further explain later in my testimony, the requirements for efficacy supplements are often significantly simpler than the requirements for applying for permission to market a product in the first place. Moreover, the Agency is considering a number of measures that will make the supplement process a more effective tool for getting additional uses on the label of drug and device products.

S. 1447

The Food and Drug Administration Performance and Accountability Act of 1995, S. 1447, bypasses the current approach. It would permit drug and device companies to use journal articles, textbook chapters, continuing medical education program materials, and compendial information relating to uses

recognized for purposes of third party coverage or reimbursement that discuss off label uses to promote the sale of their products for those uses. The bill also would permit drug companies to use summaries of journal articles, textbook chapters, CME program materials, or information relating to uses recognized for purposes of third party coverage or reimbursement to promote the sale of their products for off label uses. Device companies could distribute oral and written information about off label uses that are part of an "exchange" among health care practitioners, health care reimbursement officials, and the industry, that is exchanged for "educational or scientific purposes," or that is presented at CME programs, seminars, workshops, or demonstrations for devices to promote the sale of their products for those uses.

We recognize that the purpose of the bill is to enhance dissemination of information and not to facilitate or encourage promotion of off label uses. But we strongly believe that if the bill is enacted, that will be its effect. Drug and device manufacturers market their products principally by sending sales representatives, referred to as detail men and women, out to talk one on one with physicians who might prescribe their products. A detailer's job is to convince those physicians to use and prescribe their products. They do this by providing information that purports to describe the usefulness of their products in the patient population. Written materials such as journal articles

that discuss favorable studies of these products are powerful tools in the hands of a detailer. If the bill is enacted, drug and device companies will be free to use these materials to promote off label uses.

Pursuant to the bill, after a company receives FDA approval of a drug or device for one use, it would be permitted to promote that product, through these other means, for other uses. The material that companies could distribute often would be very preliminary, based on poorly designed or wholly uncontrolled studies. Companies could promote the use of a product even when the evidence merely suggests or can be interpreted as suggesting that a product may work for a specific use. Effectiveness would not have to be demonstrated. Thus, if drug X is approved for cancer patients, and there is some preliminary data that suggests it is beneficial for patients with crippling arthritis, the drug's manufacturer would be permitted to promote the drug and encourage its use for arthritis on the basis of this preliminary or unsubstantiated data. This promotion would be permitted even though the data have not been reviewed by independent scientific FDA experts.

In addition, the clinical information that appears in the materials that the bill allows manufacturers to distribute has not been validated in any way. For example, neither peer reviewers nor textbook editors review the data underlying a study

described in a journal article or textbook chapter. In fact, peer reviewers and editors do not even see that data.

FDA has serious concerns regarding the promotion of indications that have not been reviewed and approved by the Agency. Because promotional activities of drug companies and others are substantially motivated by profit and market expansion, the widespread promotion of prescription drugs and devices for uses that have not been determined to be safe and effective could be detrimental to the health and safety of the public. Permitting companies to promote drugs and devices for off label uses could have a number of devastating consequences for the quality of medical care in this country.

PROBLEMS WITH PERMITTING PROMOTION OF OFF LABEL USES

The fundamental problem with permitting the promotion of off label uses is that not all off label uses are safe and effective. The only way to know which ones are safe and effective is to collect and analyze the data supporting a finding of safety and efficacy. Because the data on off label uses have not been collected and analyzed, their promotion raises a number of serious concerns.

Undercutting the Efficacy Standard

Permitting the promotion of off label uses based on studies reported in journal articles or other texts that clearly are an

inadequate basis for approval by FDA would undercut the efficacy standard.

A fundamental precept of drug and device regulation in this country is that these products must be proven safe and effective before they can be sold. The requirement that these products must be proven effective, on the basis of well-controlled clinical studies, was first adopted by Congress in 1962. Congress specifically added the concept of effectiveness to the definition of "new drug" in order to ensure that the efficacy requirement would apply not only to initial claims made for a drug, but also to claims made after the initial new drug application had been approved. 108 Cong. Rec. S22044-46 (daily ed. October 3, 1962); S. Rep. No. 1744, 87th Cong., 2d Sess. Part 2 at 267, 271 (1962) ("On what logical basis can one possibly argue that the initial claim for a drug . . . should be supported by "substantial evidence" but that successive claims . . . should not be so supported?" 108 Cong. Rec. at S22045.)

The addition of the "efficacy standard" revolutionalized drug development and approval, not only in the United States, but worldwide, as well. Essentially, a manufacturer cannot just <u>say</u> that a product works for a particular disease or condition, it must <u>prove</u> that the product works for that disease or condition. The only way manufacturers can prove efficacy is by submitting data from well-controlled clinical trials for evaluation by

independent experts at FDA. Anecdotal reports and poorly controlled observations do not suffice because those kinds of reports may be wrong or may not be an adequate basis for conclusion. We know this because we have had experience with this type of information. Many drugs approved before 1962 turned out not to work when, after 1962, they had to be (and were) studied. Even when such reports suggest efficacy, they fail to provide important guidance in areas critical to the effective use of a therapy such as dosage and patient selection and management.

The solid foundation that is laid down by the efficacy standard is one of the main reasons that there is a strong sense of confidence in the drug products that are on the U.S. market today. Because the standard requires well-controlled clinical trials, once FDA has made a determination of effectiveness, there can be a high degree of confidence that the drug will work. Thus, when a manufacturer claims that a product is safe and effective for a particular disease or condition, doctors can be confident that the product is in fact safe and effective for that disease or condition. Patients, in turn, can have confidence in the quality of the products they are receiving.

Eliminating the need for well-controlled studies would be a major setback for the first-rate medical care that the health care system in this country provides. Consider some of the

additional uses that FDA has approved on the basis of such studies -- for example, timolol, propranolol, metoprolol, and atenolol to improve the survival of heart attack patients, taxol for breast cancer, and interferon-alpha 2b for chronic hepatitis B and C. Without the requirement to submit clinical studies to prove that drugs are effective for their intended uses, it is far less likely that we would know that these drugs will work to decrease mortality in heart attack patients, to delay or prevent breast cancer recurrence, or to treat chronic hepatitis B and C. In the absence of the efficacy requirement, the market will be filled with drugs that manufacturers claim work and that physicians use because of a belief that they work, but for which there is relatively little evidence.

Disincentive to Conduct Studies

One of the most serious consequences of allowing companies to freely promote off label uses is that companies would have no incentive to conduct or fund the necessary scientific research and to present data to FDA to verify the safety and efficacy of those off label uses. In fact, because the Agency might determine that the new use is not supported by the evidence, there would be an incentive to avoid FDA review. To use the example of the cancer drug that may be useful for crippling arthritis, why would the drug company undergo the expense of actually studying whether the drug works for arthritis if it could promote the drug for arthritis based on preliminary

evidence, particularly since a thorough study might fail to establish efficacy for arthritis?

In a world where off label uses can be widely promoted, manufacturers would have an incentive to do the minimal amount of studies necessary to obtain approval for the first, narrowest/easiest indication and then heavily promote the product for other broader (and possibly more speculative) uses. For example, interferon-alpha 2b was approved for use in hairy cell leukemia, of which there are approximately 300-400 cases per year. It subsequently was approved to treat chronic hepatitis B and C, of which there are tens of thousands of cases per year. If S. 1477 had been in effect, the manufacturer of interferon-alpha 2b could have sought approval for hairy cell leukemia and then just promoted for chronic hepatitis B and C -- the much broader use -- based on preliminary data. Interferon-alpha 2b is just one of many examples of a second, very different use being significantly broader than the original use for which a drug was approved.

Under the approach taken in the bill, we might never learn whether interferon alpha actually works to treat hepatitis B -- yet the manufacturer could promote its use. This is precisely the scenario that Congress sought to prevent when it added the effectiveness requirement to the definition of a new drug. A group of Senators, lead by Senator Kefauver, argued that unless

the effectiveness requirement was added to the definition of drugs, "the expectation would be that the initial claim would tend to be quite limited, which of course, would expedite approval of the new drug application. Thereafter, 'the sky would be the limit' and extreme claims of any kind could be made," subject only to FDA's enforcement authority. 108 Cong. Rec. at S22046.

Because the incentive to conduct research on uses of drugs and devices will decrease, the end result will be that the dissemination of off label information pursuant to this bill will actually reduce the amount of information that health care providers receive about drugs and devices.

Safety Issues

Widespread promotion of unapproved uses also raises significant safety concerns. Even under the current law, which prohibits the promotion of off label uses, we know of a number of instances where physicians have used drugs for off label uses that have resulted in disastrous consequences.

For example, the drugs encainide and flecainide were approved for life-threatening and symptomatic arrhythmias, which are abnormal rhythms of the heart. In the late 1980's, physicians began to prescribe these two drugs for heart attack victims who were experiencing ventricular premature complexes

(VPCs), a type of asymptomatic or minimally symptomatic arrhythmia. (Asymptomatic arrhythmias are arrhythmias that can be detected by tests, but which the patients do not feel.) This off label use, which was supported by published peer-reviewed journal articles, was intended to prevent the well-documented increased mortality of heart attack victims who have a high level of VPCs by suppressing those VPCs. The use was logical and became so widespread that the National Institutes of Health decided to study the effectiveness of encainide and flecainide in these patients. To the surprise of almost everybody, that study demonstrated not only that the drugs were ineffective in reducing the risk of death but that the drugs were actually harmful in patients for whom it was being prescribed off label -- that is the death rate among those receiving the drug was more than twice the rate of those receiving a placebo. If these unapproved uses had been heavily promoted by drug companies, it is estimated that thousands more unnecessary deaths would have occurred.

Another example relates to the widespread off label use of a class of drugs called calcium channel blockers (CCBs). These drugs are effective for patients suffering from angina, which is chest pain caused by insufficient oxygen to the heart muscle. CCBs have no established role in patients who have had a heart attack but have no symptoms. These patients do, however, benefit from another class of drugs, beta-blockers, which are known to reduce mortality by 25-30% after heart attacks. Nevertheless,

CCBs are widely used in this patient population and there are publications that could be interpreted as supporting this use. Because CCBs and beta-blockers generally should not be used simultaneously, patients are receiving CCBs _in lieu_ of clearly life-saving beta blockers. Many, probably thousands, of lives are lost each year because a drug of no known benefit is being used for an unapproved use in place of a drug with known value. Widespread promotion of this use would make the problem even worse.

Yet another example of a case where the distribution of published articles on off label use could have resulted in very serious harm to the public involves the fentanyl transdermal system (Duragesic). Approved for use in chronic pain in patients requiring opioids, the fentanyl patch was not approved for acute post-operative pain because of concern that it would cause respiratory depression (a serious condition in which less air reaches the lungs) in those patients not used to the effect of opioids. A number of publications prior to the time of approval, however, described the drug as safe and effective for post-operative pain. After approval, reports to FDA and the literature documented life-threatening respiratory depression in post-operative patients given the patches. Extensive promotion of this off label use could have been disastrous.

There are many other claims that could be promoted through

peer-reviewed journal articles describing off label uses that could be detrimental to a large number of patients if they were heavily promoted. FDA fears that problems illustrated by these examples would be multiplied if manufacturers were given free rein to promote unapproved uses.

Unbalanced View

Another significant problem with permitting companies to promote unapproved uses by distributing the type of information described in the bill is that physicians may not receive a balanced view of the available information. It is well documented that there is publication bias. Studies with favorable results have a greater likelihood of getting published; studies with less favorable results less often get published. More importantly, even if less favorable or contradictory results have been published, companies have no incentive to distribute articles, textbook chapters, or other information recommending against a particular use. Because the bill permits companies to distribute certain chapters of textbooks or mere summaries of journal articles, chapters, and CME materials, with no obligation for balance or comprehensiveness, physicians may see only one side of an off label use story.

The current law governing promotion requires balance. Changing the law to allow the distribution of journal articles and other similar materials that discuss off label uses will

allow drug detail men and women to provide materials that describe favorable study results of their product for a particular use, but without providing copies of materials that go the other way.

I would like to illustrate with an example. Human growth hormone currently is indicated for use only in children who are short because they lack sufficient growth hormone and children who are short because of kidney problems. Its use in children who are short, but have no growth hormone deficiency or underlying kidney problem, is an off label use of uncertain value and safety. We identified four journal articles that discuss this off label use -- two more or less supported the off label use and two did not. If a physician receives information about this off label use from a detail person, it is possible that he or she will receive only the two favorable articles. On the other hand, if the physician were conducting his or her own research into the subject, he or she would likely locate both the pro and con articles. Given the approximately $20,000 per year price tag of human growth hormone, the pain a child must endure because of multiple drug injections each week, and the potential adverse effects that growth hormone may cause (such as diabetes and possibly tumor growth), it is important that physicians see all pieces of the scientific puzzle until the answer is clear.

By using this example, I am not targeting a specific drug or drug company. I am merely trying to illustrate what the bill would permit and why FDA has serious concerns.

What makes this situation even more troubling is that when we have evidence that a particular use is unsafe or ineffective, federal confidentiality laws frequently prohibit FDA from disseminating that information. Thus, there are off label uses about which positive studies appear in the literature and negative data are contained in our files. However, depending on its source, FDA may be unable to use that information to ensure that the medical community has all of the available facts on which to base treatment decisions.

Even under current law, physicians have access to positive articles about off label uses and FDA may be unable to counter those positive articles with any negative information that might be in our files. However, under current law, company detail men and women cannot use those articles to promote potentially dangerous off label uses.

The Bill's Requirements Are Not Substitutes for FDA Review

The bill imposes very few requirements on the off label use information that companies could disseminate. Basically, the unapproved use must appear in a peer-reviewed journal article, a chapter from a recognized text, text from an approved CME

program, information relating to a use recognized under Federal law for purposes of third party coverage or reimbursement, or a summary of one of the above. For devices, the information may also be from oral and written information that is part of an "exchange" among health care practitioners, health care reimbursement officials, and the industry, is exchanged for educational or scientific purposes, or is presented at CME programs, seminars, workshops, or demonstrations. None of these sources has procedures that confirm the validity of the data and information contained therein.

The purpose of the "peer review" process, for example, is to determine if an article is worthy of publication. At its best, peer review can ensure that the reader is provided with enough detail and clarity to make a general judgment about the strengths and weaknesses of the study. However, there are no generally accepted standards for what constitutes "peer review." Essentially, anyone can establish a "peer review" journal; the rigor of the review varies considerably.

Regardless of the rigor, there are severe limitations inherent in the peer review process that make it inappropriate to rely solely on a peer-reviewed journal article for efficacy determinations. For example, peer reviewers almost never receive the study protocol. They cannot tell what the initial hypothesis was or whether the final analysis represents the planned analysis

or an analysis crafted with the results in hand. Peer reviewers do not have access to the underlying data. The peer reviewers must rely on the data and facts as they are presented by the author. FDA, on the other hand, does have access to the data and can verify the critical statistical outcomes and the conclusions of a study. Moreover, peer reviewers do not necessarily have the time or the expertise in all aspects of the subject matter to adequately review the information. In fact, a survey reveals that a peer reviewer spends on average less than three hours reviewing a prospective article. The peer review process cannot guarantee the correctness or authenticity of the article, nor can it detect fraudulent or flawed research.

The data and information supporting off label uses that appear in reference textbook chapters, which could highlight off label uses of particular drugs or devices, CME materials, and materials related to third party coverage and reimbursement are even less likely to be validated than that in peer-reviewed journals. In fact, we have no reason to believe that such data have been reviewed or validated at all. Textbook editors do not review the data underlying information about off label uses that appear in those books. The recognition of suggested uses in texts or treatment guidelines for purposes of third-party reimbursement serve different societal purposes. The decision to include such uses is not based on the standards used by FDA to substantiate safety and efficacy. FDA has serious concerns about

a provision that allows companies to use these types of unproven/unvalidated information for promotional purposes.

There are many instances when uncontrolled studies have supported a use and subsequent well-controlled studies have failed to show effectiveness. Moreover, the literature is laden with studies that report preliminary findings -- e.g., studies that involve a small number of patients and case reports or are not properly controlled. Although the studies or reports may be scientifically accurate, they are not sufficient to show safety and efficacy. Thus, companies should not be allowed to use these less rigorous studies to promote off label uses of approved products.

GETTING SUPPORTED OFF LABEL USES ON THE LABEL

As you know, a drug is approved for its initial indications via a new drug application, which includes data on the drug's safety and efficacy. A subsequent indication is added via a supplemental new drug application, which usually needs to present only efficacy information to support that new use. After review and approval by FDA, the new use is added to the approved labeling and can be promoted by the drug's manufacturer.

There are several good reasons for drug companies to submit these "efficacy supplements":

- Approval usually ensures that third-party payers will reimburse for the use, as insurance companies virtually always pay for approved uses of drugs and devices.

- As health maintenance organizations continue to grow in size and number, a sponsor's ability to get their drug included in the HMO's drug formulary will be significantly enhanced.

- The physician, via the approved labeling, is given more complete information about the drug's uses, contraindications, adverse effects, and other important information about the manufacturer's product.

- Drug companies can present the FDA findings to drug approval bodies in other countries, thus enhancing their ability to gain approval (and reimbursement) for uses in other markets.

- And, of course, the manufacturer can promote the use, whether through the use of journal articles or other means.

Unfortunately, in many instances these incentives have been insufficient to persuade drug sponsors to submit efficacy supplements. There appear to be two reasons for their reluctance. First, they fear they will be expected to spend millions of additional dollars conducting new clinical studies to convince FDA reviewers that the new use should be approved. And

second, they have often complained that efficacy supplements are given low priority by FDA, resulting in delays of years in getting new indications approved. These concerns -- or at least the perception -- have been valid in the past, and we at FDA must address them.

We have been working on ideas for encouraging and expediting efficacy supplements for unapproved uses and for otherwise addressing industry concerns. We are doing a number of things and have several ideas for additional progress in this area. Let me summarize them for you:

Expediting Review of Efficacy Supplements

As you know from yesterday's testimony, the Prescription Drug User Fee Act of 1992 (PDUFA) is helping resolve the problem of timely reviews for drugs and biologics. Under PDUFA, by 1997, the Agency will make approval decisions on all new drug and biologic applications (NDAs, PLAs, and ELAs) within 12 months and within 6 months for priority drugs and biologics. These time frames apply to efficacy supplements as well. The approval times for NDAs, PLAs, ELAs, and efficacy supplements have decreased significantly, and the backlog of pending applications has also decreased markedly. In fact, for NDAs, PLAs, ELAs, and efficacy supplements, the Agency has exceeded the interim goals established by Congress. For applications submitted in FY 1994, the Agency reviewed and acted upon 96% of the NDAs, PLAs and ELAs

and 73% of efficacy supplements on time. [The interim goal for all of these was 55%.] With adequate resources, we are confident that we can make the same progress for medical devices.

We should, however, be able to exceed the PDUFA targets. I believe we should try to reduce the 6-12 month timeframes. To do so, we will need to give supplements a greater priority than they have had in the past, and we are committed to that.

Fewer Data Are Needed Than Commonly Believed

In addition to assuring companies that we can and will expedite their supplemental applications, we also need to address the industry perception that many efficacy supplements do not warrant the expense associated with getting them approved. Companies fear that they must conduct multiple and expensive new clinical trials and collect and analyze thousands of pages of medical data, with no assurances of approval. We need to more clearly explain that in the vast majority of cases this is just not so. Some off label uses could be approved by FDA if the sponsor would simply compile the existing literature and submit it to us. Others may need only limited data or data about the studies, such as protocols, data tapes, or verification of endpoints, all of which is already in existence but simply needs to be found and copied. In any event, because FDA has already learned much about the drug's actions and effects in humans from the original application and has considerable experience relevant

to safety, the data required for second and subsequent indications is often far less than for the original indication. It is, in sum, Madam Chairman, a much simpler process than generally believed and we must convince sponsors of that. To that end, we intend to draft a new policy statement articulating the data needs of the Agency for efficacy supplements for new indications.

Pediatric Labeling

We are already demonstrating how limited data can get more uses on the label in the pediatric area. We have recently promulgated new regulations that provide, in certain cases, for pediatric uses to be included on the approved labeling without new clinical studies. Pursuant to these regulations, when there is sufficient basis to conclude that the course of the disease and the effects of the drug are sufficiently similar in children and adults, drug firms can rely on existing studies in adults, extrapolate the data to children, and get those uses on the label with relative ease. The only new data that will ordinarily be needed are information about the drug's course throughout the body (e.g., blood and tissue levels) that will allow the proper dosage to be established for the use of that drug in children.

Seek Out the Most Appropriate Off Label Uses

As I said earlier, many off label uses are quite appropriate, and some may even be the treatment of choice.

Although off label use is seen in all medical specialties, it seems to be most widespread in certain areas, such as oncology and pediatrics. Beginning with those specialties, we will work with practitioners and their specialty associations to identify the off label uses that are most appropriate. We will then present those findings to the sponsors of those drugs and urge them to work with us to get the indications in the labeling. In many, if not most, cases that will entail only the compilation of existing information, not the design and conduct of new clinical studies. We have not done enough to reach out to the medical profession and to drug sponsors on this issue, but we believe we can get the majority of the most appropriate current off label uses in the labeling through this process.

The best way to get information to physicians about the best uses of the drug and device armamentarium, Madam Chairman, is to have it in the product's labeling. Our collective goal ought to be to get this done.

CONCLUSION

Public confidence in drug and device therapy has been built on the recognized rigor of FDA's approval process. It is important that we not change a system that has the respect and confidence of the health care community and the public. FDA recognizes that there are important lifesaving off label uses. FDA believes, however, that the best way to address any concerns

that the information about those uses is not reaching medical practitioners is to get those uses in the labeling. We believe that the risks of allowing drug companies to distribute journal articles and other information about off label uses far outweigh any benefits.

I would be happy to answer any questions.

ORGANIZATIONS & INDIVIDUALS ENDORSING
THE ACCESS TO MEDICAL TREATMENT ACT
HR 2019/S 1035

American Academy of Anti-Aging Medicine
American Academy of Environmental Medicine
American Academy of Pain Management
American College for Advancement in Medicine
American Herbalist Guild
American Holistic Centers
American Holistic Medical Association
American Holistic Health Association
American Massage Therapists Association
American Preventive Medical Association
American Academy of Metabolic Medicine
American Association of Naturopathic Physicians
American Association of Acupuncture & Oriental Medicine
Association of Applied Psychophysiology & Biofeedback
Calello Martinez P.C.
Cancer Control Society
Cancer Awareness Coalition
Center for Mind-Body Medicine
Center for Natural and Traditional Medicine
Citizens for Health
Citizens for Nutrition Choice
Council for Responsible Nutrition
Direct Access for A.I.D.S. Research
Direct Action for Treatment Access
Dr. Mohammed Ranavaya, of Academy of Disability Evaluating Physicians *
Ed Hudgins , of Cato Institute *
Great Lakes Association of Clinical Medicine
Healing Alternatives Foundation
H.I.V. Complimentary Therapy Center
Institute for Naturopathic Medicine
Institute of Pain Management
International Academy of Compounding Pharmacists
International Association of Cancer Victors & Friends
International Oxidative Medical Association
Lyme Disease Foundation
National Center for Homeopathy
National Council for Improved Health
National Nutritional Foods Association
Mr. Duke Pearson and Ms. Sandy Shaw
People Against Cancer
Physician's Committee for Responsible Nutrition
Physician's Association for Anthroposophical Medicine
Pure Food Campaign
Southwest College of Naturopathic Medicine & Health Sciences
Traditional Acupuncture Associates
Traditional Acupuncture Institute
Utah Natural Products Association
Vegetarian Awareness Network

* - Signifies a personal endorsement and is not intended to convey endorsement by the Association
July 29, 1996

Prepared by the American Preventive Medical Association
459 Walker Road Great Falls, Virginia 22066
703-759-0662 Fax 703-759-6711

COMPETITIVE ENTERPRISE INSTITUTE

CARDIAC AND CANCER SPECIALISTS ON THE NEED FOR FDA REFORM

Polls Show Need for Access to Unapproved Therapies

Cardiology and oncology are two medical specialties whose members understand the need for new, life-saving drugs and devices. They know, on a first-hand basis, that such technologies can frequently mean the difference between life and death for many patients.

What do cardiologists and oncologists think of FDA and of access to new therapies? In the past year, CEI commissioned two polls to examine the views of these specialists. The first, a poll of oncologists, was released in August, 1995. It involved a total of 160 telephone interviews with randomly selected hospital-based oncologists. Its margin of error was ±5.1% at the 95th percentile confidence level--that is, similar results would have been obtained in 19 out of 20 cases.

The second poll, of 216 randomly selected cardiologists and cardiac surgeons, was released last week on July 24, 1996. Its margin of error is ±4.8 percent at the same high confidence level.

Both polls demonstrate highly negative views of FDA on such issues as whether the agency is too slow in approving new drugs and devices, whether the public understands the human cost of FDA delays, and whether FDA delays impair the ability of these specialists to give the best possible care to patients. Both polls also demonstrate overwhelming opposition to FDA's policy of restricting information about off-label use.

Majorities of both specialties support allowing physicians to use unapproved drugs and devices, provided those products carried a warning about their unapproved status (Question 8). Both specialties believed they could rely on published research, on foreign governments' approvals, and on their colleagues' opinions to determine whether such therapies were suitable for their patients (Question 9).

Cardiologists and oncologists agree that FDA regulation has prevented them from giving their patients the best possible care. *Something is wrong when an agency charged with protecting public health is viewed this negatively by physicians fighting for their patients' lives.* The Access to Medical Treatment Act (S. 1035), on which the Senate Labor and Human Resources Committee is holding hearings today, is an important step toward giving doctors the freedom to treat their patients to the best of their abilities.

Sam Kazman
July 30, 1996

1001 Connecticut Avenue, N.W. • Suite 1250 • Washington, D.C. 20036
Phone: (202) 331-1010 • Fax: (202) 331-0640 • E-mail: info@cei.org • Web site: http://www.cei.org

Summary of Poll Results

1. On balance, do FDA regulations *help* or *prevent* you from using promising new drugs or medical devices in the treatment of your patients? Would that be *strongly* or just *somewhat*?

	Cardiologists	Oncologists
TOTAL HELP	**42%**	**44%**
Strongly help	20%	8%
Somewhat help	22%	36%
TOTAL PREVENT	**46%**	**43%**
Somewhat prevent	33%	35%
Strongly prevent	13%	8%
Neither	7%	14%
Don't know/Refused	5%	-

2. The FDA is too slow in approving new drugs and medical devices.

	Cardiologists	Oncologists
TOTAL AGREE	**65%**	**77%**
Strongly agree	30%	31%
Somewhat agree	35%	46%
TOTAL DISAGREE	**30%**	**20%**
Somewhat disagree	18%	14%
Strongly disagree	12%	6%
Neither	3%	2%
Don't know/Refused	2%	1%

3. The additional time it takes for the FDA to approve drugs and medical devices costs lives by forcing people to go without potentially beneficial therapies.

	Cardiologists	Oncologists
TOTAL AGREE	**57%**	**47%**
Strongly agree	17%	11%
Somewhat agree	40%	36%
TOTAL DISAGREE	**37%**	**48%**
Somewhat disagree	21%	34%
Strongly disagree	16%	14%
Neither	5%	4%
Don't know/Refused	2%	1%

4. In your opinion, to what extent does the general public understand the "human cost" of the FDA approval process, that is, that some people may suffer or die waiting for the FDA to act? Do they . . .

	Cardiologists	Oncologists
TOTAL UNDERSTAND HUMAN COST	**24%**	**19%**
Completely understand	4%	1%
Somewhat understand	20%	18%
TOTAL DON'T UNDERSTAND HUMAN COST	**63%**	**74%**
Understand only a little	33%	51%
Don't understand at all	30%	23%
Refused/Disagreed with statement/Don't know	12%	9%

5. If a drug or medical device has already been approved for one use by the FDA, should the FDA restrict information about off-label uses, that is, other unapproved uses of that drug or device?

	Cardiologists	Oncologists
YES	**21%**	**16%**
NO	**67%**	**76%**
Sometimes	5%	4%
Don't know	5%	1%
Refused	2%	3%

6. To what extent does this FDA policy of limiting information make it more difficult for ***you*** to learn about new uses for drugs or devices?

	Cardiologists	Oncologists
TOTAL MORE DIFFICULT	**60%**	**60%**
Much more difficult	13%	17%
Somewhat more difficult	47%	43%
TOTAL LESS DIFFICULT	**28%**	**28%**
Somewhat less difficult	14%	22%
Much less difficult	14%	6%
No impact	7%	-
Don't know	4%	8%
Refused	1%	5%

7. Would you say the FDA's approval process has hurt your ability to treat your patients with the best possible care frequently, some of the time, at least once, or never?

	Cardiologists	Oncologists
TOTAL HURT ABILITY TO TREAT	**71%**	**63%**
Frequently	7%	11%
Some of the time	45%	37%
At least once	19%	15%
NEVER	**28%**	**36%**
Refused	1%	1%

8. What would your position be on a proposal to change FDA law so that unapproved drugs or devices could be made available to physicians as long as they carried a warning about their unapproved status? Would you strongly favor, somewhat favor, somewhat oppose, or strongly oppose such a proposal?

	Cardiologists	Oncologists
TOTAL FAVOR	**53%**	**61%**
Strongly favor	21%	24%
Somewhat favor	31%	37%
TOTAL OPPOSE	**44%**	**37%**
Somewhat oppose	24%	24%
Strongly oppose	20%	13%
Don't know/refused	3%	2%

9. Assume for a moment that a system was in place where unapproved drugs or devices were available to you for treating patients. Which of the following would be the ***most*** important factor in your decision to use such an unapproved drug or device?

	Cardiologists	Oncologists
Whether persuasive published research exists about the drug or device	47%	59%
Whether the drug or device has received approval in other medically advanced countries	25%	29%
Whether the drug or device was well-regarded by physician colleagues	19%	10%
Don't know/Refused	10%	2%

10. And finally, how many years have you been in practice?

	Cardiologists	Oncologists
5 years or less	7%	14%
5-8 years	7%	14%
8-12 years	14%	14%
12-15 years	17%	11%
More than 15 years	56%	47%

11. Gender

	Cardiologists	Oncologists
Male	94%	89%
Female	6%	11%

COMPETITIVE ENTERPRISE INSTITUTE

For Immediate Release: Contact: Greg Smith (202) 331-1010

PHYSICIAN ACCESS TO UNAPPROVED THERAPIES SUPPORTED BY NEW LEGAL STUDY AND BY TWO NATIONAL POLLS OF MEDICAL SPECIALISTS

WASHINGTON, DC July 30, 1996—A public interest group today announced the release of a new legal study on giving physicians access to drugs and devices that have not been approved by FDA. On Tuesday, July 30, the Senate Labor & Human Resources Committee holds hearings on the Access to Medical Treatment Act (S. 1035), a bill which increases physician access to such therapies.

The CEI study, *Breaking the FDA's Drug Approval Monopoly--Implications for Tort Law and Consumer Welfare*, is written by George Mason Law Professor Michael I. Krauss. It concludes that FDA's current command-and-control approach to therapeutic approval cannot be justified by the "market failure" arguments that are usually offered to support it. Physician access to unapproved therapies would serve the interests of patients who frequently suffer under FDA delays, and would ultimately force FDA itself to earn its credibility.

A CEI poll of cardiologists, released on July 24, demonstrates that support for this approach is far wider than commonly assumed. A majority of the over 200 cardiologists polled (53%) supported physician access to properly labeled unapproved therapies, while 44% opposed it. Similarly, a 1995 CEI poll of cancer specialists found 61% favoring this approach. Both groups stated that "persuasive published research" would be the single most important factor in their deciding whether to use such therapies.

CEI General Counsel Sam Kazman stated: "Physician access to unapproved therapies is often derided as opening the door to snake oil. The fact that such an approach is favored not only by the public, but by majorities of these two life-saving specialties indicates that FDA is far more of a health problem than its supporters will admit."

Under CEI's proposal, FDA would continue to evaluate new therapies, but it would not have the power to veto unapproved therapies, which would be available under medical supervision and with clear warning of their unapproved status.

CEI is a non-profit, non-partisan public policy group dedicated to free markets and limited government. For more information, or a copy of the study or the polls, call Greg Smith at (202) 331-1010.

1001 Connecticut Avenue, N.W. • Suite 1250 • Washington, D.C. 20036
Phone: (202) 331-1010 • Fax: (202) 331-0640 • E-mail: info@cei.org • Web site: http://www.cei.org

THE FEDERATION OF STATE MEDICAL BOARDS OF THE UNITED STATES, INC.

400 FULLER WISER ROAD, SUITE 300
EULESS, TEXAS
76039-3855

817 868-4000
FAX 817 868-4099

PRESIDENT
ROBERT E. PORTER, MD
ONE MEDICAL CENTER DR.
LEBANON, NH 03756

PRESIDENT ELECT
JAMES E. WEST, MD
901 EAST LEIGHTON AVENUE, SUITE 702
ANNISTON, AL 36207

VICE PRESIDENT
SUSAN M. SPAULDING
P.O. BOX 222
MONTPELIER, VT 05601

TREASURER
BRUCE H. HASENKAMP, JD
900 HYDE ST., SUITE 1208
SAN FRANCISCO, CA 94109

IMMEDIATE PAST PRESIDENT
GERALD J. BÉCHAMPS, MD
P.O. BOX 2698
WINCHESTER, VA 22601

DIRECTORS

LEROY B. BUCKLER, MD
640 SOUTH STATE ST
DOVER, DE 19901

WILLIAM H. FLEMING, III, MD
7777 SW FREEWAY, SUITE 1004
HOUSTON, TX 77074

JOHN T. HINTON, DO, MPH
655 EDEN PARK DR.
CINCINNATI, OH 45202

PHILIP M. MARGOLIS, MD
900 WALL ST.
ANN ARBOR, MI 48105

DINESH PATEL, MD
15 PARKMAN ST., SUITE 510
BOSTON, MA 02114

ALAN E. SCHUMACHER, MD
3020 CHILDREN'S WAY / MC 5008
SAN DIEGO, CA 92123

GEORGE J. VAN KOMEN, MD
745 EAST 300 SOUTH
SALT LAKE CITY, UT 84102

RAY Q. BUMGARNER, JD
77 SOUTH HIGH ST., 17th FLOOR
COLUMBUS, OH 43266

JAMES R. WINN, MD
EXECUTIVE VICE PRESIDENT

DALE L. AUSTIN, BSN, MA
DEPUTY EXECUTIVE
VICE PRESIDENT

CAROL CLOTHIER, BA
ASSISTANT VICE PRESIDENT
P/R, PUBLICATIONS, EDUCATION

I. KATHRYN HILL, MEd
ASSISTANT VICE PRESIDENT
EXAM/BADB SVCS. DIV.

STATEMENT OF THE FEDERATION OF STATE MEDICAL BOARDS OF THE UNITED STATES, INC. ON

S.1035, ACCESS TO MEDICAL TREATMENT ACT TO THE

COMMITTEE ON LABOR AND HUMAN RESOURCES UNITED STATES SENATE

JULY 30, 1996

The Federation of State Medical Boards is pleased to provide comments about S.1035, The Access to Medical Treatment Act. The Federation is a national organization, the members of which are the state medical boards empowered to license and discipline physicians in the United States. The mission of the state medical boards is to protect the public from unqualified practitioners of medical services, through enforcement of standards established by state laws. The Federation assists boards with this mission, acting as a clearinghouse for the latest information on licensure and discipline, and assists in the credentialling process through maintenance of a comprehensive database of board actions involving physician disciplinary matters, that is available for query by state boards and other credentialling agencies.

The evaluation of a medical practitioner is best performed at a level of government that allows regulators to take advantage of professional and personal relationships with individuals whose judgment they trust. Since being established in the late nineteenth century in response to a number of incidents in which patients were harmed, state medical licensure boards have evolved into sophisticated regulatory agencies dedicated to ensuring that the public is protected from unfit and/or unqualified practitioners.

During the last century each state has enacted and amended its own version of a medical practice act. While the specifics of each medical practice act differ, each prescribes through statute and implementing regulation the process by which the initial granting of a license and the monitoring of the privilege to practice medicine shall be accomplished.

Today, there are 54 allopathic and 16 osteopathic state medical boards which have the authority to license physicians, to regulate the practice of medicine within the state, and to discipline those who violate the relevant medical practice act. In particular, state medical boards:

- Establish academic and clinical skill standards for all license applicants;
- Establish rules and regulations promoting the safe and effective practice of medicine;
- Require periodic re-registration of medical licensees in order to review the qualifications of licensees on a regular basis; (the frequency of re-registration required varies from state to state);
- Investigate and adjudicate allegations of physician misconduct;
- Take appropriate disciplinary actions against any physician who is found to have violated the state medical practice act. The action taken may involve sanctions that range from license revocation to reprimands and fines.

These central functions of state medical boards serve to accomplish the primary purpose of medical licensure; protecting the public from sub-standard medical care.

The member Federation boards recognize that patients have a right to participate with their physicians and other health care practitioners in the decisions to pursue a particular therapy as long as risks, benefits, costs, and alternatives are discussed between practitioners and patients

before a particular course of treatment is begun. A number of our boards have had to discipline practitioners for providing treatment without adequate disclosure to the patient. For that reason the Federation is supportive of several provisions in S.1035 that recognize the need for full disclosure prior to treatment. Unfortunately, other provisions in the bill seriously undermine the ability of state licensing boards to take actions against physicians who may jeopardize public health.

S.1035 grants every patient a right to be treated by a health care practitioner with any medical treatment that such individual desires (including one not approved, certified, or licensed by the Secretary of Health and Human Services), provided: a) that such practitioner has personally examined the individual and agrees to treat such individual, and b) the administration of such treatment does not violate licensing laws. The Federation has grave concerns about this central provision and does not believe that the limitations (e.g. requiring a personal examination and prohibiting treatment that violates licensing laws) provide adequate safeguards for patients.

First, although the bill requires a personal examination of a patient by a practitioner, it does not specify the nature of the examination; whether it may be perfunctory, or must be exhaustive, nor whether it shall include particular attention to the patient's mental and emotional state if a treatment involving products that have not been approved by FDA is being recommended.

Second, The bill prohibits the administration of any treatment that violates licensing laws. For the most part, licensing laws do not contain prescriptive lists of dos and don'ts for practitioners to follow. State licensing laws are designed to give boards wide latitude in making determinations whether a particular practitioner is practicing competently. A practitioner contemplating the use of an unapproved therapy will not be able to find in statute a definitive answer to the question of whether its use violates his or her state licensure law. In fact, a practitioner is not likely to find out if use of an unapproved product violates state licensure law until a board makes a determination after the treatment has been provided. For this reason, the Federation does not believe that the limitation in the bill indicating that a procedure must not violate licensing laws will be effective in preventing a practitioner from engaging in activities specifically authorized by this new legislation but not explicitly prohibited under a state licensure statute.

Further, the protocol that must be followed by a practitioner who provides an unapproved therapy is inadequate and provides only illusory protection for the patient. The first element of this protocol is that the practitioner must determine that there is no reasonable basis to conclude that the treatment poses an unreasonable and significant risk of danger to a patient. This stands the Hippocratic Oath on its head. "First, do no harm" has been transformed to, "Do no harm that is unreasonable <u>and</u> poses a significant risk of danger." It will be very difficult for state licensure boards to accept this standard. Many boards will find it contradictory with standards they have developed over years of experience in dealing with both responsible and irresponsible practitioners.

The legislation also require that a practitioner who provides a treatment that involves a product not approved by FDA provide the patient with written notice of the product's lack of approval, the treatment's anticipated benefits, foreseeable side effects, and the results of past treatments. While this appears to be a fairly complete list of information that will allow a patient to make an informed decision, in most cases, the information will not be very useful and could be misleading. Information about the risks, benefits, contraindications, and side effects of treatments that have not been subjected to clinical studies is anecdotal possibly misleading and not reliable. As suggested at the outset, the concept of providing extensive information to a patient so that he or she can make an informed decision about therapy is laudable. Application of that concept to therapies for which there is little or no verifiable clinical data is useless in most cases and fraudulent in others.

The Federation also believes that other provisions in the bill need significant revision. Many of the definitions are imprecise. For instance, the definition of a health care practitioner is someone "who is legally authorized to provide health services in the State in which the services are provided." In order to make it clear that an individual may only provide those health services for which he or she is licensed, the definition should reference licensure for a specific type of practitioner. Similarly, Section 8 of the bill requires that a health care practitioner who discovers that a treatment was a danger to the individual receiving such treatment must immediately report to the Secretary of HHS. Unfortunately, this section does not go on to require the practitioner to immediately cease using the treatment until further investigation or study about the treatment has been conducted. It appears that the practitioner's obligation is met by filing a report, despite the apparent danger of the treatment.

In summary, the Federation of State Medical Boards is very concerned that S.1035 if enacted would interfere with state medical boards' ability to make appropriate decisions about the competency of physicians. Our member boards are constantly balancing the right of individuals to make informed choices about their health care and the boards' obligation to protect vulnerable people who may not be fully informed about the benefits and risks of different therapies from being exploited or harmed by licensees of the state. If S.1035 is enacted, the public will no longer be confident that licensure is an indication that the safety of the individual being treated by the licensees is of paramount importance.

COMPETITIVE ENTERPRISE INSTITUTE

HEALTH CARE
REFORM PROJECT

BREAKING THE FDA'S DRUG APPROVAL MONOPOLY

IMPLICATIONS FOR TORT LAW AND CONSUMER WELFARE

MICHAEL I. KRAUSS

July 1996
ISSN#1085-9055

BREAKING THE FDA'S DRUG APPROVAL MONOPOLY

Implications for Tort Law and Consumer Welfare

Michael I. Krauss

EXECUTIVE SUMMARY

The Food and Drug Administration's monopoly over approving new medical therapies is premised on the idea that information markets fail. In fact, competitive forces produce information much more readily than is commonly believed through advertising, testing publications, and companies' reputations for quality. This holds important implications for FDA reform.

The common law inspires confidence in information produced without the need for heavy-handed regulations. Tort and product-liability law can and do result in increased informational output from manufacturer to physician and consumer precisely in those instances where such output might otherwise be insufficient.

The market failure argument supposes that private corporations have insufficient incentives to produce information, but that government incentives to inform consumers are somehow not distorted. But FDA is subject to its own set of perverse incentives. For the agency, the political consequences of mistakenly approving a bad drug or device are far worse than those of mistakenly delaying or disapproving a needed therapy. As a result, FDA is inherently overcautious — an approach which serves its interests but not those of the public.

The path to reform can be found in a gap in FDA's current monopoly. Under existing law, manufacturers may not market drugs or devices that have not received FDA approval. But if a drug or device is approved by the agency as safe and effective for one purpose, then doctors are free to prescribe it for other purposes as well.

Despite its efforts to suppress these "off-label" uses, FDA has not stemmed the tide. Off-label prescriptions have proliferated despite tort law's implicit bias in favor of FDA-approved uses.

A proposal by the Competitive Enterprise Institute suggests a way to preserve FDA's evaluative functions while expanding therapeutic choice. Under this proposal, FDA would function not as a veto agency, but as an evaluation agency. Rather than being banned across the board, unapproved therapies would be available under medical supervision and with clear warning of their unapproved status. That is, "off-label *manufacturing*" would be permitted, much as "off-label prescribing" is presently allowed.

FDA would lose its veto power over new therapies, but it would continue to act as a state-funded evaluator of therapies.

Manufacturers might still choose to seek FDA approval if that approval was sufficiently valued by the public and by physicians. Moreover, under this proposal FDA approval would confer a shield against design defect liability. But patients and their doctors would be free to go beyond the circle of government approved therapies. The arena of initial therapeutic evaluation would itself expand to encompass such private entities as testing laboratories and medical journals, so that FDA itself would be subject to competition in producing credible, *and timely*, evaluations of new drugs and devices.

FDA's legal control over medicine has never been all-encompassing, but its exercise of that power has had deadly consequences. The "off-label" use gap in FDA's power has mitigated its potentially disastrous effects, and contains the kernel of a regulatory approach that would be far safer and more effective than our current system.

BREAKING THE FDA'S DRUG APPROVAL MONOPOLY

IMPLICATIONS FOR TORT LAW AND CONSUMER WELFARE

by Michael I. Krauss[1]

INTRODUCTION

Origins and Characteristics of the FDA's "Certification Monopoly"

In the 1970s, a configuration of geo-political factors resulted in a serious but temporary tightening of oil supplies. Several sets of sweeping federal fuel economy regulations were enacted. The institutionalization of this expanded federal mandate led to the production and sale of relatively dangerous and unattractive automobiles.[2] In a similar way, federal drug regulation has been driven by reactions to sensational occurrences. For ethical drugs as for cars, the belief that markets (tempered by common law) can provide safe and effective products has been a notable casualty of federal regulation.

Federal drug regulation has been driven by reactions to sensational occurrences.

The first statute regulating pharmaceutical products in the United States was the *Pure Food and Drug Act of 1906*,[3] which established federal offenses for adulteration and mislabeling of ingredients in food and drugs.[4] The statute was apparently Congress' response to the "literary emergency" generated by Upton Sinclair's *The Jungle*, a turn-of-the-century *Soylent Green* portraying a world in which all medicines were deleterious, all milk tainted and all sausages once human. Both before and after the 1906 bill's passage, non-narcotic drugs were as freely available as newspapers (as they remain in many countries today[5]). No government approval was required before drugs were manufactured or marketed, nor was a physician's prescription legally required (though doctors' advice was relied on by many, with prescriptions accounting for almost one third of all drugs consumed).[6]

Patent medicines of dubious effectiveness were available on the market in 1906. Amendments to the 1906 law in 1912 criminalized false and misleading claims of a medication's efficacy. It is worthwhile noting that, federal criminal law aside, even at this early stage of its development[7] the common law already provided recourse to those injured by negligently mislabeled or poorly manufactured drugs.[8] Economic analysis suggests that

market forces will tend to provide correct incentives for manufacturers to design and produce safe drugs if tort remedies are available in such cases.[9] Of course, tort law has little effect on insolvent tortfeasors, and in any case the national ruckus generated by *The Jungle* provided an impetus for federal officials anxious to be seen "doing something" about drug problems. Perhaps not surprisingly, criminal enforcement also presented difficulties (insolvent producers are often "fly-by-night" and hard to locate; criminal intent is more difficult to prove than tortious negligence; etc.). All of these factors curtailed enforcement of the 1906 Act.[10]

Federal drug regulation was of little consequence until a tragedy in 1937.

Federal drug regulation was of little consequence until a tragedy in 1937. In attempting to formulate a liquid form of sulfanilamide (a sulfa drug) one Samuel E. Massengill, a Tennessean doing business as the Massengill Company, marketed a syrup that employed diethylene glycol as its solvent. One hundred seven children died after ingesting this poisonous concoction.[11] Though Massengill was of course found liable in tort for his gross negligence,[12] the political temptation to provide additional "protection" to voters proved irresistible for the Roosevelt administration, which was enjoying the huge expansion of federal jurisdiction produced by the "switch in time that saved nine."[13] The President signed the *Food, Drug and Cosmetic Act of 1938*, which for the first time required firms to submit New Drug Applications (NDA's) to the FDA before introducing pharmaceuticals into interstate commerce. Each NDA enumerated the proposed uses of a drug and demonstrated that tests "proved" it safe[14] at recommended dosages. NDA's were approved after 60 days unless the FDA determined before that period that they did not reveal sufficient safety testing. [The 1938 act contained another, seemingly innocuous, provision allowing discretionary exemptions from labelling requirements. This provision was subsequently interpreted by the FDA to greatly expand its authority (and physicians' income) by creating a category of "ethical drugs," that could henceforth be sold only by prescription.[15]]

FDA safety evaluations obviously caused delays in the marketing of new drugs. But lag times were relatively short: by the end of the 1950's record levels of new drugs were being marketed with mean regulatory delays of seven months. The 1938 act is most renowned, however, for the delay it occasioned in the introduction of the German sedative Thalidomide in 1960. While an FDA reviewer investigated reports (published in Europe for years[16]) that Thalidomide caused peripheral nerve damage, news of a different side effect, deformities in the fetuses of pregnant users of the sedative, led to its withdrawal from markets worldwide in 1961.[17]

The 1938 act had indirectly prevented any Thalidomide tragedies in the United States. Congress nonetheless sprang to action to dramatically expand federal powers. In 1962 a hastily drafted *Food and Drug Act* required that drugs henceforth be found safe *and effective* by the FDA before they could be marketed.[18] Whereas under the 1938 act NDAs were approved

unless the FDA denied them, after 1962 *disapproval* was the default position: for an NDA to be approved the FDA must affirmatively conclude that a new drug is safe and effective.[19] While the 1938 bill allowed firms to test the safety of their own products (subject to documenting their tests for FDA review), after 1962 all human testing of new drugs had to be pre-cleared by the agency. The FDA acquired, additionally, the power to pre-approve all drug advertising and all labels, and set out "good manufacturing practices" regulations.

As others have noted,[20] the combined effect of the 1938 and 1962 legislation was to fundamentally alter the nature of American pharmaceutical production and distribution. Whereas the 1906 act had essentially sought to make markets work better through the prohibition of false claims and information,[21] after 1962 the judgment about what was desirable or undesirable was to be made by a central regulatory authority rather than by the choices of suppliers, physicians, and patients.

As might be expected, one effect of the FDA's post-1962 "certification monopoly" is a much more lengthy "drug lag." By 1967, average post-test review times for an NDA had increased from seven to thirty months.[22] Largely because of agency involvement in testing, total pre-authorization development time for a new drug (which had averaged from 4 to 6 years before 1962) increased to over 16 years by 1990.[23] Only one out of 5,000 new drugs now completes this process successfully, at an average manufacturer's cost of $200 million.[24] Economic theory leads to the prediction that these substantial increases in the cost of developing a drug for the US market affect both the number of new drugs developed (at the margin, otherwise marketable drugs will now be unprofitable *ex ante* to a manufacturer)[25] and the market price of developed drugs during what remains of their patent monopoly.[26] Both these forecasts have been amply documented in practice.[27] Also increasingly chronicled is the net cost in lost lives of not approving effective drugs quickly, as the following section relates.

FDA safety evaluations obviously caused delays in the marketing of new drugs.

THE RATIONALE FOR THE FDA CERTIFICATION MONOPOLY: ANALYSIS AND CRITIQUE

The 1938 and 1962 amendments came during "New Deal" and "Great Society" administrations, when confidence in government as an efficient provider and allocator of goods and services was high. General preference for government over markets is typically accounted for in "welfare economics" by the existence of "market failures." In the case of drugs, the lay version of the "market failure" argument is that the profit motive leads manufacturers to produce too many drugs too quickly, that these drugs would consequently either be poorly manufactured,[28] designed[29] or marketed,[30] and that consumers would suffer losses that could be avoided if manufacturers

were forced through regulatory hoops. Several "consumer watchdog" groups embrace this market failure theory wholeheartedly. Dr. Sidney Wolfe of Public Citizen, for example, recently warned Congress not to privatize *any* FDA functions because drug manufacturers "mak[e] decisions based more on who fills their pocketbook than what is best for the public health."[31]

In economic theory, the "market failure" popularly attributed to pharmaceutical manufactures' profit motive is ascribed to "imperfect information." The theoretical argument goes roughly as follows:

- Private choice of goods and services maximizes global satisfaction only if consumers *perfectly* know what they want and *flawlessly* calculate whether products offered for sale will give them what they want. These conditions imply an elimination of all risk;

- A risk-free universe exists nowhere, of course, and is especially absent where disease is concerned. Consumers of drugs in fact have doubts both about what ails them and about the effects of proposed remedies for that ailment;

By 1967, average post-test review times for an NDA had increased from seven to thirty months.

- Producers of a remedy can of course provide useful information on the latter subject to consumers, but (as statements like Dr. Wolfe's above indicate) informational asymmetry is held to encourage false or biased reports;

- Furthermore, information is a "public good:" once originated, it can be reproduced or broadcast. Since others can copy costly-to-produce information, the argument goes, insufficient quantities of data about pharmaceuticals are likely to be produced by the private market. Notably, it is held to be unlikely that disinterested third parties would spring up to provide correct evaluations of a drug's safety and effectiveness;

- Thus, concludes the argument, government must fill the gap created by informational market failure. This government can do by testing and certifying drugs, and by requiring exceptional quality before authorizing drug marketing.

There are many difficulties with the market failure rationale for a government drug certification monopoly. Some can be usefully sketched here:

- The market failure argument explains little because it explains too much. Virtually *all* consumer goods and services are purchased by buyers with incomplete information. How long will that pair of panty hose last, and will its chemical formulation provoke allergic reactions? Will this champagne bottle explode in my face, scarring me for life? Is the doctor operating on me this morning recovering from last night's party? Will the university I just applied to have an excellent reputation when I graduate four years from now? On all these issues, should I trust the information I receive from the not disinterested department store, bottler, surgeon or law school? Consumer information is never perfect, and ignorance (i.e., risk) therefore inevitably influences all choices relevant to our well-being. But few are confident enough in *government's* ability to discover and process information to argue for the replacement of market allocation and

consumer choice by regulatory agencies merely because information is imperfect.[32]

• The major premise of the market failure argument, that information is a "public good" underproduced by markets and therefore efficiently provided only by government, is flawed. Competitive forces privatize information much more readily than is commonly believed by welfare economists.[33] Competitors with better products profit by pointing out imperfections in their rivals' merchandise. Testing publications from *Consumer Reports* to *Car and Driver* find markets for information, ranging from open evaluation to formal certification of products.[34] The value of these publications (and for that matter, the value of pharmaceutical manufacturers' products) derives from the reputation for quality they acquire. In fact the "good will" value of brand names, trademarks, and other intellectual property, which both product manufacturers and consumer publications ferociously protect,[35] is largely a function of this reputational effect. Commercial activity (whether by automobile manufacturers or drug producers) consists not of one-shot events but rather of a series of repeat dealings; only myopic producers generate false product information if it is likely that the misinformation will become known. Admittedly, fly-by-night operators by definition don't feel reputational risk: but that is precisely why the market values their products less than it does those of a Proctor & Gamble or a Merck. That is why the used car sold through classified ads costs less than the same car sold by a reputable dealer. In the absence of any federal regulation, market prices for products already compensate *ex ante* for informational imperfections.

The market failure argument explains little because it explains too much. Virtually all *consumer goods and services are purchased by buyers with incomplete information.*

• Of course, reputational markets are not perfect. Most notably, "agency problems" incite misbehavior. Managers may, for example, deceive drug (or car, or pantyhose, or surgery, or law school) "purchasers" because by the time the misinformation is discovered the manager will have comfortably retired, personally reaping the short term gain while the corporation is left with the long-term pain. While agency problems do exist (in government[36] as well as in private industry), it is important to note that tort and contract law create powerful incentives for private firms[37] to monitor managerial behavior. The common law inspires confidence in information produced without the need for heavy-handed regulations.

• For example, incorrect information dispensed by manufacturers typically constitutes a "breach of express warrant," giving rise to strict liability suits by consumers injured as a consequence.[38] Poor manufacturing techniques, shoddy design work, inadequate warnings or careless preparation (whether by a too-hasty marketer of a drug with side-effects or by a partying surgeon) result in tort or products liability. This liability is designed to fully compensate wrongfully harmed victims, thereby forcing wrongdoers to internalize the cost of their misbehavior. Some believe that tort law undercompensates plaintiffs, while others feel that tort recovery is too generous. Depending on who is right, tort should be made more plaintiff- or defendant-friendly. But that is a question of tort law, **not** of government regulation.[39] If the amount manufacturers (or service providers) must pay injured parties in tort suits is greater than the long term gain they derive from deceiving their clientele (and such gain should not be easily assumed: reputational costs make it problematic, as seen above), information will be improved. This will occur precisely in cases where we want to modify the manufacturer's (or service provider's) behavior.[40] Tort and product liability law can and do result in increased

informational output from manufacturer to consumer precisely in those instances where such output might otherwise be insufficient.[41]

• The market failure argument supposes (incorrectly, as seen immediately above) that private corporations' incentives to produce information are insufficient. It also believes that *government* incentives to inform consumers are *not* distorted. But this benign view of government has been challenged by political theorists ever since the *Federalist Papers*. Scholars who monitor civil servants know that "agency problems" are notoriously likely to reduce bureaucrats' efficiency.[42] "Public Choice" analysis teaches that we should expect government agencies to be *over*cautious in approving new drugs. The loved ones of those who have died because a non-approved (or non-developed) drug they have never heard of *might* have saved them *had* it been developed and marketed are unlikely to protest to their elected representative. On the other hand, every crippled victim of a defective drug is visible to journalists and to politicians, lawyers and judges.[43] Every new drug is therefore potentially another Thalidomide to bureaucrats. As Sam Kazman has written,

> "From the FDA commissioner to the bureau heads to the individual NDA reviewers, the message is clear: if you approve a drug with unanticipated side effects, both you and the agency will face the heat of newspaper headlines, television coverage and congressional hearings. On the other hand, if the FDA insists on more and more data from a manufacturer, and finally approves a drug which should have been on the market months or years before, there is no such price to pay. Drug lag's victims and their families will hardly be complaining, because they won't know what hit them.... They only know that there is nothing their doctors can do for them. From the standpoint of ... politics, they are invisible."[44]

Drug lag's victims and their families will hardly be complaining, because they won't know what hit them.

As between what might be called "Type 1" certification error (a drug is approved that turns out to cause more harm than good) and "Type 2" certification error (a drug is not approved, but that drug would have caused more good than harm), the above analysis indicates that market forces (tempered by contract and tort remedies) tend to *minimize the sum* of these two errors: anything less would reduce profits. *Government regulation, in contrast, is acutely sensitive to Type 1 error but relatively unfeeling to Type 2 error.* In sum, Public Choice theory leads us to predict that government monopoly over drug certification would exacerbate, not solve, informational failure.

Theory has been borne out by practice, as is revealed by recent illustrations of the informational failure resulting from the FDA's certification monopoly:

• The cardiopump is standard equipment in ambulances in many countries. But it is not available in the United States. Initial tests in the US in 1992 showed that, though not universally effective, use of a cardiopump led to a survival rate 35% greater among unconscious heart attack victims. However the FDA ordered in 1993 that tests on the pump cease because unconscious patients could not give "informed consent" before the device was "tested" on them.... The cardiopump may help many people: one

estimate is that up to 7,000 Americans could be saved each year through its use.[45] We will never know who these "missing dead" are, of course.

• A 42-month delay in making Interleukin-2 available to patients with kidney cancer cost nearly one hundred unidentified deaths per month.[46]

• Delays in the approval of the emergency blood-clotting drug TPA are estimated to have resulted in more than 100,000 preventable heart-attack deaths.[47]

• The FDA took seven years before approving tacrine (or THA), which would have greatly improved (and in some cases saved[48]) the lives of thousands of Alzheimers patients.[49]

• Wyoming physician Michael Werner had the knowledge and wealth needed to visit Japan in 1993 for experimental treatment for his rare form of brain cancer. The treatment has not been approved by the FDA for use in the US. According to Dr. Werner, 120 patients with brain tumors like his had been treated in Japan with a 52% five-year survival ratio. In the US 90% of patients with Dr. Werner's disease die within twelve months; only 1% survive five years.[50]

• FDA regulations require that the clinical studies needed to obtain approval of a new drug or medical device be "randomized" and "concurrent;" i.e., new devices or drugs must be blind-tested against placebos or FDA-approved products. This poses ethical problems if the new device or drug is so superior to existing technology that the "placebo" half of the "double-blind" cohort is virtually condemned to death. However, the FDA tolerates this state of affairs and tends to intervene only when real victims are publicly identified. For example, the agency ordered hospitals to stop using specialized baby ventilators (irreplaceable in saving very sick infants because they provide uniquely tiny breaths of air) because hospitals refused to "blind-test" them (and thereby condemn 50% of air-deprived "neonates"). Dr. Martin Kessler of Georgetown University Medical Center estimates that scores of babies died as a result. Subsequent to the FDA decision, protests from doctors *who pointed to specific infant deaths* were aired on the television show "20/20." Only then did the agency allow use of the ventilators.[51]

Government monopoly over drug certification would exacerbate, not solve, informational failure.

• The pre-market approval process for new medical devices, required since 1976,[52] averaged 840 days during the first six months of fiscal 1994 compared to 420 days in 1990. If manufacturers wish to *improve* devices already on the market before 1976, they must file a notification (or "510(k)") application with the agency.[53] Although the FDA is legally obliged to rule on 510(k) applications within 90 days, in fact the *average* review time has increased from 98 days in 1990 to 213 days in 1994.[54] These expensive delays, obviously a product of the agency's zealous desire to control for Type 1 error, result at the margin in decisions not to introduce new or improved devices.

These and other illustrations of FDA behavior[55] are *not* mere technical failings that could be addressed through more careful oversight.[56] Rather, they are the inevitable result of the institutional incentives of public regulators. The more complete the government's monopoly, the more pernicious

these results are. Fortunately, however, the FDA's monopoly has never been complete.

THE GAP IN THE FDA'S CERTIFICATION MONOPOLY: OFF-LABEL PRESCRIPTIONS

The FDA's certification monopoly for drugs and new devices has hastened the death of thousands of Americans. But, as seen in Section 1 above, the use of ethical drugs and devices in America pre-dates mandatory pre-certification rules. This chronology has left "gaps" in the FDA's certification monopoly: pockets of market-oriented behavior that have not yet been stifled by the agency.

Fortunately, the FDA's monopoly has never been complete.

One important breach of the monopoly results from "off-label prescriptions." Physicians may not prescribe, nor may manufacturers market, drugs or devices that have not received FDA approval.[57] Both doctors and pharmaceutical companies have been found "per se negligent" in tort if they defy the FDA's power in this area.[58] But if a drug or device is approved by the agency as safe and effective for a one purpose, *no FDA regulations prevent doctors from prescribing the approved drug or device for any other purpose*. Thus, doctors, hospitals and researchers may discover that a drug approved, labeled and marketed for treatment of one kind of cancer is effective at treating other diseases. They write up these discoveries in refereed medical journals and other publications.[59] Physicians read or hear about these other uses and then prescribe the drug for an "off-label" use. Under common law, an "off-label prescription" is *not* "per se" negligent. Tort law will, of course, sanction independently negligent prescriptions (if a doctor has misread the journal literature, if he has neglected to prescribe the correct dose, etc.).

The FDA has had mixed success in its sporadic efforts to suppress off-label prescriptions.[60] In 1979 the agency attempted to prevent a physician from prescribing a drug that had been approved as a medication for lead poisoning for a patient with arteriosclerosis. The Fifth Circuit Court of Appeals rejected the FDA's claim that the physician had "misbranded" (falsely claimed that the agency had approved the proposed use of) the drug by prescribing it or by advertising the new therapy.[61] FDA power has been more successfully invoked against manufacturers, however. Pharmaceutical companies routinely publicized (to doctors and to the general public) the results of new research on their already-approved drugs, thereby alerting physicians (the vast majority of whom do not subscribe to, say, the *New England Journal of Medicine*) to new ways to help their patients. In 1991 FDA Commissioner Kessler successfully cracked down on this "misbranding."[62]

These efforts to extend the FDA's certification monopoly to off-label prescriptions have cost lives and money, in several ways. For example, many insurers, following Medicare's lead,[63] deny or limit drug cost reimbursement for off-label use. Nearly 25% of oncologists surveyed by the Government Accounting Office in 1991 reported varying from their preferred treatment because of anticipated denial of Medicare reimbursement.[64] But because Medicare reimbursement for costly hospital stays is fixed, hospitalization is used to work around the out-patient system. Five of every eight surveyed oncologists admitted patients to hospitals solely to ensure reimbursement for drug therapy that would be denied to an out-patient.[65] However, case law has limited state governments' (and, to a much lesser degree, private) health insurers' discretion to rely exclusively on FDA approved use in determining coverage, however.[66]

More direct illustrations of health risks created by the FDA's crack-down on manufacturers' "misbranding" include one case involving an "over-the-counter" drug. Influential studies suggest that the risk of heart attacks for males over 50 is cut in half by taking one aspirin every other day. According to a 1988 article in the *New England Journal of Medicine,* widespread publicity of the aspirin treatment could save from 10,000 to 100,000 American lives each year.[67] Yet the FDA has prohibited aspirin manufacturers from distributing such notices, and since aspirin is no longer patented no company has the incentive to spend the millions of dollars for clinical trials and other tests necessary to lead the agency to authorize publicity for this "new use."[68] Even when drug patents are effective, unless a manufacturer is willing to submit an NDA supplement for an unapproved use it has little incentive to generate information on its safety and effectiveness. Nor may manufacturers even distribute reprints of peer-reviewed journals or textbooks in which off-label uses are documented, even though drug producers are an efficient clearing house for such material.[69]

Widespread publicity of the aspirin treatment could save from 10,000 to 100,000 American lives each year. Yet the FDA has prohibited this.

Despite its efforts, the FDA has not stemmed the tide of off-label prescriptions. According to one officer of the American Medical Association, off-label uses may presently account for *60 percent of all prescription drug use today.*[70] A recent study by the Government Accounting Office found off-label prescribing to be the rule for many types of therapy.[71] Common law suits recognize this common practice, and there is no requirement that physicians inform patients that they are prescribing a medication for a non-FDA-approved use.[72]

It is interesting to note that off-label prescriptions have proliferated despite tort law's implicit bias in favor of FDA-approved uses. A physician has a qualified tort immunity in that he is never negligent merely for prescribing a drug for a purpose approved by the FDA (though he still must transmit appropriate warnings, check for possible drug allergies, etc.).[73] If, on the other hand, a doctor prescribes an drug "off-label," there is no such immunity.[74] Common-law negligence principles apply; i.e., a doctor will be

liable to an injured patient *if* the current state of research or customary medical practice impugn the off-label use.[75]

Obviously, many more would die (and the clamor about FDA-induced "drug lag" would be more intense) if off-label prescriptions were suppressed. In an important sense, the medical profession has reduced public pressure on the FDA by privately performing research and issuing recommendations that manufacturers find too costly due to agency regulations. Just as obviously, private research and recommendations only deal with already-approved drugs and devices, for despite the gap in the agency's certification monopoly the FDA retains legal control over the approval of a drug or device for its "first" approved use. The proliferation of beneficial off-label prescriptions demonstrates the illogical character of this monopoly, though: why should FDA approval be a *sine qua non* to "first use" when, once approved, the drug can be put to any number of other non-approved uses, subject only to the general rules of tort liability?

A recommendation initially formulated by the Competitive Enterprise Institute could preserve all FDA evaluative functions while saving hundreds of thousands of lives.

The intolerable features of the *status quo* make it worthwhile to elaborate on a recommendation initially formulated by the Competitive Enterprise Institute.[76] This proposal, properly developed, could preserve all FDA evaluative functions while saving hundreds of thousands of lives. It consists of terminating the FDA's unsound "first use" monopoly by permitting "off-label manufacturing," much as "off-label prescribing" is presently allowed. This proposal would resolve asymmetries of incentives and result in consideration of both "Type 1" and "Type 2" certification errors. The proposal is clarified and defended in the remainder of this paper.

LOOSENING THE CERTIFICATION MONOPOLY: FROM OFF-LABEL PRESCRIPTION TO "OFF-LABEL MANUFACTURING"

To recap this paper's findings:

- FDA authority has expanded piecemeal in reaction to scattered occurrences. The result of this expansion is that the agency has metamorphosed from a guardian against consumer fraud to a prime determinant of the production of ethical drugs and medical devices;

- The FDA's present role cannot be justified by economic or political theory. The agency's skewed informational incentives, which contrast with those of manufacturers and physicians, have had the effect of aggravating illnesses and accelerating deaths;

- The FDA has attempted to suppress what remains of the private selection of ethical drug use. Despite all its efforts, a significant proportion of medications are used in non-FDA-approved ways. If private defiance of FDA hegemony had not been allowed, the perverse effects of the agency's disincentives would have been far more severe.

What measures can be taken to reconcile economic and political theory with FDA practice? The outright abolition of the agency, or even its reinstatement as a "consumer protection" department devoted to policing and prosecuting fraudulent claims about drugs, are likely nonviable solutions. A significant segment of the public is probably convinced that the agency should retain a role in the *ex ante* evaluation of drug safety and efficacy. On the other hand, the phenomenon of off-label prescriptions demonstrates that the FDA has never exercised hegemony over the therapeutic use of medication; practitioners (controlled by common-law tort, not by federal regulation) do "end-runs" around the FDA with quite desirable effects.

Once this is grasped, it becomes apparent that the FDA's social function would not change if practitioners could recommend non-approved *drugs* as easily as they can now recommend non-approved *uses* of drugs. Just as any doctor may today legally write "off-label" *prescriptions* of drugs or devices, it could be lawful to *manufacture* drugs and devices "off-label." The FDA would, under this proposal, remain accessible as a state-funded monitor of safety and efficacy.

In at least two areas this plan enhances the value of FDA certification.

Note that this proposal does not create a windfall gain for manufacturers of dangerous drugs. By analogy to physicians writing "off-label prescriptions," manufacturers producing "off-label drugs" would not benefit from tort immunity.[77] They would be liable for design defects in these drugs, while (as is the case for "on-label" prescriptions today) producers of FDA-approved drugs would be immune to design defect liability.[78] All producers of drugs would of course still be liable for manufacturing defects and failures to warn[79] (e.g., if a batch of the drug is contaminated, or if a label incorrectly indicates the appropriate dosage, etc.) just as physicians are liable for negligently mis/prescribing approved drugs under current law. But liability for design defect[80] (marketing a drug that should never have been put on the market) would be precluded only if the FDA has approved a drug.

This is not, therefore, a revolutionary proposal to sterilize the FDA. In fact, in at least two areas this plan enhances the value of FDA certification. As just stated, it provides "on-label" manufacturers with a "design defect shield" they presently lack, courtesy of agency approval.[81] Second, while physicians are presently not compelled by statute or common law to inform patients that they are writing "off-label" prescriptions,[82] this proposal would assuage nervous consumers and increase FDA visibility by requiring doctors to obtain "informed consent" from patients if an ethical drug they recommend is not approved by the agency.

What effect would this modification of the FDA's authority have on the allocation and distribution of ethical drugs? The remainder of this paper will explore this question Socratically, by answering a series of hypothetical

criticisms dealing with the interface between tort liability and drug production and use decisions.

Critique #1: "Without an FDA right to reject market decisions to commence production of a drug, manufacturers would massively produce "snake-oil" cures harming millions."

- Readers who have followed the analysis in this paper will hopefully recognize that this critique is unfounded. Manufacturers interested in maintaining a presence in the market and in enhancing their brand image will not market "snake oil." Excellent quality automobiles, croissants and knives are produced despite the absence of mandatory pre-market government approval, even though defective versions of any these products are extremely detrimental to our health.

- In rebuttal, it might be contended that government pre-approval of drugs is more prized by the public than pre-certification of the neighborhood baker or cutler. This argument fails to recognize that all certifications tend to become valuable over time. It may well be the FDA's structural obsession with avoiding Type 1 headlines that instills misplaced public confidence.[83] If the public retains this confidence, manufacturers will make the investment needed to obtain FDA approval, which they could then recoup by exacting a premium in the marketplace. Over time, market valuation of FDA approval would stabilize (formally stated, a demand function for the agency's services would emerge). The label "FDA inspected and approved," if truly esteemed by the public, would add more than enough value to a drug or device to ensure the agency's survival even in the absence of a statutory monopoly. The government could then engage in informed cost-benefit analysis of the FDA's policies, including its fixation with Type 1 errors.

The label "FDA inspected and approved," if truly esteemed by the public, would add more than enough value to a drug or device to ensure the agency's survival even in the absence of a statutory monopoly.

Critique #2: "Without mandatory FDA approval, manufacturers would refuse to produce most drugs or devices because of their fear of product liability."

- Both economic theory and present-day practice tell us that this is not so. Manufacturers produce motorcycles and ladders despite the absence of pre-market government approval. They are held liable when their product is defectively designed.[84] Conversely, FDA approval does not presently immunize manufacturers of pharmaceuticals (as distinguished from Class III medical devices[85]) from product liability.[86] This proposal's proposed immunization of manufacturers (against design defect liability only) for FDA-approved drugs might therefore *increase* the availability of ethical drugs.[87] At the very least, it is clear that the elimination of the agency's certification monopoly would not remove ethical drugs from the market.

- It was observed above that manufacturers now decline to develop certain drugs because pre-approval expenses render such development unprofitable. If Critique #2 is to be accepted, this would imply that manufacturers will refuse to produce drugs with or without agency oversight. This is a *non sequitur.* It is clear that the elimination of the agency's certification monopoly would not remove ethical drugs from the market.

Critique #3: "Doctors would never prescribe non-FDA approved drugs or devices, for fear of malpractice liability."

• The prevailing "gap" in the FDA's certification monopoly dulls this criticism. Fear of malpractice liability has not precluded off-label prescriptions, despite the loss of tort protection that derives from FDA use approval. Doctors are clearly willing to be held to common law negligence standards[88] when prescribing drugs for off-label uses. They would arguably agree to be held to the same standards when prescribing off-label drugs. Indeed, common law tort has evolved to the point that a physician's decision *not* to prescribe a drug for a widely accredited "off-label" use could well constitute malpractice. In this way again has the private sector mitigated the effects of the FDA's disdain for "Type 2" error. Legislation permitting prescription of off-label drugs would further palliate this problem.

• One might wonder how doctors would learn of "off-label manufactured drugs." After all, off-label *uses* of FDA-approved drugs are presently described in medical journals, which can be admitted into evidence at a malpractice trial; how would "off-label drugs" be introduced? The procedure would likely be very similar. Journals and other producers of knowledge about the safety (and efficacy) of drugs would find it in their interest to produce information on manufacturers' products. The same reputational pressures that encourage the *New England Journal of Medicine* to refrain from publishing unscientific drivel on new *uses* will promote accuracy on the part of private reviewers of new *drugs*.[89] Note that these new drugs would likely fill very urgent medical needs; the relative tort protection of FDA certification means that physicians would likely need good reasons[90] for utilizing non-FDA approved drugs or devices if there exist FDA-certified alternative treatments.

Doctors are clearly willing to be held to common law negligence standards when prescribing drugs for off-label uses. They would arguably agree to be held to the same standards when prescribing off-label drugs.

• It is important to see that agencies already provide informational services in fields where government has not snatched a legal monopoly. Private firms regularly evaluate and certify design and production parameters (or "standards"[91]) for goods and services as diverse as bricks and law schools. Reliance on these evaluations and certifications, even when they lack mandatory legal authority,[92] is an important element of malpractice defense for (in the above examples) architects and guidance counsellors. Unlike government agencies like the FDA, private firms cannot be politically constrained to accredit (or to refuse to accredit) new products or designs.[93] But (also unlike government agencies) if a sufficient number of knowledgeable parties belittle a certifying agency's inefficiency or corruption the creation of a rival agency is permissible.[94] Competing agencies exist in many fields,[95] some of them well known to physicians.[96]

Critique #4: "Private firms will not be willing to certify drugs and devices, because (unlike the FDA)[97] they will be liable for the unexpected side effects of drugs they have 'approved'."

• This is another baseless critique. It begs two important questions:

— As regards *reasonably foreseeable* side effects (for example, Thalidomide-type side effects that were clearly discernable through testing), the critique impliedly assumes that such calamities will occur frequently as a result of private drug certification; i.e., that market incentives will not lead

private certifying agencies to discover and prevent drug tragedies. The burden of much of this paper has been to challenge that assumption. Markets (supplemented by tort law) do provide strong incentives for certifying agencies to do their jobs well;

— As regards *unknowable* future side effects, it is not clear why a non-negligent certifier should be liable for results it could not have reasonably prevented. Manufacturers of ethical drugs are most certainly not liable for such side effects today,[98] and there is no reason why a certifying agency would assume presently non-existent liability in their place.[99]

• More fundamentally, this paper's critique of the "informational market failure" argument emphasizes that profits can be earned from certification even if there is a risk of liability. Some firms (like Underwriters' Laboratories) charge manufacturers directly for their services. Others (like Consumers Union, publisher of *Consumer Reports*) earn money solely from the public sale of evaluative information. Both types of companies devote considerable resources to protecting their intellectual property, which of course enables them to privatize the information they produce.[100] Still other companies (like Hearst, publisher of *Good Housekeeping*, whose "Seal of Approval" is affixed to products) earn money from subscribers (purchasers of their evaluative information) *and* from manufacturers. Although payment of fees might blur the distinction between publicity and certification, both protection of trademark value and tort liability[101] furnish incentives to accurately assess products.

The UL model has particular relevance for the ethical drug industry under this proposal.

• It seems likely that insurance companies would have a comparative advantage in competing as quality certifiers. Liability insurance companies already have a vital incentive to accurately evaluate products whose quality is likely to affect their exposure. One of America's most venerable private certifiers, Underwriters' Laboratories, is in fact a cooperative venture of insurance companies that presumably lower total risk (thereby increasing their profit)[102] by assuring that only certified products are produced or used by their clients. Since UL certification incurs the venture's liability to consumers injured by a defectively designed product that never should have been certified,[103] and since insurance companies are typically solvent, UL accreditation can be seen as a kind of surety bond paid for by manufacturers, assuring purchasers[104] that a product design is effective.[105]

• The UL model has particular relevance for the ethical drug industry under this proposal. Drug manufacturers could offer to "hold harmless" (i.e., to indemnify, as if they had issued a surety bond to) any physician found liable for prescribing a (non-government-approved) drug they produced, just as, analogously, Ford Motor Company contractually holds harmless independent dealers for liability they incur as a result of selling a defective new (non-government-approved) Ford. In both cases, of course, manufacturers either self-insure or purchase their own insurance against concomitant risks.[106] Drug manufacturers deciding to forego FDA certification could, by risking their capital ("self-insurance") or by purchasing liability insurance, produce quality guarantees for products in which they already have an interest and an expertise. Poor certification practices for ethical drugs would obviously directly cut into the profits of these "insurers," who in fact are serving as a bond for the quality of their pharmaceuticals. Good certification practices, accomplished through the establishment of reputable independent agencies (such as Underwriters' Laboratories), maximize insurers' and manufacturers' profits. Both tort

liability and self-interested monitoring by insurers will hold cooperative certifying agencies in check.

CONCLUSION

The FDA's legal control over medicine has never been all-encompassing. What monopoly the agency does possess was acquired episodically and accidentally. The agency's power over drug certification is not justified by economic or political realities, and its exercise has had deadly consequences. However, a gap in the FDA's power, resulting from the *ad hoc* process through which its jurisdiction was granted, has mitigated its potentially disastrous effects. This current process itself contains the kernel of a safer and more effective drug regulation policy.

This paper argues that the FDA's authority should be modified by allowing doctors to prescribe non-approved drugs and devices just as they today promote non-approved uses. Indeed, the FDA itself has recently presented a (very diluted) version of this proposal[107] in an effort to calm hostile critics on both sides of the aisle[108] in Congress.

Since this proposal in no way eliminates the FDA, consumers who remain troubled by non-FDA-approved products will be able to insist on FDA certification.

Although the relaxation of the agency's monopoly that this paper proposes would not substantially alter the FDA's everyday work, it would have far-reaching and beneficial effects. It might well lead to the establishment of a drug certification industry likely be composed of different types of competitive firms, as is the case in other fields. Non-profits (like Consumers Union), for-profits (like Hearst Publications) and insurers' cooperatives (like Underwriters' Laboratories) could be expected to enter the drug certification industry. To compete successfully, these firms would have to convince producers, consumers and doctors that their evaluation process is of high quality. Physicians and manufacturers would not decline to make and use privately certified products under these new ground rules, while risks of liability will be transferred (*via* insurance and bonding mechanisms) to efficient risk bearers.

Of course, no private evaluation industry will be viable if consumers balk at non-FDA certified drugs. Since this proposal in no way eliminates the agency, consumers who remain troubled by non-FDA-approved products will be able to insist on FDA certification. If consumers remain unconvinced that the market has provided efficient substitutes for the agency, drug manufacturers will continue to submit their products to the FDA for pre-market approval. On the other hand, if the FDA becomes perceived as an inefficient agency focused exclusively on the elimination of Type 1 testing errors (at the cost of an inefficiently high number of Type 2 errors), the agency's "market share" of certifications will decline. Sick people will increasingly opt to consume privately certified ethical drugs. If this happens, an FDA that wishes to prosper *sans* certification monopoly can be expected to put patients' best interests at heart by balancing Type 1 and Type 2 errors

instead of responding to bureaucratic pressures at the cost of thousands of lives. At that point consumers will finally benefit from an FDA which will put their interests first.

ABOUT THE AUTHOR

Michael I. Krauss is a professor of law at George Mason University School of Law in Arlington, Virginia. He is a graduate of Carleton University, and received his degrees in law from the Université de Sherbrooke and Yale University. He has published numerous law review articles on issues of tort law, market processes and comparative law. His writings have also appeared in publications ranging from the *Wall Street Journal* to *Reason* magazine and *Policy Review*. In 1994 he received George Mason University's first "Teacher of the Year" award for excellence in teaching.

A slightly different version of this monograph will shortly be published in the *George Mason University Law Review*.

END NOTES

[1] Professor of Law, George Mason University, 3401 North Fairfax Drive, Arlington, Virginia USA 22201. Internet: mkrauss@vms1.gmu.edu. Assistance from the Law and Economics Center of George Mason University and from the Competitive Enterprise Institute is gratefully acknowledged. Thanks to Richard Jacobus and to Sam Kazman for their useful comments, and to Kenneth Rossman for valuable research assistance. Any remaining errors are, of course, solely the author's responsibility.

[2]*See Competitive Enterprise Institute v. NHTSA*, 956 F.2d 321 (D.C. Cir. 1992) (holding NHTSA must consider reduced safety effects when determining fuel efficiency standards). *See also* R.W.Crandall & J.D.Graham, "The Effect of Fuel Economy Standards on Automobile Safety," 32*J. L. & Econ.* 97 (1989).

[3]Federal Food and Drugs Act of 1906, ch. 3915, 34 Stat. 768.

[4]See Peter Temin, *Taking Your Medicine: Drug Regulation in the United States*, Harvard U. Press, 1980, for a good history of drug regulation.

[5]*See* S. Peltzman, The Health Effects of Mandatory Prescriptions, 30 *J.L. & Econ.* 207 (1987).

[6]Federal regulations did not determine which drugs would be controlled by the prescription process until 1951. Humphrey-Durham Act, ch. 578, 65 Stat. 648 (1951). In fact, until that time drug manufacturers decided on their own how to label and sell their drugs, subject to state laws. *See DeFreese v. United States*, 270 F.2d 730 (5th Cir. 1959), *cert. denied*, 362 U.S. 944 (1960).

[7] Notably, the requirement of privity for successful products liability lawsuits was in the process of being relaxed at this time. See, e.g., *Macpherson v. Buick*, 111 N.E. 1050 (1916).

[8]See, e.g., *Thomas v. Winchester*, 6 N.Y. 397 (1906) (liability for manufacturer of incorrectly labelled drug, even if no privity is involved); *Osborne v. McMasters* (1906) (liability of druggist for mislabeling a poisonous drug); *Macpherson v. Buick*, 111 N.E., 1050 (1916) (liability for manufacturer of misrepresented vehicle). Contrary to popular belief, even early products liability law didn't preclude recovery from a defendant manufacturer whose misrepresented product caused injury.

[9]See M. Polinsky, *An Introduction to Law and Economics*, 1983, ch. 4. Assume, for example, that one million "units" (of an ethical drug) currently sell for $5 each, but that for $1 per unit more the manufacturer could add a safety device that would reduce total consumer injuries by two million dollars (for instance, manufacturers could substitute a hypo-allergenic substance for an ingredient that randomly affects a very tiny number of users). Assume that if the drug is not improved consumers cannot cheaply avoid these injuries at any cost less than five million dollars (because, say, no consumer knows whether they are allergic to the substance). The drug manufacturer should realize that it can maximize profits by choosing this new ingredient and selling the improved drug at a price above $6. If the manufacturer fails to realize this, tort law will "help" it figure this out. When sued by a consumer who suffers an allergic reaction to the non-improved drug, the manufacturer will be found to have marketed a negligently designed drug (under comment k, §402A, Restatement on Torts (2nd)), since it could have improved the drug for less ($1 million) than the damages the unimproved drug caused ($2 million). Internalizing these damages, the firm will realize that it is cheaper for it to add the safety device to the drug.

[10]Drug regulation was originally the responsibility of the Bureau of Chemistry in the Department of Agriculture. *See* Federal Food and Drugs Act of 1906, ch. 3915, 34 Stat. 768. The Bureau became the Food, Drug and Insecticide Administration in 1927. That name was shortened to the Food and Drug Administration in 1930. McNary-Mapes Amendment, ch. 874, 46 Stat. 1019 (1930).

[11]The syrup had already been marketed in pill form, and Mr. Massengill decided to produce it as a syrup by liquefying it with diethylene glycol. For further discussion of the relationship between the Elixir Sulfanilamide tragedy and the 1938 Act, see David F. Cavers, Food, Drug and Cosmetic Act of 1938: Its Legislative History and Its Substantive Provisions, 6 *Law & Contemp. Probs.* 2.

[12]Tort liability was rendered difficult by the fact that Mr. Massengill apparently owned assets only in Tennessee, which had a very short statute of limitations for wrongful death suits. Ultimately, Massengill was found liable under Tennessee law by applying the statutes of limitations of the states where the injury occurred. See, e.g., *Wilson v. Massengill*, 124 F.2d 666 (C.C.A.6 (Tenn.), Jan. 9, 1942, *cert. denied, Massengill v. Wilson*, 316 U.S. 686. In addition, Massengill was fined $26,100 under the 1906 Act for misbranding violations under the 1906 Act.

[13]The phrase refers to Justice Roberts' vote in *West Coast Hotel v. Parrish*, 300 U.S. 379 (1937), reversing a series of cases which held unconstitutional various components of "New Deal" legislation. These cases displeased President Roosevelt, prompting his threat to increase the number of Supreme Court Justices until he obtained a majority which would validate to his platform. *See* The Oxford Dictionary of American Legal Quotations 393 (Fred R. Shapiro ed., 1993); Gerald Gunther, *Constitutional Law* 457 (12th ed., 1991). No one is certain who authored the phrase. *See* Michael Ariens, *A Thrice-Told Tale, or Felix the Cat*, 107 Harv. L. Rev. 620, 623 n.11 (1994).

[14]It is important to note that the *safety* of a new drug had to be established. The *effectiveness* of the drug was not the FDA's concern, however. Presumably, market forces were still relied on to distinguish effective from ineffective medications.

[15]See Temin, supra note 4, pp. 46-51; Peltzman, supra note 5.

[16]Chemie Grünenthal, the producer of Thalidomide, had been alerted to the drug's neurological hazards by many European physicians. But the firm, in a move that did not serve its long-term commercial interests, constantly dissimulated the problem. W. S. Ross, *The Life/Death Ratio* 22 (1977)

[17]It should be noted that there is no reason to believe that the FDA ever suspected that Thalidomide had any teratogenic effect. The delay in US approval for the drug was entirely due to the above-mentioned adverse neurological reactions, whose theoretical link to birth deformities is still unclear. See Ross, supra note 16, at 39.

[18]For a summary of the modifications to Food and Drug law in 1962, see H. Grabowski and J. Vernon, *The Regulation of Pharmaceuticals*, American Enterprise Institute, 1983, p. 2-4.

[19]The agency was required to render decisions within 180 days, but no sanctions were provided for longer deliberation time. See Pub. L. 87-781, Title I, Part A, 76 Stat. 781-83, 784, 785 (codified in relevant part at 21 U.S.C. § 355(c)).

[20]Grabowski and Vernon, supra note 18, p. 5.

[21]In other words, the 1906 bill recognized the primacy of the market in the production and distribution of medicines, and saw a purely informational role for government. Of course, it is not clear that government is even efficient in evaluating information accurately. See on this point M. Krauss, "Regulation v. Markets in the Development of Standards," 3 *S. Cal. Interdisciplinary L. J.* 781 (1994)

[22]S. Peltzman, *Regulation of Pharmaceutical Innovation*, American Enterprise Institute, 1974, p. 18.

[23]Grabowski, supra note 18, p. 30; K. Kaitin, Written Testimony Before House Subcommittee on oversight and Investigations, Tufts Center for the Study of Drug Development, May 25, 1995. The process for new drug approval begins with preclinical testing of a compound in a laboratory and on animals. This stage takes on average 3.5 years to satisfy the FDA. If successful, researchers then file an IDA (Investigational New Drug Application) with the agency. This requires a three-stage clinical testing procedure on human subjects, monitored constantly by the agency: **Phase 1** determines safety and dosage on a small group of volunteers, over about one year. **Phase 2** measures the effectiveness of the drug on hundreds of volunteers, over about two years. **Phase 3** confirms the efficacy of the drug in double-blind tests involving hundreds if not thousands of volunteers and control groups, lasting on average three years. See 21 C.F.R. §312.21

[24]San Francisco *Chronicle*, Oct.26, 1992, p. A1.

[25]The pharmaceutical industry introduced an average of more than three times as many drugs (54 to 16) before

1962 as after. See H. Grabowski, "The Prescription for High Drug Prices: Factors Contributing to Rising Prescription Drug Prices," (December 1992) *Consumers' Research* 10.

[26]If fewer drugs are available, lessened competition will increase prices.

[27]See K. Kaitin *et al.*, "The drug lag: An update of new drug introductions in the United States and in the United Kingdom, 1977-87," 46-2 *Clinical Pharmacology & Therapeutics* 121 (1989).

[28]For example, using poor sterilization processes.

[29]For example, with insufficient care given to allergic or other abreactions, or to drug interaction effects.

[30]For example, firms might exaggerate a drug's therapeutic effects, or not draft labels that would alert users to abreactions or optimal dosage.

[31]"FDA to leave firms to devices," *Washington Times*, 4-7-95, p. A6.

[32]Some readers might have the following reaction to the above examples: "Yes, we almost always have incomplete information, but in the case of ethical drugs imperfect information is especially severe, and its consequences can be especially bad." Later in this paper I try to show that government monopoly over drug certification is, neither in theory nor in practice, the best way to combat this informational problem. At this point my modest claim is that informational problems are endemic to daily life in a free society.

[33]See M. Krauss, "Property, Monopoly, and Intellectual Rights," 12 *Hamline L. Rev.* 305 (1989) for an in-depth discussion of this point. See also Krauss, supra note 21. The privatization of information will not be possible, of course, if legislation prevents it (say, by denying copyright or patent protection to information producers).

[34]The burgeoning growth of private on-line information systems (e.g., America Online, LEXIS-NEXIS, etc.) and the anticipated streamlining of Internet services will likely make the diffusion of such information much less costly. Once dangerous side effects emerge in users of a particular product, the "Net" may allow extremely rapid dissemination of this information. Arguably, news of Thalidomide's neurological side-effects would become much more difficult to hide today.

[35]See infra, note 100.

[36]Janet Novack has repeatedly detailed FDA corruption scandals in articles written for *Forbes* magazine. *See*, e.g., Oct. 16, 19989, p. 10; April 29, 1991, p. 34.

[37]Unfortunately, tort law provides less incentive to monitor negligent *government* workers, since their managers (unlike corporate owners) have no direct ownership claims which allow them to directly profit from good monitoring. Tort law's inability to adequately motivate government officials is a contemporary justification for sovereign immunity (excluding tort liability to limit drains on tax dollars).

[38]See, e.g., *Seely v. White Motor Co.* 63 Cal.2d 9 (1965) (Privity between consumer and manufacturer is not required for manufacturer to be sued for breach of express warranty.)

[39]See M. Krauss, "Tort Law and Private Ordering", 53 *St. Louis U. L. J.* 423 (1992).

[40]If it would have cost more *ex ante* to modify the manufacturer's behavior than would be saved through such a change, then of course the modification is not socially beneficial. See R. Coase, "The Problem of Social Cost," 3 *J. of L. & Econ.* 1 (1960), and supra note 9.

[41]Again, a strong argument can be made that the consumer is presently paying for more information than she wants because tort law is skewed to over-compensating victims. Any reader who has seen the labels on new ladders will understand this point.

[42]A "Public Choice" vision of government and bureaucracy largely based on these agency problems garnered a Nobel prize for one of my George Mason colleagues. See J. Buchanan, with G. Tullock, *The Calculus of Consent*, 1961.

[43]During the Thalidomide episode the regulatory authority and one of its employees was praised by both the President and Congress for the purely negative action of delaying (*not* disapproving) endorsement of Thalidomide. The employee and the FDA had never been praised for *approving* a drug, or for expediting approval or, in fact, for any positive decision.

[44]See S. Kazman, "Deadly Overcaution: FDA's Drug Approval Process," 1 *J. of Regulation & Social Costs* 35 (1990), 41.

[45]See, "Feel a Heart Attack Coming? Go to France," *Wall Street Journal*, August 2, 1994, p. A14. In April, 1995 the *Journal of the American Medical Association* published a study questioning the claimed superior efficacy of the cardiopump: see Schwab *et al.*, "A Randomized Clinical Trial of Active Compression-Decompression CPR v. Standard CPR in Out-of-Hospital Cardiac Arrests in Two Cities," JAMA 1995: 273:1261-1268. However neither this nor any other study has found any added risk from cardiopumps, and the article underlined the need for further research, which hospitals would presumably be free to conduct were it not for the FDA prohibition. An editorial in the same issue of the AMA *Journal* expressed "astonish[ment] and dismay..." at the FDA's policy on research of emergency devices. A 1993 Congressional report, "Less than the Sum of its Parts," found that 26 US-made life-sustaining cardiovascular products were not available in this country, but have been approved and are in widespread use overseas. *Less Than the Sum of its Parts: Reforms Needed in the Organization, management, and Resources of the Food and Drug Administrations Center for Devices and Radiological Health* (Comm. Print 103-N) 103d Cong., 1st Sess. (1993).

[46]Competitive Enterprise Institute, "Consumer Advocacy Group Attacks FDA For Slow Approval of Cancer Treatment" (press release, May 14, 1992).

[47]*Investor's Business Daily*, May 3, 1994, p.1.

[48]An Alzheimers patient whose symptoms are controlled is less likely to wander off from home, etc.

[49]*Baltimore Sun*, May 10, 1994, p. 1.

[50]"Dr. Went to Japan for Treatment He Couldn't Receive in America," Minneapolis *Star Tribune*, June 26, 1994, p. 12A.

[51]See *20/20*, August 12, 1994, transcript, p. 7.

[52]See Medical Device Amendments to the Food and Drug Act, 21 USC § 360 et seq. (90 U.S. Stat. 539).

[53]Referring to section 510(k) of the Act.

[54]Testimony of Mr. Robert O'Holla, Vice-President for Regulatory Affairs, Johnson & Johnson. *Medical Device User Fee Act of 1994: Hearings on H.R. 4728 Before the Subcomm. on Health and the Environment of the House of Representatives Committee on Energy and Commerce*, 103d Congress, 2d Session (1994).

[55]See, for other examples, J. DiMasi *et al.*, "New Drug Development in the United States from 1963 to 1992," *Clin. Pharm. Therap.*, pp. 609-622.

[56]Such is the recurrent claim of FDA Chairman David Kessler. *See, e.g.*, "Statement Before the Subcommittee on Human Resources and Intergovernmental Relations, Committee on Government Operations." *Council on Competitiveness and FDA Plans to Alter the Drug Approval Process at FDA: Hearings Before the Subcomm. on Human Resources and Intergovernmental Relations of the House of Representatives Comm. on Government Operations*, 102d Congress, 2d Session 47-145, 226-357 (March 19, 1992).

[57]Except for those drugs and devices which are "grandfathered" by the 1976 amendments.

[58]See Stanton by Brooks v. Astra Pharmaceutical Products Inc., 718 F.2d 553 (3d Cir.1983); Orthopedic Equipment Co. v. Eutsler, 276 F.2d 455, 460-61 (4th Cir.1960).

[59] See Richard M. Cooper, *Unapproved Uses of Drugs: An Analysis and Some Proposals*, 49 Food & Drug L.J. 533 (1994); William L. Christopher, *Drug Prescription: Filling the Regulatory Vacuum*, 48 Food & Drug L.J. 247 (1993), for examples of this process involving journals, textbooks, and even the Internet.

[60]In a position paper over twenty years ago, the FDA admitted that "Once the new drug is in a local pharmacy..., the physician may, as part of the practice of medicine, lawfully ... vary the conditions of use from those approved on the package insert... without informing or obtaining the approval of the Food and Drug Administration." 37 Federal Register 16,503 (1972). This acknowledgment by the FDA was in fact

part of a proposal to curb off-label uses, if necessary by revoking approval of any drug used "too often" in an off-label fashion. The 1972 proposal was abandoned, however, and in 1982 the FDA issued a bulletin formally emphasizing that it condoned off-label use as "accepted medical practice." 12 FDA DRUG BULLETIN, April 1982, at 4. The 1982 bulletin was seen by some as an abdication by the FDA of its desire to control off-label use. See, e.g., American Medical Association, 1991 *Drug Evaluations Manual* 13. But see *infra*, note 62 where more recent efforts to discourage off-label prescriptions are detailed.

[61]United States v. Evers, 643 F.2d 1043 (5th Cir. 1981).

[62]See T. Randall, "FDA Scrutinizes 'Off-Label' Promotions," 266 *JAMA* 11 (1991). See also 21 C.F.R. §§310.3(h)(4), 312.7(a), 314.70(b)(3) (1994).

[63]See 54 Fed. Reg. 4302, 4306, 4316 (1989) (providing reimbursement only for "safe and effective" drug use, and defining FDA approved uses as "safe and effective."

[64]United States Government Accounting Office, *Off-Label Drugs: Reimbursement Policies Constrain Physicians in their Choice of Cancer Therapies*, GAO/PEMD-91-14, (1991) at 35.

[65] See supra note 64, at 37.

[66]In *Weaver v. Reagan*, 886 F.2d 194 (8th Cir. 1989), Missouri defended its refusal to provide Medicaid coverage to certain AIDS patients on the grounds that their preferred therapy, AZT, had only been approved by the FDA for patients with a different HIV profile than the plaintiffs'. The Eighth Circuit reasoned that Medicaid was required to provide "medically necessary" care, and that the distinction between "medically necessary" and "experimental" care should be established by the medical community, not by the FDA approvals. In *Pirozzi v. Blue Cross-Blue Shield*, 741 F.Supp. 586 (E.D.Va.1990), a district court enjoined an insurer from denying reimbursement for a new cancer therapy known as high dose chemotherapy-autologous bone marrow transplant (HDCT-ABMT), a therapy in which standard cancer drugs are used at levels far higher than approved by the FDA. The grounds for the injunction were narrow: the court held that the insurer's contract with the plaintiff did not disclose that the insurers could refuse to reimburse a non-FDA-approved use.

[67]See D. Thompson, "Aspirin: the Cardiologist's Dream?" 131 *Time* 56 (Feb. 8, 1988).

[68]This is one area where, *because* of legislation, there is indeed an informational "market failure." See supra note 33 and accompanying text.

[69]According to one critic, this new FDA interpretation has actually intimidated textbook publishers, who now fear that including the latest information on drug use may result in restrictions on the sale of their textbooks. See J. Bovard, "FDA's pharmaceutical hide-and-seek," *Washington Times*, April 9, 1995, p. B4.

[70]See J. Calfee, "The Leverage Principle in FDA's Regulation of Information" in R. Helms, ed., *Competitive Strategies in the Pharmaceutical Industry*, American Enterprise Institute, 1995. S. Lane, "Medical Precautions," *Washington Times*, April 9, 1995, p. B4.

[71]United States Government Accounting Office, *Off-Label Drugs: Reimbursement Policies Constrain Physicians in their Choice of Cancer Therapies*, GAO/PEMD-91-14, at 3. The report notes that off-label use of three drugs, ifosamide, interferon and mitoxantrone, constituted 85% of total prescriptions. Id. at 22.

[72]No appellate cases have been found holding that a doctor's failure to disclose that a frequently prescribed drug therapy was "off-label" violated the rigorous "informed consent" requirements of tort law.

[73]The Food and Drug act has generally been seen as preempting state tort law liability holdings in such cases. See, e.g., *Slater v. Optical Radiation Corp.*, 961 F.2d 1330 (7th Cir., 1992); *Evraets v. Intermedics Intraocular*, 34 Cal.Rptr. 2d 852 (1995). The Supreme Court recently granted a certiorari petition in a case in which the Eleventh Circuit had ruled that the "grandfathering" of a medical *device* (under the Medical Device Amendments to the Food, Drug and Cosmetic Act) precluded any state-based products

liability suit. See *Medtronic, Inc. v. Lohr*, cert. granted, Jan. 19, 1996. The issues posed in *Lohr* to the Supreme Court are not relevant to the qualified tort immunity discussed in this paragraph.

[74] *Mulder v. Parke Davis*, 181 N.W.2d 882 (Minn., 1970) is occasionally cited as contrary authority. In *Mulder*, the Minnesota court held (at 887) that when the drug manufacturers' warnings and contraindications have been clearly communicated to the physician, who then deviates from them, prima facie evidence of negligence has been established, requiring the physician to explain his deviation. *Mulder* clearly rejects any "per se" rule for off-label prescriptions, as it does not preclude a demonstration by the defendant physician of the reasonableness of his use of the drug, given current medical practice. See, e.g., *Lhotka v. Larson*, 238 N.W.2D 870 (Minn. 1976).

[75] See, e.g., *Salgo v. Leland Stanford Jr. Univ. Board of Trustees*, 317 P.2d 170 (CA, 1957) (finding, at 180, that drug manufacturers' recommendations are always conservative and are quickly outdated, and after a drug has been available for a period of time physicians rely on their own experience concerning its use in actual practice); *Craft v. Peebles*, 893 P.2d 138 (HI, 1995) (holding that manufacturers' instructions about use and dosage, which are presumably those approved by the FDA, do not establish the standard of medical care as a matter of law).

[76] See Competitive Enterprise Institute, "The Food and Drug Administration: A Modest Proposal" (press release, January 6, 1995); see also Kazman, supra note 44, at 51-52.

[77] See supra note 74 and accompanying text.

[78] The situation is analogous in that, under present law, a doctor prescribing a drug for an "on-label" (i.e. FDA approved) use could not successfully be sued on the grounds that the drug was inappropriate for that use. However an "off-label" prescriber is vulnerable to this type of lawsuit.

[79] I.e., when the drug as sold is not identical to the drug as advertised.

[80] See comment k, §402A Restatement (Second) of Torts: *k. Unavoidably unsafe products*. There are some products which, in the present state of human knowledge, are quite incapable of being made safe for their intended and ordinary use. These are especially common in the field of drugs. An outstanding example is the vaccine for the Pasteur treatment of rabies, which not uncommonly leads to very serious and damaging consequences when it is injected. Since the disease itself invariably leads to a dreadful death, both the marketing and use of the vaccine are fully justified, notwithstanding the unavoidable high degree of risk which they involve. Such a product, properly prepared, and accompanied by proper directions and warning, is not defective, nor is it *unreasonably* dangerous. The same is true of many other drugs, vaccines, and the like, many of which for this very reason cannot legally be sold except to physicians, or under the prescription of a physician. It is also true in particular of many new or experimental drugs as to which, because of lack of time and opportunity for sufficient medical experience, there can be no assurance of safety, or perhaps even of purity of ingredients, but such experience as there is justifies the marketing and use of the drug notwithstanding a medically recognizable risk. The seller of such products, again with the qualification that they are properly prepared and marketed, and proper warning is given, where the situation calls for it, is not to be held to strict liability for unfortunate consequences attending their use, merely because he has undertaken to supply the public with an apparently useful and desirable product, attended with a known but apparently reasonable risk. Restatement (Second) of Torts § 402A, comment k.

[81] Absolute design defect immunity for FDA approved drugs is not presently enjoyed by manufacturers: indeed, in only five states (Arizona, New Jersey, Ohio, Oregon and Utah) does FDA approval currently preclude *punitive* damages for faulty design. See Viscusi, Rowland, Dorman & Walsh, "Deterring Inefficient Pharmaceutical Litigation: an Economic Rationale for the FDA Regulatory Compliance Defense," 24 Seton Hall L. Rev. 1437 (1994). It follows that in an important way this proposal would *increase* the present value of FDA approval. It is thus incorrect to think that implementation of the proposal contained in this paper would "emasculate" the agency. However, just as some doctors currently

prescribe "off-label" despite the lack of tort immunity, some manufacturers would, for reasons explicated below, produce non-approved drugs despite the risk of liability for design defect. This would eliminate the noxious drug lag described above.

[82]See supra note 75.

[83]Reputable certifications are relied on in many areas unrelated to drugs. Well-heeled consumers (of products as diverse as shotguns, wallets and four-wheel-drive vehicles) prize the knowledge that a product has achieved "appointment to Her Majesty the Queen," who therefore acts as a certifier of exceptional quality control throughout the British Commonwealth. In the food industry, registration with the Pennsylvania Department of Agriculture was likely a sign of high quality a generation ago. Perhaps the governmental nature of the certifier led to insufficient cultivation, and thus a slow deterioration, of its "brand name." But private food certifiers continue to thrive. For example, consumers of Kosher food products are often fussy about the identity of the agency which has certified that a product complies with Jewish dietary rules. "Star K," "Circle U" and "MK" logos on products are brand marks of three of many competing rabbinical inspection boards, which contract with manufacturers to inspect and certify their manufacturing and packaging facilities. These marks add value to food for consumers of Kosher goods who trust the agency owning the relevant trademark. If (as has occasionally happened in the past) it is revealed that a certification board has erroneously (or even intentionally, as a result of corruption) certified a non-Kosher product, the commercial effect on the board is devastating.

[84]Many experts in Tort law, including this author, feel that manufacturers are presently being held liable even if their motorcycle or ladder was properly designed and manufactured. See Krauss, supra note 39. Again, this is a problem that substantive tort reform can handle. Mandatory government certification is not needed.

[85]See *Michael v. Shiley, Inc.*, 46 F.3d 1316 (3d Cir. 1995) (ruling that the 1976 amendments to the Food and Drug act preempt state actions for negligence, strict liability and implied warranty for Class III medical devices, the only devices subject to formal pre-market FDA approval).

[86]Numerous cases have held that FDA approval does not preempt state products liability. See, e.g., *MacDonald v. Ortho Pharm. Corp.*, 475 N.E.2d 65, *cert. denied*, 474 U.S. 920 (1985) (holding state not preempted from imposing higher duty of warning); *Allen v. G.D. Searle & Co.*, 708 F. Supp. 1142 (D. Or. 1989) (holding state law claim of defective labelling for IUD was not preempted because the device was classified as a prescription drug).

[87]For example, Bendectin, the most effective anti-nausea drug for pregnant women, was withdrawn from the market after many successful (but expensive) product liability defenses against claims that it induced birth defects. Had these suits been "demurrable" (i.e., seen as ill-founded on the basis of a preliminary motion) on the grounds that Bendectin had been tested and found safe by the FDA, the drug would most certainly still be marketed.

[88]E.g., allowing doctors to defend themselves by citing medical studies showing the utility of the drug, etc.

[89]In a recent survey, the Competitive Enterprise Institute asked oncologists how they would obtain reliable information about drugs that had not obtained FDA approval: 59% of respondents stated that they would rely on studies published by refereed journals. CEI, "A National Survey of Oncologists Regarding the Food and Drug Administration," p. 5 (Aug. 1995).

[90]E.g., superior effectiveness, enhanced safety, much lower price (due to the high costs of FDA certification) for low-income patients, etc.

[91]See Krauss, supra note 21.

[92]See, e.g., In the Matter of Analysis of Wash Trucking, 521 A.2d 883 (N.J.Super., 1987) (confirming the voluntary nature of Underwriters' Laboratories).

[93]See, e.g., *Roofire Alarm Co. v. Underwriters' Laboratories*, 188 F. Supp. 753 (E.D. Tenn., 1959) [UL cannot be forced to change its standards as to fire warning devices, as it is a private entity.]; *Consolidated*

Metal Products v. American Petroleum Institute, 846 F. 2D 284 (5th Cir., 1988) [Trade association that evaluates products and issues private "licenses" does not violate § 1 of Sherman Act when it fails to favorably evaluate a product.]

[94]Of course, it is conceivable that private certification firms may be bribed or otherwise corrupted; but this is a risk that has also afflicted the FDA. See, e.g., Novack, supra note 36. If a private firm is corrupted it loses most or all of its goodwill, while a government monopolist does not have this fear. The likelihood of corruption is thus lower for private certifiers than for the FDA.

[95] For example, for metal gasoline containers standards have been privately proclaimed by Underwriters' Laboratories (Standard #30 for Metal Safety Cans), by the National Fire Prevention Association (NFPA Flammable and Combustible Liquids Code #30-77), and by Factory Mutual Insurance (Standard for Safety Containers and Filling Supply and Disposal Containers #FM 6051).

[96]Medical malpractice trials are replete with expert testimony from various hospital and physicians' associations, which have adopted competing standards for surgical techniques.

[97]See *Sun Up Foods, Inc. v. Florida Dept. of Citrus*, (M.D. Fla., Dec. 31, 1991) (holding FDA's sovereign immunity bars suits for damaging business through manner of enforcement); *Giles v. Villanileea*, No. C 93-2461 BAC (N.D. Cal. Dec. 14, 1993); *Daley v. Weinburger,* 400 F. Supp. 1288 (E.D.N.Y. 1975) (denying injunction request because of the FDA's sovereign immunity).

[98]Comment k, § 402A, Restatement (second) of Torts. This comment applies to prescription drugs, so in fact a negligence rule applies to manufacturers of FDA approved drugs. See, e.g., *Carmichael v. Reitz*, 95 Cal. Rptr. 381 (Cal. App., 1971). Strict liability is also held inapplicable to medical devices, whether approved by the FDA or grandfathered. See, e.g., *Phillips v. Baxter Healthcare*, 1993 WL 524688 (Cal. App. 2 Dist.) (1993).

[99]See, e.g., *Yassin v. Certified Grocers of Illinois*, 502 N.E.2d 315 (Ill. App., 1986) at 331 (refusing to hold Underwriters' Laboratories to a "strict liability" standard under § 402A of the Restatement (Second) of Torts, as UL is a testing facility and not a manufacturer).

[100]Their efforts are not always successful. In *Consumers Union of the United States v. General Signal Corp.*, 730 F.2d 47 (2nd Cir., 1984), the Union (publisher of *Consumer Reports*) sued to prevent a manufacturer from using that magazine's research findings about Regina vacuum cleaners in its advertising. A majority of the court opined that quoting *Consumer Reports*' ratings of a product constituted "fair use" under 17 U.S.C. § 107. Oakes, J., in dissent (*ibid*, at 47), correctly observed that the majority's opinion prevented Consumers Union from maximizing profits by deciding what mix of endorsement revenues and newsstand sales is optimal. Buyers informed about Regina's high *CR* rating directly from the manufacturer have less of a need to purchase the *CR* "vacuum cleaner" issue to see "who won." In practice, of course, the Union can refuse to evaluate products manufactured by corporations which violate its prohibition of citations. Even in Second Circuit states there is a strong economic incentive to refrain from using *CR*'s name. See also *Toman v. Underwriters' Laboratories*, 707 F.2d 620 (5th Cir., 1983) (Underwriters' Laboratories may sue manufacturer and distributor of hair dryer if they place laboratory approval marks on their product without authorization).

[101]See, e.g., *Hanberry v. Hearst Corp.*, 81 Cal. Rptr. 519 (Cal. App., 1969) (recognizing the possible liability for negligent issuance of "Good Housekeeping Seal of Approval" for a dangerous product). Acceptance of an advertisement by a magazine does not constitute an endorsement (see, e.g., *Walters v. Seventeen Magazine*, 241 Cal. Rptr. 101 (Cal. App. 1987)), but *Good Housekeeping* purports to evaluate, not just advertise, products which gain its seal of approval.

[102]Insurance companies derive profits in two ways: by investing the premiums they receive, and by accurately gauging their risk exposure. High absolute risks are more variable; it follows that if insurance companies can lower their risk they can (by definition) more accurately gauge their exposure. Risk is lowered in three ways: intrinsically through the aggregation of identical risks into pools (*via* the "law of large

numbers"); through production of more accurate information about the extent of risk; and through reinsurance (by which insurance companies "contract out" the aggregation of some risks). Certification agencies test products and thereby produce new information about their risk potential. Insurance companies are "natural" certifiers of risk, and therefore of quality. Note that managed care providers are typically insurers in this sense.

[103]See Restatement of Torts, § 324A. See: *United States Lighting Service v. Llerrad Corp.*, 800 F.Supp. 1513 (N.D.Ohio, E.D., 1992) (UL can be considered a "product endorser," and is liable when it fails to exercise reasonable care when performing its testing procedures, or if inaccurately communicating its testing results). See also *Toman v. Underwriters' Laboratories*, 532 F. Supp. 1017 (D. Mass. 1982) (reversed on other grounds, 707 F.2d 620).

[104]The reputational effect of UL certification is significant. See, e.g., *Brazos Graphics v. Arvin Industries*, 574 S.W.2d 240 (Tex App., 1978) (evidence of UL approval of an electric heater admissible in defense against claim that the heater was defectively designed).

[105]Robert Cooter has produced analogous and interesting work on insurers' purchase and sale of tort claims. Robert Cooter, *Towards a Market in Unmatured Tort Claims*, 75 Va. L. Rev. 383 (1989).

[106]*See* Frank H. Easterbrook, Limited Liability and the Corporation, 52 Chi. L. Rev. 89 (1985) (discussing reasons why corporations insure, despite the portfolio diversification of their owners and their presumed resulting risk neutrality).

[107]On April 6, 1995 the agency, in a package of reforms announced at the White House, announced that for a two-year trial period it would contract out testing of low-risk devices (like laboratory cholesterol tests and electronic stethoscopes) to private certification firms, *but only if those firms are accredited by the agency.* The agency reserved the right to nullify private certifications in any case. See *Washington Times*, April 7, 1995, p. A6. Note that no drugs (and no devices affected by long time lags, such as pacemakers) are affected by the FDA's offer. Note also that the FDA accreditation requirement would have the effect of exporting many of the bureaucratic pressures afflicting the agency, and would preclude free competitive entry into a nascent "certification industry."

[108]Senator Barbara Mikulski (D-MD) insisted that the FDA have a "passion for change" if it did not wish to be "rolled right over" by Congress. *Ibid.*

The Competitive Enterprise Institute

The Competitive Enterprise Institute is a public policy organization committed to advancing the principles of free enterprise and limited government. Founded in 1984 by Fred Smith, Jr., CEI promotes classical liberal ideals through analysis, education, coalition-building, advocacy, and litigation. A non-profit, tax exempt organization under Section 501 (c) (3) of the Internal Revenue Code, CEI relies entirely on donations from foundations, corporations, and private individuals. Contributions are tax deductible to the extent allowed by law.

For more information, contact:

COMPETITIVE ENTERPRISE INSTITUTE

1001 Connecticut Avenue, N.W.
Suite 1250
Washington, D.C. 20036
Phone: (202) 331-1010
Fax: (202) 331-0640
E-mail: info@cei.org
Web site: http://www.cei.org

THE WHITE HOUSE
WASHINGTON

Michael Large

479-0694

Pre Disasters

4 copies

Jim Arcdala's
202-260-1847

Lindsey Morse
Paul Shuda

FDA Reform 7/12/96

JD / Rich - finalized ground rules for Donna-Bliley discussion. He called her! She said she couldn't support if they were going to go forward w/ mark-up ~~and~~ within next two weeks. He agreed - pending blowup.

{ Alan Roth
Kay Holcomb
Karen Nelson - Waxman

Think it's a good opportunity - though 1½ issues -

[Kassebaum, Mikulski, Dodd - met w/ Phil Lee. -]

Ground rules - Dingell-Waxman at table
- FDA
- at Table
- Agreement on language / not concepts
- 2 weeks w/ Bliley / Donna -
- No Food -

Bliley - wants something on devices - Rich - but we're far apart - Barton is committed to his bill.
Bliley - recognize they have "Barton" problem Drugs and Devices. -

Meetings starting Mon p.m. 4:30 —
- First negotiation sessession Wed.
- (Tues is pesticide mark-up) —

"Keep Dan Tate involved" —
- bridge to conservative democrats —

Pesticides —
Safe-drinking H_2O. —
Rich apprised them of agreement w/Bliley — Donna —
Tues or Wednesday —

→ Wed, Thurs, Fri — Tracy called about FDA reform —

Senate — Hammer
Kassebaum said explicitly — never want hammer
to be triggered. —
spreading out trigger
lowering perception each year
HHS — made argument — wasn't realistic in
terms of resources —
Rich — member level understanding is thin —
Flexibility about lowering percentage and
stretching out time frame.
Has to be cliff — David and Bill —

No hammers on drug side on House bill —
House now has a more acceptable

drug hammer — Senate has better approach on 3rd party review — on devices agreed to our parameters — excluding life threatening implantable and some therapeutic/diagnostic devices. —

Guidance — uniform standards for diff reviewers on same device.
- II and Class III — w/notice of intent to reclassify —
"supporting or sustaining human life"
"diagnostic of which

Health Claims — flexibility
Med Guides — flexibility
Prod Approval
Mun Changes
Off label — Dodd work out w/Frist, Mack, Wyden
Bill and Peggy Dorrell — Jane Loewenson working hard on off-label —
- Phil also seeing Frist Tuesday

- Off Label — that's where Senators are most dug in — Sully — that's where they don't have as much to

off-label Bush
- Dodd would oppose an immediate cloture vote — so at least 4 days on floor. —
Senate way behind —

Withdrawal/Redaction Marker
Clinton Library

DOCUMENT NO. AND TYPE	SUBJECT/TITLE	DATE	RESTRICTION
001. note	re: FDA Reform [partial] (1 page)	07/12/1996	b(6)

COLLECTION:
Clinton Presidential Records
Domestic Policy Council
Elizabeth Drye
OA/Box Number: 10452

FOLDER TITLE:
FDA Reform 1996 [2]

2014-0046-S
rc1402

RESTRICTION CODES

Presidential Records Act - [44 U.S.C. 2204(a)]

P1 National Security Classified Information [(a)(1) of the PRA]
P2 Relating to the appointment to Federal office [(a)(2) of the PRA]
P3 Release would violate a Federal statute [(a)(3) of the PRA]
P4 Release would disclose trade secrets or confidential commercial or financial information [(a)(4) of the PRA]
P5 Release would disclose confidential advice between the President and his advisors, or between such advisors [a)(5) of the PRA]
P6 Release would constitute a clearly unwarranted invasion of personal privacy [(a)(6) of the PRA]

C. Closed in accordance with restrictions contained in donor's deed of gift.
PRM. Personal record misfile defined in accordance with 44 U.S.C. 2201(3).
RR. Document will be reviewed upon request.

Freedom of Information Act - [5 U.S.C. 552(b)]

b(1) National security classified information [(b)(1) of the FOIA]
b(2) Release would disclose internal personnel rules and practices of an agency [(b)(2) of the FOIA]
b(3) Release would violate a Federal statute [(b)(3) of the FOIA]
b(4) Release would disclose trade secrets or confidential or financial information [(b)(4) of the FOIA]
b(6) Release would constitute a clearly unwarranted invasion of personal privacy [(b)(6) of the FOIA]
b(7) Release would disclose information compiled for law enforcement purposes [(b)(7) of the FOIA]
b(8) Release would disclose information concerning the regulation of financial institutions [(b)(8) of the FOIA]
b(9) Release would disclose geological or geophysical information concerning wells [(b)(9) of the FOIA]

FDA Reform

• Have VP or Leon call

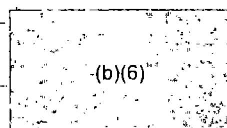
• Dodd said – he's done everything he can to get our support –

Phil has Frist at 4:00 or early afternoon –

– Tracy 2:00 or 5:30
– John
– George

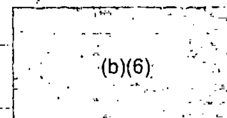
Phyllis
7956856

[001]



• Line is said M – Phil Lee.
– Sally
– Greg
– Nancy-Ann
– Jonathan
Tracey / Dan Tate

{– Tarplin : 690-7627
{– Phil-Lee's . 690-7694
{– Shultz : 827-3370
– Bill Corr. 690-7694



– John Angell –

– 3:00 –

Off Label Use —

26th - Day on Colt's internal calendar for FDA reform —

- Mack / Frist / Dodd

Focus — undercut incentive to do research —

Basic principle — done research — represented it to the FDA → before you disseminate journal article that could be basis for supplemental —

→ -3 months before submit data to FDA —

Patient Groups —

Dr's in boonies — won't get this info. —
Need database → have it for cancer, (NCI)
AIDS,

(2) - in-House bill

(3) - fixing supplement process - Reg type thing
(1) simplifying
(2) one-study largely

Dodd — see some circumstances where supplementals wouldn't be necessary.
- has said research incentive is important
- Mack's intense interest. —

2 weeks - Bursell / Bliley / Waxman / Admin. —
- narrow indication for approval / promote of

Tues. 5:30

FDA Conf-call
7/26

Devices House — pilot resolved (3rd)
—

open - efficacy std; off-label

Howard Kohn; non-idealogical —

Monday expects current draft. —

R's will make a judgment early in the week —

LOH is telling Kassebaum — agreement and no more than ½ day.

Senate
New issues Jane Williams is raising —
tissue issue

pharmacy compounding issues

- off-label
- health claims
-

Agreed to:
- third party review — (excepts coats)
- efficacy stds. —
- manufacturing changes —
- health claims —
- med guides off the table — (resolved in approps.)

12 issues
4 Done
5 close
3 humanitarian devices; efficacy (we offered language); initial classification of devices (we gave language)

FDA Reform - Letters

July 3, 1996

Ms. Susan Panico
Executive Director
National Depressive and
Manic-Depressive Association
Suite 501
730 North Franklin Street
Chicago, Illinois 60610

Dear Susan:

Thank you for writing to me. I'm glad to have the perspective of the National DMDA.

Since taking office, I have worked hard to reform the Food and Drug Administration so that it can function more efficiently and rapidly to benefit the American people. As you know, we have successfully reduced the length of the approval process for many new drugs and therapies, and recently, my Administration put forward a series of regulatory reforms designed to make the FDA even more responsive to those in need of new treatments.

I appreciate your suggestions, and as we work to build on our progress, I will certainly keep your views in mind.

Sincerely,

BILL CLINTON

BC/SEM/JFB/JFB/emu-jfc (Corres. #3005417)
(6.panico.s)

cc: Barbara Woolley, OPL
~~cc: Elizabeth Drye, ODP~~

ATL

CONCERNS RE: DEVICE BILL (H.R. 3201)

A. Major Concerns

1. Privatization of Review/GMP Inspections (Sections 9, 11, 12, and 17)

2. Off Label Promotion (Section 18)

B. Serious Concerns

1. Effectiveness Standards (Section 8 -- no well controlled clinical trials and no clinical outcome results for devices)

2. Devices: Modifications Without FDA Review and Specific/General Use (Section 9)

C. Other Significant Concerns

1. Dispute Resolution (Section 3)

2. Investigational Device Exemptions (Section 4)

3. Humanitarian Use of Devices (Section 6)

4. Performance Standards (Section 7)

5. Initial Classification of Devices (Section 9)

6. Scientific Advisory/Classification Panels (Section 10)

7. Device Tracking (Section 14)

8. Postmarket Surveillance (Section 15)

9. GMP and Device Reports (Section 20)

10. Information Systems (Section 22)

11. Environmental Impact Review (Section 23)

D. Other Concerns

1. Annual Report (Section 2)
2. Harmonization (Section 16)
3. Informal Agency Statements (Section 24)
4. Research and Education (Section 25)
5. Public Notice of Deviation (Section 26)
6. Civil Penalties (Section 21)

CONCERNS RE: DRUG ~~DEVICE~~ BILL (H.R. 3199)

A. Major Concerns

1. Privatization of Review/GMP Inspections (Sections 7 and 8)
2. Off Label Promotion (Section 19)

B. Serious Concerns

1. Effectiveness Standards (Section 5 -- one versus two clinical trials and new uses of drugs)
2. Medication Guides (Section 29)
3. Human Tissue (Section 25)

C. Other Significant Concerns

1. Annual Report (Section 2)
2. Streamlining Clinical Research in Drugs and Biological Products (Section 3)
3. Content and Review of New Drug Application (Section 4)
4. Scientific Advisory Panels (Section 6)
5. Dispute Resolution (Section 9)
6. GMPs (Section 10)
7. Nonprescription Drugs (Section 14)
8. Pharmacy Compounding (Section 17)
9. Access to Unapproved Therapies (Section 26)
10. Protection of Confidential Information (Section 28)

D. Other Concerns

1. Information Systems (Section 15)
2. Environmental Impact Review (Section 16)
3. Harmonization (Section 18)
4. Informal Agency Statements (Section 20)
5. Research and Education (Section 21)
6. Public Notice of Deviation (Section 23)
7. Radiopharmaceuticals (Section 27)