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Rare Diseases

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b(7) Release would disclose information compiled for law enforcement purposes [(b)(7) of the FOIA]
b(8) Release would disclose information concerning the regulation of financial institutions [(b)(8) of the FOIA]
b(9) Release would disclose geological or geophysical information concerning wells [(b)(9) of the FOIA]

Carol briefing

[ ]

4-06-1995 3:17PM FROM NORD 2037466481 P.2

[illegible]

- Alliance of Genetic Support Groups
- Alpha 1-Antitrypsin Deficiency National Association
- ALS Association
- American Brain Tumor Association
- American Porphyria Foundation
- American Society of Adults with Pseudo-Obstruction, Inc. (ASAP)
- American Syringomyelia Alliance Project, Inc.
- Aplastic Anemia Foundation of America
- Association for Glycogen Storage Disease
- Batten Disease Support & Research Association
- Benign Essential Blepharospasm Research Foundation, Inc.
- Carpal Tunnel Syndrome/RSI Association
- Charcot-Marie-Tooth Association
- Chromosome 18 Registry and Research Society
- Cornelia de Lange Syndrome Foundation, Inc.
- Cystinosis Foundation, Inc.
- [illegible] Foundation, Inc.
- [illegible] Medical Research Foundation
- Dystrophic Epidermolysis Bullosa Research Association (D.E.B.R.A.)
- Ehlers-Danlos National Foundation
- Epilepsy Foundation of America
- Families of Spinal Muscular Atrophy
- Fanconi Anemia Research Fund, Inc.
- Foundation for Ichthyosis & Related Skin Types, Inc. (F.I.R.S.T.)
- Guillain-Barré Syndrome Foundation International
- Hemochromatosis Research Foundation, Inc.
- Hereditary Disease Foundation
- Histiocytosis Association of America
- Human Growth Foundation
- Huntington's Disease Society of America, Inc.
- Immune Deficiency Foundation
- Inclusion Body Myositis Association
- International Fibrodysplasia Ossificans Progressiva (IFOP) Assoc., Inc.
- International Joseph Diseases Foundation, Inc.
- International Rett Syndrome Association
- Interstitial Cystitis Association of America, Inc.
- Lowe's Syndrome Association
- Malignant Hyperthermia Association of the United States
- Mothers' Network (FAR Foundation)
- Myasthenia Gravis Foundation
- Myelin [illegible] Disease Center
- Narcolepsy Network, Inc.
- National Adrenal Diseases Foundation
- National Alopecia Areata Foundation
- National Ataxia Foundation
- National Chronic Fatigue Syndrome and Fibromyalgia Association
- National Foundation for Ectodermal Dysplasias
- National Fragile X Foundation
- National Leigh's Disease Foundation
- National Marfan Foundation
- National Mucopolysaccharidoses Society, Inc.
- National Multiple Sclerosis Society
- National Neurofibromatosis Foundation
- National PKU News
- National Retinitis Pigmentosa Foundation, Inc.
- National Sjogren's Syndrome Association
- National Spasmodic Torticollis Association (NSTA)
- National Tay-Sachs & Allied Diseases Association, Inc.
- National Tuberous Sclerosis Association, Inc.
- National Urea Cycle Disorders Foundation
- National Vitiligo Foundation, Inc.
- Neurofibromatosis, Inc.
- Obsessive Compulsive Foundation
- Osteogenesis Imperfecta Foundation
- Oxalosis and Hyperoxaluria Foundation
- Paget Foundation
- Parkinson's Disease Foundation, Inc.
- PXE Foundation
- Prader-Willi Syndrome Association
- Reflex Sympathetic Dystrophy Syndrome Assn.
- Scleroderma Federation, Inc.
- Scleroderma Info Exchange, Inc.
- Sickle Cell Disease Association of America, Inc.
- Sjogren's Syndrome Foundation, Inc.
- Tourette Syndrome Association, Inc.
- Trigeminal Neuralgia Association
- United Leukodystrophy Foundation, Inc.
- United Parkinson Foundation
- United Patients' Association for Pulmonary Hypertension, Inc.
- Vestibular Disorders Association
- VHL Family Alliance
- Wegener's Granulomatosis Support Group, Inc.
- Williams Syndrome Association
- Wilson's Disease Association

[illegible]

- Aicardi Syndrome Newsletter, Inc.
- ALS Association/Greater Philadelphia Chapter
- American Behcet's Association, Inc.
- American Pseudo-Obstruction & Hirschsprung's Disease Society, Inc.
- American Self-Help Clearinghouse
- Arc of Ohio
- Association for Children with Russell-Silver Syndrome, Inc.
- Ataxia Telangiectasia Children's Project
- Center for Research in Sleep Disorders
- Charcot-Marie-Tooth International
- Children's Leukemia Foundation/MI
- Christian Lazar Foundation for Juvenile Laryngeal Papillomatosis
- Chronic Granulomatous Disease Assoc., Inc.
- Earl J. Goldberg Aplastic Anemia Foundation
- Family Caregiver Alliance
- Fragile X [illegible]
- Freeman-Sheldon Parent Support Group
- Help Hospitalized Children's Fund
- HHT Foundation International, Inc.
- Hydrocephalus Association
- JCN Resource Center
- Just for the Kids of NPC, Inc.
- Klippel-Trenaunay Support Group
- Lethbridge Society for Rare Disorders/Canada
- L.I.F.T. (Living in Faith Together)
- Lyme Disease Foundation
- Mt. Rogers Community Mental Health and Mental Retardation Services Board
- National Association for Pseudoxanthoma Elasticum
- National Coalition for Research in Neurological & Communicative Disorders
- National Cushings Association
- National Niemann-Pick Disease Foundation
- Parent to Parent of GA, Inc.
- Parent to Parent of New Zealand
- Recurrent Respiratory Papillomatosis Foundation
- Research Trust for Metabolic Diseases in Children/England
- Restless Legs Syndrome Foundation
- Sarcoidosis Research Institute
- Shy-Drager Syndrome Support Group
- Sickle Cell Association of the Texas Gulf Coast
- Society for Progressive Supranuclear Palsy, Inc.
- Sotos Syndrome Support Group
- Sturge-Weber Foundation
- Tourette Syndrome Association of MD, DC & VA
- Tourette Syndrome Association of OH
- Treacher Collins Foundation
- Tuberous Sclerosis Association of IL
- Vaincre les Maladies Lysosomales/France
- West Central Head Start

...out of the darkness, into the light...®

NORD®
National Organization for Rare Disorders
PO Box 8923
New Fairfield, CT 06812-8923
Phone: (203) 746-6518

What Is NORD®?

Mission Statement

The National Organization for Rare Disorders (NORD) is the federation of voluntary health organizations dedicated to helping people with rare "orphan" diseases and assisting the organizations that serve them. NORD is committed to the identification, treatment, and cure of rare disorders through programs of education, advocacy, research, and service.

NORD–The Beginning

Begun in 1983, NORD was an outgrowth of a unified effort by rare disease support groups who were determined to solve the "orphan drug" dilemma. Treatments for these disorders were not being developed by the pharmaceutical industry because they were "drugs of limited commercial value." Consequently, voluntary health agencies and support groups banded together to urge passage of federal legislation that would encourage pharmaceutical companies to develop "orphan drugs." In 1983, when the Orphan Drug Act was enacted, NORD formalized into a national non-profit health agency dedicated to the welfare of those with rare disorders.

Some Facts

Each rare disorder affects fewer than 200,000 people in the United States.

There are more than 5,000 orphan diseases affecting some 20 million Americans. One out of every 12 people suffers from a rare disorder.

NORD is unique. It is the only organization of its kind—a federation of more than 135 not-for-profit health organizations, and thousands of individuals and medical professionals—serving people with rare disorders throughout the world.

NORD Programs and Services

Education

NORD's primary program is education of the public and medical professionals. NORD is a worldwide clearinghouse for information about orphan diseases, answering more than 75,000 inquiries each year from throughout the world. The rare disease information is written in simple, understandable language so that patients and families can understand it. NORD's information is also made available to the public through our Rare Disease Database (RDB) which is available on the CompuServe electronic information system.

- The NORD literature order form lists more than 1,000 rare disorder entries from NORD's Rare Disease Database.
- NORD's book, *Physicians' Guide to Rare Diseases*, is a printed version of the database written in technical terminology for medical professionals.

Research

Besides advocating for increased government research funds, and referring patients to clinical trials and genetic investigators, NORD funds grants on new treatments for rare diseases. Clinical research has historically been underfunded, and NORD attempts to fill this void, creating hope for millions whose disorders are presently hopeless and untreatable.

Family Programs

- NORD's "Networking Program" puts families with the same diagnosis in touch with each other. This helps people find mutual support and encourages the formation of new voluntary health agencies for specific diseases.
- NORD's Patient Services Program provides counseling and advice to people seeking help with accessing social services and learning about appropriate programs for people with disabilities.
- NORD's Medication Assistance Programs provide several free prescription drugs to needy patients who cannot afford treatments.

Information & Referral

NORD provides information to medical professionals, libraries, educators, corporations and individuals. NORD refers patients and families to appropriate sources of assistance and support. When patients are needed for clinical trials, we refer them to the researchers through NORD's confidential patient registry. NORD can usually locate patients with even the rarest diagnoses.

Support Groups and Advocacy

- NORD provides technical assistance to support groups, helping them to start and grow with minimal waste of precious resources.
- NORD monitors implementation of the Orphan Drug Act and advocates for increased government funding of medical research. NORD participates in efforts to assure that people with disabilities maintain the rights and services they deserve.
- NORD is an advocate for the interests of all people with orphan diseases, helping to assure that government programs and services are available and accessible to patients and families.

The NORD Story–Who Is Helped

- More than 75,000 people contact NORD directly each year for information and help.
- More than 210,000 people access NORD's Rare Disease Database (RDB) each year through CompuServe or on touch-screen computers in pharmacies and medical waiting rooms.
- Through NORD's Networking Program more than 7,000 families are linked to other families each year who have similar disorders.
- More than 4,000 financially needy individuals are provided critical, life-saving drug therapies through NORD's Medication Assistance Program each year.
- NORD's newsletter, *Orphan Disease Update*, is published three times annually. This newsletter is mailed to thousands of people throughout the world.
- NORD publishes the *Physicians' Guide to Rare Diseases*. This book enables physicians to find accurate and timely diagnostic information. One out of three individuals with a rare disease does not receive a correct diagnosis for up to five years, and one out of six wait more than six years.
- Sponsorship of an Annual Patient/Family Conference, which is aimed at providing help to patients and families who must cope with the impact of living with a rare disease. Information, networking opportunities and creating an environment of hope are the principal goals. NORD also convenes an Annual Membership Conference providing training and technical assistance to leaders of support groups and voluntary health agencies.

NORD Membership and Support

NORD is reliant on membership and charitable contributions to continue providing its programs of education, advocacy, research and services to people with rare disorders. NORD spends your contribution dollars wisely; less than 15 cents of every dollar donated to NORD is spent on fundraising and administration.

Your membership in NORD will insure that you continue to receive the NORD newsletter, *Orphan Disease Update*, which reports on:

- Progress in research on rare disorders.
- Recent government, health-related industries and scientific community activities.
- Personal accounts of courageous struggles by people with orphan diseases.

N H Drops Its Policy on Drug Prices

Agency Had Required 'Reasonable' Charge

By David S. Hilzenrath
Washington Post Staff Writer

The National Institutes of Health yesterday ended a requirement that drugmakers and other companies charge a "reasonable" price for products developed with government research.

The pharmaceutical and biotech industries had lobbied against the requirement, arguing that it discouraged companies from using federal research that might lead to the development of needed drugs. Consumer advocates had sought the requirement as a way to prevent manufacturers from charging exorbitant prices.

The policy had never been tested, because no products governed by it had been brought to market.

NIH Director Harold Varmus said his agency found that "the pricing clause has driven industry away from potentially beneficial scientific collaborations" with government scientists "without providing an offsetting benefit to the public."

The theory behind the so-called "reasonable pricing" clause was that the public should benefit when drugs are produced with the advantage of taxpayer-funded research.

The policy, which applied to federal research that corporations and others use under agreements with the government, was adopted in 1989 amid protests over the price of the AIDS therapy AZT, which cost about $8,000 to $10,000 per patient annually when Burroughs Wellcome Inc. introduced it in 1987. Critics protested that the drug should have been priced lower because NIH research had contributed to its development.

Once the policy was implemented, companies refrained from using NIH research because they could not be assured they would recoup an investment in product development, said Carl Feldbaum, president of Biotechnology Industry Organization, which represents biotech companies. "Biotech companies said, 'It's not worth

See DRUG PRICES, F4, Col. 1

F4 WEDNESDAY, APRIL 12, 1995 ... THE WASHIN

NIH Drops Drug Price Policy Requiring 'Reasonable' Charge

DRUG PRICES, From F1

dealing with NIH,' " Feldbaum said.

The private sector's frustration is not reflected in the number of research-sharing agreements between NIH and outside organizations, which has fluctuated over the years. There were 31 such agreements last year, up from 20 in 1988, the year before the pricing rule was adopted.

"There's really no pattern," said NIH spokesman Donald Ralbovsky.

"There's a lot of anecdotal evidence . . . where industry or people outside the government were indicating they were just put off by the reasonable-pricing concept."

Rep. Ron Wyden (D-Ore.), a member of the House Commerce Committee, said the NIH's policy shift "puts the burden of proof on NIH and the medical technology firms to show that what they're doing protects the taxpayers' interests." Without the reasonable pricing clause, "it's not at all clear at present how the taxpayers' interests are protected."

Wyden said NIH could ensure that the public interest is served by demanding royalties from companies that use federal technology, sharing product ownership or requiring manufacturers to make their products available to the poor. But current NIH guidelines don't ensure that those things will happen, he said.

Among patient and consumer advocates, views of the pricing policy were mixed.

"We need affordable drugs, and this thing didn't really do much," said Derek Link, research issues director of AIDS Action Council, which represents providers of services to AIDS patients. "I don't think it's a major issue one way or the other what happens with this clause."

bc: [illegible] Larson

National Organization for Rare Disorders, Inc.®

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(203) 746-6518 • FAX : (203) 746-6481 •TDD (203) 746-6927

. . . out of the darkness, into the light . . .

February 15, 1995

Ms. Carol Rasco
Assistant to the President
for Domestic Policy
The White House
Washington, DC 20500

Dear Ms. Rasco:

I have asked our good friend and NORD member, Kathy McClanahan, to forward this invitation to you personally because it is so difficult to ensure that we can get through the right channel at the White House. We want to invite you to speak at our 1995 Annual Tribute Banquet, which is scheduled for the evening of April 24 at the Madison Hotel in Washington, DC.

Each year for the past twelve years the National Organization for Rare Disorders (NORD) holds an Annual Tribute Banquet honoring outstanding individuals and corporations who have made a significant contribution to the welfare of approximately 20 million Americans with rare "orphan diseases." A list of former honorees is attached for your review. This year we will be honoring an academic research scientist who developed a drug for a rare fatal kidney disease, Cystinosis, which affects only 150 children in the United States. For more than a decade he could not find a pharmaceutical company willing to manufacture the drug. Our second honoree, **Ken Larson**, is a retired CEO of several generic drug companies. He took the responsibility of locating a corporation who would produce the drug and apply for FDA approval. Ken located **Mylan Laboratories**, our third honoree, and the drug was finally approved by the FDA in 1994. Today, all the children with Cystinosis are alive and well thanks to these individuals.

We will also be honoring **NIH**, and Dr. Varmus will accept the award. Additionally, we will be honoring **Gene Therapy Inc.**, which was the first biotechnology company to bring the concept of gene therapy out of the laboratory and into human clinical trials. Notably absent from these award winners is a large research intensive company. We simply could not identify one major PhRMA corporation that has developed a true orphan drug in the last few years on a humanitarian basis. Instead, the lion's share of orphan drug development is being pursued by small and medium sized companies.

The audience at our Tribute Banquet is primarily composed of individuals and companies from the pharmaceutical industry, national voluntary health agencies, representatives of health-related industries, people from Capitol Hill, biomedical researchers and the press. About 200 to 250 people usually attend. Since everyone in the room has an overwhelming interest in health care reform, your presentation would be a matter of great interest. Indeed, it would give you an opportunity to send a message from the administration to the two disparate health-related communities: The voluntary health sector representing patients, and the corporate sector representing health-related industries.

When I met with you in the White House in 1993, we discussed the probable opposition of health industry groups to the President's health care reform efforts. Subsequently, the scope of their opposition was even stronger than anyone had predicted, and defeat of the President's reform plan has left them elated and somewhat arrogant. The patient community is devastated. Last year we saw the light at the end of the tunnel, but it turned out to be a fleeting glance. The patients need hope, which will come only from the President's pledge not to give up and not to give in to the forces that selfishly oppose health care reform. On the other hand, health related industries need to understand that they should give back to society a portion of what they have taken. What better way than to develop orphan drugs for small numbers of suffering people, even though they may not be very lucrative.

Carol, this is a very frightening time for people with any serious health condition, and especially for those with neglected and little known orphan diseases. It is vitally important to tell our members that the President and Mrs. Clinton are fighting for us, they will not forget our plight, and they are still pledged to giving us health insurance that can never be taken away. On the other hand, the industries that manufacture drugs, run hospitals, or issue health insurance policies should feel a responsibility to be fair, to meet the needs of society in areas where the free market has failed, and to be responsive to their customers. This is why your presentation at the NORD Annual Tribute Banquet would be extraordinarily meaningful.

I sincerely hope you will agree to attend the Banquet and speak to the audience on April 24. I eagerly look forward to your reply.

Very truly yours,

Abbey S. Meyers
President

ASM:aa

Attachment

cc: Kathy McClanahan

FORMER NORD TRIBUTE BANQUET HONOREES

1994

Miles Inc.
Roberts Pharmaceutical Corp.

Philip R. Lee, M.D.
Head of U.S. Public Health Service
& Assistant Secretary of Health, Dept. of Health & Human Services
Larry Thompson, Author, *Correcting the Code: Inventing the Genetic Cure for the Human Body*
Francis S. Collins, M.D., Ph.D., Director of the National Center for Human Genome Research
National Institutes of Health

1993

Bristol-Myers Squibb Company
Mission Pharmacal

Bruce Fried, Senior Vice President
& Deputy Council of the Weider Group
Senator Nancy L. Kassebaum
Jack Klugman, Actor
Melvin Van Woert, M.D., Neurologist & Pharmacologist
Mount Sinai School of Medicine
Congressman Henry A. Waxman

1992

Allergan, Inc.
Teva/Lemmon/Gate Pharmaceuticals
Sigma-Tau Pharmaceuticals, Inc.

David Kessler, M.D., J.D., Commissioner
Food & Drug Administration

1991

Enzon, Inc.
Schering-Plough Corp.

Senator Mark Hatfield
Theodore Cooper, M.D., Chairman of the Board
& Chief Executive Officer, The Upjohn Company
Marion Finkel, M.D., Vice President
Sandoz Pharmaceuticals

1990

Burroughs Wellcome Co.
Somerset Pharmaceuticals, Inc.

Senator Tom Harkin
Congressman Silvio Conte
Jacob Schein
James B. Wyngaarden, M.D.

1989

Warner-Lambert Company
Kendall-McGaw Laboratories
American Airlines

Congressman Doug Walgren

1988

Merck & Company
Lyphomed, Inc.
Sandoz Pharmaceuticals

Senator Lowell P. Weicker, Jr.
Dr. Frank Young, Commissioner
Food & Drug Administration
Alice Ferdyce, Executive Vice President
Albert and Mary Lasker Foundation

1987

Bristol-Myers Squibb Company
Hoffman-LaRoche
Revco Drug Stores

Senator Orrin Hatch
Congressman Jamie L. Whitten

1986

Senator Nancy L. Kassebaum
Senator Howard M. Metzenbaum
Congressman Henry A. Waxman

NORD (orphan drug act
longer patent period

- relationship to Carol
- Bill Schultz FDA
- Mark Childers (Kennedy) 224-7677 did not call
- David Kim? 2241467

DEPARTMENT OF HEALTH & HUMAN SERVICES Public Health Service

National Institutes of Health
Bethesda, Maryland 20892

DATE: April 10, 1995

TO: Karen Guss
White House Domestic Policy Staff

FROM: Director, Office of Rare Disease Research, NIH

SUBJECT: S:184 - Creation of an Office of Rare Disease Research at the NIH

Attached is a short synopsis of the Provisions of S.184 and the current status of the activities included in the proposed legislation. I had created this for DHHS earlier in the year. The information is still applicable. The one major concern is the establishment of the Advisory Council to the Director of the Office of Rare Disease Research.

NIH received $750,000.00 in fiscal year 1995 for this activity. The two major functions are to(1) create the Rare Disease Clinical Research Database and (2) provide support for scientific meetings, workshops, and symposia to stimulate research on rare diseases.

If you have any additional questions, I can be reached on 301-402-4336 (FAX 301-402-0420).

Stephen C. Groft, Pharm. D.

Attachment

DEPARTMENT OF HEALTH & HUMAN SERVICES Public Health Service

National Institutes of Health
Bethesda, Maryland 20892

DATE: February 9, 1995

TO: Mitchell Goldstein
Budget Office, OS, DHHS

FROM: Director, Office of Rare Disease Research, NIH

SUBJECT: Establishment of the Office of Rare Disease Research at the National Institutes of Health - S.184

The National Institutes of Health (NIH) does not object to the proposed legislation (S.184) as offered by Senator Hatfield.

As you know, the Office of Rare Disease Research was created in January, 1994 and has made progress along the lines in the proposed legislation. Several of the activities proposed in the legislation are already in place. For example, the Office is developing the Rare Disease Clinical Research Database with funds provided in Fiscal Year 1995. This System will be constructed to be compatible with the Physician Data Query System (PDQ) of the National Cancer Institute. The Office also prepares an extensive annual report on advances in rare disease research.

Additional funds would be required to establish patient registries, conduct epidemiological studies of the prevalence of rare diseases, support research training, and develop a comprehensive plan for conducting and supporting rare disease research at the NIH. Attached you will find a status report on the proposed provisions of S.184 and a copy of the Functional Statement of the Office when it was established. The only major concern with the proposed legislation is the provision to establish an advisory council to serve in an advisory capacity to the Director of the Office of Rare Disease Research.

If you have any questions on the activities of the Office or the Status Report, please give me a call on 301-402-4336.

Stephen C. Groft

Stephen C. Groft, Pharm. D.

Attachment A - Comparison of the Provisions of S.184 and the Current Status

Attachment B - Administrative Activities of the Office of Rare Disease Research at the NIH

DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

National Institutes of Health
Bethesda, Maryland 20892

DATE: April 10, 1995

TO: Karen Guss
White House Domestic Policy Staff

FROM: Director, Office of Rare Disease Research, NIH

SUBJECT: S:184 - Creation of an Office of Rare Disease Research at the NIH

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If you have any additional questions, I can be reached on 301-402-4336 (FAX 301-402-0420).

Steve Groft

Stephen C. Groft, Pharm. D.

Attachment

ATTACHMENT A
PROPOSED S.184
Office for Rare Disease Research at the NIH

Provisions of S.184	Current Status
Establish an Office of Rare Disease Research at NIH.	Completed
Develop and Maintain a Rare Disease Clinical Research Database.	Under Development with a Project Oversight Committee. Expected Completion 18 Months After Award of Contract.
Establish an Advisory Council to the Office.	No Action Until Legislation is Enacted.
Develop Comprehensive Plan for the Conduct and Support of Rare Disease Research at NIH.	No Action Until Legislation is Enacted. Previous Study Revealed Nearly 20% of NIH Research Budget Directed to Rare Disease Research.
Coordinate and Disseminate Information Among the Institutes and the Public.	No Action Until Legislation is Enacted. Utilize Existing NIH Information Resources. Database Development Activity at NIH and Clearinghouse Function at Other PHS Agencies.
Support Research Training and Encourage a Diversity of Individuals to Participate in the Conduct of Rare Disease Research.	No Action Until Legislation is Enacted. Identify Existing Training Opportunities for Investigators Interested in Rare Disease Research.
Identify Projects or Research on Rare Disease Research to be Conducted or Supported by NIH.	Review of Research Advances Reported in the Annual Report of the DHHS Orphan Products Board to Congress. The Office Plans to Co-sponsor and Support with the Institutes 7-10 Symposia and Workshops This Year.
Determine the Need for Patient Registries and Epidemiological Studies on Rare Diseases.	Review Results of Recently Completed "Needs Analysis". Review Previous Plans for Epidemiological Studies of Rare Diseases with the Orphan Products Board.
Prepare Biennial Report on the Activities of the Office.	Office with Information from the Institutes Currently Prepares Annual Report.

ATTACHMENT B

Office of Rare Disease Research
Functional Statement

(1) Guides and coordinates NIH-wide activities involving research into combating and treating the broad array of rare diseases (orphan diseases); (2) manages the NIH Rare Diseases and Orphan Products Coordinating Committee (INTERNAL NIH OVERSIGHT COMMITTEE); (3) develops and maintains centralized database on rare diseases research; (4) coordinates and provides liaison with Federal and non-Federal national and international organizations concerned with rare disease research and orphan products development; (5) advises the OD/NIH on matters relating to rare diseases and orphan products; (6) prepares Director's annual report to Congress on rare disease and condition research activities sponsored by NIH; and (7) responds to requests for information on highly technical matters and matters of public policy relative to rare diseases and orphan products.

Current and Future Activities

Activities of the Office of Rare Disease Research would include the following:

Preparation of the Annual Report to Congress from the Director, NIH on the Rare Disease Research Activities of the NIH.

Establish the Rare Disease Research Database with the assistance of the ICD Rare Disease Coordinators, the Division of Research Grants and the National Library of Medicine.

Assist intramural and extramural investigators to obtain the Orphan Drug Designation from the FDA and help locate commercial sponsors for orphan products.

Continue to assist the Division of Research Grants expand the NIH Consultant Reviewers Reserve with particular emphasis on the rare diseases. Recruit reviewers with the assistance of the voluntary rare disease organizations.

Assist voluntary organisations to develop patient, physician, and research investigator registries for specific rare diseases or related rare diseases.

Assist the ICDs in the development and revision of rare disease related information, e.g., fact sheets or brochures on specific conditions.

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409 Third Street SW
Second Floor
Washington, DC 20024

Telephone: (202) 479-6694
FAX: (202) 479-6959

FAX

To: Karen Guss

Fax: 436-7431

Number of Pages (including cover sheet): 10

Date: 4-7-95

From: **Michael S. Langan**

Remarks: As Discussed.

Have a nice weekend!
- Michael

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. . . out of the darkness, into the light . . .

Testimony of

The National Organization for Rare Disorders (NORD)

By

Michael S. Langan
Director of Public Policy

Before the

Subcommittee on Agriculture, Rural Development, Food and Drug Administration and Related Agencies

The Honorable Joe Skeen, Chairman

Committee on Appropriations

U.S. House of Representatives

April 3, 1995

Mr. Chairman and Members of the Subcommittee:

Good afternoon. I am Michael Langan, Director of Public Policy for the National Organization for Rare Disorders (NORD), a national non-profit voluntary health agency dedicated to the identification, treatment and cure of rare "orphan diseases." We are the consumer group that worked for passage of the Orphan Drug Act of 1983. We continue to advocate for and monitor the development of treatments that would not be developed without the incentives of this lifesaving legislation.

In general, an orphan drug is a drug of "limited commercial value" because each orphan disease affects fewer than 200,000 Americans. However, there are more than 5,000 of these disorders cumulatively affecting an estimated 20 million Americans. Our interest is not limited to pharmaceutical products, but includes medical devices, foods and procedures that will cure or alleviate the symptoms of serious, debilitating and life-threatening ailments that strike small patient populations.

FDA Orphan Products Research Program:

Mr. Chairman, this Committee, which appropriates funds to the Food and Drug Administration (FDA), has historically appropriated funding for the FDA's Orphan Products Research Grant Program since 1982 -- the year before the Orphan Drug Act was enacted. Last year, you provided $15 million for this biomedical research program, which was the same amount as the previous year. These limited funds encompass the entire federal commitment to research on new treatments for rare diseases. Since there are more than 5,000 orphan diseases, $15 million is hardly sufficient to make an impact on this problem. Yet every penny has been used wisely and effectively throughout the years, leading to the development of several breakthrough treatments that have prevented death and avoided painful disability for thousands of Americans.

What is the problem? Treatments for rare diseases -- orphan drugs and orphan devices -- are not ordinarily developed by the pharmaceutical and device industries because the small markets for such products limit their potential profitability. This is a unique area of science and health care where the free market has failed to work properly, and where targeted government intervention has had a major impact on the public's health. Because of the Orphan Drug Act, we now have approximately 110 orphan drugs approved by the FDA and on the market, in addition 590 designated orphan drugs are in development.

However, some orphan products need more than the incentives of the Orphan Drug Act to entice the interest of commercial sponsors. Very often, new treatments are discovered by academic scientists at university affiliated hospitals. They cannot attract the interest of companies to commercialize a product until they have conducted controlled clinical trials proving that the product is safe and effective. For these scientists, the **FDA's Orphan Products Grant Program** is the only source of funding available to support this research. Ordinarily, the National Institutes of Health (NIH) will not support these types of studies because the Institutes tend to fund basic research, not clinical research. In those instances when NIH does fund clinical research projects, they usually support very early trials rather than later phases of clinical studies which are required by the FDA for approval of a new product.

The data culled from the FDA's Orphan Products Grants often result in attracting a commercial sponsor. To date, 11 orphan products have been developed with these FDA grant funds, they have achieved commercial sponsorship and are currently on the market. Two of these products are orphan devices, and the rest are pharmaceuticals including treatments for lead poisoning in children, Severe Combined Immune Deficiency (known as the "Bubble Boy Disease"), severe spastic muscles, hairy cell leukemia, and Cystinosis which is a hereditary disorder causing kidney failure, blindness and death among children.

For Fiscal Year 1996, we request **$20 million** for the FDA's Orphan Products Grant Program. By way of comparison, Mr. Chairman, Japan enacted an Orphan Drug Act in 1994. The Japanese government subsidizes 50% of the cost of research on all new orphan products, totaling several millions of dollars each year. Germany has reserved $840 million in an annual fund to support biotechnology research. Last year they solicited applications for funding of 30 gene therapy protocols, but they received 180 applications for those funds, mostly for rare genetic diseases. France allocated $50 million for gene therapy research last year, but the United States has reserved zero. The European Union (EU) has set aside $336 million for pharmaceutical R&D, encompassing nine priority areas (article 20 of the Treaty of European Union). One of those priority areas is rare diseases. Here in the United States, however, where the orphan drug/orphan disease movement started, a mere $15 million was appropriated last year for this research. Only $12 million of that sum actually went to research grants ($3 million went to other FDA orphan product related activities).

Mr. Chairman, we Americans are falling behind in the highly competitive world of medical technology. For example, we virtually invented gene therapy, yet European and Asian governments are investing millions of dollars in this technology and are likely to surpass us. Here, because the commercial sector relies on investment capital for funding, gene therapy companies are focusing almost exclusively on the most prevalent and potentially most profitable diseases (e.g., cancer and HIV/AIDS).

In Europe and Asia, gene therapy is focusing on the hereditary diseases where the technology actually has the highest probability of succeeding. Moreover, European and Asian countries have targeted substantial funding for conventional orphan drugs and biologics, while we Americans spend so little.

The infusion of an additional $5 million into the Orphan Products budgets for the next two years will have a major impact on the number of orphan products developed and ultimately manufactured by the private sector, enabling the FDA to invest in areas of new technology, such as gene therapy and cell therapy, that are so important to America's competitiveness. Most importantly, the appropriation of $20 million for FY'96 will save thousands of lives next year and thousands more in years to come.

Mr. Chairman, the National Organization for Rare Disorders celebrates one of the newest orphan drugs to reach the market. Twenty years ago, academic scientists were studying a rare hereditary kidney disease, Cystinosis, which killed children during adolescence. They discovered that the drug cysteamine could prevent these children from losing their kidneys and going blind. Over the next two decades, the scientists searched for and indeed begged manufacturers to adopt this drug, but no company was interested because less than 300 children in the United States have Cystinosis. The scientists could not allow the children to die, so they continued to buy the raw chemicals and distribute cysteamine as an investigational drug. Periodically they would run out of money and would have to beg and borrow in order to find the resources to keep the experimental treatment available. Finally, a steady supply of the ingredients was assured through the FDA's Orphan Products Grants, which also supported the clinical data necessary to attract a corporate sponsor. Last year, after 20 years of research, cysteamine was approved by FDA. It is now available from Mylan Pharmaceuticals as "Cystagon."

The 300 children with Cystinosis in the United States are alive today because of the funds which this Subcommittee appropriated to the Orphan Products Grant Program. Recently, I spoke with a man whose children have a deadly hereditary disease known as Ataxia Telangiectasia (AT). He is in the shrimp business. He asked me why the federal government is spending $12 million each year to investigate a disease that affects shrimp, but it is spending nothing on research of Ataxia Telangiectasia which is killing his children, and only $15 million to develop treatments for 5,000 orphan diseases in humans. I could not answer him, nor do I believe that many members of this Subcommittee would rationalize the apportionment of federal funds in this manner. We request, therefore, that you direct federal appropriations to a proven program with a track record of having made a major impact on people's lives, and indeed kept them alive -- the FDA's Orphan Products Grant Program.

FDA Restructuring:

There has been much public discussion about reviewing the structure and role of the Food & Drug Administration (FDA) in recent months. This discussion ranges broadly from dismantling the agency to preserving it intact.

Mr. Chairman, most Americans agree that while some things are wrong with the FDA, there is still a lot right about the agency. At the heart of the issue is the very basic question: What is the proper role of government? A quick review of history indicates that major Food, Drug and Cosmetics laws and amendments were enacted after major tragedies occurred, killing or maiming people. The proper role of government should have been prevention of these tragedies, instead of intervening after they occurred.

Protection of public health is, therefore, a proper and indispensable role for government. No one wants needless death and disability to occur as a result of unsafe drugs. Nor should consumers be the victims of ineffective medications. It is ludicrous to believe that in this day and age we would return to the status of turn-of-the-century medicine where snake oil was touted as the cure for everything from arthritis to cancer. Nor can our health care system afford to pay for useless therapies that may be safe but do not alleviate the pain and disability associated with human diseases.

The FDA is the gold standard for drug approval in the rest of the world, so any attempt to weaken its regulatory authority over safety and efficacy would be foolhardy and dangerous. Quicker approvals of safe and effective medications and devices is a laudable goal that industry and consumers all share. To accomplish this, the National Organization for Rare Disorders recommends that this Committee review the dozens of new responsibilities Congress has added to the FDA during the past 25 years, and the appropriations this Committee has enacted during this time period. Funding for space, equipment and staff has not kept up with the FDA's ballooning responsibilities including laws governing generic drugs, medical devices, nutritional supplements, orphan drugs, as well as monitoring entirely new technologies such as gene therapy, biotechnology and cell therapy.

It is clearly an "**unfunded mandates**" problem, Mr. Chairman, because Congress has required the FDA to fulfill expanding responsibilities without sending enough money back to the agency for it to do its job. Then Congress complains that FDA is not doing its job!

We suggest that Congress clearly delineate the roles of the Department of Agriculture and the FDA. The FDA's role should encompass health when it is related to medical practice. A hundred years ago it was created to monitor the food supply, today this responsibility could be carried out by the Agriculture Department. For example, the Department of Agriculture monitors the meat and chicken

industries, but the FDA currently monitors the seafood industry! Why? And why, when the FDA suspected that Chilean grapes had been sabotaged with poison, or announced that orange juice be recalled, should the divisions which oversee drugs and devices be forced to cut staff?

We should enable the FDA to approve drugs and medical supplies more quickly and focus exclusively on the **medical** aspects of consumer goods. If the scope of the FDA's responsibilities could be narrowed, and if they could maintain staff and appropriations at adequate levels, then medical experts would not be diverted from their most important responsibilities. Reviews would be carried out in a more timely manner.

It is also of interest to note that orphan drugs are approved by the FDA very quickly, even though there is no requirement that the FDA give any special considerations to orphan compounds. A review of all new drugs approved in 1993 indicates that the FDA averaged 33.1 months to review New Drug Applications (NDA's). However, approval times for orphan drug applications that year averaged only 12.8 months. Similarly, review of all NME's (New Medical Entities) that year took an average 25.58 months, whereas orphan NME's took 12.4 months.

These shortened review times were not mandated by laws or regulations, but instead occurred because of the importance of the compounds -- There was usually no other treatment available for that disease, the diseases were often life-threatening, and the compounds were considered "breakthrough" drugs. The FDA **always** gives breakthrough drugs highest priority, especially when diseases are considered serious or life-threatening. Thus, complaints about the slowness of new drug approvals at the agency usually involve "me-too drugs" that are not considered to be major medical advancements. If this committee wants to speed the FDA approval process for these less important drugs, please give the agency adequate resources to do so. As far as we are concerned, Mr. Chairman, no one is dying for lack of **another** beta blocker for hypertension, or anti-inflammatory for arthritis. It is this type of copy-cat drugs that primarily clog up the FDA's pipeline. The breakthrough drugs, many of which are orphan drugs, are being speeded through the process without any need to dismantle the FDA.

We sincerely hope that this committee will weigh the seriousness of its responsibilities when deliberating any possible changes to the FDA. You would not want your children or your spouse to take an unsafe drug, and you certainly would not want to waste your money on an ineffective drug that would delay or prevent your recovery. Mr. Chairman, we thank you for the opportunity to present our views, and offer our continuing cooperation and advice.

Thank you.

II

104TH CONGRESS
1ST SESSION

S. 184

To establish an Office for Rare Disease Research in the National Institutes of Health, and for other purposes.

IN THE SENATE OF THE UNITED STATES

JANUARY 9, 1995

Mr. HATFIELD introduced the following bill; which was read twice and referred to the Committee on Labor and Human Resources

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A BILL

To establish an Office for Rare Disease Research in the National Institutes of Health, and for other purposes.

Be it enacted by the Senate and House of Representatives of the United States of America in Congress assembled,

SECTION 1. SHORT TITLE.

This Act may be cited as the "Office for Rare Disease Research Act of 1995".

SEC. 2. ESTABLISHMENT OF OFFICE FOR RARE DISEASE RESEARCH.

Part A of title IV of the Public Health Service Act (42 U.S.C. 281 et seq.) is amended by adding at the end thereof the following new section:

"SEC. 404F. OFFICE FOR RARE DISEASE RESEARCH.

"(a) ESTABLISHMENT.—There is established within the Office of the Director of the National Institutes of Health an office to be known as the Office for Rare Disease Research (in this section referred to as the 'Office'). The Office shall be headed by a director, who shall be appointed by the Director of the National Institutes of Health.

"(b) PURPOSE.—The purpose of the Office is to promote and coordinate the conduct of research on rare diseases through a strategic research plan and to establish and manage a rare disease research clinical database.

"(c) ADVISORY COUNCIL.—The Secretary shall establish an advisory council for the purpose of providing advice to the director of the Office concerning carrying out the strategic research plan and other duties under this section. Section 222 shall apply to such council to the same extent and in the same manner as such section applies to committees or councils established under such section.

"(d) DUTIES.—In carrying out subsection (b), the director of the Office shall—

"(1) develop a comprehensive plan for the conduct and support of research on rare diseases;

"(2) coordinate and disseminate information among the institutes and the public on rare diseases;

"(3) support research training and encourage the participation of a diversity of individuals in the conduct of rare disease research;

"(4) identify projects or research on rare diseases that should be conducted or supported by the National Institutes of Health;

"(5) develop and maintain a central database on current government sponsored clinical research projects for rare diseases;

"(6) determine the need for registries of research subjects and epidemiological studies of rare disease populations; and

"(7) prepare biennial reports on the activities carried out or to be carried out by the Office and submit such reports to the Secretary and the Congress.".

○

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DOCUMENT NO. AND TYPE	SUBJECT/TITLE	DATE	RESTRICTION
001. note	Personal (Partial) (1 page)	n.d.	P6/b(6)

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FOLDER TITLE:
Rare Diseases

2012-0820-S
ms481

RESTRICTION CODES

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

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

C. Closed in accordance with restrictions contained in donor's deed of gift.
PRM. Personal record misfile defined in accordance with 44 U.S.C. 2201(3).
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Freedom of Information Act - [5 U.S.C. 552(b)]

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

[001]

Carol is a hero to them [redacted] P6/b(6)
NORD represents patients and families w/rare (5000) diseases that effect 20 milllion Amers. Diseases are usually genetic.

Around since 1983. Came together as result of Oph drug act. Govt Incentives to pham industry to do research on drugs for rare diseases. Statute – disease that effects 200,000 or fewer. Tax credit to companies for research.

Federal appropriations for research.

Passed senate labor committee -- change NIH by creating office for rare disease research. Hope it passes this year -- passed entire senate last year. Now various institutes have capacity to research rare diseases but we're not maximizing our efforts because they don't appropriate. Funds already appropriated. Senator Hatfield was very active in appropriations process. Already allocation FY1995-97 for this purpose. Waxman and Wyden both want to sponsor.

FDA reform proposals.
-preserving efficacy and safety standards at the FDA. Don't want total dismantlement.

Orphan Drug Act -- orphan drug tax credit provision has to be reauthorized for FY 1996 -- so has to be reauthorized this year. The industry is pushing for more permanent tax credit.

Health care reform -- increased insurance coverage
preexisting conditions

Managed care -- they want to see their patients continue to have access to the specialists that they need -- may need to go out of state, to academic health centers, to participate in trials.

doesn't need to get real specific

audience -- invited Cong members and staff, pharm and biotech industry, alot of members b/c having a board meeting that day

Jeff-
These are notes I took during phone call w/ NORD's policy [redacted]dir.
Following doc. is ltr. from Abbey Meyers.
Any help would be appreciated.
/

- 10 minutes
- no Q&A will be first

NORD – Cong staff
– NORD board
– pharm+biotech

call NIH ○
call Bill Hubbard

① NIH Office for Rare Disease Research Act
② increase $ for FDA Orphan Products Grant Progr.
③ FDA restructuring
④ health care reform – increase ins. co.
– no preexisting cond.
⑤ managed care - access to specialists, etc.
⑥

301 496 2433

NIH's
statement
re: reasonable
prices

OPTIONAL FORM 99 (7-90)

FAX TRANSMITTAL # of pages ▶ 10

To: Judith Ann Scourfield | From: Dan Rabovsky

Dept./Agency: | Phone #: NIH

Fax #: DC R. Conv. | Fax #: 301 496-5787

NSN 7540-01-317-7368 5099-101 GENERAL SERVICES ADMINISTRATION

National Institutes of Health
Public Health Service
U.S. Department of Health and Human Services

FOR RELEASE:
April 11, 1995

Contact: Anne Thomas
(301) 496-5787

The Director of the National Institutes of Health (NIH), Harold Varmus, M.D., today announced removal of the "reasonable pricing" clause from the Public Health service (PHS) model Cooperative Research and Development Agreement (CRADA) and the PHS model Exclusive License Agreement.*

"An extensive review of this matter over the past year indicates that the pricing clause has driven industry away from potentially beneficial scientific collaborations with PHS scientists without providing an offsetting benefit to the public," said Dr. Varmus. "Eliminating the clause will promote research that can enhance the health of the American people," he said.

Over the past year, NIH analyzed its CRADA activities, including the scope of scientific research under CRADAs, the resources brought to the collaborations by NIH scientists and industry, intellectual property arising from the CRADAs, and the effect of the "reasonable pricing" clause on products developed under CRADAs. NIH also sought advice from scientists, patient advocacy groups, and representatives of academic institutions and industry on how the clause has affected research and development collaborations and the advancement of scientific discoveries.

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*NIH is the lead technology transfer office on behalf of PHS.

compete with one another. Thus, even where a product results from an exclusively licensed technology, the commercial licensee is not assured a monopoly position in the marketplace. NIH

Reasonable pricing clauses were first placed in PHS CRADAs and exclusive licenses in response to the widely criticized launch price of AZT, an HIV therapy developed with assistance from the National Cancer Institute. However, AZT was not developed under a CRADA or exclusive license nor, to date, has it been determined that the government has a patentable interest in this medication. Today, PHS has an active technology transfer program that negotiates commercialization milestones, royalties, and termination provisions for every technology licensed to a commercial partner. PHS exclusive licenses can be terminated on various grounds, including the failure to reasonably satisfy unmet health and safety needs.

# # #

Contact: Anne Thomas
(301) 496-5787

Backgrounder

NATIONAL INSTITUTES OF HEALTH

■ To encourage commercialization of Government conducted research, the Federal Technology Transfer Act of 1986 (FTTA) authorizes Federal laboratories to enter into CRADAs with numerous entities, including private businesses. Under a CRADA, companies may provide funds, personnel, services, and equipment in support of collaborative research with Public Health Service (PHS) scientists, most of whom are at the National Institutes of Health (NIH). Federal laboratories may provide all of these resources except funds, and the Government may also grant to their collaborators, in advance, exclusive license options to intellectual property rights on any invention made by a Federal employee under the terms of the agreement. In addition, under separate authority, Federal agencies are authorized to enter into exclusive licenses with companies for the commercialization of new technologies developed solely within the intramural research programs of Federal laboratories. Often the CRADA and exclusive licensing mechanisms are used together to further develop, through collaborative research, a new technology first discovered within a Federal laboratory.

- In fiscal years 1987 through 1994, the NIH executed a total of 237 CRADAs, most of them with industrial partners. These agreements covered a broad range of research, from the initial application of basic discoveries to advanced clinical trials. In the vast majority of cases, because of the nature of the research or the intellectual property position of either NIH or the collaborator at the inception of the CRADA, no new inventions (and hence no new intellectual property) were expected and none resulted. Frequently in these situations, NIH had extensive intellectual property protection on a technology that was licensed by a CRADA collaborator and further developed under a CRADA. Other times, the industrial partner had extensive intellectual property coverage and entered into the CRADA primarily to allow NIH access to the proprietary technology for the purposes of further basic research. In a small minority of cases, new intellectual property was developed during the CRADA. In no case has a product been brought to market based upon technology developed under a CRADA and exclusively licensed to the collaborator, although future products may be anticipated to arise out of exclusively licensed CRADA technologies currently in development.

- In 1989 the PHS, acting through the NIH Patent Policy Board, adopted a policy statement and three model provisions addressing the pricing of products licensed by PHS research agencies on an exclusive basis to industry or jointly developed with industry through CRADAs. The most critical

factor in adoption of the pricing provisions by the PHS was the substantial Congressional and public concern over the $8,000-$10,000 per patient per year launch price of AZT in 1987. The involvement of National Cancer Institute (NCI) scientists in development of this compound created a public expectation that this medication would reach the public at a more accessible price. Although there was no CRADA or exclusive license executed between the NCI and the drug company to govern the commercialization of AZT, in response to the issue, the NIH Patent Policy Board, in consultation with the Deputy Assistant Secretary for Health, PHS, decided to require pricing clauses in model CRADAs and exclusive license agreements.

- On the matter of pricing, the PHS CRADA Policy Statement provides:

"DHHS has responsibility for funding basic biomedical research, for funding medical treatment through programs such as Medicare and Medicaid, for providing direct medical care, and, more generally, for protecting the health and safety of the public. Because of these responsibilities and the public investment in research that contributes to a product licensed under a CRADA, DHHS has a concern that there be a reasonable relationship between the pricing of a licensed product, the public investment in that product, and the health and safety needs of the public. Accordingly, exclusive commercialization licenses granted for the NIH/ADAMHA intellectual property

rights may require that this relationship be supported by reasonable evidence."

The model PHS CRADA and exclusive license each include similar provisions. The model PHS exclusive license states as well that the agreement"... shall not restrict the right of the Licensee to price a Licensed Product or Licensed process so as to obtain reasonable profit" and "... does not permit PHS or any other government agency to set or dictate prices...."

The DHHS is the only federal agency to include the "reasonable pricing" clause in its CRADAs and exclusive licenses, other than the Bureau of Mines.

- The current pricing clauses apply in two circumstances: first, when new intellectual property arises out of a CRADA and then is licensed exclusively to the collaborator by the PHS; and second, when NIH develops through its intramural research new intellectual property that is then exclusively licensed to the private sector for commercialization.

- NIH held two public meetings on the subject of the "reasonable pricing" clauses: one on July 21, 1994 and one on September 8, 1994. These meetings included representatives from patient advocacy groups, industry, academia, and the scientific community. Attendees generally supported the public access purpose of the clause, but few believed the clause currently functions as intended. Many registered the

view that the clause was driving industry away from potentially beneficial scientific collaborations without providing a compensating benefit to the public. Both of the two most relevant trade organizations, Pharmaceutical Research and Manufacturers of America (PhRMA), representing traditional research and development based pharmaceutical firms, and the Biotechnology Industry Organization (BIO), representing over 500 biotechnology firms, are on record as strongly opposing the model PHS pricing clauses. In addition, numerous PHS intramural research scientists have reported difficulty in entering into CRADAs due to the reluctance on the part of potential CRADA collaborators to accept the "reasonable pricing" clauses. Several scientists reported difficulty in obtaining research materials and interacting with industry scientists even outside the context of a CRADA, due to the reluctance of some companies to become involved with NIH. (A report of the two public meetings is available by calling the NIH Office of Communications at (301) 496-5787.)

- NIH also obtained advice from the NIH Director's Advisory Committee, the PHS Technology Transfer Policy Board, and the NIH Technology Transfer Advisory Committee. All three of these groups concluded that the clause should not be permitted to impair NIH's ability to do collaborative research to improve public health. Further, these committees found that the NIH lacked the requisite legislative mandate or expertise to regulate prices and that such a role would conflict with its technology transfer mission.

NIH found that CRADAs, although they represent only a small fraction of NIH intramural research activities, significantly advance biomedical research by allowing the exchange and use of experimental compounds, proprietary research materials, reagents, scientific advice, and private financial resources between government and industry scientists. The "reasonable pricing" clause, however, discourages the execution of exclusive licenses and CRADAs and inhibits the ability of PHS scientists to obtain access to research materials and scientific expertise from their private sector counterparts, even outside the context of a license or a CRADA.

NIH also determined that very few CRADAs have directly resulted thus far in new intellectual property or products. The six products developed under NIH CRADAs since 1987 either are non-exclusively licensed to one or more companies or had no patent protection and did not require licensure for development. Thus, to date, no CRADA product has been developed under an exclusive license, although several CRADA technologies have been exclusively licensed and may result in future products. The vast majority of CRADAs result in new scientific knowledge, not new products.

NIH also found that research on several technologies had resulted in CRADAs and exclusive licenses with different companies for the development of similar products that would compete with one another. Thus, even where a product results from an exclusively licensed technology, the commercial licensee is not assured a monopoly position in the marketplace. NIH

believes that competition should be fostered by removing barriers to CRADAs and ensuring, where possible, that competing products are developed for the same area of technology.

No law or regulation requires or expressly authorizes the inclusion of the "reasonable pricing" clauses. No other Federal agency except for the Bureau of Mines includes a reasonable pricing clause in their CRADA or license agreements with the private sector. Licensees of PHS and other Federal agencies routinely pay fees and royalties to fairly compensate the Government for using intellectual property developed through taxpayer-supported research.

"The clause attempts to address the rare breakthrough product at the expense of a more open research environment and more vigorous scientific collaborations," said Dr. Varmus. "One has to have a product to price before one can worry about how to price it, and this clause is a restraint on the new product development that the public identified as an important return on their research investment."

NIH shares the concern voiced by participants at the public meetings about potential inaccessibility of such products due to cost. However, NIH agrees with the consensus of the advisory panels that enforcement of a pricing clause would divert NIH from its primary research mission and conflict with its statutory mission to transfer promising technologies to the private sector for commercialization. "NIH's primary programmatic mission, legislative mandate, and expertise is in biomedical research, not in product pricing," said Dr. Varmus.

- Six products have been developed under CRADAs since 1986. None of these products are exclusively licensed. The products fall in the following categories: therapeutics (taxol, pilocarpine), vaccines (Hepatitis A vaccine), research tools (D2 Short Dopamine Receptor, Patient Activity Monitor), and research services (cDNA megabase sequencing).

- NIH CRADA and licensing strategy has resulted in several CRADAs and licenses aimed at developing products which will eventually compete with each other. Examples include:

1) AIDS: Two AIDS therapeutics, dideoxycytidine (DDC) and dideoxyinosine (DDI), were co-developed by NIH and compete with AZT in the marketplace.

2) Cancer: Taxotere, an analog of taxol, is being developed by the NCI and will compete with taxol as a cancer therapeutic.

3) Gaucher's Disease: Two CRADAs are underway to develop two different forms of recombinant glucocerebrosidase for the treatment of Gaucher's disease. In addition, a CRADA for gene therapy to permanently treat Gaucher's disease is ongoing.

4) Chlamydia infections: Three CRADAs are underway using the same NIH technology to develop a Chlamydia vaccine. The three collaborators have brought their own proprietary delivery systems to the CRADAs and will obtain exclusive rights to the NIH technology only for use in conjunction with specific delivery systems.

# #

April 1995

NORD

coverage - ironic & disappointing that most Covg. proposals seem to be aimed @ reducing Mcd + MC. As a result, likely creating a situation that will reduce rather than expand coverage. Only pt. that has been exp is Mcd, private has been dumping, dropping depend. covg.

States expanding covg for most vulnerable - children & disabled.

We need to make more efficient, but big cuts being considered fundamentally undermine delivery system by harming the system + cost shifting → add'l uncomp. care.

We will: POTUS not giving up - Mcd + MC + cuts s/b considered in broader context of reform. He has laid out vision that addresses problems in step by step manner. Most recently, he has talked re assisting working families access of affdable health care by assisting temp. unemployed. This would build on his ~~com~~understanding of Amer's fear of losing health care during personal crisis + portability + preexisting.

In State of Union he said ~~[redacted]~~ kids coverage may take some time. Plus temp. unemployed would assist both.

drugs - has been price inflation moderation. Hope it is long-term trend. But largest unaddressed issue continues to be too many Amers w/no perscription drug coverage + w/inadequate coverage + Medicare-paying for drugs is lgest out-of-pkt. health care $ for 3/4 elderly. As we step by step to expand coverage in general -- [redacted]

We think drug bene is cost effective - it would be expensive for Medicare population. Discussions re additional cge for elderly, including mgd. care, which frequently include perscription drug coverage.

Look forward to wkng w/consumers groups + pharms on this.

FDA - Things we can do legislatively but regardless, we are doing what we can administratively - regulatory review process. 2 wks ago we released first reg. reform report on FDA.

Recs have been widely acclaimed by drug+device ind. should help FDA better target resources, ~~and~~ reduce unnec reg. burdens on ind. + enable FDA to further improve upon its record of bringing high qual. drugs to mktplace

in a timely manner.

User indust fee → FDA → help them approve drugs faster. [redacted]

- Kessler testimony
- Bill Hubbard 301 443 2854

Managed care - w/greater utilization of mgd. care & use of formularies, there has been some success in mging drug prices. Concurrent w/that trend is a larger amt. of scrutiny from public, Cong, media, policymkrs on how mgd care orgs do things & potential for unduly restricting options. We are currently reviewing this issue thru prism of trying to assure adequat choice, quality control & all the while moderating price in Medicare & Medicaid. Can learn/apply to privat sector.

New Covenant community stuff

- separate funding, codification
so many rare diseases
- software in place

Associate Director for Disease Prevention
Dr. Steven Groft
301 402 4336
Head of Office of Rare Diseases

****

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DATE: 4 / 13 /1995

TO: Judith Ann Scourfield

FROM: Bill Hubbard

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COMMENTS:

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STATEMENT BY

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BEFORE THE

COMMITTEE ON LABOR AND HUMAN RESOURCES

UNITED STATES SENATE

APRIL 6, 1995

TO BE RELEASED ONLY UPON DELIVERY

save $ for industry/ resources for FDA + maintain high stds of safety & effectiveness

(1) FDA has been reforming and just announced more reforms as part of Pres. & VP's Nat'l Performance Review
- devices + drugs

(2) drugs incl. biotech.
- minor changes
- environ. review

(3) new challenges
- quicker review
- work w/ industry

(4) conclusion
- POTUS quote
- intend to maintain independence + scientific expertise
- despite attempts to undermine.

I. **INTRODUCTION**

Next year we will celebrate this country's commitment to consumer protection that began ninety years ago with the passage of the Pure Food Act of 1906. It is a commitment that has been renewed through the decades with the passage of consumer protection statutes in 1938, 1944, 1958, 1962, 1976, and 1990 -- all aimed at assuring Americans that the food they eat is safe, the drugs and devices they use are safe and effective. It is a commitment the Food and Drug Administration makes each and every day.

The FDA's consumer protection mission is absolutely vital -- as vital today as it was the day that the Pure Food and Drug Act was passed 90 years ago.

Our mission is to protect and promote the public health by protecting the foods we eat, and by assuring the safety and effectiveness of the drugs we take and the devices we use. The assurance that FDA is there, every day, doing its job, is so fundamental to what we know and expect as public health

protection, that Americans have the luxury of taking their safety for granted.

By what we do, we also give credibility to industry and bolster consumer confidence in its products.

When the makers of Diet Pepsi faced a crisis following reports of syringes in their product, they welcomed FDA's investigators, and when on the basis of our investigation we stood up and reassured consumers that the products posed no hazard, the crisis turned on a dime.

Consistent with the purpose of this hearing, the Administration is announcing a list of reforms that streamline drug and medical device regulation while preserving our critical health and safety standards. In my testimony today, I will talk about some of what the agency has done already and highlight some of the reforms now being recommended.

We are committed to maintaining high standards so that consumers can continue to have confidence in FDA-regulated products. But high standards alone are not enough. We also have a responsibility to get these products to consumers as quickly as

possible. One of FDA's top priorities has been to reduce product review time while maintaining high standards of safety and effectiveness. Let me explain what we have done.

II. MAKING IMPORTANT NEW PRODUCTS AVAILABLE SOONER

The reforms we are announcing in a few minutes were developed as part of President Clinton and Vice President Gore's National Performance Review. They can be fully understood, Madam Chairwoman, only in the context of our work to speed the availability of new products over the past several years. It is an effort on which we have been working very hard indeed.

FDA has made two types of changes over the past several years: we have expanded access to promising therapies before approved for marketing, and we have set up a process of "accelerated approval" for drugs designed to treat serious and life-threatening diseases.

A. ACCELERATING DRUG AND BIOLOGIC REVIEW

Over the last decade we have developed a number of mechanisms that give seriously ill and dying patients access to potential therapies before they are approved for marketing. For

example, FDA's "Treatment IND" provides patients access to a promising drug after clinical trials show that it may be effective, but before the FDA has approved it for marketing. Our parallel track program gives HIV-infected patients who are unable to join a controlled trial access to the experimental drugs. Tens of thousands of patients with serious and life-threatening diseases have received therapies that have not yet been approved through these and other expanded access mechanisms.

In addition to these innovative pre-approval policies, we have also developed a process to accelerate approval of drugs for serious and life-threatening diseases. FDA now can approve these drugs for marketing before the data from clinical trials is complete, if the drug shows an effect on a "surrogate marker," a laboratory measurement used to predict actual clinical outcome.

"Accelerated approval" is also called "conditional approval," because in the end the drug must meet our traditional standards for safety and effectiveness. If the studies do not verify a clinical benefit, FDA will revoke the approval.

We have already approved five drugs under the accelerated approval policy since it was put in place in December 1992.

This process is not without its risks. But when it comes to getting needed therapies to dying patients, the riskiest thing we can do is to be unwilling to take risks.

B. THE IMPACT OF DRUG USER FEES

But administrative innovations to product review can go only so far. That is why, during the summer of 1992, the Congress, the pharmaceutical industry, and the FDA directed their considerable energies toward enacting the Prescription Drug User Fee Act (PDUFA). This innovative law has given FDA the additional resources that it needed to speed up our drug and biologic reviews without sacrificing their quality. In conjunction with enactment of the legislation, FDA also agreed to demanding performance goals for the Agency. I am pleased to report that we have not only met its goals to date, but in some areas we are substantially ahead of schedule.

The charts at the end of the testimony show that we are solving the problem of long drug delays. In the past, our median approval time for new drug applications was 26.7 months. Last year, we reduced the median approval time for all new drug applications to 19 months. The subset of these approvals which

product area with enormous implications for the public health. Often, its products are designed to function for years and even decades.

I hardly need to point out the inherent tension between FDA's dual and inseparable goals: to protect consumers against unsafe or ineffective products, while at the same time making new medical technologies available as soon as possible. Where medical devices are concerned, we must do better on both scores.

Progress in Medical Device Review

We are also making significant strides in strengthening our medical device program. We're working hard on a several fronts. For example, we have:

- Instituted an expedited review process for breakthrough devices, -- those with significant clinical advantages over marketed devices.

- Increased the percentage of the medical device budget targeted to reviews -- up 11 percent to 46 percent of the Center's resources.

- Established a pilot approach to the pre-market approval of medical devices which achieves defined objectives under pre-established time and resource constraints.

These strategies are beginning to pay off. In January 1994, our median review time for 510(k) medical devices was 160.5 days. By January 1995 we cut the median review time to 98.5 days. In addition, the backlog of 510(k) submissions (chart 4) has been reduced from 1,824 submissions in January 1994 to 371 submissions at the start of this year. However, the slowest 5 percent of 510(k) reviews still take more than 500 days and we are working hard to bring those times down as well.

III. REINVENTING REGULATION OF DRUGS AND MEDICAL DEVICES

Today, the Clinton Administration is announcing a number of initiatives to improve the speed and efficiency of the drug and device review processes. The Administration is committed to making government work better while maintaining the services and protections the American people deserve. I would like to submit for the record FDA's report on regulatory reform in drug and medical device review. These reforms, which have been developed

under the leadership of Vice President Gore's National Performance Review, build on what the Agency has accomplished over the last several years in speeding reviews and expanding access for promising therapies.

Some of the reforms we announce today 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. We believe that cumulatively they can make a difference for the companies that seek to market new drugs and devices or to make improvements to existing products. They will result, we estimate, in annual cost savings for the industry of $500 million.

Let me tell you how some of these reforms will do so. First, we believe many medical devices simply don't pose a sufficient risk to be reviewed by FDA prior to marketing. We already have exempted hundreds of categories of devices from such review, and are proposing to exempt more than 100 today. Thus, we will have exempted a third of the 1700 categories of devices from premarket review, covering thousands of actual products.

During the past several months there has been considerable discussion about the European system of device review, whereby third-party, non-government bodies review device applications. There are legitimate, serious questions as to whether such a system would work in this country--such as whether the capacity exists in this country for such reviews, whether it would provide the same quality control, and whether private reviewers could be independent.

We will not know if the concept of third party review can successfully speed device reviews unless we try it. So we will initiate a pilot study for such reviews of medical devices with low to moderate risk. We expect to begin this study this fall, have it cover hundreds of device applications, and complete it in about two years.

We also will be eliminating the so-called "reference list," a controversial program that deferred clearance of device applications until good manufacturing practice violations discovered during plant inspections were corrected. Under the new program, applications will be held up only where there is a relationship between the violation discovered and the pending

application, thus ensuring that devices not affected by the violations continue to move to the market.

Even with the many exemptions for medical devices, there are still numerous devices that pose potential health concerns and will need some premarket review. We are urging Congress to authorize user fees for those reviews, which we believe are essential to our commitment to both reducing application backlogs and speeding review times. We are hopeful that the user fee proposal negotiated last year by FDA, Congress, and the medical device industry will provide an acceptable framework for action this year. With sufficient resources, the Agency can commit to reviewing the simplified device applications submitted under section 510(k) of the law within 90 days. These applications account for 99% of all device submissions. The longer PMA applications would be reviewed within 180 days to one year. Our success with drug user fees demonstrates that we can meet ambitious goals if given sufficient resources, and we can make similar progress in medical device reviews if the user fee authority is granted.

Making changes re devices & drugs

We also are making major changes with respect to the regulation of drugs, including drugs made using the new science

of biotechnology. As I've described earlier, we are making significant progress in bringing down drug review times, and we believe the regulatory reforms we are announcing today will greatly enhance and continue that progress.

First, drug companies are frustrated that it often takes them months to get FDA approval--via a manufacturing supplement to their original approval application--for even minor changes in the content or manufacturing process of a drug or biologic. We believe there are many such changes that do not need to be reviewed by the Agency or which should only require brief notice to the Agency.

For biologics, which include many biotech products, we intend to reduce the number of supplements by fifty percent. Under this approach, 250 of these changes could made unilaterally each year, and another 250 could be made by giving the Agency 30 days notice. This policy change is being published in the Federal Register today. A similar publication covering other drugs will be completed soon, which will eliminate our current review of more than 800 supplemental applications.

We are also clarifying an important issue with respect to construction of biotech manufacturing plants. In the past, some companies have built full-scale plants, at a cost of millions of dollars, only to have approval of their product denied. In the future, we will be very clear that biotech companies will have the flexibility to build a pilot facility, if they choose.

We also looked at environmental requirements that pose significant costs for drug and biologic manufacturers in getting a new drug approved--complying with the National Environmental Policy Act. For many years, FDA has required drug companies to submit with new drug applications a formal assessment of the impact of approving the drug on the environment. In virtually all cases, there is no significant impact. Yet these evaluations each cost tens of thousands of dollars.

We intend to issue categorical exclusions to the requirements to prepare these assessments that will eliminate the need for them, except in rare cases, which will free millions of dollars of industry resources to be applied to other avenues of drug development.

We are also announcing reforms in the regulation of antibiotics and insulin, which have been subject to special controls since the 1940s. Today, these products can and should be regulated like other drugs, and we will be asking Congress to repeal the special requirements for those drugs.

Finally, I would like to mention the issue of exports of unapproved drugs and devices. This is an especially difficult issue, and today the Federal Food, Drug and Cosmetic Act has differing, inconsistent standards. I want to emphasize that this is not an issue on which I or the Agency has any particular expertise. In fact there is a strong argument to be made that this is not really an issue of public health since products not approved in the United States will inevitably get to other countries, whether we allow their export or not. Instead the issue turns on the extent to which we, as a country, are comfortable with permitting the export of products which cannot be sold here, but which are sold in other countries.

Current law allows drugs to be exported to 21 industrial countries identified in the Federal Food, Drug and Cosmetic Act, if FDA has permitted investigation of the drug in the United States, the foreign country approves of the shipment, and certain

other conditions are met. Export of unapproved drugs to other countries is not permitted by law. The Administration proposes to reduce administrative burdens on the export of drugs to the 21 countries. 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.

For devices, current law treats all countries the same. In general, low risk devices may be exported without restriction. On the other hand, the more risky devices may be exported only if FDA makes a finding that export would not be contrary to the public health and safety. If permission to test the device has been granted, then the Agency always makes the finding that public health and safety is being adequately protected.

The Administration is proposing to reduce administrative burden on the export of devices to permit export to countries on a list of industrialized countries if the product conforms with the requirements that country.

As to countries that are not on the list, we would propose to leave current law where it is, with one exception. The

exception is devices approved in other countries and for which investigational permission has been granted in this country. In that case, we propose to eliminate the necessity for the administrative review since, in reality, the result is always the same -- export is permitted. Under this aspect of the proposal there would be no loss of protection to citizens in foreign countries, but we would relieve American companies of the administrative burden of having to wait for FDA clearance.

These export recommendations will free U.S. drug and device firms from substantial impediments to exporting their products, and will result in significant savings in costs of applying--and waiting--for FDA export permission.

FDA is pursuing these reforms in recognition of its dual mission to protect the public health and expedite the availability of safe and effective drugs and devices.

As I noted earlier, the reforms I've outlined today are part of a series. We expect to be announcing later this spring a number of reforms being developed for the regulation of foods and veterinary products. We have done a number things in recent

years that are consistent with the changes we are announcing today.

First, last December we exempted almost 150 categories of low-risk medical devices from premarket approval requirements. These are devices such as stethoscopes, manual surgical instruments, and neurosurgical stockings. Manufacturers submitted about 600 applications per year in these categories. The device industry had made these exemptions a high priority.

Second, the Nutrition Labeling and Education Act has been a great success, and the nutrition label that law required is extremely popular. But there have been instances where the strict deadlines required by the law placed an unnecessary burden on American business, particularly small business. We were able to use the discretion allowed by the law to permit an additional year for final implementation of the new label requirement. And we worked with you on yet other legislation providing an exemption for small businesses who would be financially distressed by the new labeling requirements. These provisions have saved food companies, particularly small businesses, millions of dollars.

IV. FUTURE CHALLENGES TO ENSURING PUBLIC HEALTH PROTECTION

A. DRUGS

We recognize that getting drugs to patients as expeditiously as possible also involves another critical challenge. Academia, industry and government all agree that although the basic methodology is sound, there are probably faster and more efficient ways to conduct the clinical trials that generate data about a drug's safety and efficacy. There is an important opportunity here to shorten the time it takes for a drug to get from the laboratory to the bedside.

Today, some companies conduct dozens of clinical trials in support of one product. Sometimes this results from a company's perception that this is necessary to meet different regulatory requirements of different countries. FDA is working closely with our counterparts in other countries to harmonize regulatory requirements in many areas. But the challenge goes beyond that. It goes to the heart of clinical trial methodology.

The expectations of what needs to be known about a new drug are increasing worldwide. How can trials be designed to generate

information in the fastest, most efficient way? Finding ways to obtain the data without needlessly delaying drug development will require creativity and innovation in clinical trial designs. New paradigms for trials designed to simultaneously fulfill multiple information requirements are needed.

The past 20 years of clinical research has produced a tremendous accumulation of information on successful and unsuccessful trials and a wealth of information on what works and what doesn't in testing new drugs. Analysis and dissemination of this material, through a collaboration between FDA and outside scientists, could advance the science of drug development. One outgrowth of such a project might be standardized protocols for certain diseases. For example, several years ago FDA contracted with the Infectious Disease Society of America to develop a set of standardized protocols for evaluating anti-infective agents. Such standardized protocols can reduce uncertainty about how to proceed with studies of these agents. It may be possible to develop standardized protocols for other conditions as well.

FDA cannot bring about these changes alone. The Agency reviews applications, but we do not conduct the drug trials. Achieving greater efficiency will obviously require a commitment

by scientists and industry, as well as FDA, to identify obstacles and devise creative solutions. Success will mean some drugs will get to patients sooner, industry will save money and both the pharmaceutical industry and the FDA will be able to make more efficient use of our resources.

FDA plans to take a leadership role in this effort over the next several years. This agency has accumulated a tremendous amount of sophistication in study design and new drug evaluation. We believe we can make an important contribution in this very important area.

B. MEDICAL DEVICES

The critical challenge we face in the device area goes to the most fundamental question about the safe and effective use of complex and changing technologies.

Let me briefly put this in context. With the 1960's came both tremendous advances in biomedical technology and a heightened realization that such products are potentially harmful. A commission formed by President Nixon to assess the need for regulatory intervention at the national level documented

10,000 device-related injuries, 750 of which were fatal. Among them were deaths and miscarriages in women who used the Dalkon Shield; serious eye infections and impaired vision resulting from improperly manufactured intraocular lenses; and thousands of defective pacemakers.

Six years later, the Congress enacted the Medical Device Amendments of 1976. For the first time, FDA had the authority to regulate devices prospectively. This represented an enormous task and presented some challenges different from those involved in drug approvals. In short, evaluating devices raises new scientific challenges. The experience of FDA and the device industry in designing clinical trials to answer key safety and effectiveness questions is far less mature than with drugs.

A few years ago we undertook a study of the device review process and found the quality of the data submitted by companies in support of their devices was lacking. We have taken a number of steps to improve the quality of the data submitted to the Agency so that we can make sound scientific and medical decisions.

I cannot emphasize enough the importance of sound scientific studies of new medical devices, particularly where the safety and effectiveness of the type of device has not been established or where changes in the device could influence its safety and effectiveness. These are devices that people rely on -- diagnostic tests, pacemakers, hip replacements -- and we have to get it right. FDA is faced with thousands of new or modified devices every year whose safety and effectiveness is unknown, and we have to be able to assess whether they work, for whom and under what circumstances.

Some of these devices are associated with dramatic changes in medical care. For example, less invasive surgical techniques offer tremendous potential benefits to the patient and the health care system. But we can't realize that potential -- and we risk serious harm to patients -- if our understanding of how these devices can be used safely and effectively is not well grounded. You can't guess, you can't rely on anecdotes and you can't always predict clinical impact based on nonclinical testing.

Many of the medical devices being developed today are very sophisticated. Frequently they are software driven. These technologies require a different model of regulation than do

devices such as, for example, hand held surgical instruments and make testing in clinical trials all the more important.

The challenge for FDA is to make sure that approval of these new technologies, as well as of the more traditional devices, is based on sound scientific studies that can determine for the American people that these products work and benefit patients.

C. FOODS

The United States' food supply is one of the safest in the world. The current regulatory regime relies on the marketplace to take responsibility for the safety and integrity of the food supply. FDA is working on improvements in this system that will further ensure that problems are prevented before they occur.

Our challenge in the foods area is to develop a comprehensive approach for assuring food safety that is built on preventing problems in the food supply. Our food safety system must be based on a broad view, encompassing from the laboratory to the field; from farm or fishery to the dinner table; from the foreign processing plant to the local retail establishment.

Our current system of food safety regulation is often reactive. What we need is a system that focusses on preventing problems in the food supply. This is a shared responsibility of industry and FDA.

FDA oversees the safety of all fresh and processed foods except meat and poultry. This universe encompasses 230,000 separate foods, which contain over 10,000 additives. These foods are made and distributed by 60,000 domestic manufacturers, warehouses, and distributors. In addition, there are over 1.2 million imported food products. These foods are produced by a wide variety of people. The distribution chain ranges from entirely local operations to large cross-country and cross-continent operations. The products range from selectively bred plants and animals to products from the wild, such as seafood and game meats. No one regulatory approach works for this wide variety of products.

Increasingly, the American consumer is relying on foods produced in high-tech, centralized processing facilities, shipped over long distances, and packaged and stored in new ways. Increasingly, we will see the introduction of new and novel foods produced by biotechnology. We already have seen the successful

introduction of a number of such foods, such as the Calgene tomato and yellow squash that is resistant to viral disease. The consumption of prepared foods sold ready-to-eat at retail outlets is expanding rapidly. And an increasing amount of the food that we eat originates overseas--over a million shipments a year and growing.

Food-borne illness has always been a public health problem. New pathogens have appeared. There is more opportunity for food to be contaminated than in the past because food today is more extensively processed, handled at more steps between the farm or fishery and the table, and transported to and from more distant locations.

We also have to address the ongoing, unsolved problems associated with the need for safe, effective drugs for use in food-producing animals, industrial chemicals used in processing and packaging, and the range of environmental contaminants that come into play at various points in the process.

Today we examine a modest number of the food shipments coming into this country, but only after they have arrived at our

shores. And we have no authority to inspect foreign food plants, unless we are invited to do so.

Both FDA and the industry must have the tools appropriate to the tasks we each face in this new paradigm. We have taken the first step in creating the comprehensive scheme for the future with our HACCP (Hazard Analysis Critical Control Points) proposal for seafood that we issued last year. We have also published an Advanced Notice of Proposed Rulemaking to ask for public comments on how and when HACCP should be extended to the rest of the food supply. Implementation of a HACCP system will be a major priority over the next decade.

FDA will need to maintain the scientific expertise in the areas of toxicology, microbiology, nutrition, and genetics, that has provided us with the ability to evaluate the safety of new technologies and products. FDA is determined to take the approach that results in safe new food products, without needlessly impeding the use of safe biotechnology techniques that can give manufacturers the ability to produce better foods and provide consumers expanded choices.

D. THE GLOBAL MARKETPLACE

Increasingly, FDA's work must be seen within the context of the global marketplace. One important sign is the increase in imports. The number of imported shipments of FDA-regulated products has doubled in the 1990's, to more than two million shipments per year. FDA is responsible for ensuring that these imports meet the same safety, effectiveness, and quality standards as products produced domestically.

Obviously, this is an enormous task. We cannot begin to look at every item, yet we need a way to ensure the safety of each product imported. We need to know what is coming into the country, yet the process to clear imports had become laden with time-consuming paperwork. To make this process more effective and efficient, we have begun development of a phased information systems initiative to support automation of the import clearance process. Phase I was implemented nationwide in 1994 in conjunction with the U.S. Customs Service. The new FDA system enables the import broker to enter additional FDA-specific data, which passes through a screening process that recognizes the product, the country of origin, the manufacturer or producer, and the shipper. FDA has developed a set of decision criteria based

on its past experience with import risks and surveillance sampling techniques to determine whether the shipment is admissible, or whether FDA needs to look more closely at it. Within minutes, the broker receives a return message, advising whether FDA has cleared the shipment, or whether examination and testing by FDA is needed. Shipments in which FDA has no further interest can move immediately into commercial channels.

FDA is also addressing other challenges in the international arena. FDA and its international counterparts have been working very hard toward the goal of harmonizing drug regulations and developing international standards for devices, foods, and veterinary medicine products. One important activity that is producing harmonized scientific and technical guidelines is the International Conference on Harmonization (ICH), a unique partnership of regulatory authorities and the pharmaceutical industry in the United States, Japan, and the European Union.

Science-driven harmonization can curtail duplication and thereby significantly reduce the cost of new drug development--not just in dollars spent by the industry, but in the risks taken by patients, the experimentation with laboratory animals, and the regulatory effort of our governments. It has the potential

for a major breakthrough in the drug approval process by making a common registration package a realistic possibility.

E. CHANGES IN SCIENCE AND TECHNOLOGY

Perhaps the most important change is the staggering pace of scientific and technological innovation that affects almost everything we do. New science and technology result in new types of products, which require us to expand our scientific expertise to comprehend the complexities of these products so that we can make sound judgements about their safety and effectiveness.

Devices such as virtual reality image-guided surgery, digital mammography systems, and totally artificial organ replacements are on the horizon. Our Center for Biologics is continually faced with new product technologies such as somatic cell and gene therapy, xenotransplants, and the genetic tests spawned by the Human Genome Project. The technologies used to produce and administer biological therapeutics and vaccines and to regulate the blood supply are changing rapidly, raising a host of new challenges for the Agency. For example, the potential for direct injection of nucleic acids to induce humoral and cellular immunity against infectious disease is one of the hottest

emerging topics in vaccine research today. FDA is currently considering the safety issues that developers of these DNA vaccines may need to address before these vaccines are tested on humans.

These new technologies offer tremendous opportunities for patients and it is imperative that FDA be prepared to evaluate them and get promising products to patients expeditiously. It is a challenge we are working very hard at.

V. CONCLUSION

In this country, we sit down to dinner without even thinking about whether the food on the table is safe. We purchase drugs for our children without even thinking about whether they work. When we are treated in the emergency room of a hospital, we often don't think twice about the new technologies being used.

Americans don't have to worry about the safety and effectiveness of these products because of the high standards the Food and Drug Administration has set. Today this Agency has the confidence of the American people.

In recent months there have been numerous proposals for major changes in how FDA conducts business; proposals which could only serve to undermine the dual mission of the agency -- ensuring the safety of foods, and the safety and effectiveness of drugs and medical devices.

As the President said in his announcement last month of regulatory reforms in FDA and EPA, the guiding philosophy in our own examination of FDA has been "protect people, not bureaucracy; promote results, not rules; get action, not rhetoric." We have followed the President's charge and we are working hard to make FDA more efficient and maintain its high quality of work.

By our past actions, the regulatory reform report we are releasing today, and our continuing regulatory reform process, we have shown our commitment to improve FDA consistent with the President's charge. However, proposals that would completely privatize or weaken the public health mission of FDA might only serve to undermine the reforms FDA is pursing and the confidence the public has in the Agency.

The two pillars of FDA's success are its independence and its scientific expertise.

In the end, it is FDA's independence that gives the American people confidence in the Agency's decisions. The American people know that when the FDA approves a drug, that approval decision is made independent of commercial interests.

In recent months there have been numerous proposals to make radical inroads into the independence of the agency, ranging from requiring it to use advisory committees with industry experts who have conflicts of interest, to wholesale delegation of critical functions to private third parties, to requiring it to hire industry employees who would review drug and device applications.

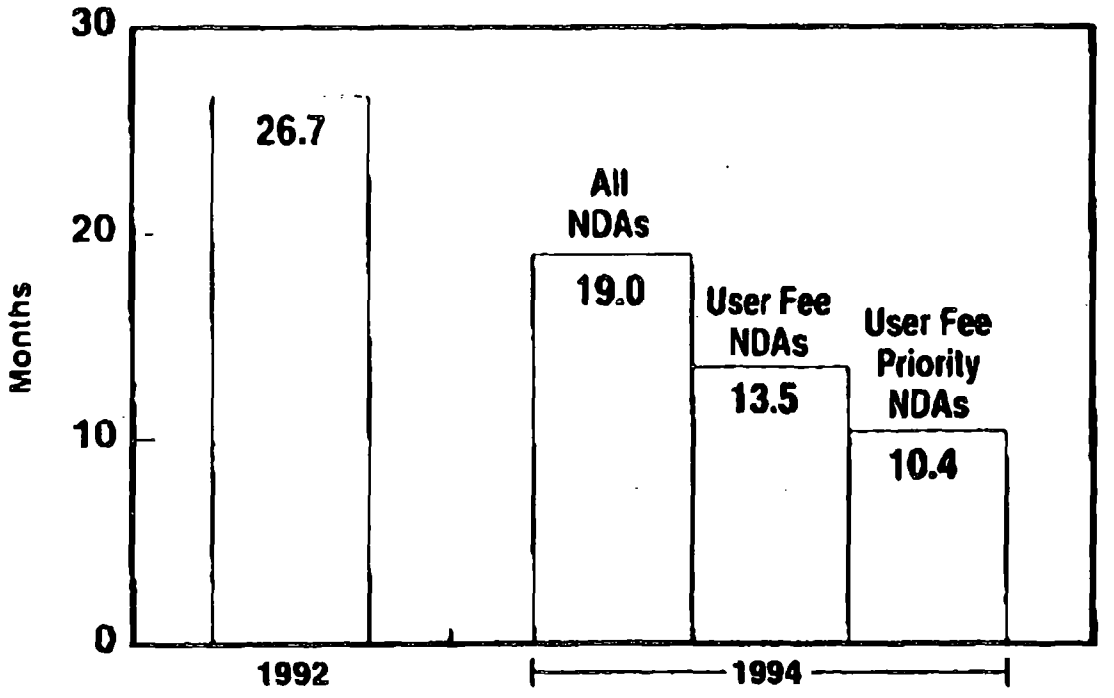
We recognize that working with industry and consumers to get the best expertise is important. But we also recognize the importance of making regulatory decisions in an environment of independence.

The second pillar of this agency is its scientific capability. Some of the leading experts on clinical trials work for FDA. This is one reason why drugs approved here are an immediate international success. Our laboratories can detect food contaminants ranging from illegal pesticide residues to

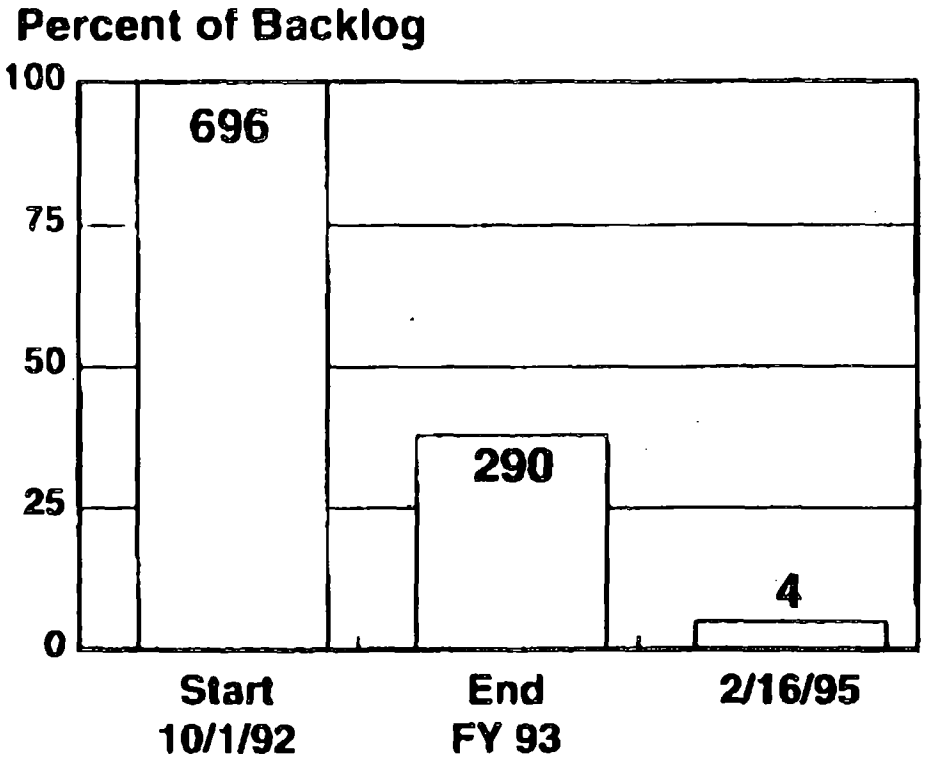
unlawful levels of lead. This is one reason why we are justifiably confident in the safety of our food supply.

In closing it is important to remember, particularly as we consider proposals for reform, that we not lose the best of what we already have.

Median Drug Approval Times

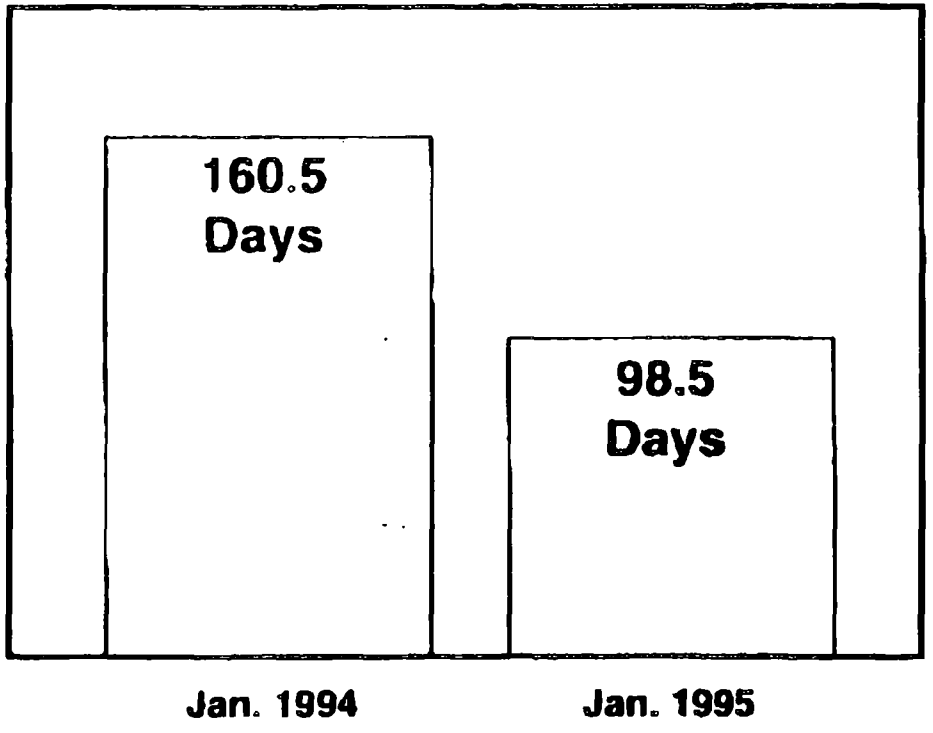


Overdue Drug and Biologic Submissions



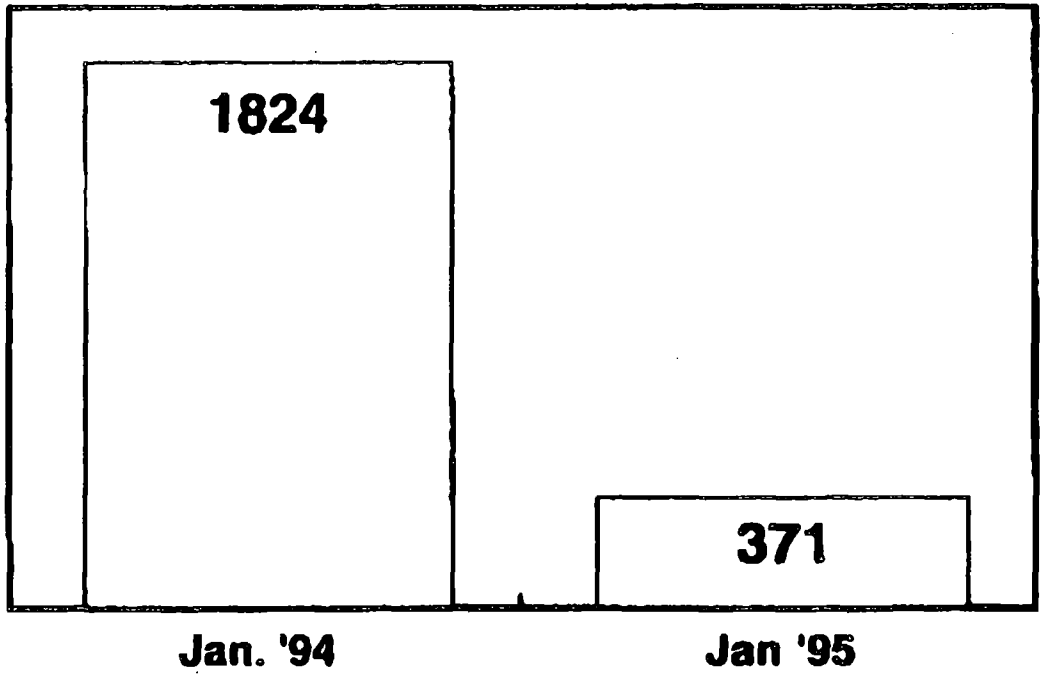
Goal: Eliminate Backlog by July 2, 1995

Median Review Times - 510(k) Devices



But the slowest 5% is still more than 500 days

Overdue* 510(k) Device Submissions



*More than 90 days