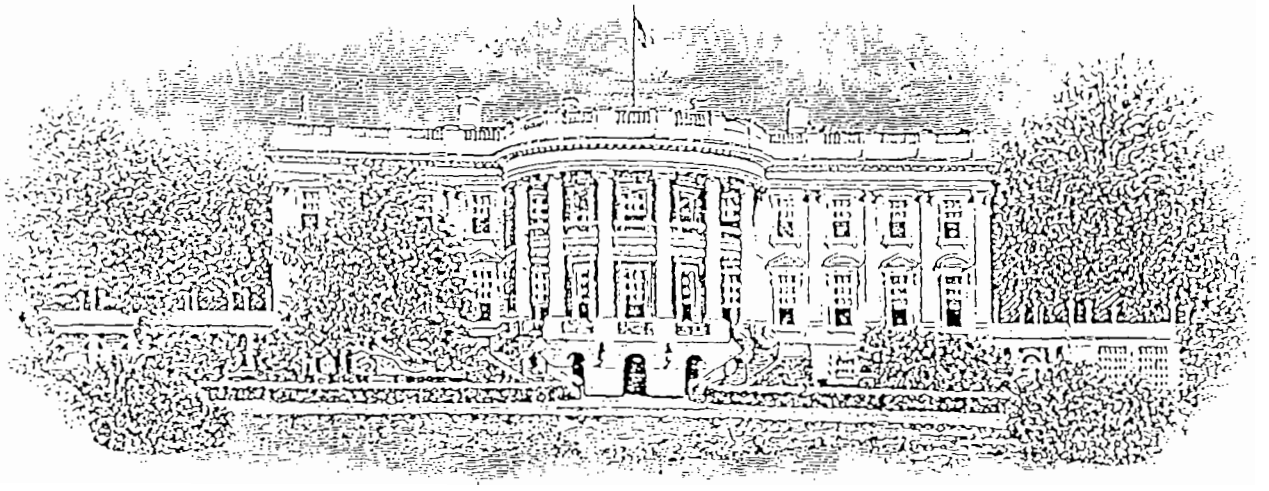
The White House



DOMESTIC POLICY

FACSIMILE TRANSMISSION COVER SHEET

TO: Jennifer Boulanger

FAX NUMBER: 690-6262

TELEPHONE NUMBER:

FROM: Jon Klein

TELEPHONE NUMBER:

PAGES (INCLUDING COVER):

COMMENTS: As we discussed in meeting this week...

MEMORANDUM

TO: Carol Rasco
FR: Chris Jennings
RE: Today's release of FDA reg reform report
cc: Bill, Jeremy, Jen, Paul

April 6, 1995

This morning, the Administration is releasing the attached FDA regulatory reform report. It follows on the print shop event a few weeks ago in which the President released the EPA report and made references to a number of the FDA reform initiatives that are included in today's report.

The FDA report proposes numerous regulatory reforms that are estimated to save the drug and device industries at least $500 million per year in unnecessary regulatory costs and will also free up FDA to better target its resources toward improving and expediting market access of new products. The recommendations are significant, not only for their substance but because the Agency has committed to specific timetables for implementation. There will be additional recommendations to come. The FDA has committed to the Vice President to build on these recommendations through a bottom-up review, which will more fully include font line FDA personnel. I anticipate additional regulatory reforms being produced from this process by no later than June.

The report is being released in conjunction with Commissioner David Kessler's testimony today before the Senate Labor and Human Resources Committee. The regulatory reform review process and the product it has produced has been and will be referenced as a joint White House/FDA effort.

Yesterday we briefed Congressional staffs of relevant Committees, representatives of drug and biotech manufacturers, device manufacturers, and consumer groups. Almost universally, the Administration is being praised for this initiative. While the industry will still push for more, the relationships with the Administration and the FDA have improved markedly. The report also seems to position the Administration and the FDA well for the upcoming and inevitable debate on the need to reform -- but not to undermine -- the agency and its charge to assure that the drugs and devices on the market are safe and effective.

FYI, apparently the first AP story on this report is quite good for us. Attached for your information is a three page summary of the report. I hope these materials are useful.

FDA BACKGROUNDER

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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Reinventing

DRUG & MEDICAL DEVICE

Regulations

PRESIDENT BILL CLINTON
VICE PRESIDENT AL GORE

APRIL 1995

REINVENTING

REGULATION OF DRUGS

AND MEDICAL DEVICES

President Bill Clinton
Vice President Al Gore

National Performance Review

April 1995

OVERVIEW

"Today, Americans don't have to worry about safety or effectiveness when they buy [drugs and medical devices]—from cough syrups to the latest antibiotics or pacemakers. The Food and Drug Administration has made American drugs and medical devices the envy of the world and in demand all over the world. And we are going to stick with the standards we have—the highest in the world. But strong standards need not mean business as usual in every area."

President Clinton — March 16, 1995

Introduction

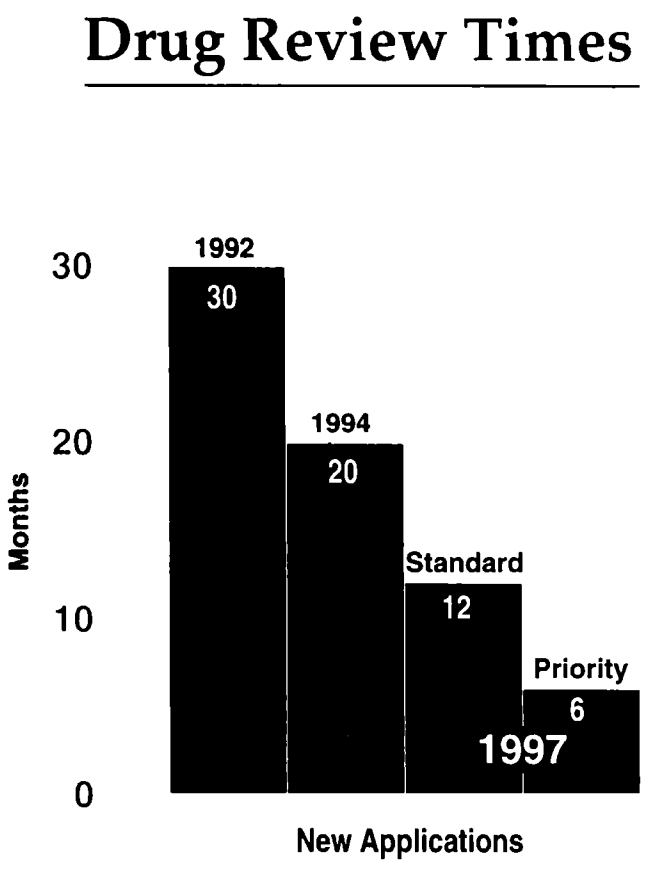
Reforming the Federal government's regulatory processes, while maintaining critical public health and safety standards, has been and will continue to be a top priority for the Clinton Administration. Consistent with this commitment, President Clinton and Vice President Gore asked Health and Human Services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

As part of the Vice President's reinventing government initiative, 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 the review of drug and medical device regulation.

Background

FDA 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 annually oversees more than $1 trillion worth of products, which account for 25 cents of every dollar spent 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 additional authority over medical devices. During this Administration, FDA has taken significant initial steps to streamline the regulatory process. These recent initiatives, building on earlier reforms to ensure access for patients to new drugs and to accelerate approval of treatments for life-threatening illnesses, 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. This law authorizes FDA to charge user fees for 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.[1] By 1997, FDA will be getting these products to market in a year or less, as fast as 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, resulting in a record number of 38 new drugs approved in 1994.

Eliminating Unnecessary Regulatory Burdens

1) 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) 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 FDA to implement the requirements of the 1992 law quickly and with minimum burden on accredited and certified facilities.

3) FDA has begun a joint program with the Customs Service to automate the entry of imported products into the United States. The program allows an importer to notify FDA by computer of import entries and receive prompt permission for the products to enter this country.

4) FDA has issued a proposed regulation to permit regulated companies to use electronic records and signatures in place of paper. This will save industry substantial costs by simplifying record-keeping and speeding the filing of applications and other regulatory documents.

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

[1] The 1994 *median* review time for all new chemical drugs was 17.5 months; (the subset of drugs reviewed in 1994 under the user fee program was reviewed in a median time 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. It looked for ways to eliminate these burdens so that its regulatory systems would not be a bar to bringing beneficial new products to market. In reforming its procedures and requirements, FDA followed these 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 public health; and
- **Utilizing modern automated technology** as a tool in streamlining internal Agency management and as an aid to industry in meeting its 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 toward expediting market access of new products:

- **Reducing or eliminating** many of the FDA requirements for companies to get approval for changes in their manufacturing facilities or processes for manufacturing drugs, biotechnology drugs, and other biologics;
- **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 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 eliminating nearly 700 pages of Federal regulations);

- **Excluding** drug and biologic manufacturers from requirements for most environmental assessments, which currently cost tens of thousands of dollars each time a new product is developed yet provide no real benefit to the environment;

- **Exempting** nearly 125 additional categories of low-risk medical devices from premarket review;

- **Eliminating the "Reference List" by clarifying** that market clearances of 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 and that a single, multi-center study may support approval of a drug;

- **Harmonizing** FDA's drug and device testing 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 reviewing new products and speeding up import entries.

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

FDA'S PROPOSALS FOR REFORM

Drugs

New drugs must be approved by FDA prior to marketing. Under the provisions of the Federal Food, Drug, and Cosmetic Act, they are tested first in animals, then in humans, and the data are submitted to FDA scientists for review via a New Drug Application. Biologics include vaccines and blood products, and drugs made using biotechnology. They are licensed under a different legal authority from drugs, and are therefore subject to somewhat different requirements. Before marketing a new biological product, the sponsor must submit for FDA's approval a Product License Application, which presents safety and efficacy data. The facility making the product must submit an Establishment License Application demonstrating that the product can be accurately and safely manufactured.

Although full marketing of drugs must await FDA review and approval, in recent years the Agency has established ways for patients to gain early access to treatments for life-threatening diseases.

FDA also approves such changes as substituting different ingredients by reviewing a "supplement" to the original application for approval.

This section of the report describes reforms in the regulation of biologics and drugs. The reforms include: permitting biologics manufacturers to demonstrate their capability to make the product without first building a full-scale production plant; changing biologics labeling requirements to remove an impediment to flexible manufacturing, packaging, and distribution arrangements; allowing manufacturing changes for both drugs and biologics to be made with less FDA prior approval; eliminating certain manufacturing requirements concerning antibiotics and insulin; and eliminating most environmental impact assessments for both biologics and drugs.

Drugs and Biologics: Eliminating Many Requirements For FDA Approval of Manufacturing Changes

Background: FDA regulations governing drugs and biologics require applicants to obtain FDA approval before implementing many manufacturing changes for those products. To obtain approval, manufacturers submit "supplemental" applications to FDA, of which the Agency receives several thousand each year. These changes range from the addition or subtraction of an ingredient, to the use of a different production facility or different equipment within the same facility, to changes in packaging. Manufacturers must often wait six to twelve months to receive FDA approval, during which time the manufacturers are prevented from making changes to the product or production facility that they believe are more efficient or otherwise necessary.

Proposal and Justification: ***FDA will reduce the number of changes that require pre-approval.*** Described below are the procedures for implementing this new policy for drugs and biologics.

DRUGS

FDA's Center for Drug Evaluation and Research (CDER), the Agency component responsible for oversight of human drug products, is developing a guidance document for drugs in tablet and capsule form (other than those for controlled release). This document, designed to ease pre-approval requirements for certain manufacturing changes, would distinguish changes that are unlikely to have any detectable impact on a drug product's quality and performance from those that could have a significant impact. Examples of changes unlikely to have an impact include the deletion of a color from a product or changes from non-automated or non-mechanical equipment to automated or mechanical equipment for moving ingredients. The proposed FDA guidance would ease the pre-approval requirements for these and other manufacturing changes when the proposed manufacturing change does not affect the drug's quality or performance.

In all instances in which prior approval would no longer be required, FDA would still receive notification of the manufacturing changes from the drug manufacturer, either when the change takes effect or through annual reports on the drug application.

BIOLOGICS

The Agency will create a reporting process tailored to the severity and complexity of the change. Less

stringent reporting requirements will apply when the changes do not pose demonstrable effects on product purity, potency, or safety — or when changes are readily amenable to on-site scrutiny during routine inspection of the production facility. FDA will classify its oversight of manufacturing changes for biologics as follows:

Category I: Changes where no supplement submission will be required. The sponsor will generate and retain all relevant data defining (and validating, if necessary) changes being made. The firm may voluntarily notify the Agency of the changes and dates of implementation.

Examples: Changes in the supplier of components (such as stoppers, vials, seals) that meet established specifications; changes which tighten existing specifications to provide greater assurance of product purity and potency; relocation of equipment in appropriate areas within approved facilities.

Category II: Changes for which the sponsor submits a standard supplement; unless the Agency objects, the sponsor can automatically implement the change in 30 days.

Examples: Expansion of existing manufacturing support systems (such as heating, ventilation, and air conditioning); modification of an approved manufacturing area which does not adversely affect safety, purity, or potency of product (such as adding new interior partitions or walls to increase control over the environment or replacing or adding new surfaces to enhance cleaning); replacement of equipment with that of similar but not identical design and operating principle that does not change the manufacturing process.

Category III: Changes requiring Agency approval prior to implementation.

Examples: Change in processing conditions (such as process time, process temperature, or filtration process); change in dosage form (such as a change from a liquid to a powder); extension of dating period; use of a previously unapproved manufacturing area or facility.

Impact: These changes will benefit industry by: (1) saving resources that would have been spent on preparing supplemental applications; (2) permitting changes to occur without waiting for prior FDA approval; and (3) encouraging certain manufacturing improvements. Under the new procedures, the manufacturing site changes described above for drugs could be carried out—and the new site could begin operating—in a matter of weeks, and with significant cost savings. And the new policy will permit a drug manufacturer to change automated equipment without prior FDA approval, an improvement that will make newer facilities and equipment available to manufacturers much more quickly. Similar changes for biologics manufacturers will speed their ability to make changes in production facilities or make other manufacturing improvements.

FDA will also benefit from these changes. The Agency estimates that this reform will eliminate its current review of more than 800 supplemental applications for drugs and 500 for biologics annually[2].

Implementation and Timeline: For **drugs**, by the end of the year FDA will issue guidance for most products sold in tablet form that will describe how these requirements will be relaxed. By the end of 1996, FDA will develop a similar guidance document for other dosage forms, including controlled release drugs, liquids, and semi-solids.

For **biologics,** FDA will immediately issue a guidance document to implement the new three-category plan. The document will identify the types of changes in manufacturing procedures and establishments that may be carried out without prior approval. It will clarify which changes will not require a supplement at all. Within nine months, in a second step, FDA will propose amending its regulations to further reduce the instances requiring its approval before products may be marketed. Likewise, the Agency will review its policy on lot release of some biologics (i.e., a procedure whereby the Agency approves each batch of biologics prior to distribution), to determine how those burdens can be minimized as well.

[2] For biologics, approximately 25 percent of supplemental applications (250 a year) will fall into Category I, 25 percent (250) will fall into Category II, and 50 percent (500) will fall into Category III.

New Policy to Permit Use of Small-Scale and Pilot Facilities During Development of Biologics

Background: Lack of clarity about establishment licensure requirements has led some biologics manufacturers to make major capital investments in full-scale manufacturing facilities before initiating the large clinical trials necessary to demonstrate the safety and efficacy of their products. Such investments can result in significant financial losses if the product is not ultimately brought to market.

Proposal and Justification: ***FDA will specifically state that manufacturers may use pilot and small-scale facilities to demonstrate safety and effectiveness and to support approval.*** Under this reform, companies may immediately submit applications for clinical studies or approval of products manufactured in small-scale or pilot facilities.

Although the manufacture of biologics warrants a high degree of quality control and regulatory oversight, FDA believes that licensure of pilot and small-scale facilities provides industry with the flexibility it needs without diminishing public health protection. As a result, FDA will issue product and establishment licenses on the basis of demonstrated safety, purity, and potency of the product manufactured in the pilot or small-scale facility. Moving to a full-scale facility will require only a supplement to the manufacturer's product/establishment license applications.

Impact: Of 1,500 active and pending investigational new drug applications (INDs) (the manufacturer's application to begin testing a drug product in humans) for biologics, 100 to 500 current applicants need to decide whether to construct new facilities. Under this reform, a significant number of these companies may choose not to construct a new full-scale manufacturing facility. Instead, they may decide to use a pilot or small-scale facility, with potentially great cost savings. It has been estimated to cost $25 million to construct a biologics manufacturing facility, and about $15 million a year to operate it.

Implementation and Timeline: Companies may apply immediately for licensure of small-scale and pilot facilities and their applications will be considered. FDA will issue a guidance document to clarify its policy on licensing small-scale and pilot facilities within the next three months.

Revision of Labeling Requirements for Biological Products

Background: Companies that develop a product sometimes find it advantageous to have their product manufactured by another company. Many small start-up companies, such as many biotechnology firms, prefer this option because they do not always have the manufacturing capabilities necessary to produce commercial quantities of a drug. However, FDA's current labeling regulations are a disincentive to such arrangements: The manufacturer's name must be displayed on the label more prominently than that of the developer (which can be listed only as a selling agent or distributor).

Proposal and Justification: ***FDA will allow the distributors' and selling agents' names to be displayed prominently on biological product containers, package labels, and labeling.*** This change will provide the biological products industry with the flexibility that it wants, and, at the same time, maintain current label information on product manufacture and origin.

Impact: The change in labeling requirements will allow prominent display of the name of the distributor or selling agent, thereby removing an impediment to flexible manufacturing, packaging and distribution arrangements.

Implementation and Timeline: FDA will publish a proposal to revise its biologics labeling regulations within six months.

Antibiotic and Insulin Standards and Insulin Certification

Background: Section 506 of the Federal Food, Drug, and Cosmetic Act requires FDA to certify individual batches of drugs containing insulin as meeting the standards of identity, strength, quality, and purity that are described by FDA regulations.

Section 507 of the Act imposes similar requirements for antibiotic drugs. The regulatory specifications for antibiotic drug products occupy almost 700 pages in the *Code of Federal Regulations.*

Antibiotics and insulin are subject to more stringent requirements than those applied to other drug products. For example, section 505 of the Act, which applies to most human drugs, does not require FDA to certify individual batches of drug products or to issue product specifications prescribed in regulations. Moreover, in some cases, the insulin and antibiotic regulations known as "monographs" are outdated, reflect old technology or methodology, prescribe standards for products that are no longer marketed, or conflict with the standards found in the United States Pharmacopeia (USP). The USP, a compendium of standards of strength, quality, and purity for drug products, is published by the United States Pharmacopeial Convention, a private entity. Because the FDA can change its standards for insulin and antibiotic products only by regulation, the USP standards are often more up to date. The existence of conflicting standards can be confusing to the industry and to FDA staff who must determine whether a particular product meets the correct specifications.

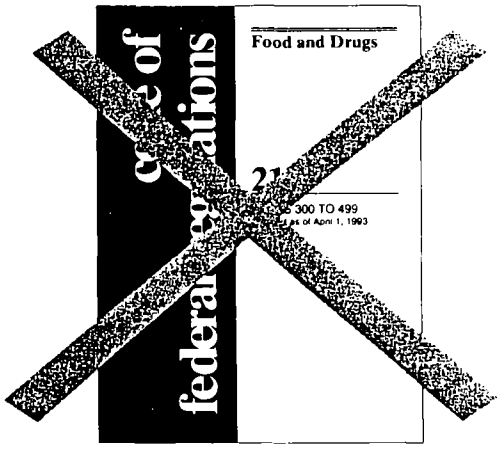
Proposal and Justification: ***FDA proposes to support the repeal of the certification requirement for insulin.*** Congress enacted this statutory requirement decades ago, when insulin products were new and manufacturing and testing technology was rudimentary. Since then, the Agency and industry alike have become much more sophisticated and experienced with insulin manufacturing, so that certifying each batch of insulin is no longer necessary. Moreover, only two firms currently market insulin in the United States, and in the past 8 years FDA has found no failures in more than 500 batches of insulin that it has tested for certification purposes.

FDA also proposes to support the repeal of the statutory requirements for the FDA monographs that are now issued for insulin and antibiotics. In the 1940's, when Congress enacted those sections of the Federal Food, Drug, and Cosmetic Act, detailed regulations setting forth standards and tests were thought to be necessary to ensure the quality and the safety of these products. At that time, Congress also expressly recognized, at least with respect to antibiotics, that a time would come when manufacturing technology would overcome the need for such detailed regulation and that the manufacturing controls used for chemically synthesized drugs would suffice for antibiotics as well.

FDA also supports the repeal of the statutory provisions which provide for the certification of antibiotic drugs. The ability to control antibiotic drug quality is also well-established. For example, a GAO study published in 1981 reported that from 1977 through 1980, less than one percent of all antibiotic products did not comply with monograph standards. FDA therefore concludes that the additional controls are no longer necessary to ensure the safety and efficacy of antibiotic drug products.

The Agency therefore proposes to regulate the approval of new insulin and antibiotic drug products, and generic antibiotic drug products, much as it does for other human drug products. Concerning tests and methods of assay, the USP will maintain the standards for insulin and antibiotics in the same way that it maintains such standards for other drugs.

Antibiotic and Insulin Standards/Certificates



Eliminate 700 Pages

Impact: Under this reform, insulin manufacturers would no longer be required to submit applications and samples to obtain batch certification. And because the insulin industry is subject to certification fees under section 506 of the Act, the change would eliminate those fees.

Eliminating the statutory requirement for FDA to issue antibiotic monographs that set forth product standards, tests, and methods of assay for particular drugs would benefit antibiotic drug product manufacturers. This change would eliminate the confusion created by actual and potential differences between FDA regulatory standards and the USP.

Eliminating the regulations specifying insulin and antibiotic drug standards and tests will remove nearly 700 pages from the *Code of Federal Regulations.*

Implementation and Timeline: The Administration will promptly propose legislation to repeal section 506 of the Act (which pertains to insulin) and to repeal section 507 of the Act (which pertains to antibiotic drug products). FDA would seek to have both insulin and antibiotic drug products regulated under section 505 of the Act.

Environmental Assessments for Human Drugs

Background: The National Environmental Policy Act (NEPA) requires all federal agencies, including the FDA, to assess the environmental impact of their actions which may significantly affect the quality of the human environment. A drug cannot be approved unless the manufacturer has submitted an acceptable Environmental Assessment (EA). On the basis of FDA analysis of the EA, the Agency can either issue a "finding of no significant impact" (FONSI), or decide that a full environmental impact statement (EIS) must be prepared. Preparation of an EA is usually quite expensive; yet, in virtually every case, FDA issues a FONSI.

Each year, the pharmaceutical industry submits approximately 50 to 60 full EAs and about 50 abbreviated EAs to CDER. Pharmaceutical firms also send 20 to 25 EAs annually to the Center for Biologics Evaluation and Research (CBER), some in abbreviated form. It can take up to 6 months to review an EA, obtain additional information from the firm to correct any deficiencies, and issue a FONSI.

And yet, in recent years, FDA has identified only one product, Taxol, as presenting any potentially significant environmental concerns. In the case of Taxol, the environmental impact was due to harvesting of Pacific yew trees, an endangered species. In Taxol's case, CDER incorporated by reference the EIS prepared by the U.S. Forest Service to address the resource question; the manufacturing process and use were addressed through the routine EA and were found to have no significant impact.

Proposal and Justification: ***FDA proposes to increase the number of categorical exclusions from the EA and EIS requirements.***

FDA proposes to reduce the number of EAs required to be submitted by industry and, consequently, the number of FONSIs prepared by the Agency under NEPA by increasing the number of categorical exclusions based upon little or no impact on the environment from the use of the drug. Based upon its experience to date in reviewing environmental assessments, FDA believes that nearly all product approvals will qualify for categorical exclusion. For example, virtually all drug approvals would result in only minute releases of the drug into the environment as a result of human use and such releases would not be environmentally significant. FDA procedures will provide for extraordinary circumstances in which a normally excluded action may have a significant environmental impact—circumstances that would require at least an EA. Taxol is an example of such an extraordinary circumstance.

Impact: These changes will substantially benefit industry and will improve regulatory efficiency

without having any adverse impact on public health or the environment. Industry would save from $40,000 to $150,000 on each EA.

Implementation and Timeline: These changes will be implemented by amending FDA regulations, in consultation with the President's Council on Environmental Quality (CEQ), to increase the number of categorically excluded actions for which an EA or EIS is not required. New regulations will be proposed in consultation with CEQ in six to nine months. Policy guidelines clarifying current procedures will be published sooner.

Medical Devices

There are three classes of medical devices. Class I devices, such as tongue depressors, are subject only to general regulatory controls and receive little Agency oversight. Class II devices, such as infant incubators, are subject to special controls, such as performance standards, to ensure their safe and effective use. Class III devices, such as implantable pacemakers, are generally life-sustaining or life-supporting, are implanted in the body, or present potential unreasonable risk of illness or injury.

New devices enter the market in one of two ways: (1) through a premarket notification process, known as a "510(k)" because it is authorized under section 510(k) of the Federal Food, Drug, and Cosmetic Act; and (2) through a more extensive premarket approval application (PMA).

Under the 510(k) process, FDA must determine whether a device is "substantially equivalent" to a device that is already legally marketed. A manufacturer using the premarket notification process informs FDA about the device and why any changes in its device can be made safely. (Some low-risk devices have been exempted from premarket notification.) If FDA finds the device to be "substantially equivalent," the manufacturer may market the device and must then comply with good manufacturing practice (GMP) requirements to ensure that the device is properly made. More than 90 percent of all devices enter the market under the premarket notification process. The more extensive premarket approval application is targeted toward Class III devices.

The reforms below are: additional exemptions from premarket notification; elimination of the current reference list program, which links GMP inspections to new device approvals, and its replacement by a process that focuses on serious GMP problems and how they may be applicable to individual premarket notification actions; a pilot program for external review of new devices; and, a user fee program to speed device approvals.

Medical Device Exemptions from Premarket Notification

Background: Currently, the Federal Food, Drug, and Cosmetic Act requires that manufacturers of most medical devices submit information to FDA and receive FDA clearance before putting a device on the market, even if the device has an extremely low risk. Review of low-risk devices is not necessary to protect the public health, places an unnecessary regulatory burden on device manufacturers, and delays introduction of new devices.

FDA currently regulates about 1,700 types of medical devices. Of these, 441 categories of low-risk devices (such as stethoscopes, hernia supports, and surgical microscopes) have already been exempted from the requirement of premarket notification, including 148 exempted in December 1994.

Proposal and Justification: ***FDA will exempt up to an additional 125 medical device categories from premarket notification requirements. As a result, about 570 categories, or one-third of all categories of devices, will be exempt from premarket notification requirements.***

Public health will not be compromised by the exemption of these devices from premarket review. These devices will reach the market sooner and will remain subject to good manufacturing practice requirements, which include regular factory inspections, record keeping and device problem reporting. (Of course, continuation of an exemption is dependent upon a safe marketing history, and exemptions can be revoked if safety problems are later identified; a review of whether these exemptions should be continued, or others added, will be conducted in two years.)

Impact: The device industry will no longer have to prepare and submit—and the Agency will not have to process and review—510(k) premarket notification submissions for the exempted device categories. FDA receives about 700 submissions each year for devices in these 125 categories and will be able to redirect the resources for the review of these products to more complex products.

Implementation and Timeline: FDA device advisory panel chairs are now reviewing the proposed exemptions. The majority of the device categories are currently in Class II and, under the law, must be reclassified to Class I before being exempted from FDA review. By June 1995, FDA will propose to reclassify these devices from Class II to Class I and to exempt them from premarket notification requirements.

Elimination of the Reference List

Problem: Under a program known as the "Reference List," FDA tracks medical device manufacturers found by FDA field inspections to have serious GMP violations. GMP violations are flaws in the manufacturing process that have the potential to affect the safety or efficacy of the product. If a firm is on the list, FDA may defer authorization for the firm to market a new product under section 510(k) of the FD&C Act.

The basis for placing a firm on the list has been an inspectional finding of serious GMP problems. In issuing the manufacturer a warning letter about its GMP violations, FDA has advised the manufacturer that the Agency may not give marketing clearance to pending applications until the violations are corrected. A company is removed from the list only after FDA has re-inspected the firm and found that all serious GMP violations have been corrected. This process can take up to 6 months.

Industry has criticized the list as not needed to protect the public health. Industry views the list as a "blacklist" because it feels that the Agency does not make clear which firms are placed on the Reference List or when they are removed from it. Moreover, because it takes time to re-inspect after violations are found, manufacturers may be delayed in marketing their products.

Proposal and Justification: ***FDA will eliminate the Reference List and instead focus attention on the appropriate linkage between serious GMP deficiencies and individual pending 510(k) applications.*** FDA will also clarify that market clearances of Class I and II devices will not be deferred unless FDA finds a reasonable relationship between the nature of the current GMP violations and the application under review. A reasonable relationship will be found only if there are GMP violations that are directly related to the product under review or if there are systemic violations that are generally applicable. FDA will not defer 510(k) applications if no such reasonable relationship is found.

Second, if market clearance of a 510(k) is deferred because of GMP violations, FDA will either reinspect the firm within 60 days after being notified that corrective actions have been taken, or clear the 510(k) application without a reinspection.

Finally, FDA will prepare clear written policies and procedures so that companies will know if they have an outstanding GMP violation, will understand when their 510(k) applications may be held up due to GMP violations, and will know the procedures to follow to correct the problems and obtain marketing clearance.

Impact: The proposed changes benefit industry by providing assurance that no market clearance will be deferred unless a clear linkage between GMP violations and the device under review is found. In addition, by clarifying FDA's procedures, any industry fear of indiscriminate delay in the clearance of a 510(k) application will be eliminated. Finally, the fixed time frame for reinspection benefits manufacturers by removing uncertainty about when they will be able to market their products after they correct GMP violations.

Implementation and Timeline: The Agency will implement these new policies and procedures by publication of a notice in the *Federal Register* by May 1995. FDA will immediately review all deferred applications to determine if the GMP violations are reasonably related to the pending applications. Firms with GMP violations unrelated to the pending applications will have their applications cleared unless there are other problems.

Medical Device External Review Pilot Program

Background: Almost all medical devices enter the market by an application process in which the manufacturer demonstrates that the device is "substantially equivalent" to a device already marketed. The device industry contends that this process inhibits innovation and competitiveness because, due to limited resources, FDA takes too long to review these applications. (A comprehensive assessment of FDA's device review resource needs, conducted by FDA and audited by the device industry, documented an annual shortfall of about $24 million and more than 200 staff positions.)

Industry recommends that FDA adopt an approach similar to that used in the European Community, in which device firms have their device applications reviewed by a third-party scientific organization accredited by the government. Under this approach, a manufacturer pays a third-party organization for its review, the third-party organization notifies the government of the results of its review, the device is marketed without government review, and the government monitors the device after it is on the market for subsequent safety problems. This concept has not been tried in the United States, so its applicability in this country is unknown.

Proposal and Justification: ***FDA proposes to create a pilot program for external reviews of devices.*** This pilot program will contain several key elements of the European model to test whether that model is appropriate for the United States. The program will have the following elements:

- At least ten categories of devices, comprising at least 100-400 device applications annually, will be identified for eligibility in the program;
- Those categories of devices will have a low to moderate risk profile, clear standards for market clearance, and no requirement for clinical data as part of their application (e.g., applications which principally raise engineering issues);
- The outside reviewers will be accredited by FDA as capable of assessing the design, performance, and safety of devices;
- The accredited review organization will be responsible for conducting the entire review of the device application, producing a written review document, and making a recommendation to FDA. The review will be checked by FDA, and the final decision will be made by FDA and communicated to the company;
- The program will be funded by the manufacturer's payment to the reviewer for its services.

Participation by manufacturers will be voluntary; and

- The accredited reviewing organization will be expected to demonstrate independence from device manufacturers for whom it will be doing reviews and adherence to conflict of interest standards.

Impact: The pilot program will allow FDA and the device industry to determine the feasibility of third-party reviews of devices. It will answer questions such as whether private groups can conduct a thorough, rapid review; whether such groups exist or will need to be created; whether safeguards against improper influence of non-government reviewers can be established; and how much groups will charge for these services.

Implementation and Timeline: The pilot program will begin early in the next fiscal year. The pilot program will operate for two years, and during the second year FDA will evaluate its success and potential for expansion and permanent continuation.

Device User Fees

Background: Even if the medical device external review pilot program and other streamlining efforts detailed in this report are successful in reducing resource demands upon FDA's device program, the Agency will still lack sufficient resources to ensure timely review of device applications. Each year, FDA receives approximately 40 to 60 Premarket Approval Applications (PMAs), 400 PMA supplements, and 6,000 premarket notification actions for marketing devices under section 510(k) of the Federal Food, Drug, and Cosmetic Act. In fiscal year 1994, the average review times were about 2 years for PMAs, 1 year for PMA supplements, and 215 days for premarket notifications[3]. Compare that to fiscal year 1990, when the average review times were 10 months for PMAs, 6 months for PMA supplements, and 100 days for premarket notifications. These lengthy review times delay the introduction of devices to the market. FDA can reduce these review times, without diminishing the public health protections it provides, if it has adequate resources to review applications.

Proposal and Justification: ***FDA proposes to authorize user fees for applications.*** FDA will collect fees for reviewing PMAs, PMA supplements and premarket notification actions — 510(k)s — and dedicate them to funding premarket review and related activities. In addition, FDA will commit to specific performance goals.

FDA will agree to performance goals of (1) eliminating the backlog of applications within 24 months; (2) completing a comprehensive, substantive review for 90 percent of PMAs in 180 days; and (3) taking a final action on 95 percent of 510(k)s in 90 days. These performance goals were negotiated with the industry as part of legislation proposed last year, and major segments of the device industry supported them.

Impact: The proposed solution will address a major complaint about federal premarket review times for devices. The device industry will benefit from increasingly faster review and approval times, will be able to market new and innovative products faster, and will become more competitive in foreign markets. Consumers inside and outside the United States will benefit from easier access to new and improved products.

Implementation and Timeline: User fees will require statutory changes to the Federal Food, Drug, and Cosmetic Act. The Administration has proposed these changes in the budget for fiscal year 1996.

[3] However, premarket notifications, which have been the most controversial, were down to a median time of 98 days as of January 1995.

Device user fees would account for $23,740,000 of the Agency's budget for the entire fiscal year, and the funds would include associated start-up costs and the hiring of over 200 staff people over the first two years.

Cross-Cutting

Several issues confronting FDA cut across product lines and affect both the pharmaceutical and medical device industries. Two such issues involve exports. One of them is the different mandatory requirements that the Agency must follow in approving exports of drugs and medical devices. The other export issue stems from the varying standards for regulated health care products in the United States and in many of its trading partners. FDA plans to ease some of the current export restrictions. Also, the Agency will intensify its efforts to bring into harmony international standards for health care products, so that firms developing new products will have to deal with only one set of requirements.

Another issue raised by both the drug and device industries is whether FDA requires new products to be shown to be superior, as opposed to equal, to products that are already on the market. An upcoming policy statement will clarify the Agency position. FDA also proposes to take steps to advance the development of an electronic information system to support the review processes, and to implement the second phase of an automated system for the processing of imports.

Drug and Device Exports

Background: Drugs and medical devices not approved for sale in the United States are now exported under different statutory requirements.

Drugs may be exported only to the 21 developed countries listed in the statute if, among other things, (1) the sponsor has an investigational new drug (IND) exemption in effect that permits testing in humans, and (2) the drug is approved in the importing country.

Devices may be exported if FDA determines, based on information supplied by the exporting company, that (1) export of the device does not harm public health and safety, and (2) the device is approved for importation by the importing country.

Manufacturers have contended that these requirements place them at a competitive disadvantage and that FDA review of exportation to foreign countries is both time-consuming and unnecessary.

Proposal and Justification: ***It is proposed to allow the export of drugs to any of the countries listed in the statute without an IND.*** In addition, the Administration proposes to work with Congress on changes in the current law based on an examination of whether to amend the present list of 21 countries, and whether to adopt other changes.

FDA proposes two new criteria for allowing devices not approved in the United States to be exported for marketing abroad without prior FDA permission: (1) devices can be exported to advanced industrialized countries (the list of which would be determined in consultations with Congress) if the devices conform to the importing country's laws; (2) devices can be exported to countries not on the above-mentioned list if the exporter has an Investigational Device Exemption (IDE) permitting testing on humans in the United States, the importing country has given FDA a letter providing blanket import approval for IDE-type devices, and the device is in compliance with the importing country's laws.

This change from current procedures would significantly relax restrictions on exports to industrialized countries, while leaving intact existing protections for countries that are not industrialized.

Impact: For drugs, companies will be able to export their products for marketing in the 21 developed countries listed in current law, even if they do not have an IND in the United States.

For devices, exports to the most significant markets—industrialized nations such as Japan and the European Community—will be exempt from FDA's oversight. The U.S. industry will be spared the expense of developing and submitting export requests to FDA and would not need to await FDA review, which now averages 16 days but can take as long as 150 days. Furthermore, a firm with an approved IDE will be able to export the unapproved device to less developed countries which have agreed to such importation, without going through FDA review, currently averaging 10 days. The U.S. device industry believes that these changes will encourage firms to remain in the United States rather than moving their operations abroad. FDA could redirect the resources used for the current export approval program to more pressing public health matters.

Implementation and Timeline: Discussions with Congress on both drug and device legislation could begin immediately. Permitting devices with an IDE to be exported without further FDA clearance to countries which have provided prior agreement can be accomplished administratively by FDA, and proposed regulations will be issued within 4 to 6 months.

Effectiveness of Drugs and Devices

Background: The pharmaceutical and medical device industries have argued that FDA requires a new drug or Class III (highest risk) device to be shown to be more effective for its intended use than comparable therapies that are already approved for marketing. Representatives of these industries believe FDA's requirements for demonstrating efficacy present unreasonable difficulties in developing new therapies and bringing them to market.

Proposal and Justification: ***FDA proposes to issue a public statement to respond to this concern.*** The statement will make the following points:

Under the Federal Food, Drug, and Cosmetic Act, new drugs and Class III devices must be shown to be safe and effective for their intended uses. In evaluating the safety of a new drug or Class III device, the Agency weighs the demonstrated effectiveness of the product against its risks to determine whether the benefits outweigh the risks. This weighing process also takes into account information such as the seriousness and outcome of the disease, the presence and adequacy of existing treatments, and adverse reaction data.

In evaluating effectiveness, as with safety, FDA reviews new drugs and Class III devices on their merits. The Agency does not require new drugs and Class III devices to be more effective than therapies for the same disease or condition that are already approved for marketing. In general, both new drugs and Class III devices must be shown to be effective through evidence consisting of well controlled investigations that provide a basis on which it can be concluded that the drug or Class III device will have the effect it is represented to have.

For the majority of new drugs and Class III devices, i.e., new products intended to treat less serious illness or provide relief from symptoms, a showing of effectiveness is usually based on a clinical trial comparing the product to a placebo. Such a showing does not involve a comparison to any other product.

In certain circumstances, however, it may be important to consider whether a new product is less effective than available alternative therapies, when less effectiveness could present a danger to the patient or to the public. For example, it is essential for public health protection that a new therapy be as effective as alternatives that are already approved for marketing when:

1. the disease to be treated is life-threatening or capable of causing irreversible morbidity (e.g., stroke or heart attack); or

2. the disease to be treated is a contagious illness that poses serious consequences to the health of others (e.g., sexually transmitted disease).

It should be noted that new products are often developed for particular subpopulations who either do not respond to or are not able to tolerate an existing approved therapy. FDA will generally approve for use in such a subpopulation a product that is shown to have effectiveness in this group, regardless of whether the product can be shown to be as effective in the broad target population as the alternative therapy. This is because, in effect, there is no available alternative therapy for the subpopulation. For example, a number of patients cannot tolerate a widely used therapy for an AIDS-related pneumonia. FDA approved the drug atovaquone for use in these patients, even though it had been shown to be less effective than the standard therapy when tested in a broad population.

Impact: Placing such a statement in the public record would clarify for sponsors of drugs and Class III devices how FDA addresses and evaluates effectiveness in the context of overall review for product approvability. This clarification should be helpful to product sponsors in the planning and development of new products.

Implementation and Timeline: Within the next 3 months, FDA will publish a statement for comment in the *Federal Register.*

Additional Effectiveness Issue:

Industry representatives also argue that the Food, Drug, and Cosmetic Act should not be read to require multiple clinical studies when one pivotal study could suffice.

Clarification: FDA believes that a showing of effectiveness must be replicated to constitute an adequate demonstration of effectiveness for a new product. While a second study may well be needed to replicate results demonstrated in a first study, in some instances it is possible to replicate results within one large, well-designed multi-center study. It should be emphasized that this approach can be successful only when results are strong. A statistically marginal result, even in a very large study, cannot provide convincing evidence of replication.

The biotechnology drug Pulmozyme was recently approved to treat cystic fibrosis on the basis of one multi-center study with features that provided elements of replication. Similarly, the drug timolol was approved to treat people after a heart attack following a demonstration of improved survival in a single study. In that study, the favorable effect was seen in patients at several levels of severity at

three different hospitals. A simple multi-center double-blind placebo-controlled trial led to prompt approval of zidovudine for AIDS in 1987 when it was found that 16 deaths had occurred in the placebo group, as opposed to one death in the group receiving the drug. FDA has also approved vaccines, including a vaccine for hepatitis A, that have been studied for effectiveness in a single controlled multi-center study.

Harmonization of Standards

Background: Nations have differing requirements for approval of new drugs, biologics, medical devices, and animal drugs. This results in multiple tests on animals and humans and different applications for marketing approval. Nations also have differing standards for manufacturing practices and regulatory inspections. There is a substantial need to harmonize standards wherever possible, while retaining the United States' high level of public health protection.

Proposal and Justification: ***Seek common international standards.*** FDA will work with other countries, particularly the European Community, Japan, and North American Free Trade Agreement (NAFTA) partners, to harmonize product testing and development standards with those of the United States. Work has already begun on drug development and should be expanded to other areas of FDA regulation.

In addition, where appropriate, FDA will adopt international standards developed by multilateral or private-sector standards-development bodies.

Impact: Increased harmonization offers clear benefits for U.S. public health. It increases the safety and quality of imports into the United States. It can also improve the safety and quality of products sold in foreign countries and may help increase the availability of new products.

Harmonization benefits industry by replacing many different standards with one international standard that industry must meet. In the long run, this brings cost savings to industry and enhanced opportunities for export of U.S. goods, and may lessen the time needed to bring new products to market.

Harmonization permits FDA to make more efficient use of its resources, as other countries share the workload of developing new standards. Harmonization also may save future FDA resources by enabling cooperation with other countries in the assessment of new products. (However, it should be noted that a sizable up-front investment of FDA resources is needed to reach harmonization.)

Implementation and Timeline: FDA will build on and expand efforts to achieve international harmonization by:

1. Launching work on new harmonization topics in the testing of human drugs, biologics, and

devices related to clinical trials, biotechnology, medical terminology, and standards for the electronic transfer of regulatory information. Harmonized standards will be issued as guidelines for industry. Substantial progress on guideline development is expected within 2 years.

2. Accelerating work on harmonizing drug Good Manufacturing Practices, Good Laboratory Practices, and Good Clinical Practices standards and inspections. A number of proposals for harmonized guidelines should be completed within 2 years; however, harmonization of inspections will probably take longer.

3. Beginning an initiative to harmonize registration requirements for animal drugs. The first proposal for harmonized guidelines should be completed within 3 years.

4. Initiating work towards more harmonization with our NAFTA partners. Such harmonization efforts should become part of the work plans of existing technical working groups formed under the Canada/U.S. Free Trade Agreement.

Submission Management and Review Tracking (SMART) Program

Background: The current premarket review processes (preparation, handling, and storage of information related to product applications) are paper intensive with limited electronic means of accessing, sharing, or archiving product-related information within the Agency. Many applications consist of hundreds of volumes of detailed scientific information. The regulated industry is similarly affected by the need to generate an overwhelming amount of paper.

The Prescription Drug User Fee Act of 1992 (PDUFA) mandates significant reductions in the time required to review new drug applications. PDUFA funds the hiring of additional review staff to accomplish these goals. However, one of the longer term objectives is to improve the efficiency of the review process and to begin addressing ways to improve regulated industry's data handling efficiencies as well. FDA has begun to develop a comprehensive, standardized information management system (SMART) to support the review processes.

Proposal and Justification: ***FDA proposes to proceed with the development of SMART by pursuing a series of information systems pilot projects which will directly support FDA's meeting the near-term PDUFA goals.*** The Agency is already putting in place a system to identify, evaluate, and prioritize these pilots. A longer term SMART strategic plan has been developed that articulates how these pilots will serve as building blocks toward integrated drug development/review information management.

The pilots will focus on upgrading and interconnecting the hardware and software on the reviewer's desk; establishing standards; developing applications which will directly support the receipt, review, tracking, and archiving of industry submissions; and provide analytical tools to support the review process. This proposed approach will provide the most immediate benefit to shortened review times and will be funded with PDUFA fees.

Impact: The drug and biotechnology industries will continue to see progress in meeting the PDUFA review time goals. Through information systems design, the review processes will be clarified and managed for greater consistency, better documentation, and improved efficiencies. As standards are developed and implemented, the regulated industry will achieve greater internal efficiencies in its development and formatting of regulatory submissions and significant savings on paper record generation, handling, storage, and retrieval.

Implementation and Timeline: Over the next 12 to 24 months, FDA's drug review programs will complete the upgrade of reviewer hardware and software and networking capability, and develop and implement a number of automated applications (e.g., electronic Establishment Licensing Applications, electronic lot release testing, gene therapy patient registry, pre-approval inspections, and other pilots). The program offices will also begin selecting and implementing electronic data interchange standards which are acceptable to the regulated industry and to regulatory authorities in Europe and Japan.

Operational and Administrative System for Import Support (OASIS)

Background: FDA is responsible for ensuring that the imported products it regulates meet the same safety, efficacy, and quality standards as products produced domestically. Importers must have FDA clearance for each shipment before it can enter the United States. The number of imported shipments of FDA-related products has doubled in the 1990s to more than 2 million per year.

FDA's traditional process for clearing import shipments has required that importers prepare and submit a prescribed form, with invoices and any other documentation attached, for each shipment. FDA staff reviews the documentation, decides whether to admit the shipment in the country, and sends a paper response back to the importer. This paper process often takes days to complete, and delays in clearing shipments are a serious problem for importers. Reductions in government resources and increasing workload make it clear that FDA's traditional paper system for clearing imports must be improved. Automation of the process is essential.

Proposal and Justification: FDA has begun developing a phased information systems initiative to support automation of the import clearance process. Phase I was implemented nationwide in 1994. It operates in conjunction with the Customs Service, with which import brokers are already on line.

The new FDA system enables the import broker to enter additional FDA-specific data, which pass through a screening process that recognizes what the product is, country of origin, producer, and shipper. FDA has developed a set of decision criteria based on its experience with import risks and surveillance-sampling techniques to determine whether the shipment is admissible, or whether FDA needs to look at it more closely.

Within minutes, the broker receives a return message, advising either that FDA has cleared the shipment or that further examination testing is needed. Shipments in which FDA has no further interest can move immediately into commercial channels.

FDA will proceed with implementing Phase II of the Operational and Administrative System for Import Support (OASIS). Whereas Phase I automated the initial submission and screening of import data from import brokers, Phase II will automate FDA's internal handling of those import transactions requiring FDA review beyond the initial screening. The Phase II system will provide automated links between FDA laboratories and inspection and compliance units.

FDA will achieve national uniformity in tracking and enforcement of suspect products and a more rapid final response to brokers on import disposition. In addition, full implementation of the OASIS

system will permit electronic links with other FDA data bases that must be accessed during the import entry review process. For example, FDA must confirm that an imported drug has an effective NDA or an IND, that medical devices are approved and have been properly registered, and that manufacturers of low-acid canned foods have registered.

Impact: In February 1995, 67 percent of all shipments processed in FDA's electronic system received final clearance within minutes. Import brokers need not prepare and submit to FDA any paperwork for these shipments that are cleared electronically. Importers' costs for holding up shipments awaiting FDA clearance are reduced markedly. Perishable shipments no longer risk spoilage from clearance delays.

The American consumer is the major beneficiary. The freeing up of FDA resources that would have been required to handle and review the paperwork submitted by importers for all shipments allows the Agency to focus its attention on those shipments that may not conform to required standards. Implementation of the full OASIS system will speed the clearance of the one-third of shipments that require some form of FDA detailed review. FDA can target its resources on those import shipments that are suspected of not meeting quality requirements.

Implementation and Timeline: The full system will take several more years to complete, assuming funding is available. FDA is seeking user fees, to be paid by the importers, to fund full development and implementation of the OASIS system.

MEMORANDUM

TO: Carol Rasco
FR: Chris Jennings
RE: Today's release of FDA reg reform report
cc: Bill, Jeremy, Jen, Paul

April 6, 1995

This morning, the Administration is releasing the attached FDA regulatory reform report. It follows on the print shop event a few weeks ago in which the President released the EPA report and made references to a number of the FDA reform initiatives that are included in today's report.

The FDA report proposes numerous regulatory reforms that are estimated to save the drug and device industries at least $500 million per year in unnecessary regulatory costs and will also free up FDA to better target its resources toward improving and expediting market access of new products. The recommendations are significant, not only for their substance but because the Agency has committed to specific timetables for implementation. There will be additional recommendations to come. The FDA has committed to the Vice President to build on these recommendations through a bottom-up review, which will more fully include font line FDA personnel. I anticipate additional regulatory reforms being produced from this process by no later than June.

The report is being released in conjunction with Commissioner David Kessler's testimony today before the Senate Labor and Human Resources Committee. The regulatory reform review process and the product it has produced has been and will be referenced as a joint White House/FDA effort.

Yesterday we briefed Congressional staffs of relevant Committees, representatives of drug and biotech manufacturers, device manufacturers, and consumer groups. Almost universally, the Administration is being praised for this initiative. While the industry will still push for more, the relationships with the Administration and the FDA have improved markedly. The report also seems to position the Administration and the FDA well for the upcoming and inevitable debate on the need to reform -- but not to undermine -- the agency and its charge to assure that the drugs and devices on the market are safe and effective.

FYI, apparently the first AP story on this report is quite good for us. Attached for your information is a three page summary of the report. I hope these materials are useful.

FDA BACKGROUNDER

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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Reinventing

DRUG & MEDICAL DEVICE

Regulations

PRESIDENT BILL CLINTON
VICE PRESIDENT AL GORE

APRIL 1995

welcome ★ _____ mailed 6/28

THE WHITE HOUSE
OFFICE OF DOMESTIC POLICY

CAROL H. RASCO
Assistant to the President for Domestic Policy

To: JENKLEIN

Draft response for POTUS
and forward to CHR by: _____

Draft response for CHR by: _____

Please reply directly to the writer
(copy to CHR) by: X 6/27

Please advise by: _____

Let's discuss: _____

For your information: _____

Reply using form code: _____

File: _____

Send copy to (original to CHR): _____

Schedule ? : ☐ Accept ☐ Pending ☐ Regret

Designee to attend: _____

Remarks: _____

PLEASE respond to Assemblyman
on Dodd's behalf ASAP

✓cc: Dodd. Thanks

THE WHITE HOUSE

WASHINGTON

June 28, 1995

The Honorable Paul A. Tokasz
Member of Assembly
State of New York
General Donovan State Office Building
125 Main Street
Buffalo, NY 14203

Dear Assemblyman Tokasz:

I am writing in response to your letter of June 9 to Doug Sosnik, which outlined your concerns about the Food and Drug Administration's (FDA) oversight of vitamins.

I am pleased to inform you that most of the issues you raised have been addressed in recently enacted legislation. When the President signed into law the Dietary Supplement Health and Education Act (DSHEA), the burden of proof that a product is unsafe was shifted to the FDA so that the FDA must demonstrate that a product is unsafe before it can be removed from the market. The law also gives manufacturers flexibility. For example, statements about nutritional value may be made under certain conditions without preclearance and without subjecting the product to regulation as a drug. Further, materials produced by independent sources, such as health journals, may be used without the constraints that apply to labels, so long as certain content and presentation conditions are met.

Thank you again for your letter. I have taken the liberty of advising the FDA of your views. Please feel free to contact me with any further questions or concerns.

Sincerely,

Jennifer Klein

Jennifer Klein
Senior Policy Analyst

cc: The Honorable Doug Sosnik
The Honorable Carol Rasco

THE WHITE HOUSE

WASHINGTON

June 15, 1995

MEMORANDUM FOR CAROL RASCO

FROM: DOUG SOSNIK

SUBEJCT: ASSEMBLYMAN TOKASZ

Enclosed please find a letter from Assemblyman Tokasz.

As you can see he is concerned about potential FDA action affecting vitamins.

As you can imagine, I know nothing about this issue. I told him I forwarded the letter to your office.

Can someone please get him a response?

Thank you for your assistance

THE ASSEMBLY
STATE OF NEW YORK
ALBANY

PAUL A. TOKASZ
Assemblyman 143rd District

DISTRICT OFFICE:
General Donovan State Office Building
125 Main Street
Buffalo, New York 14203
(716) 852-2791
FAX (716) 852-2794

ALBANY OFFICE:
Room 727
Legislative Office Building
Albany, New York 12248
(518) 455-5921
FAX (518) 455-3962

CHAIRMAN
Committee on Election Law

COMMITTEES
Environmental Conservation
Higher Education
Local Governments
Transportation

June 9, 1995

Mr. Doug Sosnick
Assistant to the President for Political Affairs
Executive Office of the President, 2nd Floor, West Wing
1600 Pennsylvania Avenue, Northwest
Washington, DC 20500

Dear Mr. Sosnick:

As a Democratic elected official representing a district that voted Republican in the last State-wide election, I am concerned about any policy that adds to government.

The Food & Drug Administration has received a lot of publicity recently about Dr. Kessler's anti-vitamin crusade. This is just what we need - more regulations! Surely, There are enough life and death matters pending to keep the FDA busy.

At a time when the United States is losing its cutting edge in high-tech medical devices to Europe because of the lengthy approval process required by the FDA, I would think raiding health food stores for vitamins would be a low priority. Vitamins do not pose a health risk.

The President should point out this obvious fact to his FDA commissioner.

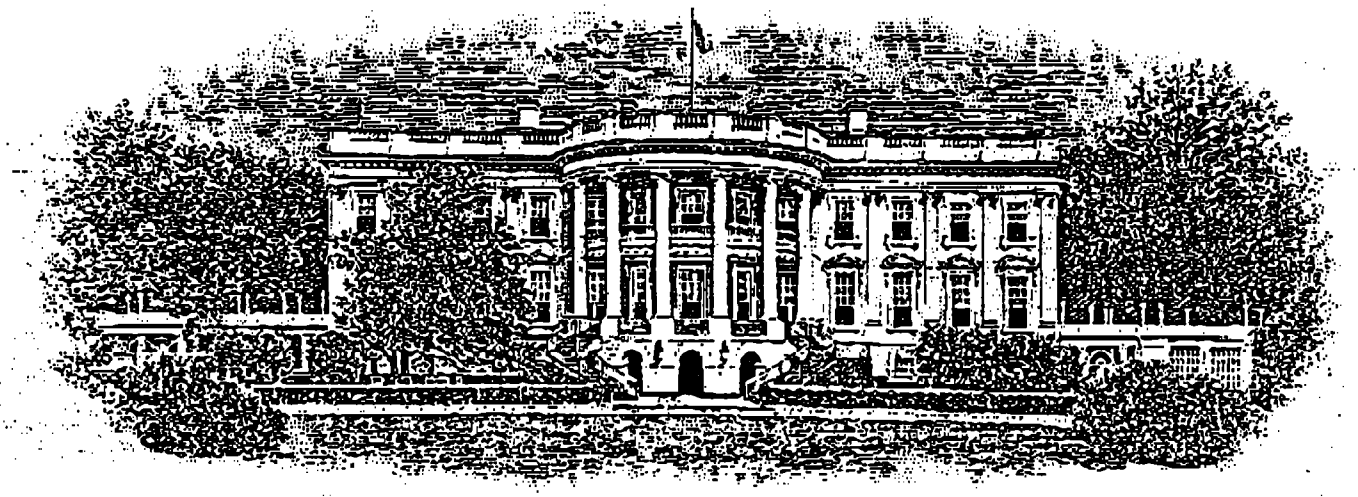
Sincerely,

Paul A. Tokasz
Member of Assembly

PAT\kab

cc: Mr. Leon Panetta, Chief of Staff to the President
Executive Office of the President, 1st Floor, West Wing
1600 Pennsylvania Avenue, Northwest
Washington, DC 20500

The White House



DOMESTIC POLICY

FACSIMILE TRANSMISSION COVER SHEET

TO: Jen Klein

FAX NUMBER: 6-2878

TELEPHONE NUMBER:

FROM: Chris

TELEPHONE NUMBER:

PAGES (INCLUDING COVER): 7

COMMENTS:

DRAFT – 3/30/95

REINVENTING

REGULATION OF DRUGS

AND MEDICAL DEVICES

National Performance Review

April, 1995

OVERVIEW

"Today, Americans don't have to worry about safety or effectiveness when they buy [drugs and medical devices]--from cough syrups to the latest antibiotics or pacemakers. The Food and Drug Administration has made American drugs and medical devices the envy of the world and in demand all over the world. And we should never forget that, either. And we are going to stick with the standards we have--the highest in the world. But strong standards need not mean business as usual in every area."

President Clinton, March 16, 1995

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-President's 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:

o ***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. This law authorizes FDA to charge user fees for 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.[1] 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. [APPROVAL CHART]

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.

o ***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.

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[1] The 1994 median review time for all new chemical drugs was 17.5 months; (the subset of drugs reviewed in 1994 under the user fee program were reviewed in a median time of 13.5 months).

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 a proposed regulation to permit regulated companies to use electronic records and signatures in place of paper. This will save industry substantial costs by simplifying record-keeping and speeding the filing of applications and other regulatory documents.

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 necessary regulation. In so doing, they will strengthen the economy while maintaining health and safety.

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 these 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 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.

- **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;

- **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 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);

- **Excluding** drug and biologic manufacturers from requirements for most environmental assessments, which currently cost tens of thousands of dollars each time a new product is developed and provide no real benefit to the environment;

- **Exempting** nearly 125 additional categories of low-risk medical devices from premarket review;

- **Eliminating the "Reference List" by 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;

- o Issuing a public statement clarifying how FDA determines the effectiveness of new drugs and devices;

- o Harmonizing FDA's drug and device approval requirements with those of other countries, thus expediting worldwide marketing of new products by reducing duplicative testing;

- o Expanding and standardizing the use of new information technologies for review of new products and 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 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.

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.

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.

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," Kessler responded. 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|

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

ASSOCIATED PRESS

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 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."

Administration Offers Plans o 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 fety 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."

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 who say the U.S. should switch to a 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.

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."

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.

A package of FDA reforms announced by the White House yesterday 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.

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 "commonsense 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. Mukulski 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 those that are 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.

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," it's "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.

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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," Kessler responded. 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|

BC-FDA-NEW-PRODUCTS-NYT
FDA MOVES TO HASTEN MARKETING OF NEW DEVICES
(bl)
By PHILIP J. HILTS

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.