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**Number of pages (includes cover)**

14

**Message:**

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By LAURAN NEERGAARD  
Associated Press Writer

WASHINGTON (AP) - The Food and Drug Administration is preparing to allow private organizations to review whether certain medical devices are safe and effective enough to offer American patients, Clinton administration documents show.

The move is part of a package of FDA reforms announced by the White House today that could save medical industries \$500 million annually in regulatory costs.

FDA critics, who say the agency takes too long to approve new treatments, have clamored for the United States to copy Europe. There, new medical devices from X-rays to heart valves are reviewed by government-accredited firms that decide whether they can be sold.

The FDA won't go that far.

In an experiment set to begin early next year, FDA will accredit private firms to review certain low-risk medical devices such as the cholesterol and drug-abuse tests performed in doctors' laboratories and electronic stethoscopes for measuring heartbeats.

Those firms will decide whether the devices work properly and are safe. The FDA retains the final say, but is expected to quickly follow the outside reviewers' decision unless it finds evidence that the devices shouldn't be used on patients.

The two-year pilot program will demonstrate whether critics are right in contending that outside scientists can do the medical testing and safety review faster than the government. If so, private firms might be allowed to review other FDA-regulated products, the reform plan says.

The plan comes as the Republican-controlled Congress, prompted by complaints from medical companies and conservative think tanks, prepares to overhaul the FDA. Although agency approval times are improving, it still can take two years to approve a new medicine for sale. FDA Commissioner David Kessler was addressing those issues at a Senate hearing today.

Some critics have called for even more drastic revamping of FDA, including having the agency only certify drugs' safety and letting individual doctors determine whether they actually work.

The privatization plan is very cautious, resembling one put forth earlier this week by FDA supporter Rep. Ron Wyden, D-Ore. But consumer advocates fear privatizing FDA functions will endanger public health.

These private firms "may be making decisions based more on who fills their pocketbook than what is best for the public health," said Dr. Sidney Wolfe of Public Citizen, a consumer watchdog group.

He said that the program is likely to cost more in training private firms on FDA standards. Companies that choose to participate in the pilot program will have to pay the reviewers a yet-to-be-determined fee.

The FDA two weeks ago took its first tentative reform steps, including eliminating 125 very low-risk medical devices, such as bandages, from agency review.

The reforms announced today go much further:

-Biotech firms would no longer have to build full-scale manufacturing plants before the FDA determined whether their drugs could be sold. This rule stemmed from biotech's earliest days, when doctors feared drugs made from living material might turn out differently when they moved from pilot-sized facilities to huge plants after FDA approval. The change would save 100-500 companies now awaiting FDA approval some \$25 million apiece in construction costs.

-Medical companies would no longer have to get special FDA approval to export products that aren't yet approved here but are wanted by other industrialized countries. The industry says this red tape has sent dozens of U.S. firms overseas.

-FDA will harmonize its requirements for new medicines with those of other nations, so companies don't have to redo international research in Americans before the FDA will approve a product.

The reforms are "a significant step in the right direction," said Alan Magazine of the Health Industry Manufacturers' Association, who lobbied for several of the changes.

04-06 4:54p

With AM-Retooling FDA  
By The Associated Press.

Some reforms the Food and Drug Administration announced Thursday to speed new therapies to market:

-A two-year pilot program to see if private companies can determine the safety and effectiveness of certain low-risk medical devices faster than the FDA, although the agency retains the final decision.

-Ending a requirement that makers of genetically engineered drugs build a full-scale factory before the drugs are approved.

-Ending FDA review before drugs and medical devices not approved for sale in the United States can be exported to countries that have approved them. The FDA says it has never blocked an export, so the rule was unnecessary. But it is federal law, so Congress must formally adopt this measure; legislation already has been introduced.

-Exempting an additional 125 categories of very low-risk medical devices, such as dermatology lasers and oxygen masks, from any FDA review. The FDA already has exempted 440 categories.

-Harmonizing FDA standards with international medical standards so the FDA can accept drugs tested abroad instead of insisting they be rechecked in Americans.

-Accepting a single major clinical trial as evidence a drug works, something the agency has already done on occasion.

-Reducing or eliminating requirements for companies to get FDA approval before improving the way they manufacture products.

AP v5200 rw 3exec Retooling FDA, 540

04-06 4:46p

## Clinton Reforms to Include Test of Partial FDA Privatization

With AM-FDA Reform List

By LAURAN NEERGAARD

Associated Press Writer

WASHINGTON (AP) - The Food and Drug Administration is turning part of its job over to private companies in an attempt to speed new medical devices to American patients, officials said Thursday. But senators said that's not nearly enough reform.

"We need a sense of urgency, we need a commitment, we need a passion for change, and if not, I think the Congress is going to roll right over you," Sen. Barbara Mikulski, D-Md., warned FDA Commissioner David Kessler.

A package of FDA reforms announced by the White House on Thursday would save medical industries \$500 million a year in regulatory costs.

The changes make it easier for companies to export therapies that aren't approved for sale here and to get FDA approval for medicines tested abroad and those given just one major trial in people, instead of multiple testing. Also, the FDA would begin approving genetically engineered drugs before companies build the full-scale plants to produce them, and thousands of low-risk medical devices could be sold without any FDA inspection.

But the biggest change is a two-year experiment to see if private firms can do part of the FDA's job faster than the government.

FDA critics say the agency takes too long to approve new treatments. They have clamored for the United States to copy Europe, where government-accredited firms decide whether new medical devices, from X-ray equipment to heart valves, can be sold.

The FDA's pilot program won't go that far. The FDA will accredit companies to decide whether certain low-risk medical devices, such as laboratory cholesterol tests and electronic stethoscopes, are safe and effective.

The FDA retains the final say, but is expected to quickly follow the outside reviewers' decision unless it finds evidence that the devices shouldn't be used. If the experiment succeeds, private companies might be allowed to review other FDA-regulated products.

Consumer advocates said the plan is dangerous.

Private firms "may be making decisions based more on who fills their pocketbook than what is best for the public health," said Dr. Sidney Wolfe of Public Citizen, a consumer watchdog group.

But critics said the FDA isn't going far enough.

The FDA reforms are "common-sense and, in some cases, long overdue first steps," Sen. Nancy Kassebaum, R-Kan., told a Labor and Human Resources Committee hearing. "More profoundly, basic change must occur in the very way that the FDA sees its mission."

Sen. Judd Gregg, R-N.H., accused Kessler of delaying lifesaving medicine for Americans.

"I don't know of a drug today that is an important therapeutic advance, that could be lifesaving, that we are holding up,"

But, he added, "we are also a regulatory agency

... and sometimes when you're a regulatory agency, you have to say no, the data's not there" to support a new medicine.

Gregg said Americans don't know about delays because companies are too afraid of FDA retaliation to speak up.

Kessler said he was bewildered by such allegations, but added: "There's no excuse for an environment or culture of confrontation."

(FDA)

A26 FRIDAY, APRIL 7, 1995

THE WASHINGTON POST

## FDA: Reforms That Address Industry's Lasting Complaints



FDA Commissioner David A. Kessler discusses proposed agency streamlining on Capitol Hill. "It's not very popular being a regulator today," he said.

By John Schwartz  
Washington Post Staff Writer

There are two points of view concerning the Food and Drug Administration. The agency's critics say, "There's much that could be improved—but the FDA has made great strides in recent years."

Then there's the agency's defenders, who say, "The FDA has made great strides in recent years—but much could be improved."

The conflict is sometimes bitter. But the two sides appear to be heading toward common ground.

Yesterday FDA Commissioner David A. Kessler announced several reforms within his agency as part of the Clinton administration's National Performance Review, continuing streamlining that has been going on for more than two years. The reforms involve nuts-and-bolts changes that might make the typical consumer's eyes glaze over but which address some long-standing industry complaints.

FDA will lift many requirements for companies making minor changes to their manufacturing processes. It will let biotechnology companies set up small pilot plants to prove that they can meet standards for their new products instead of requiring them to have full-scale plants in place.

The agency also proposed eliminating outdated manufacturing standards for insulin and some antibiotics.

Also, the FDA exempted 125 kinds of low-risk medical devices from agency review requirements, adding to the list of nearly 150 product categories recently exempted from the review process. Kessler promised to develop a pilot program to let outside organizations review some medical devices, and pledged to more closely align FDA and foreign approval procedures.

But there are limits to how far reform can go without compromising safety. Kessler told the Senate Labor and Human Resources Committee. "In this country, we sit down to dinner without even thinking about whether the food on the table is safe. We purchase drugs for our children without thinking about whether they work. We often don't think twice about the new technologies being used when we go to the emergency room. . . . In the end, it is FDA's independence that gives the American people confidence in the agency's decisions."

One of the FDA's strongest critics had harsh words for the new proposals. Paul Beckner, president of Citizens for a Sound Economy, a pro-business think tank, said, "The FDA reforms are too few and come too late. They are a cosmetic fix to an agency that needs a fundamental shaking."

But Alan H. Magazine, executive director of the Health Industry Manufacturers Association, described the proposals as an encouraging trend. The plan and legislation sponsored by Rep. Ron Wyden (D-Ore.) show that Democrats are ready to work on a bipartisan basis, he said.

"I think now that the dust is settling, cooler heads are prevailing—and the right and left are moving to the middle," Magazine said.

When asked why the agency was under attack from so many quarters—including a tongue-lashing yesterday from Sen. Barbara A. Mikulski (D-Md.)—Kessler said, "It's fair to say it's not very popular being a regulator today."

He added, "Sometimes you have to say no—and you don't make any friends when you have to say no."

WASHINGTON EDITION / LOS ANGELES TIMES

NATION

A4 FRIDAY, APRIL 7, 1995

# Administration Offers Plans to Reform FDA

■ **Health:** Proposals include program to let outside experts review safety and efficacy of certain experimental medical devices.

By MARLENE CIMONS  
TIMES STAFF WRITER

WASHINGTON—In an apparent effort to head off a Republican-driven overhaul of the Food and Drug Administration, the White House on Thursday proposed a series of agency reforms, including a pilot program that would allow outside experts to review certain experimental medical devices for safety and efficacy.

The FDA, which in recent years has speeded up the approval process for breakthrough and life-saving drugs, has been under increasing attack by GOP lawmakers, the device industry and conservative think tanks for being overly cautious—and too sluggish—in getting new devices onto the marketplace. Critics repeatedly have cited the model in many European countries, where such non-governmental reviews are permitted.

FDA Commissioner David A. Kessler, who announced the proposals in an appearance before a Senate committee, in the past has acknowledged that the agency could do better in device regulation. But he also has pointed out that the agency has limited resources to meet its numerous responsibilities, which—in addition to regulating foods, drugs, cosmetics and devices—include responding to public emergencies, such as product tampering.

Kessler, testifying before the Senate Labor and Human Resources Committee—which has jurisdiction over the FDA—stressed that the agency is engaged in a constant "balancing act" that must weigh protecting the consumer from unsafe or ineffective products against making new technologies available as quickly as possible. The agency must never lose sight of that equation, he said.

"People want access [to new drugs and devices] but, if something goes wrong, they want to be able to blame somebody," he said. "It's not very popular being a regulator today. You don't make any friends when you say no. [But] you can't deregulate the safety of food and drugs. It's just not going to work."



Associated Press

FDA's David A. Kessler told senators: "It's not very popular being a regulator today."

He added: "My bottom line is that the agency should be able to make decisions in an environment of independence."

Sen. Nancy Landon Kassebaum (R-Kan.), who chairs the committee, called the Administration's proposals "common-sense and . . . long overdue first steps toward eliminating obsolete and marginally important regulatory requirements." The measures "are a start, but [I] would look for much greater strides if we are truly going to address the issue," she added.

And Sen. Judd Gregg (R-N.H.), in stressing the need for changes within the agency, told Kessler: "We don't sense it [the FDA] is in balance right now."

Kessler predicted that the reforms could save industry \$500 million annually.

Alan Magazine of the Health Industry Manufacturers' Assn., which also has been lobbying for reforms, called them "a significant step in the right direction."

The two-year experiment with non-government experts, which will begin next fall, will allow the outside review of low- and moderate-risk devices, such as electronic stethoscopes and cholesterol and drug-abuse test kits used in laboratories. These experts would then make a recommendation to the agency, which would have the ultimate say.

Kessler cautioned, however, that "there are legitimate, serious questions as to whether such a system would work in this country—such as whether the capacity exists . . . for such reviews, whether it would provide the same quality control and whether private reviewers could be independent."

Kessler also called on Congress to approve "user fee" legislation in connection with medical devices, similar to what already exists for drug approvals. This would require companies to pay fees that would be used to cover the costs of reviews. Such additional resources "are essential" in reducing backlogs and speeding review times, Kessler said. Device user-fee

legislation was introduced in the last Congress but time ran out on the session before lawmakers could act.

Two weeks ago, the agency announced the elimination of 125 low-risk medical devices—such as bandages—from FDA review and Thursday proposed exempting more than 100 additional items, such as powered finger exercisers and certain kinds of syringes.

Kessler said the agency also would end the so-called "reference list," a program that deferred agency clearance of device applications until a company corrected manufacturing violations identified during plant inspections. Applications will be delayed "only where there is a relationship between the violation discovered and the pending application," he said.

Under the new proposals, manufacturers no longer will be required to obtain special agency approval to export unapproved products overseas if other industrial countries want them, Kessler said.

Kessler said the agency also will try to work with other countries in using research conducted abroad so that studies might not have to be duplicated in the United States for approval.

Friday, April 7, 1995

Los Angeles Times

"Administration Offers Plans  
to Reform FDA"

Drug companies no longer will have to construct full-scale manufacturing facilities before their drugs are approved—a requirement that arose from past fears that drugs made from living material could change when they moved from smaller plants to larger ones.

Kessler also said that except in rare instances, the agency will no longer require environmental impact assessments for new drugs because "in virtually all cases, there is no significant impact." Yet, he said, "these evaluations costs tens of thousands of dollars."

**THE WALL STREET JOURNAL FRIDAY, APRIL 7, 1995 B3**

## *White House Moves to Speed Up Action At FDA as Agency Is Scolded in Senate*

By LAURIE MCGINLEY

Staff Reporter of THE WALL STREET JOURNAL  
WASHINGTON — The Clinton administration took steps to speed up approvals of drugs and medical devices, even as senators scolded the Food and Drug Administration about a "culture of confrontation" and urged more-sweeping changes.

Two of the biggest changes announced by the White House involve creating a pilot program that would use outside experts to review certain low-risk medical devices to determine if they should be approved, and easing restrictions on the export of unapproved drugs and devices to other industrialized countries.

The changes, which administration officials claimed would save industry an estimated \$500 million annually in regulatory-compliance costs, went beyond steps announced at a "reinventing government" news conference held last month at the White House.

### **Warning From Sen. Mikulski**

"Congress is going to roll right over you" if more improvements aren't forthcoming, Sen. Barbara Mikulski (D., Md.) warned FDA Commissioner David Kessler at a hearing of the Senate Labor and Human Resources Committee. Her criticisms were especially notable coming from a Democratic lawmaker. The FDA is located in Sen. Mikulski's state, as are several biotechnology companies that have expressed frustrations with the agency.

Although the senators pointed to some specific difficulties, much of the criticism focused on such intangibles as the general attitude of FDA employees toward industry. Sen. Judd Gregg (R., N.H.) said he hears frequent complaints from constituents about a "culture of confrontation rather than cooperation" at the agency.

The two-year pilot program announced yesterday would allow the agency to explore a notion pushed by many of the FDA's critics — that outside analysts can get certain jobs done more quickly and efficiently than FDA bureaucrats. The agency, however, will have the final word on whether any device is actually approved.

The pilot program also is a nod to critics

### **Legislation on Exports**

Easing export restrictions on unapproved drugs and devices would require legislation, Dr. Kessler said. Some members of Congress recently have introduced legislation to ease the export rules.

Alan Magazine, president of the Health Industry Manufacturers Association, which represents device makers, called the

changes "important first steps toward ensuring that patients receive more timely access to safe and effective medical technology." Sen. Nancy Kassebaum (R., Kan.), who heads the Labor and Human Resources Committee, said that although the changes announced yesterday "are common sense and long overdue," more are needed.

But the announced changes are unlikely to assuage conservative critics of the agency. For example, the Competitive Enterprise Institute, a Washington-based group, has recommended that drugs and devices that don't meet the FDA's standards shouldn't be banned, but should be available under doctors' supervision with a warning of their unapproved status. Other critics say the FDA's efficacy standard should be weakened or eliminated, allowing the marketplace to decide which treatments work.

After the hearing, Dr. Kessler said, "We're open to thoughtful reforms, but my bottom line is making sure that the agency is able to make these decisions in an environment of independence."

European-style review process. In Europe, device makers pay a third-party organization to conduct reviews, and if the device gets a favorable rating, it is marketed without prior government approval; the government monitors the device after it goes on the market.

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## FEDERAL REPORT

# FDA to leave firms to devices

## Privatization of some functions part of agency reform

ASSOCIATED PRESS

The Food and Drug Administration is turning over part of its job to private companies in an attempt to speed new medical devices to American patients, officials said yesterday.

But senators said that's not nearly enough reform.

"We need a sense of urgency, we need a commitment, we need a passion for change — and if not, I think the Congress is going to roll right over you," Sen. Barbara A. Mikulski, Maryland Democrat, warned FDA Commissioner David Kessler.

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The changes make it easier for companies to export therapies that aren't approved for sale here and to get FDA approval for medicines tested abroad and those given just one major trial in people, instead of multiple testing.

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proving genetically engineered drugs before companies build the full-scale plants to produce them, and thousands of low-risk medical devices could be sold without any FDA inspection.

However, the biggest change is a two-year experiment to see whether private firms can do part of the FDA's job faster than the government.

FDA critics say the agency takes too long to approve new treatments. They have clamored for the United States to copy Europe, where government-accredited firms decide whether new medical devices, from X-ray equipment to heart valves, can be sold.

The FDA's pilot program won't go that far. The FDA will accredit companies to decide whether certain low-risk medical devices, such as laboratory cholesterol tests and electronic stethoscopes, are safe and effective.

The FDA retains the final say but is expected to quickly follow the outside reviewers' decisions

unless it finds evidence that the devices shouldn't be used. If the experiment succeeds, private companies might be allowed to review other FDA-regulated products.

Consumer advocates said the plan is dangerous.

Private firms "may be making decisions based more on who fills their pocketbook than what is best for the public health," said Dr. Sidney Wolfe of Public Citizen, a consumer watchdog group.

Critics said the FDA isn't going far enough.

The FDA reforms are "common-sense and, in some cases, long overdue first steps," Sen. Nancy Landon Kassebaum, Kansas Republican and chairman of the Senate Labor and Human Resources Committee, said during a hearing. "More profoundly, basic change must occur in the very way that the FDA sees its mission."

Sen. Judd Gregg, New Hampshire Republican, accused Dr.

Kessler of delaying lifesaving medicine for Americans.

"I don't know of a drug today that is an important therapeutic advance, that could be lifesaving, that we are holding up," Dr. Kessler responded. "We are also a regulatory agency ... and sometimes when you're a regulatory agency, you have to say no, the data's not there" to support a new medicine.





**Sen. Barbara A. Mikulski says  
Congress is impatient with FDA.**

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**Life Science**

April 7, 1995

**FDA HEAD LAYS OUT SPECIFICS OF REGULATORY REFORM TO SENATE  
CLAIMING PROPOSALS WILL SPEED UP DRUG AND DEVICE REVIEW PROCESS**

Food and Drug Administration (FDA) Commissioner David Kessler arrived at a Senate hearing yesterday armed with a sheaf of regulatory reforms he claimed would get drugs and medical devices to market faster while saving industry \$500 million annually.

Kessler, under fire from Republicans--and some Democrats as well--for running an agency whose "culture" they say has become "hostile" and "obstructionist" in its dealings with industry, told members of the Senate Labor and Human Resources Committee that the Clinton administration was presenting that very day "a number of initiatives to improve the speed and efficiency of the drug and device review process."

"These reforms, which have been developed under the leadership of Vice President Al Gore's National Performance Review, build on what the agency has accomplished over the last several years in speeding reviews and expanding access to promising therapies," Kessler said in a prepared statement. "Some of the reforms...speak directly to reduced time for review and approval. Others aim to reduce excessive regulatory burdens that cost industry unnecessary time and money, and cost the agency precious resources."

According to documents Kessler submitted with his testimony, the regulatory changes announced by FDA, and published in the April 6 Federal Register, will accomplish a number of things:

- They will allow companies that make drugs and biological products to change the manufacturing process for an approved drug without first getting clearance from FDA, if risks are shown to be negligible.
- Biotech companies will be able to use "pilot" facilities instead of large manufacturing plants to produce their products, a move FDA says will "lower start-up costs" and hasten production.
- Special requirements for manufacturing insulin and antibiotic drugs will be eliminated.
- Pharmaceutical and biotech companies will largely be excluded from rules requiring environmental assessments.
- Up to 125 categories of low-risk medical devices will be added to the list of devices exempted from pre-market review.

- A pilot program will be initiated to test the review of medical devices by experts outside of FDA, and FDA will ask Congress to approve a regimen of user fees designed to further speed medical device review.
  - Industry will be given greater freedom to export unapproved drugs and medical devices to industrialized countries.
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Page 2 of 2 (LS - WASFAX 4/7/95)

FDA (Cont'd)

Sen. Nancy Kassebaum, R-KS, who chairs the Senate Labor and Human Resources Committee, said the changes outlined by Kessler were "common sense, and in some cases long-overdue, first steps toward eliminating obsolete and marginally important regulatory requirements." However, she said that "more profoundly, basic changes must occur in the basic way that the FDA sees its mission."

Though Republicans have generally been viewed as the party leading the charge for reform at FDA--House Speaker Rep. Newt Gingrich, R-GA, is particularly harsh in his assessment of Kessler--it was a Democrat, Maryland Sen. Barbara Mikulski, who delivered the day's sternest admonition.

Mikulski was unsatisfied with the response she received from Kessler about why FDA cannot agree with industry to classify certain genetically engineered materials as chemicals, thus reducing some of the regulatory burden for biotech companies.

After telling Kessler that FDA needs a "21st century (regulatory) framework and not a 1970s framework," she went on to say that "there is enormous frustration" in the private sector about FDA's "attitude," its "approval" process and its "nitpicking."

"We really have to get with the program," Mikulski told Kessler. "We need a passion change (at FDA)...or Congress is going roll right over you."

Sen. Judd Gregg, R-NH, said Mikulski "touched on the core issue here."

"There is a view out there that the culture of FDA is stifling the capacity of the market," Gregg said, adding that the biggest problem is "not the regulatory structure" but what he perceived was a pervasive anti-industry attitude at FDA.

Kessler responded that FDA is working hard to respond to the concerns of industry, calling attention to its efforts to dramatically expedite the approval process for potentially life-saving drugs.

"Senator, I don't know of any drug today that has important therapeutic advances than can be life saving that we are holding up," Kessler told Gregg. "When it comes to products that don't have important therapeutic advances then we have to play by the rules."

Mikulski told Kessler that "no one would want FDA not to play by the rules," but that what many Senators hear is that there is an "adversarial environment" at FDA, that agency officials don't return phone calls and that industry officials worry that they'll face retaliation from FDA if they complain.

Compiled and Published by WASHINGTON FAX: AN INFORMATION SERVICE

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04-06 4:46p

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[FDA]

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04-06 7:07p

BC-FDA-NEW-PRODUCTS-NYT

FDA MOVES TO HASTEN MARKETING OF NEW DEVICES

(bl)

By PHILIP J. HILTS

c.1995 N.Y. Times News Service

WASHINGTON - Hoping to head off greater changes that might be proposed in Congress, the Clinton administration announced plans Thursday to have the Food and Drug Administration ease the way to market for some new drugs and medical devices.

Among the plans is a two-year pilot program in which review of a number of medical devices will be turned over to private groups.

The commissioner of food and drugs, Dr. David A. Kessler, outlined the changes at a hearing of the Senate Labor and Human Resources Committee, saying the FDA was committed to eliminating red tape while continuing to make sure that drugs and medical instruments are both safe and effective.

Sen. Barbara A. Mikulski, D-Md., joined several Republican members of the committee in warning the agency about what they described as a confrontational attitude toward companies like the biotechnology concerns in Senator Mikulski's own district.

"There is an enormous frustration in the private sector about the agency's attitude, about nit-picking," she said. "We need a passion for change at the FDA. And if not, I believe Congress is going to roll right over you."

Kessler assured her that change had begun. "We believe many medical devices simply don't pose a sufficient risk to be reviewed by FDA prior to marketing," he said.

Accordingly, the two-year pilot program will enable 10 categories of medical devices - a total of 100 to 400 such instruments that the FDA deems of low or medium risk - to be reviewed not by the agency itself but by private medical groups. These groups have not yet been chosen, or even solicited.

The manufacturers will pay for the private reviews, which are expected to get under way in 1997.

Throughout the pilot program, the FDA will retain final decision-making authority. That makes the program less sweeping than the standard review procedure in some European countries that have been approvingly cited by the American health manufacturing industry.

Private groups accredited by the governments there have the power to grant applications for medical devices.

Another of the changes announced Thursday will allow 125 categories of devices, which account for about 700 applications a year, to be exempted from the need for FDA approval before going to market. These categories include syringes, oxygen masks and simple surgical lasers.

The agency has already exempted 441 categories of devices, including stethoscopes and surgical microscopes. The new

exemptions, and all medical devices will now be exempt from review before marketing.

In another change, companies will be allowed to export drugs that are not approved for use in the United States but that do have the approval of the countries to which they are sent.

The FDA plans to permit export to 21 countries with the best safety records at first, and then consider expanding that number.

NYT-04-06-95 1912EDT<

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DATE: **4 / 10** /1995

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COMMENTS:

**GATT/URAA Info.**

**OUTLINE OF LEGAL ISSUES RAISED BY THE URUGUAY ROUND  
AGREEMENTS ACT WITH RESPECT TO FDA APPROVALS  
OF ABBREVIATED NEW DRUG APPLICATIONS:**

Patent Submissions by NDA Holder and Publication by FDA

- NDA applicants submit patent information on the listed drug or its uses to FDA. 21 U.S.C. § 355(b)(1).
- "Orange" and "Green" book publication.
- Patent information available after approval of NDA - new patent, Waxman-Hatch patent extension provisions - FDA publishes.
- URAA-extended patent expiration dates will be published.

Patent Certifications by ANDA Applicants

- ANDA must certify to each patent in Orange Book. 21 U.S.C. § 355(j)(2)(A)(vii).
- ANDA applicant amend certification if learns certification is not accurate. 21 C.F.R. § 314.94(a)(12)(viii)(C).
- ANDA applicants amend certifications to acknowledge URAA-extended patent expiration dates.
- ANDA applicant submits a paragraph III certification - will wait to market until URAA-extended patent term expires, or paragraph IV certification - patent is invalid or will not be infringed. 21 U.S.C. § 355(j)(2)(A)(vii).

FDA Approval of ANDAs

- Paragraph III certification - approval effective no earlier than expiration of patent. 21 U.S.C. § 355(j)(4)(B)(ii).
- Paragraph IV certification - approval effective immediately, unless litigation over the patent. If litigation, wait at least 30 months. 21 U.S.C. § 355(j)(4)(B)(iii).

Effect of URAA Patent Extensions

- Patents in force on June 8, 1995 - the patent term shall be 20 years from date of filing or 17 years from the date of granting. Section 532(a)(1).
- Limits availability of infringement remedies (injunctions, damages, and attorney's fees) for acts commenced, or for which "substantial investment" was made, before June 8, 1995, and which become infringing because of extension. Acts may continue with "equitable remuneration" to the patentee.
- Not included among remedies unavailable during the transition period: remedies (injunctions, damage awards, and attorney's fees) for infringement of drug-related patents. 35 U.S.C § 271(e)(4).
- Remedies apply to submission of an ANDA, an ANADA, or a 505(b)(2) application to obtain approval before expiration of patent.



## DEPARTMENT OF HEALTH &amp; HUMAN SERVICES

Office of the General Counsel  
Food and Drug Division

## Memorandum

Date April 4, 1995

From Elizabeth Dickinson EHD

Subject Effect of the Uruguay Round Agreements Act on the Approval of ANDAs under the Waxman-Hatch Amendments

To Margaret Jane Porter

I have been asked to address the relationship between certain patent provisions of the Uruguay Round Agreements Act ("URAA"), Pub.L 103-465, and the provisions of the Waxman-Hatch Amendments governing the submission of patent information for new drug applications ("NDAs") and the approvals of abbreviated new drug applications ("ANDAs") for generic equivalents of listed drugs.<sup>1/</sup> I have analyzed the relevant provisions of the URAA and the Waxman-Hatch Amendments; considered the oral and written submissions made by industry and the patent bar in conjunction with the hearing held at the Patent and Trademark Office on February 16, 1995; reviewed the letters sent to the agency by Senator Hatch and Representative Waxman, the original co-sponsors of the Waxman-Hatch Amendments; and have discussed the issues fully with the Office of Generic Drugs and the Office of Health Affairs.

For the reasons set out below, I believe that the transitional "grandfathering" provision of the URAA does not apply to FDA's drug approval process. Therefore, I recommend the following:

- The agency accept and publish in the Orange Book patent expiration dates as extended by the URAA.
- Applicants with ANDAs pending before the agency on June 8, 1995, the effective date of the URAA provisions, must amend their patent certifications to respond to the URAA-extended patent expiration dates.
- The agency treat the URAA-extended patent expiration dates as the dates that govern for approvals of ANDAs for listed drug products.

As described below, the only means by which FDA could rely on the pre-URAA patent expiration dates to approve ANDAs pending before the agency on June 8, 1995, is if the agency amends the regulations that currently require an applicant with an ANDA

<sup>1/</sup> This analysis applies as well to 505(b)(2) applications and abbreviated new animal drug applications ("ANADAs").

It shall not be an act of infringement to make, use, or sell a patented invention ... solely for uses reasonably related to the development and submission of information under a Federal law which regulates the manufacture, use, or sale of drugs or veterinary biological products.

35 U.S.C. §271(e)(1).

Further,

It shall be an act of infringement to submit ... an application under [21 U.S.C. § 355(j)] for a drug claimed in a patent or the use of which is claimed in a patent ... if the purpose of such submission is to obtain approval under such Act to engage in the commercial manufacture, use, or sale of a drug ... claimed in a patent or the use of which is claimed in a patent before the expiration of such patent.

35 U.S.C. § 271(e)(2)

For an act of infringement as described in 35 U.S.C. §271(e)(2),

(A) the court shall order the effective date of any approval of the drug or veterinary biological product involved in the infringement to be a date which is not earlier than the date of the expiration of the patent which has been infringed,

(B) injunctive relief may be granted against an infringer to prevent the commercial manufacture, use, or sale of an approved drug or veterinary biological product, and

(C) damages or other monetary relief may be awarded against an infringer only if there has been commercial manufacture, use or sale of an approved drug or veterinary biological product.

35 U.S.C. § 271(e)(4). This section also provides that these remedies are the only remedies which may be granted by a court for an act of infringement described in (2), except that a court may award attorney fees under 35 U.S.C. § 285.

## ANALYSIS

The Office of Generic Drugs ("OGD") would like the agency to approve ANDAs upon the expiration of the pre-URAA patent term.<sup>2</sup> OGD is concerned that if the agency must wait until the expiration of the URAA-extended patent term to approve ANDAs, entry onto the market of many generic drugs will be substantially delayed at a cost of millions of dollars to consumers. OGD's position is shared by most of the generic drug industry and by Representative Waxman, who argue that approval of ANDAs upon the expiration of the pre-URAA patent term would best reconcile the goals of both the URAA and the Waxman-Hatch Amendments. The section below addresses the options suggested by the generics industry and OGD, whereby FDA could approve ANDAs at the end of the pre-URAA patent term.

### Applicability of Transitional Provisions to Generic Drugs

The fundamental premise of the position favored by OGD and the generic industry ("the generic's position") is that the transitional provision of § 532 of the URAA applies to the generic drug industry, just as it does to other industries in which premarket approval of products is not required. The generic's position is that, by limiting the remedies available for infringement when infringing acts were commenced, or a substantial investment was made, before June 8, 1995, Congress intended to "grandfather" in all businesses that had relied upon the pre-URAA dates. The URAA states that the only barrier to such infringement would be the payment by the ANDA holder to the patent holder of "equitable remuneration," as determined in a court proceeding. If FDA were to refuse to approve an ANDA until the expiration of the URAA-extended patent term, FDA would, by exercise of regulatory authority, be granting the patent holder/NDA holder a de facto injunction against the marketing of a competitor product. Such a result would be inconsistent with the provision of URAA that makes injunctions unavailable.

The greatest obstacle to application of the "grandfathering" provision of the URAA to FDA's generic approval process is that Congress did not include among the remedies made unavailable during the transition period, those remedies in the patent code that apply to infringement of drug-related patents. 35 U.S.C § 271(e)(4), which provides for injunctions, damage awards, and attorney's fees for acts of infringement related to drug

<sup>2</sup> In earlier discussions of this issue, representatives from the Center for Veterinary Medicine indicated that the generic industry for veterinary medicine is relatively small, and therefore CVM would support whatever position CDER took with respect to the effect of the URAA on the generic approval process.

products, was not listed among the remedy sections explicitly made unavailable under the URAA. (§§ 283, 284, and 285). The remedies set forth at 35 U.S.C. § 271(e)(4) apply to acts of infringement defined at § 271(e)(2) as the submission of an ANDA, an ANADA, or a 505(b)(2) application, if the purpose of the application is to obtain approval to market the product claimed by the patent before the expiration of the patent.<sup>2/</sup>

In order to determine the role § 271(e)(4) plays in the current drug approval scheme, and the obstacle it poses to application of the "grandfathering" provision of the URAA to the generic drug approval process, it is crucial to understand the current requirements imposed by statute and FDA regulations upon NDA holders, ANDA applicants, and the agency with respect to patent information, patent certification, and ANDA approvals.

The Hatch-Waxman Amendments direct that NDA applicants will submit patent information to FDA. 21 U.S.C. § 355(b)(1), (c)(2). Further, the Waxman-Hatch Amendments direct that the agency "shall publish" such information. *Id.* There is a statutory timeframe for such submissions (*see supra* at 2), and the agency has recognized that there are instances when information on applicable patents will become available after approval of an NDA, such as with the issuance of a new patent or the extension of patent term under the Waxman-Hatch patent term extension provisions. 59 Fed. Reg. 50,343. As discussed below, the agency will be required under the statute to publish the URAA-extended patent expiration dates.

The Waxman-Hatch Amendments require that an ANDA contain a certification with respect to "each patent which claims the listed drug ... or which claims a use for such listed drug for which the applicant is seeking approval ... and for which information is required to be filed ... ." 21 U.S.C. § 355 (j)(2)(A)(vii). FDA regulations require that an ANDA applicant amend a submitted certification "if at any time before the effective date of the approval of the application, the applicant learns that the submitted certification is no longer accurate." 59 Fed. Reg. 50,366 (to be codified at 21 C.F.R. § 314.94(a)(12)(viii)(C)). The agency currently interprets this regulation to require that applicants update ANDAs to respond to

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<sup>2/</sup> The Supreme Court has observed that § 271(e)(2) creates these "artificial" acts of infringement so that the underlying patent issue can be resolved in a court proceeding pursuant to a paragraph IV certification. Eli Lilly and Co. v. Medtronic, Inc., 496 U.S. 661, 678 (1990). The Court further observes that the remedies of § 271(e)(4) are also artificial remedies. "Quite obviously, the purpose of subsections (e)(2) and (e)(4) is to enable the judicial adjudication upon which the ANDA and paper NDA schemes depend." *Id.*

information on Waxman-Hatch patent term extensions and on newly-issued patents submitted to the agency after initial submission of the ANDA but before any approval of the ANDA is effective. The only circumstance expressly identified in the regulations in which an ANDA applicant is not required to update a certification with respect to later-submitted patent information is when the NDA holder submits the patent information in an "untimely" manner.<sup>4</sup>

Under FDA's current regulations, ANDA applicants would be required to amend patent certifications to acknowledge the URAA-extended patent expiration dates. With respect to a URAA-extended date, an ANDA applicant may submit either a paragraph III certification, indicating that it will wait to market until the URAA-extended patent term has expired, or a paragraph IV certification, indicating that the ANDA applicant believes that the patent is invalid or will not be infringed. The appropriate course open to an ANDA applicant who wishes to challenge the URAA-extended patent term and attempt to obtain approval prior to the expiration of the patent would be to file a paragraph IV certification. See 35 U.S.C. § 271(e)(2). As noted above, the remedies available to the patent holder in patent infringement litigation arising out of the paragraph IV certification were not altered by the URAA, and the patent holder can obtain an injunction or damages for an infringement.

The Waxman-Hatch Amendments direct that FDA will make ANDA approvals effective based on the certification provided by the ANDA applicant. In the case of a paragraph III certification, FDA will make an approval effective no earlier than the expiration of the patent. 21 U.S.C. §355(j)(4)(B)(ii). A paragraph IV certification to a patent permits the agency to make an approval effective immediately, unless there is litigation on over the patent claim. If there is patent litigation, the agency must wait at least 30 months to make an ANDA approval effective, unless a shorter or longer period is ordered by the court. 21 U.S.C. § 355(j)(4)(B)(iii). Therefore, if the NDA holder submitted URAA-extended patent expiration date to the agency in a timely manner (see discussion below) and the ANDA applicant certified to the new information, as required by the regulations, the agency would be precluded from approving the ANDA prior to the URAA-extended patent expiration date or the expiration of the thirty month stay, or such longer or shorter period set by the court, as required by the Waxman-Hatch Amendments.

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<sup>4</sup> The regulations identify an "untimely" filing as the submission by the NDA holder of information on a newly-issued patent more than thirty days after the patent is issued. The agency has also interpreted this regulation to apply to a patent that was not submitted to the agency within the timeframe identified by Congress (see background material, *supra*).

Congress is well aware that generic drugs cannot be marketed without FDA approval. Further, the Waxman-Hatch Amendments require that ANDA applicants acknowledge the status of applicable patents through the patent certification process. By retaining the remedies for the patent infringement actions explicitly contemplated by Congress as the proper means for resolving patent disputes pertaining to ANDA approvals for generic drugs, while at the same time making unavailable those same remedies for challenges to acts of infringement related to non-drug patents, Congress exempts the generic drug industry from the effects of the general "grandfathering" provision. In the absence of any legislative history clearly indicating that Congress intended the "grandfather" provision to apply across the board, the retaining of the §271(e) remedies would most likely be persuasive to a court that Congress intended to treat patents for drugs differently than other patents.<sup>2</sup> See, e.g., Consolidated Rail Corporation v. United States, 896 F.2d 574 (D.C.Cir. 1990) (plain meaning of legislation is conclusive except when literal interpretation will product results at odds with intention of drafters and there is a clear indication of legislative intent).

This conclusion is further supported by the fact that Congress was apparently aware of the remedy provision that applies to drug-related patent infringement, in that it made certain changes to 35 U.S.C. § 271(e)(4) to apply the remedies to a broader range of infringing activities. Section 533(a)(1) of the URAA makes the injunction and damages remedies of 35 U.S.C. § 271(e)(4)(B) and (C) available for an "offer to sell" as well as to a "sale" within the United States, or importation into the United States.

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<sup>2</sup> The only legislative history for the transitional provisions is contained in the Joint Senate Report from the Committee on Finance; the Committee on Agriculture, Nutrition, and Forestry; and the Committee on Governmental Affairs. It states as follows:

Section 532(a) adds new sections 154(c)(2) and (3) [to the Patent Code]. These sections address the situation where a third party begins using a patented invention anytime during the six months after the enactment of the legislation and such use becomes infringing because of a change in patent term due to the operation of section 154(c)(1). In such circumstances, the patent owner will not be able to obtain an injunction, recover a reasonable royalty, or obtain attorneys fees, but will be able to recover equitable remuneration.

This passage has been characterized by a number of the commentators as a clear statement that Congress did not intend to treat patents related to drug products any differently than other patents. I don't believe that this imprecise and slightly inaccurate statement from the Joint Report can bear that burden.

One of the recommendations made by the generics is that the agency amend its regulations to provide that ANDAs submitted by June 8, 1995, need not be updated to respond to the submission of URAA-extended patent expiration dates by the NDA holder.<sup>4</sup> If the agency were to change its regulations as suggested, the paragraph IV certification process would not be called into play, and the retention by the URAA of the §271(e)(4) remedies would have no effect with respect to URAA-extended patent expiration dates.

The agency has consistently maintained the position that ANDAs must be amended to respond to patent information filed after the ANDA is submitted. The preamble to the proposed rules states that

If an applicant becomes aware, after submitting an ANDA, of a newly issued patent or if a patent is timely submitted after the submission of an ANDA, an appropriate new certification would be required in the form of an amendment to the pending ANDA.

54 Fed. Reg. 28,885 (July 10, 1989). See also 54 Fed. Reg 28,886.

The preamble to the proposed rule also described the certification obligations of the ANDA applicant with respect to patent information submitted to the FDA in an untimely manner. In that case, the applicant whose application is submitted to the FDA prior to the submission of "untimely" patent information need not amend the ANDA to respond to the late-filed information. The applicant who submits an ANDA after the untimely filing of patent information must certify as to that information. The agency has devoted considerable space in the preambles to the proposed rules and the final rules to explaining the basis for its position that an ANDA submitted prior to the submission of untimely patent information does not have to be amended to accommodate the untimely filed patent information. See 54 Fed. Reg. 28,910; 59 Fed. Reg. 50,340, 50,347. FDA has not, however, publicly articulated its basis for requiring applicants to amend ANDAs to respond to the submission of patent information that is not "untimely," but that is submitted to the agency after the ANDA is filed.

If the agency were to change the regulation currently set out at 59 Fed. Reg. 50,366 (to be codified at 21 C.F.R. § 314.94(a)(12)(viii)(C)) so that an applicant would not be required to amend an ANDA to accommodate patent information

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<sup>4</sup> Senator Hatch expressly states in his letter to FDA that the agency has "no authority" to allow ANDA applicants to retain patent certifications that do not address the URAA-extended patent terms.

submitted to the agency after the ANDA was filed, it could take one of two approaches. Either the agency could determine that no ANDA would have to be amended to respond to later-filed patent information, or it could create an exception to the amendment requirement for patent information related to URAA-extended patent expiration dates. If the agency decides to exempt applicants from any obligation to amend a pending ANDA with respect to later-filed information, it must be prepared to defend that position as one that is supported by the Waxman-Hatch Amendments. The option that would exempt just URAA-extended patents from the recertification requirement would require the agency to show both that the interpretation was supported by the Waxman-Hatch Amendments and that such treatment is supported by the URAA. The agency is entitled to deference with respect to its interpretation of the provisions of the Waxman-Hatch Amendments that fall within the Federal Food, Drug, and Cosmetic Act, however no such deference attaches to FDA interpretation of patent code provisions amended by the URAA.

In order for the agency to change the current regulations to require that no applicant need amend an ANDA to respond to patent information submitted to the agency after the ANDA was filed, it must find that this position is consistent with the Waxman-Hatch Amendments. The degree to which the Waxman-Hatch Amendments support such an interpretation is beyond the immediate scope of this memorandum. Moreover, such a change in the certification requirements may have implications for program implementation that would make such a course impracticable.

The agency would have some difficulty in defending, as supported by the Waxman-Hatch Amendments and the URAA, a position that specifically identifies the URAA-extended patent expiration dates as patent information to which a pending ANDA does not have to certify. Currently, the only patent information to which an applicant with a pending ANDA is not required to certify, if the information is submitted after the ANDA is filed, is patent information that was not filed by the NDA holder in a timely manner. The agency justifies this regulation by arguing that, if FDA were to permit NDA holders to submit patent information at any point and then required pending ANDAs to be amended to respond to the information, NDA holders could manipulate the timing of patent information submissions so as to extend the period of market monopoly in a manner inconsistent with the policies of Waxman-Hatch. See 59 Fed. Reg. at 50,340, 50,347. In the present case, there isn't the concern about manipulation the timing of patent filings because the same date triggers the patent right for all patent holders and the patent that is extended is a patent that has been in the Orange Book already. Moreover, any concerns about manipulation of such filings could be addressed by applying the same sort of timely/untimely distinction the agency has drawn with respect to other patent information.

It is the generic's position that the transitional provisions, which limit remedies for infringement, establish that Congress intended to grant to all patent holders whose patents would be extended by the URAA, something less than full patent protection, and that therefore the FDA should treat the extended patent period (the "delta" period) as something different than a period of full patent protection with respect to patent certification requirements. This argument is unpersuasive for the same reasons articulated above with respect to the applicability of the URAA to drug approvals in general. Since the remedies of 35 U.S.C. § 271(e)(4) were left intact, so as to provide comprehensive remedies for infringement of patents for drugs, the agency cannot sustain an argument that the URAA permits it to treat the "delta" period as providing anything other than full protection to the patent holder and consequently not require updated patent certifications to the URAA-extended patent expiration date.

#### Substantial Investment

If, as proposed by the generics, FDA were to interpret the transitional provisions of the URAA as applying to drug-related patents, the agency would be required to make some determination as to what constitutes "substantial investment," so as to trigger the particular application of the transitional provision to an approval of an ANDA. The URAA limits the availability of certain remedies only for acts which were commenced, or for which a substantial investment was made, before the effective date of the URAA, and that became infringing by virtue of the extension of the patent under URAA. § 532 (a)(1).

The URAA does not define the term "substantial investment," nor does it refer to other sources for explanatory material. The generic industry and OGD propose that the "substantial investment" requirement be met by the preparation and filing of an ANDA before June 8, 1995. Some support for the position that submission of a complete ANDA constitutes a "substantial investment" may be found in the Process Patent Amendments Act of 1988. P.L. 100-418, §9004. Under that Act, importation into the U.S. of a product made abroad using a process covered by a U.S. patent became an act of infringement. The new law did not apply to products for which "substantial preparation" for sale or use had occurred prior to enactment of the new infringement provision.<sup>21</sup> The legislative history states that "the

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<sup>21</sup> Like the amendments under the URAA, the Process Patent Amendments Act contained a transitional provision containing broad language that appears to cover all manufacturing sectors, including pharmaceuticals. The 1988 amendments did not raise the same issues as those raised by the URAA, in that process patents

(continued...)

grandfather clause gives an exception for the many new generic medicines that have been approved or whose applications have been submitted to the FDA." S. Rep. No. 100-83, 100th Cong. 1st Sess., p. 47. (emphasis added):

The Senate Report goes on to state that:

"Section 105(a) contains a grandfather clause exempting commercial arrangements that have been or were about to be entered into prior to May 15, 1987. The special importance of this provision for the generic pharmaceutical industry was mentioned in the Statement. Since the Drug Price Competition Act and Patent Term Restoration Act of 1984, over 100 abbreviated new drug applications (ANDAs) for generic medicines have been approved by the FDA. The committee firmly believes it would be inequitable if process patent legislation were to interfere with the marketing of these newly approved generic drugs, or with other ANDAs that were pending but not yet approved on May 15, 1987, if substantial commercial investments had been made in them prior to that date."

That is, if a generic pharmaceutical company has made substantial commercial investment in preparing and filing an ANDA and is awaiting FDA approval as of May 15, 1987 or if the company has been granted an ANDA approval before that date and starts to market a generic medicine in the United States, the pharmaceutical products that the company imports, uses and sells in connection with the ANDA are protected under the grandfather clause. The generic company may expand or contract its business with these products, shift to different suppliers as necessary and continue to come under the protection of the grandfather clause. Id., at 58-59 (emphasis added).<sup>v</sup>

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<sup>v</sup>(...continued)

are not included among the patents addressed by the Waxman-Hatch amendments, and are thus not implicated in the pre-market approval process which, in turn, calls into play the remedial provisions of §271(e)(4).

<sup>v</sup> This statement provides a clear explanation as to the applicability of the Process Patent Amendments to the FDA drug approval process. The absence of an analogous clarifying statement in the legislative history to the URAA is troubling, particularly in light of the recent congressional attention to health care costs and the detrimental effect any extension of patent protection to pioneers will have on the availability of lower-cost generic drugs.

This explanatory material from the Process Patent Amendments on the interpretation of a similar provision elucidates somewhat what Congress may have meant by "substantial investment." Congress has not, however, provided a similar definition with respect to the URAA, and without such explicit guidance, these determinations are questions of patent law and fall outside FDA's authority and expertise. The difficulty of making such determinations is further underlined by the comments made in connection with the PTO hearing that suggest that the agency provide for submission of other evidence of "substantial investment" (i.e. commencing of bioequivalency studies, expenditures for new personnel) by ANDA applicants who do not have completed ANDAs pending before FDA on the date of enactment of the URAA.

Publication of URAA-extended Patent Information in the Orange Book

We currently publish only one expiration date for each patent listing in the Orange Book, i.e., when a Waxman-Hatch patent term extension is granted, FDA substitutes the new expiration date for the pre-extension date. In order to implement any policy that would permit approval of ANDAs at the expiration of the pre-URAA patent term, the agency would be required to make available to ANDA applicants information on these patent expiration dates. This could be done either by dual listings in the Orange Book, or by annotating the Orange Book with an instruction to see earlier editions for pre-URAA patent expiration information. There is no legal bar to either course.

The agency may not refuse to publish the URAA-extended dates under these circumstances. The Waxman-Hatch Amendments direct that the agency "shall publish" patent information submitted to it by the NDA applicant or holder. 21 U.S.C. § 355 (b)(1), (c)(2). While FDA has taken the position in the preamble to the proposed and final rules that, with respect to information submitted to the agency in an untimely manner, we would have the authority not to publish the information, in the present circumstances there is no question of NDA holder manipulation of the Orange Book that would merit such a step.<sup>2/</sup> 59 Fed. Reg

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<sup>2/</sup> The information upon which URAA-extended patent expiration dates will be calculated is publicly available. The URAA-extended patent expiration dates submitted by NDA holders will be subject to the same scrutiny by the industry as is currently brought to bear on submissions of other patent information. Any person who wishes to challenge the accuracy or relevance of patent information submitted by the NDA holder is directed to notify the agency, which will contact the NDA holder to seek confirmation that the information is accurate. 59 Fed.

(continued...)

50340. Moreover, the agency has stated that notice to potential ANDA applicants of the NDA holder's patent claims is an important part of the statutory scheme. Id.

### RECOMMENDATIONS

For the reasons set out above, I believe that, unless the agency is willing to amend its regulations addressing the ANDA amendment requirements, FDA is obligated to acknowledge and rely upon the URAA-extended patent expiration dates in the ANDA approval process. This conclusion raises a number of issues related to FDA's procedures and the obligations of NDA holders and ANDA applicants. These are addressed below.

#### Publication of Patent Expiration Dates in Orange Book

As discussed above, there is no legal bar to either publishing both the pre-URAA and the URAA-extended patent expiration dates in the Orange Book or indicating by means of an annotation that the listed date includes the URAA extension. There would be two primary benefits to doing so, even if the agency determines that the URAA-extended patent expiration date is the governing date for ANDA approvals. The first is that, at least until the NDA holders have had an opportunity to update patent expiration dates as appropriate, the absence of an updated entry or of an annotation might flag for a potential ANDA applicant that it would be wise to ascertain whether a URAA patent extension applies before submitting an ANDA. The ANDA applicant would still be entitled to rely on the Orange Book for relevant patent information; providing additional information would not impose upon the ANDA applicant an affirmative duty to conduct a patent search. The second benefit to making a reference to the status of the patent expiration date is that, until these issues have been resolved in litigation, ANDA applicants may wish to pursue a paragraph IV option with respect to the URAA-extended patent period. We could consider applying this dual entry or annotation approach for a fixed transitional period.

#### Submission by NDA Holders of Updated Patent Information

The agency must determine an appropriate timetable for submission of URAA-extended patent expiration dates and what, if any, consequences should attach to failure to update in a timely

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<sup>2</sup>(...continued)

Reg. 50,364 (to be codified 21 C.F.R. §314.54 (f)). Unless the NDA holder withdraws or amends the patent information, the agency will not change the listing. Id.

manner. There are three patent updating approaches currently in effect which bear on resolution of this issue.

First, the statute requires that information on patents issued after approval of the NDA be submitted to FDA within 30 days of issuance. 21 U.S.C. § 355(c)(2). The agency was asked during the comment period on proposed 21 C.F.R. 317.54(d) to extend this period to 60 days, but declined to do so, stating that the 30 day period was established by the statute and noting that a longer submission period could result in inaccurate listings in the Orange Book. 59 Fed. Reg 50,344, 50,364. The statutory penalty for failure to submit information on newly issued patents within thirty days of notification by the agency of failure to do so, and upon notice and an opportunity to be heard, is withdrawal of the NDA. 21 U.S.C. § 355(e)(4). The agency has taken the position that it could also impose the less extreme remedy spelled out in the final regulations, whereby ANDA applicants whose applications were submitted to FDA prior to submission by the NDA holder of late patent information would not be required to update the patent certifications in the ANDA to respond to the late-filed information. 59 Fed. Reg. 50,365 (to be codified at 21 C.F.R. 314.94(a)(12)(vi)).

Second, the agency has interpreted the statutory and regulatory provisions related to submission of information on newly-issued patents to apply the same treatment to the submission of information, other than Waxman-Hatch patent term extension, on patents that were issued before the approval of the NDA and then listed, delisted and subsequently relisted.<sup>10</sup>

Finally, the agency acquires information on Waxman-Hatch patent term extensions directly from the Patent and Trademark Office. It is the agency's position that ANDAs submitted prior to the submission of information on Waxman-Hatch patent extensions must be amended to certify to the new expiration date. 59 Fed. Reg. 50,366 (to be codified at 21 C.F.R. § 314.94(a)(12)(vii)(C)).

In a Fed. Reg. notice published on March 27, 1995, the Patent and Trademark Office proposes to determine and publish the new expiration dates for patents (1) that are in force on June 8, 1995, (2) that are entitled to a term of twenty years from filing, and (3) that have received a patent term extension under 35 U.S.C. §§ 155, 156. FDA can apply the same process with

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<sup>10</sup> This latter position has been challenged by Marion Merrell Dow with respect to agency treatment of ANDAs for terfenadine that were filed prior to relisting by MMD of a patent it claims applies to a use for terfenadine. The matter is currently before the U.S. District Court for the District of Columbia on a motion for summary judgment.

respect to this URAA patent information it uses with information on Waxman-Hatch patent term extensions, although some arrangement must be made with PTO to assure that the updated information will be available within an agreed-upon time frame. In the case of Waxman-Hatch extensions, the Office of Health Affairs monitors the Federal Register for the publications and then conveys the information to the relevant offices for publication in the Orange Book and in FDA Approved Animal Drug Products (the "Green Book"). The Fed. Reg. notice did not indicate whether the PTO intends to determine and publish new patent expiration dates for patents in force on June 8, 1995 that have not received patent term extension under 35 U.S.C. §§ 155, 156. If PTO does not determine and publish that information, there will be instances in which information on URAA-extended patent expiration dates comes directly from the NDA holder. The agency must determine as well whether the NDA holder should also submit to the agency information determined and published by PTO.

OGD would like to require that information on the URAA-extended patent expiration date be submitted to the agency within 30 days of June 8, 1995.<sup>11/</sup> They also believe that the agency should take the same position with respect to late submissions of patent information in this context as it has taken in the regulations with respect to other "untimely" submissions of patent information. Under this approach, late submissions of URAA-updated patent expiration dates will be accepted and published by FDA. ANDA applicants who submit ANDAs after July 8, 1995, will not be required to update the certifications contained in the ANDA to respond to URAA-extended patent expiration dates not submitted to the agency prior to the filing of the ANDA. ANDAs submitted after the untimely submission by the NDA holder of URAA-extended patent expiration dates will be required to certify to the extended date.

The position OGD would like to take is fully consistent with the positions the agency has taken with respect to updating other patent information. Unless PTO determines and publishes all URAA patent extensions, this situation would not be comparable to the updating of information on Waxman-Hatch patent term extension

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<sup>11/</sup> OGD should determine what, if any, approvals could be made effective in the 30 days following June 8, 1995, during which new patent information may not have been submitted. In order to avoid unnecessary confusion and litigation, the agency may wish to contact the parties directly to determine whether the URAA will have any effect on the patents at issue. While this pro-active approach is somewhat inconsistent with the "ministerial" position FDA has ascribed to itself with respect to patent matters, this situation is unusual enough that such actions are unlikely to have serious ramifications in the future.

where all the information comes to the agency directly from the Patent Office and the NDA holder has no discretion as to when the information is submitted. The issue is more analogous to the issuance of a new patent or the determination by the NDA holder that an existing patent applies to the listed drug. In these instances, the information and discretion rest with the NDA holder. As discussed in the preamble to the final regulations, the failure to file patent information promptly can undermine the statutory goals of the Waxman-Hatch Amendments and could cause the agency and ANDA applicants to expend resources unnecessarily. 59 Fed. Reg. 50340. The knowledge that FDA could approve an ANDA filed before the NDA holder submits its updated patent information, if that information is not submitted by July 8, 1995, should prove an incentive to NDA holders to file the URAA-extended expiration dates promptly.

#### ANDA Applications Pending Before the Agency on June 8, 1995

ANDAs pending before the agency on June 8, 1995, will be required to submit updated certifications to respond to the URAA-extended patent expiration dates. This will also apply to ANDAs for which a tentative approval letter has been sent. See 59 Fed. Reg. 50348-9. The agency will not approve ANDAs that do not contain the new certifications to URAA-extended patent expiration dates submitted by the NDA holder because those applications will not meet the requirements for a complete ANDA and they will contain untrue statements of material fact. 21 U.S.C. § 355(j)(3)(J), (K). I would anticipate that a number of ANDA applicants will submit paragraph IV certifications to the extended patent dates. If that occurs, and the NDA holder brings suit to enforce the patent, the agency will be required to stay its approval for at least 30 months, unless the court orders otherwise.

#### CONCLUSION

For the reasons set out above, I believe that unless FDA amends its regulations to permit approval of ANDAs that do not contain certifications to later-filed patent information, FDA is required to accept and publish the URAA-extended patent expiration dates. The agency is further required to treat these URAA-extended dates as the dates that will govern for approval of ANDAs for listed drug products.

I have been told by parties representing both the innovator industry and the generic industry that they intend to file lawsuits if FDA adopts a policy that is unacceptable. We can expect litigation on this matter promptly upon the issuance of the agency's position.

\*\*\*\*\*

U.S. FOOD AND DRUG ADMINISTRATION  
OFFICE OF THE COMMISSIONER  
OFFICE OF POLICY  
5600 FISHERS LANE  
ROCKVILLE, MARYLAND 20857  
ROOM:14-105/MAIL CODE:HF-22  
OFFICE NUMBER:1-301-443-5004  
FAX NUMBER:1-301-594-6777

\*\*\*\*\*

DATE: 4/18/1995

TO: Chris Jennings

FROM: Bill Schuttz

NUMBER OF FAX PAGES: 5

COMMENTS:

**SUMMARY OF LEGAL ISSUES RAISED BY THE URUGUAY ROUND  
AGREEMENTS ACT WITH RESPECT TO FDA APPROVALS  
OF ABBREVIATED NEW DRUG APPLICATIONS:**

The Office of Chief Counsel of FDA has analyzed the relationship between certain provisions of the Uruguay Round Agreements Act ("URAA"), that extend patent terms for up to three years, and the provisions of the Waxman-Hatch Amendments governing the approvals of abbreviated new drug applications ("ANDAs") for generic equivalents of approved drugs.<sup>1/</sup>

**BACKGROUND**

Prior to 1984 and the passage of the Waxman-Hatch Amendments, FDA did not determine or consider the patent status of pioneer drugs when it approved generic copies of those drugs. In the event of an infringement of patent rights by a generic drug manufacturer, the owner of the patent sought recourse in the federal courts.

The Waxman-Hatch Amendments established new drug and generic drug approval programs that require FDA to accept and publish patent information, and to consider the patent status of innovator drugs when it approves generic versions of those drugs. This requirement was part of the legislative compromise that permits prompt marketing of lower-cost generic drugs after expiration of patents on the pioneer drugs, in exchange for an express recognition of patent rights in the generic drug approval process and the restoration to patent holders of some of the time lost on the patent life during the regulatory review process. The Waxman-Hatch Amendments generally require that FDA wait until the patents applicable to the pioneer drug have expired before the agency approves generic versions of the drug.

The URAA extends the term of patent protection by up to three years. FDA's current drug approval process requires that the agency acknowledge the URAA-extended patent expiration dates as controlling with respect to approvals of generic drugs. The generic drug industry and some other interested parties have asserted that FDA should amend its regulations so that ANDAs pending before the agency on June 8, 1995, the effective date of the patent extension provisions, can be approved upon the expiration of the pre-URAA patent term. FDA's authority to amend its regulations as proposed depends upon whether such a change is permitted by the URAA and by the Waxman-Hatch Amendments. The Office of the Chief Counsel has determined that the URAA does not permit such an amendment.

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<sup>1/</sup> This analysis applies as well to abbreviated new animal drug applications ("ANADAs"), by which manufacturers seek approval to market generic versions of animal drugs.

## THE GENERIC DRUG APPROVAL PROCESS

### **Patent Submissions by NDA Holder and Publication by FDA**

- The Waxman-Hatch Amendments direct that NDA applicants submit patent information on the pioneer drug to FDA. FDA is required to publish this information.
- Some patent information becomes available after approval of an NDA, such as when a new patent is issued or with the extension of a patent term under the Waxman-Hatch patent term extension provisions. FDA publishes this information.
- NDA holders are already submitting updated patent information to FDA that contains the URAA-extended patent expiration dates. The Waxman-Hatch Amendments require that the agency publish the URAA-extended patent expiration dates once they are effective.

### **Patent Certifications by ANDA Applicants**

- The Waxman-Hatch Amendments require that a company seeking to obtain FDA approval to market a generic copy of a drug include in its ANDA a "certification" with respect to each patent which claims the drug or a use.
- FDA regulations require that an applicant amend its ANDA if at any time before the effective date of the approval of the application for the generic copy, the applicant learns that the submitted certification is no longer accurate.
- Under FDA's current regulations, ANDA applicants would be required to amend patent certifications to acknowledge the URAA-extended patent expiration dates.
- With respect to a URAA-extended date, an ANDA applicant may submit either a certification indicating that it will wait to market until the URAA-extended patent term has expired, or a certification indicating that the ANDA applicant believes that the patent asserted by the NDA holder is invalid or will not be infringed by the generic.

### **FDA Approval of ANDAs**

- In the case of a certification indicating that the ANDA applicant doesn't intend to market the generic until the patent expires, FDA will not make an approval effective any earlier than the expiration of the patent.
- If the ANDA applicant claims that the pioneer's patent is invalid or will not be infringed by the generic copy, FDA can make an approval effective immediately, unless the

pioneer drug company sues the generic drug company over the patent claim. If there is patent litigation, FDA must wait at least 30 months to make an ANDA approval effective, unless a shorter or longer period is ordered by a court.

#### EFFECT OF URAA PATENT EXTENSIONS

The URAA extends the period of patent protection, in order to harmonize U.S. patent law with international patent standards. New patents will have a 20-year term from date of filing. Patents in force on June 8, 1995, or that result from an application filed before that date, will have a patent term that will be the greater of the 20-year term from date of filing or 17 years from the date of granting of the patent.

Section 532(a)(1) of the URAA is a transitional, "grandfathering" provision that limits the availability of certain statutory patent infringement remedies (injunctions, damages, and attorney's fees) for acts that were commenced, or for which "substantial investment" was made, before June 8, 1995, and which become infringing because of the extension of the patent period. The URAA provides that such infringing acts may be continued upon payment of "equitable remuneration" to the patentee. The URAA does not define "substantial investment" or "equitable remuneration."

The generic drug industry maintains that this "grandfathering" provision will permit any applicant who has submitted an ANDA to FDA by June 8, 1995, and therefore made a "substantial investment," to obtain approval of a generic version of a drug covered by a URAA-extended patent upon expiration of the pre-URAA patent term. Marketing of the generic drug will then require only "equitable remuneration" to the patentee.

The flaw in the generic drug industry's argument is that Congress did not include the remedies that apply specifically to the infringement of drug-related patents among the remedies made unavailable by § 532(A)(1) during the transition period. Section 271(e)(4) of the patent code, which provides for injunctions, damage awards, and attorney's fees for acts of infringement related to drug patents, was not listed among the remedy sections explicitly made unavailable under the URAA. Moreover, any argument that Congress simply overlooked §271(e)(4) is undermined by the fact that the URAA makes technical amendments to this provision to apply the remedies specified to a broader range of infringing actions (e.g. extended coverage from "sale" to "offer to sell").

The Office of Chief Counsel therefore has determined that under established canons of statutory construction, Congress did not intend to include generic drug applications within the transitional "grandfathering" provision. The clear language of

the URAA does not amend the remedies that govern infringement of drug patents. Congress clearly knew of the existence of § 271(e)(4), but it nonetheless did not include that section's remedies for infringement of drug-related patents among the remedies made unavailable for patent infringement during the transitional period.

The limited legislative history on the transitional provision of the URAA does not provide any affirmative support for the argument that it was Congress' intention to apply the provision to all industries. The language in the Agreement on Trade-Related Aspects of Intellectual Property Rights ("TRIPs") permits, but does not require, the inclusion of a transitional provision in the implementing legislation adopted by a member country. The statements contained in the Statement of Administrative Action and in the Senate report are not specific as to the parties affected by the transitional provision and are merely restatements of the general technical aspects of the provision.

Legislative History for URAA Provisions Pertaining  
to Transitional Patent Provisions

The Agreement on Trade-Related Aspects of Intellectual Property Rights ("TRIPs") provides, at Article 70.4, that:

In respect of any acts in respect of specific objects embodying protected subject matter which becomes infringing under the terms of legislation in conformity with this Agreement, and which were commenced, or in respect of which a significant investment was made, before the date of acceptance of the WTO Agreement by that Member, any Member may provide for a limitation of the remedies available to the right holder as to the continued performance of such acts after the date of application of this Agreement for that Member. In such cases, the Member shall, however, at least provide for the payment of equitable remuneration.

(emphasis added).

The Statement of Administrative Action that accompanied the URAA states that:

Section 532(a) also adds sections 154(c)(2) and (3). These sections address situations where a third party begins use of a patented invention before the date that is six months after the date of enactment of the Uruguay Round Agreements Act and such use becomes infringing because of a change in patent term due to operation of section 154(c)(1). In such circumstances, the patent owner will not be able to obtain an injunction, recover a reasonable royalty, or obtain attorneys fees as provided for in sections 283 to 285 of Title 35, but will be able to recover equitable remuneration from a third party who infringes the patent during the period in question.

The Joint Report of the Committee on Finance; the Committee on Agriculture, Nutrition and Forestry; and the Committee on Governmental Affairs contains a nearly identical, albeit slightly inaccurate, statement:

Section 532(a) adds new sections 154(c)(2) and (3). These sections address the situation where a third party begins using a patented invention anytime during the six months after the enactment of the legislation and such use becomes infringing because of a change in patent term due to the operation of section 154(c)(1). In such circumstances, the patent owner will not be able to obtain an injunction, recover a reasonable royalty, or obtain attorneys fees, but will be able to recover equitable remuneration.

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Office of Executive Secretariat  
5600 Fishers Lane, HF-40  
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**FACSIMILE TRANSMISSION RECORD**

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NUMBER OF PAGES (not including coversheet) - ~~2~~ 3

TO: Chris Jennings

Fax No.

Telephone No.

301-443-9369

FROM:

Walt Osborne  
Supervisory Policy Analyst

MESSAGE:

Per your request to Bill  
Schultz & Bill Hubbard for response  
to Jon Cherney.

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**DRAFT**

Mr. Jon Cherney  
5816 West Lindenhurst Avenue  
Los Angeles, California 90036

Dear Mr. Cherney:

Thank you for your letter of March 26, 1995. I can well appreciate the frustration you express concerning the availability of drugs to treat life-threatening diseases such as cancer and AIDS. These diseases have terribly devastating effects, not only on the patient, but on the family and loved ones as well.

The Administration places a high priority on cancer and AIDS research, and as you probably know, funding for the National Cancer Institute and the National Institutes of Health is at an all time high.

The Food and Drug Administration (FDA), under the Department of Health and Human Services (HHS), is responsible for ensuring the safety and effectiveness of all drugs and biological products in the United States. Over the past few years, FDA has taken significant steps toward making experimental drugs for HIV/AIDS more widely available and has initiated expedited procedures to speed the review and approval of promising therapies for HIV/AIDS. Tens of thousands of people have received products under expanded access mechanisms.

The Treatment Investigational New Drug regulations (Treatment INDs) establish conditions under which promising new drugs and biologics that have not yet been approved or licensed may be made available to desperately ill persons. Treatment INDs have generally been granted only after all clinical trials have been completed, or at least well into the clinical testing phase, and after the development of some reliable evidence that the product is effective. In addition to treating AIDS, approved Treatment INDs also have made therapies available to treat renal transplant rejection, cancer, obsessive compulsive disorder, and Parkinson's Disease.

The "parallel track policy," first announced in April 1992, expands the availability of promising investigational drugs to those persons with AIDS and HIV-related diseases who are without satisfactory alternative therapy and who cannot participate in controlled clinical trials. The first AIDS drug that was tested under FDA's parallel track policy was d4T, an anti-viral drug that acts by inhibiting HIV. During the testing of this product, 11,000 people were enrolled for treatment.

In December 1992, new rules to speed the approval of drugs and biologics for patients with serious or life-threatening illnesses, such as AIDS, cancer, and Alzheimer's disease, were published by FDA. These rules establish procedures for the Agency to approve a drug based on "surrogate endpoints" such as laboratory tests or physical signs that indicate that real health benefits are likely to occur. Use of surrogate endpoints for measurement of drug efficacy permits approval earlier than if traditional endpoints--such as relief of disease symptoms or prevention of disability and death from the disease--are used. These rules also allow for a streamlined withdrawal process if the postmarketing studies do not verify the drug's clinical benefit, if there is new evidence that the drug product is not shown to be safe and effective, or if other specified circumstances arise that necessitate expeditious withdrawal of the drug or biological product.

In September 1993, FDA announced the creation of its Office of AIDS and Special Health Issues. The Office serves several critical functions within the Agency. First, it is a major contact point between the FDA and people with AIDS and other serious or life-threatening diseases, including cancer. Second, it is a point of contact between FDA and other federal agencies dealing with these diseases. Lastly, where appropriate, this Office attempts to represent, within the FDA, the perspectives of people with these diseases.

Early in 1994, HHS Secretary established the National Task Force on AIDS Drug Development. Dr. David Kessler, Commissioner of Food and Drugs, is a member of the Task Force. The mission of the Task Force is to ensure that all aspects of AIDS drug development are rapidly taking place in a creative, coordinated manner, free of unnecessary barriers. The Task Force has had several meetings and has also established subcommittees to address a variety of issues concerning expedited AIDS drug development.

Many individuals at FDA have been working closely for years with pharmaceutical manufacturers, community activists, and researchers in the fight against AIDS, cancer, and other serious diseases. We all share your frustration, but assure you of our continuing commitment to finding cures.

I hope this information has been helpful, and thank you again for taking the time to write.

Sincerely,

Carol Rasco  
-----, etc.

JON CHERNEY  
5816 West Lindenhurst Avenue  
Los Angeles, CA 90036

March 26, 1995

The Honorable Carol H. Rasco  
Asst. to the President for Domestic Policy  
THE WHITE HOUSE  
1600 Pennsylvania Avenue  
Washington, DC 20500

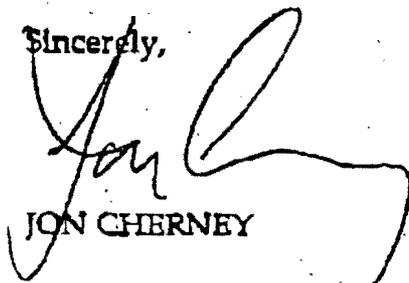
Dear Ms. Rasco:

I am writing to urge you to do something about the bureaucracy in the FDA. Drug approval for diseases such as AIDS and CANCER move at a snail's pace. Meanwhile, loved ones are dying everyday. Something must be and should be done about this. I understand that the FDA is slow to approve drugs because of fear of lawsuits and liabilities. Why can't special laws be created to approve these drugs, which have shown great promise in both Stage 1 and Stage 2 testing, that would be approved only at the risk of the patient and that the Government of the United States, the FDA and the NIH will have no liability if there should be any adverse reactions to these medications and agents.

This idea seems logical and humane. Please give it some thought and create legislation to save lives of thousands of people. The President could even initiate this by Executive Order. Please, time is of the essence here.

Thank you for your time and attention.

Sincerely,



JON CHERNEY

202 456 7431

**Office of Public Affairs  
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**301-594-6004 or 301-443-3819 (fax)  
301-443-1130 (phone)**

**TO:**

**FROM:**

CHRIS TERWIDGES

**JIM O'HARA**

**Number of pages (includes cover)** \_\_\_\_\_

**Message:** What you would have read on 7/5 A-22  
in The NY Times if they had quality control

If this is not clear, please call and we will send another fax. Thank you.

BC-FDA-NEW-PRODUCTS-NYT  
FDA MOVES TO HASTEN MARKETING OF NEW DEVICES

(b1)

By PHILIP J. HILTS

c.1995 N.Y. Times News Service

WASHINGTON - Hoping to head off greater changes that might be proposed in Congress, the Clinton administration announced plans Thursday to have the Food and Drug Administration ease the way to market for some new drugs and medical devices.

Among the plans is a two-year pilot program in which review of a number of medical devices will be turned over to private groups.

The commissioner of food and drugs, Dr. David A. Kessler, outlined the changes at a hearing of the Senate Labor and Human Resources Committee, saying the FDA was committed to eliminating red tape while continuing to make sure that drugs and medical instruments are both safe and effective.

Sen. Barbara A. Mikulski, D-Md., joined several Republican members of the committee in warning the agency about what they described as a confrontational attitude toward companies like the biotechnology concerns in Senator Mikulski's own district.

"There is an enormous frustration in the private sector about the agency's attitude, about nit-picking," she said. "We need a passion for change at the FDA. And if not, I believe Congress is going to roll right over you."

Kessler assured her that change had begun. "We believe many medical devices simply don't pose a sufficient risk to be reviewed by FDA prior to marketing," he said.

Accordingly, the two-year pilot program will enable 10 categories of medical devices - a total of 100 to 400 such instruments that the FDA deems of low or medium risk - to be reviewed not by the agency itself but by private medical groups. These groups have not yet been chosen, or even solicited.

The manufacturers will pay for the private reviews, which are expected to get under way in 1997.

Throughout the pilot program, the FDA will retain final decision-making authority. That makes the program less sweeping than the standard review procedure in some European countries that have been approvingly cited by the American health manufacturing industry.

Private groups accredited by the governments there have the power to grant applications for medical devices.

Another of the changes announced Thursday will allow 125 categories of devices, which account for about 700 applications a year, to be exempted from the need for FDA approval before going to market. These categories include syringes, oxygen masks and simple surgical lasers.

The agency has already exempted 441 categories of devices, including stethoscopes and surgical microscopes. The new exemptions, added to those earlier ones, mean that about a third of all medical devices will now be exempt from review before marketing.

In another change, companies will be allowed to export drugs that are not approved for use in the United States but that do have the approval of the countries to which they are sent.

The FDA plans to permit export to 21 countries with the best safety records at first, and then consider expanding that number.

NYT-04-06-95 1912EDT<

## **Introduction**

Reforming the Federal government's regulatory processes, while maintaining critical public health and safety standards, has been and will continue to be a top priority for the Clinton Administration. Consistent with this commitment, President Clinton and Vice-President Gore asked Health and Human Services Secretary Donna Shalala to help them carefully examine FDA's regulatory requirements.

As part of the Vice-Presidents' reinventing government initiative, the FDA has been reviewing its regulatory processes to determine which requirements could be reduced or eliminated without lowering health and safety standards. This report contains recommendations resulting from the initial phase of that review.

## **Background**

The Food and drug Administration is the Agency within the Department of Health and Human Services charged with ensuring that drugs, vaccines, and medical devices are safe and effective and that foods meet basic safety standards. In carrying out these and other responsibilities, FDA oversees more than \$1 trillion worth of products, which account for 25 cents of every dollar spent annually by American consumers.

FDA was created in 1906 to protect Americans from unsafe foods and drugs. In 1976, FDA's responsibilities were expanded to include medical devices. During this Administration, FDA has taken significant initial steps to streamline the regulatory process. These recent initiatives have resulted in new products being brought to market sooner; but more can be done.

## **A Record of Accomplishment**

FDA's recent regulatory improvements include:

### **\* Shortening Review Times for New Drugs and Devices**

- 1) FDA now uses expert review panels to expedite the review of certain biotechnology products (for example, a joint committee of FDA experts oversaw the licensing in record time of the drug interferon beta 1b to treat certain patients with multiple sclerosis).
- 2) Under the Prescription Drug User Fee Act of 1992, drugs are now reviewed more quickly than ever[?]. This law authorizes FDA to charge user fees for the review of drug applications, and to use these additional resources for the review of drug applications, and to use these additional resources for the reviews of new drugs, vaccines, and biotechnology products.

Already review times for new chemical drugs have dropped

from an average of 30 months in 1992 to 20 months in 1994.<sup>1</sup> By 1997, FDA will be getting these products to market in a year or less, as fast or faster than anywhere else in the world, with no sacrifice in review quality.

- 3) Medical devices are benefiting from a number of new processes that speed up their review; for example, devices that provide significant medical advances are now given priority review.
- 4) Animal drugs are now reviewed in a more efficient manner that resulted in a record number of 38 new drugs approved in 1994.

**\* Eliminating Unnecessary Regulatory Burden**

- 1) The FDA exempted 148 categories of low risk medical devices from premarket review in December 1994, relieving manufacturers from submitting applications to the Agency and waiting for their approval.
- 2) The FDA has helped to assure safe and high quality mammography by using existing private sector standards to certify mammography facilities, which are mostly small businesses. Utilizing these standards allowed the FDA to implement the requirements of the 1992 law that all of these facilities be accredited and certified.
- 3) FDA has begun a joint program with the Customs Service to automate the entry of imported products into the U.S. The program allows an importer to notify FDA by computer of import entries and receive prompt permission to enter this country.
- 4) FDA has issued permit regulated companies to use electronic records and signatures in place of paper under a new proposal. This will save industry substantial costs by simplifying record keeping and speeding the filing of applications and other regulatory documents.

**[JUSTIFICATION]**

As noted in the President's State of the Union address and his recent announcement highlighting some of the recommendations in this report, this Administration is committed to promoting results and not rules. The reforms this report advocates will reduce paperwork and eliminate unnecessary regulation. In so doing, will strengthen the economy while maintaining health and safety.

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<sup>1</sup> The 1994 median review time for all new chemical drugs was 17.5 months; (the subset of 1994 drugs reviewed under the user fee program were reviewed in an average of 13.5 months).

## **Principles for Reforming FDA Regulation in Carrying out this Review**

In carrying out its regulatory review, the Agency carefully considered the financial burdens that its requirements impose on industry and consumers and looked for ways to allocate or eliminate these burdens. In reforming its procedures and requirements, FDA followed the following principles:

- \* Using performance standards rather than command and control regulations, whenever possible;
- \* Expediting product review, without sacrificing the health and safety of the public;
- \* Eliminating unnecessary requirements that may have been appropriate once but are not now necessary to protect public health; and
- \* Utilizing modern automated technology as a tool in streamlining internal Agency management and as an aid to industry in meeting their regulatory requirements.

## **Regulatory Reform Recommendations**

FDA is proposing a number of reforms that reinvent how FDA regulates. The reforms included in this report are estimated to save the drug and device industries \$500 million per year in unnecessary regulatory costs. These reforms will also let FDA better target its resources.

The recommendations contained in this report are summarized below:

- \* **Reducing or eliminating** many of the FDA requirements for companies to get approval for changes in their manufacturing facilities or processes for manufacturing drugs, biotech drugs and other biologics biotech drugs;

(note: FDA please make certain that the consolidation of this paragraph with the fourth bullet which previously started out "reducing or eliminating" coincides with the consolidation of the written proposals)

- \* **Allowing manufacturers of biological drugs to get licenses for pilot facilities** instead of making them build full-scale plants. Manufacturers will still have to show that they can meet safety, purity, and potency standards.
- \* **Permitting greater flexibility** in the appearance of distributors' names on biological product containers, package labels, and labeling;
- \* **Eliminating outdated requirements** for insulin and

antibiotics and allowing a private standard-setting body to establish testing and quality standards (thus 600 pages of Federal regulations will be eliminated);

- \* **Exempting drug and biologic manufacturers from certain environmental assessments that currently cost tens of thousands of dollars each time a new product is developed and provide no real benefit to the environment;**
- \* **Exempting nearly 140 additional categories of low-risk medical devices from premarket review.**
- \* **Eliminating the reference list and clarifying that market clearances of low-risk devices will not be withheld unless FDA finds a reasonable relationship between the nature of current violations and the application under review;**
- \* **Developing a pilot program for review of low-risk medical devices by outside review organizations to determine if such a system could be developed permanently;**
- \* **Speeding the marketing of medical devices by seeking authority to charge industry user fees for device reviews, and committing FDA to meet certain strict performance goals;**
- \* **Expanding opportunities to export drugs and medical devices to industrialized countries.**
- \* **Issuing a public statement clarifying how FDA determines the effectiveness of new drugs and devices;**
- \* **Harmonizing FDA's drug and device approval requirements with those of other countries, thus expediting worldwide marketing of new products by reducing duplicative testing;**
- \* **Expanding and standardizing the use of new information technologies for review of new products to speed up import entries.**

Additional proposals for reforming the regulation of drugs and medical devices are being developed and will be announced in a later report. They will accompany additional recommendations related to the regulation of foods and veterinary products.

## MEMORANDUM

To: Carol Rasco  
Elaine Kamarck  
Greg Simon  
Sally Katzen  
Jennifer Klein  
Paul Weinstein  
Shannah Koss

From: Chris Jennings

Date: April 18, 1995

Re: FDA Report Clips

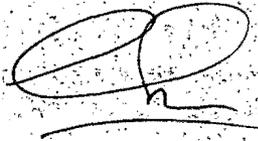
Attached for your information are the clips from the FDA report. I thought that you might like to have a set.

Stacey -

Pl. white out top and enclose w/ brief cover memo to Elaine, Greg, Sally, w/ a cc to Jim & Shannon. The cover note should say:

Attached is the implementation timeline for the reg reforms outlined in the recently released FDA report. We can all use this to keep on top of the Agency to follow through on the Administration's promised timeframe. ~~Let me know what you~~

Hope you find useful. Call me with any questions.



## DECO DEVICE PROPOSALS

Stacey -

71

pl. white out top and enclose w/ brief cover memo to Elaine, Greg, Selby, w/ a cc to Jim & Shannoh. The cover note should say:

Attached is the implementation timeline for the reg reforms outlined in the recently released FDA report. We can all use this to keep on top of the Agency to follow through on the Administration's promised timeframe. ~~Call me with any~~

Hope you find useful. Call me with any questions.



### IMPLEMENTATION/TIMELINE

reclassification and exemption by

review of products on list

program will begin Oct. 1995

proposed in 1996 budget

proposed regulation for IDE by Oct. 1995

statement by July 1995

guideline development within 2 years  
guidelines within 2 years

## REGO DEVICE PROPOSALS

PROPOSAL	IMPLEMENTATION/TIMELINE
Medical Device Exemptions from Premarket Notification	proposed reclassification and exemption by June 1995
Elimination of the Reference List	immediate review of products on list
Medical Device External Review Pilot Program	pilot program will begin Oct. 1995
Device User Fees	legislation proposed in 1996 budget
Device Exports	legislation; proposed regulation for IDE devices by Oct. 1995
Effectiveness of Devices	published statement by July 1995
Harmonization of Standards	testing: guideline development within 2 years GMPs: guidelines within 2 years

## REGO DRUG PROPOSALS

PROPOSAL	IMPLEMENTATION/TIMELINE
Eliminating Many Requirements for FDA Approval of Manufacturing Changes	<p>Drugs: tablet form, guidance document by Dec. 1995 other forms, guidance document by Dec. 1996</p> <p>Biologics: 1st round guidance document immediately 2nd round proposed regulation by Jan. 1996</p>
New Policy to Permit Use of Small-Scale and Pilot Facilities During Development of Biologics	guidance document by July 1995
Revision of Labeling Requirements for Biological Products	proposed regulation by Oct. 1995
Antibiotic and Insulin Standards and Insulin Certification	legislation
Environmental Assessments for Human Drugs	proposed regulation by Jan. 1995
Drug Exports	legislation
Effectiveness of Drugs	published statement by July 1995
Harmonization	<p>testing: guideline development within 2 years</p> <p>GMPs: guidelines within 2 years</p> <p>animal drugs: guidelines within 3 years</p>



# B A C K G R O U N D E R

U.S. FOOD & DRUG ADMINISTRATION

Contact: Jim O'Hara 301-443-1130

## Reinventing Drug and Medical Device Regulation

The Clinton Administration is committed to making government work better by reducing unnecessary regulatory burdens while maintaining the critical public health protections the American people expect and deserve. In the case of the Food and Drug Administration, reinvention of drug and medical device regulation will mean speeding up the review of these products.

The high standards of the FDA have given Americans access to drugs and medical devices that are safe and that work. In addition, FDA has worked in recent years: to make new therapies available as soon as possible, even before final approval; to accelerate the approval of life-saving drugs; and to speed up the review and approval of all drugs with additional resources from industry user fees.

The Clinton Administration is building on these high standards and efforts to speed up drug and device approval with new FDA regulatory reforms. Some of these reforms will directly speed up the review process for these products. Others will reduce unnecessary regulatory burdens on industry. All are aimed at maintaining and protecting Americans' confidence in the safety and effectiveness of the drugs they take and the medical devices they use.

FDA will reform drug and medical device regulation by:

- Allowing manufacturers of drugs and biologics (products made from biological materials) to change the way they manufacture an approved drug without FDA pre-approval if the risk is negligible.  
**Impact:** Industry can modernize facilities and processes more easily; FDA can shift resources to more critical review needs.
- Allowing manufacturers of biological drugs to get licenses for pilot facilities instead of building full-scale manufacturing plants.  
**Impact:** Manufacturers will have lower start-up costs and can more quickly begin production of new drugs.
- Permitting greater flexibility in how distributors' names appear on biological product containers, package labels, and labeling.

(more)

**Impact:** Small start-up companies, many of them biotechnology firms, may more readily enter into manufacturing arrangements with larger companies and bring products to market quicker.

- Eliminating special requirements for manufacturing insulin and antibiotic drugs.

**Impact:** Industry will no longer be burdened with outdated requirements and FDA can regulate these products the same way it does other drugs.

- Excluding drug and biologics manufacturers from requirements for most environmental assessments.

**Impact:** Industry will be spared the expense of preparing assessments that FDA has found unnecessary.

- Exempting up to 125 categories of low-risk medical devices from premarket review, adding to the 441 categories already exempted from review.

**Impact:** Industry will no longer have to wait for premarket review, meaning that these devices can reach patients sooner; FDA can shift resources to more critical review needs.

- Eliminating the "reference list" and clarifying that premarket review of medical devices can be affected only if good manufacturing practice violations are related to a specific device.

**Impact:** Industry concerns that good manufacturing practice violations for one product can slow down approval for other devices unrelated to those problems will be alleviated, and there will be more certainty about when products can be marketed.

- Developing a pilot program for the review of low to moderate risk medical devices by outside organizations.

**Impact:** This program will help determine if such a system can speed the review of these devices, whether the independence of the review process can be maintained, and if such a system will be less costly.

- Speeding the marketing of medical devices by charging industry user fees to give FDA more resources for product reviews and committing FDA to strict performance goals.

**Impact:** A similar program for prescription drugs has substantially reduced review times and FDA has met all performance goals to date.

- Expanding the opportunities for the export of unapproved drugs and medical devices to industrialized countries.

**Impact:** Industry will have wider markets for its products and will be encouraged to maintain operations in this country.

(more)

- Clarifying the effectiveness standard for new drugs.  
**Impact:** Industry will have a better understanding of how to develop new products, reducing the time it takes to bring a drug to FDA for review.
- Harmonizing international standards for the review of drugs and medical devices.  
**Impact:** The worldwide marketing of new products will be speeded up if there is less need for duplicative testing to meet the standards of different countries.
- Expanding and standardizing computer technologies used by FDA in the review of new products and in the processing of imported products.  
**Impact:** Review times for new products will be reduced as these technologies are better utilized both by FDA and industry; imported products will be allowed into the U.S. marketplace quicker as these systems are implemented.

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