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FROM: GALAS, David J.: U.S. DEPARTMENT OF ENERGY

TO: DR. D.A. BROMLEY

DATE OF CORRESPONDENCE: 12/04/92

SUBJECT: HE IS CONCERNED ABOUT THE DECISION WITHIN THE DEPARTMENT OF COMMERCE THAT AFFECTS THE BIOTECHNOLOGY RESEARCH BUDGET.

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DIRECTORATE ASSIGNED: LIFE SCIENCES

STAFF ASSIGNED: D.A. Henderson

ACTION REQUIRED: FOR DAB'S SIGNATURE

STAFF ACTION: Bromley Signature

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SENDER'S DUE DATE:

OSTP DUE DATE: 12/23/92 STAFF DUE DATE 12/23/92
DATE COMPLETED: DATE COMPLETED/DEPT: 12/30/92

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COPIES TO: D. Allan Bromley

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WHITE HOUSE TRACKING #: CONTACT PERSON:
PHONE: EXT:
REMARKS: Per D.A. Henderson, no reply is necessary.

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CENTRAL FILES:

Department of Energy
Washington, DC 20585

December 4, 1992

Dr. D. Allan Bromley
Director
Office of Science and Technology Policy
Washington, D.C. 20506

Dear Dr. Bromley:

I am writing to express my concern over a recent budget decision within the Department of Commerce (DOC) that affects the biotechnology research budget. It is reasonably clear that the Biotechnology Research Initiative will be damaged by this decision, which is therefore of concern to you. It is unclear to me what can be done at this point, but I thought it important to raise the issue, and ask for your help and advice in moving towards a solution.

The National Oceanic and Atmospheric Administration (NOAA) originally proposed a major initiative in marine biotechnology for FY 1994, totaling $10 million. The initiative came out of NOAA's National Sea Grant Office and focusses on four issues:

- development of industrial materials and processes,
- development of aquacultural technology,
- development and improvement of seafood technology, and
- improvement of fisheries science and management.

These are all important issues and each promises to make the U.S. more competitive in this important and rapidly growing area of biotechnology -- born in the U.S. and now being dominated by Scandinavia and Asia -- marine biotechnology. This NOAA initiative is in the spirit of the Biotechnology Research Initiative, and has been endorsed by the Biotechnology Research Subcommittee (BRS) process.

As you recall, the BRS is currently conducting an outside review of the Biotechnology Initiative. Based on the response to date, there is a strong sense that we are about to miss a major area of opportunity by not adequately supporting marine biotechnology research. Marine biotechnology is perceived as a critical area by academia, industry, and other nations of the world.

The DOC has just recently made the decision to go with a partial version of the NOAA initiative in marine biotechnology, at a reduced level of $3 million, but to completely exclude Sea Grant from the funding. The impact of the decision is to shift the funds to the National Marine Fisheries Service where most of the new funds will be used to hire personnel working on fisheries' issues. While I am sure these are significant issues, we cannot consider this alternative as a valid part of the Biotechnology Initiative. This decision does not seem to be in the spirit of the FCCSET process, and it will not advance marine biotechnology research efforts.

The National Sea Grant College Program has been a lead agency in marine biotechnology research since the early 1970's. All of their research support goes to academic institutions and must be matched 50 percent with non-Federal funds. I have to agree with the initial Sea Grant proposal that marine biotechnology research would best be served by placing primary responsibility for the marine biotechnology initiative in the DOC with Sea Grant.

I enclose a copy of the documents describing the initiative, and I would be happy to discuss this matter with you further.

Sincerely,

David J. Galas
Associate Director for Health
and Environmental Research
Office of Energy Research

Enclosures

FY 1994 Budget Initiative

Marine Biotechnology

For

Economic Development

- Develop Industrial Materials and Processes
- Develop Aquacultural Technology
- Develop and Improve Seafood Technology
- Improve Fisheries Science and Management

National Oceanic and Atmospheric Administration
U.S. Department of Commerce

FY 1994 Budget Initiative

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National Oceanic and Atmospheric Administration
U.S. Department of Commerce

Overview of the Initiative

What are the Issues?

Industrial Products and Processes. The majority of plant and invertebrate phyla on Earth are exclusively or predominantly marine. These plants and animals as well as marine microorganisms often exhibit processes and produce substances with no terrestrial counterparts. Some of these processes and materials are of proven or potential importance in industry, but in general little is known about them. Biopolymers, enzymes, hormones, pigments, pharmaceuticals, and pesticides are among the chemical materials of interest. For example, annual U.S. trade in marine algal polymers is over $200 million. Bioprocessing and detoxification of effluents and waste materials are among the ways in which the biochemistry of marine organisms, especially microorganisms, can be exploited. The research community worldwide is recognizing the importance of marine organisms as sources of models for industrial materials and new approaches to industrial processing. Japan's aggressive program in marine biotechnology has developed an algal strain that produces large amounts of an industrial enzyme, superoxide dismutase. The annual international market for this kind of enzyme is $700 million. A NOAA initiative in research will contribute to the scientific basis and technology for new metabolic products of commercial significance, for producing bio-materials in controlled systems, and for using marine organisms or their components in industrial processing.

Aquacultural Technology. Foreign aquacultured products continue to invade domestic markets and the annual U.S. deficit in seafood trade stands at $2.4 billion. Improved biological and engineering technology and fish strains enhanced for culture in controlled systems will enable the United States to improve its trade position in seafood, to protect fisheries through market substitution of aquacultural products, and to enhance natural stocks with hatchery-produced animals. International competition in this field is intense, especially in Scandinavia and Asia. Aquaculture in China now provides 50% of its aquatic protein. Norwegian salmon farming employs 100,000 people and generates $750 million at the farm gate. NOAA research will provide technology for regulating reproduction, growth and development of aquacultural species; DNA technology for enhancing their growth characteristics; and engineering technology for production in closed systems and at off-shore sites in order to make the U.S. competitive in this growing field.

Seafood Technology. Seafood processors are facing increasingly stringent requirements for managing wastes and effluents from their plants. These requirements often exceed the ability of standard technology in the seafood industry or require expensive modifications in these plants. Numerous plants

are closing rather than acceding to the requirements. Current technology frequently allows seafood quality to deteriorate to undesirable levels as it moves from processor to consumer. Seafood contaminated with bacteria and viruses moves in many marketing channels. Foreign and domestic seafood processors, importers, and exporters perpetrate economic fraud by selling one fish species as another. Current technology does not allow such substitutions to be easily pinpointed. Advancements and applications in biotechnology are needed through research for improving and assessing seafood quality and safety, providing economic methods for recovering byproducts and treating wastes and effluents in seafood processing, and preventing fraud in seafood marketing.

Fisheries Science and Management. Many fish stocks are not managed optimally in part because conventional meristic techniques are incapable of identifying and separating regional fish stocks. In addition, the environmental perturbations, including fishing, that regulate the size and rate of growth of populations are poorly understood. Molecular technology has the potential to provide methods for assessing genetic changes resulting from environmental perturbations, including fishing; defining and assessing fish populations for management purposes; and defining and sorting ecological parameters affecting size of populations; and determining the degree of genetic diversity within species groups.

What Actions are Proposed?

NOAA is proposing research and development of biotechnology that will enhance economic development and fisheries management. Focused research in the following seven categories will be conducted:

Molecular genetics and genetic diversity - identify unique genetic codes that may form the basis for commercial technology; develop genetic engineering technology for aquatic plants, animals, and microorganisms useful in biotechnology, including aquaculture; determine diversity in fish stocks.

Growth and production of aquatic species - improve survival of commercial species under controlled conditions, especially closed and off-shore aquacultural systems; develop technology to prevent and treat diseases and to control and synchronize reproductive and growth cycles.

Bio-organic chemistry and pharmacology - identify novel marine substances as models for new types of biopolymers, enzymes, pigments, pharmaceuticals, hormones and pesticides; define related biosynthetic pathways; determine natural function and mechanism of action of novel bioactive compounds; define chemical and physical properties and develop production technology.

Cell culture, bioreaction, and bioprocessing - develop techniques for culturing

cells and tissues as a basis for mass production of useful natural chemicals; develop technology for catalyzing industrial reactions and for producing industrial materials; determine factors that control production of useful metabolites.

Technology for seafood processing and other water-dependent industries - develop new technology, biological processes, and by-products for controlling wastes, detoxifying effluents, and reducing solutes in waste water; improve technology for producing safe and high quality seafood.

Fish species and stocks - improve fisheries management by developing better tools for defining distinct fish populations and for assessing genetic changes in stocks that result from environmental perturbations and heavy fishing.

Recruitment processes and ecological relationships - improve fisheries management and yield forecasts by applying molecular techniques to defining and sorting variables that control trophic structures and affect the size and dynamics of fish populations.

What Will be the Impact on the Problem?

This program of research will make it possible to (1) rebuild fisheries and make more resources available to the fishing industry by enhancing natural stocks with hatchery produced animals and by substituting aquacultured animals in the marketplace for those from over-fished stocks, (2) improve the balance of trade in seafood by producing more product domestically through aquaculture and by developing byproducts, (3) upgrade the seafood processing industry by improving product quality and safety and through better technology, and by better handling wastes and effluents, and (4) increase U.S. competitiveness in high technology.

In regard to competitiveness, NOAA research has shown marine organisms to be rich sources of anti-inflammatory metabolites, some of which are under commercial development. The annual world-wide market for a new anti-inflammatory drug has been estimated at $2 billion. Obviously, the potential economic importance of even a single chemical product can be enormous. The Japanese Ministry of International Trade and Industry (MITI) as part of its emphasis on developing bio-industries also is emphasizing marine biotechnology. One of the primary goals of this Japanese effort is the "industrial utilization of marine organisms" and providing the basis for new industries in the 21st century. This is being done in part through a new Marine Biotechnology Institute whose objective is to be the first full-scale marine biotechnology research and development base, not only nationally, but globally. It is based on the premise that marine biotechnology is the "greatest remaining technological and industrial frontier."

Why Now?

The United States, and NOAA, must make an immediate commitment to advance state-of-the-art technology to ensure wise use and conservation of living marine resources and competitiveness in the aquaculture and biotechnology industries, and national health. The White House has identified biotechnology as one of five topics of special focus for a proposed Presidential budget initiative. The corresponding report of **the Federal Coordinating Council for Science, Engineering, and Technology, "Biotechnology for the 21st Century," identifies marine biotechnology as a topic for special attention, and recognizes NOAA as a primary player in this field.** However, it shows the federal government's investment in marine biotechnology to be quite low. For example, a report of the National Academy of Sciences (in preparation) will recommend increased attention on research to develop and improve aquaculture in closed systems and at offshore locations. Living marine resources contribute significantly to the U.S. and world economics, and they have the potential for much more. Improvements in biotechnologies for fisheries science will enhance the regulation, management, and productively of fisheries.

Living marine resources already contribute significantly to the U.S. and world economies. For example, U.S. trade in algal products such as carrageenan and alginic acids totals several $100 million annually. Marine resources have the potential to contribute much more to the national economy. Science needs to provide (1) technology for ensuring harvest of fishes at high and sustainable levels, (2) efficient and progressive technology for producing and marketing safe seafood, (4) the basis for new approaches to producing food, feed, and industrial materials and processes in an increasingly technological and competitive world, as well as (4) human resources for application of biotechnology in industry.

Among the key needs are the following:

- technology for assessing genetic diversity and manipulating the genetic characteristics of marine plants, animals, and microorganisms,
- technology for the mass culture of food species in closed and off-shore aquacultural systems,
- methods for diagnosis and control of disease in aquacultural species,
- technology for control of reproductive cycles of aquacultural species,
- technology for use of single-celled organisms and cells of higher organisms

in bioreactors for production of chemical products,

- defining biosynthetic pathways for marine biopolymers and other biochemicals of interest to the chemical industry,
- technology for controlling the production of metabolic products, and
- defining the mechanism of action and natural function of potential new model compounds for the drug and agrichemical industries.
- technology for waste management and byproduct recovery in seafood processing and other water dependent industries, and for maintaining quality and safety of seafood,
- technology for precisely discriminating between fish species and strains,
- methods for defining ecological relationships among fishes and prey important to defining management strategies in fisheries,

What is Being Done Now?

The National Marine Fisheries Service and the National Sea Grant College Program conduct research that addresses some of the key issues. Advances in this research are encouraging. They have resulted in industrial investment and development at significant levels and improved our understanding of parameters controlling fish populations. (See Appendix I on page 17 for examples.)

The National Sea Grant College Program through its 29 coastal and Great Lakes programs conducts aquacultural research in molecular genetics and selective breeding, physiology and endocrinology, nutrition, and pathology. This research focuses primarily on penaeid shrimp, salmonids, hard clams, and striped bass - species that have yielded major commercial development. In addition, Sea Grant sponsors a small program of marine biotechnological research directed to exploiting the biochemistry of marine organisms for new approaches to industrial processing and for models for new products. It also sponsors research in seafood science directed to improving technology in the seafood processing industry.

The National Marine Fisheries Service conducts a limited program of activity in the following locations:

- o Milford, CT and Oxford, MD - bivalve culture techniques with emphasis on oyster pathogens and their control,
- o Galveston, TX - sea turtle "head start" program and shrimp culture

techniques,

o Manchester, WA - Pacific salmon broodstock development, Atlantic salmon disease reduction, and pen-rearing and holding techniques,

o Little Port Walter, AK - Pacific salmon broodstock protection (jointly with the State of Alaska).

All these efforts are directed to enhancement of wild stocks that are threatened from (1) over-exploitation, (2) habitat destruction, and (3) diseases and epizootic outbreaks.

Why is Further Effort Needed?

U.S. research in support of marine biotechnology and biotechnological research directed to solving problems in fisheries management and seafood regulation have barely begun to address the range of problems and opportunities that can be solved or exploited through modern molecular science. For the United States to properly protect and manage its living marine resources and to maintain its leadership in a world highly competitive in technology, it must increase its investment in research supporting marine biotechnology, which is developing rapidly in some industrialized countries, and in development of human resources for a competitive industrial sector.

Additional effort is needed to (1) develop fundamental knowledge about natural products and processes of marine organisms in order to provide models for new commercial products and new approaches to industrial processing and to maintain U.S. competitiveness in a developing field; (2) develop biological, engineering, and DNA technology for culture of marine species in controlled systems in order to protect fisheries through market substitution of aquacultural products, enhance natural stocks with hatchery-produced animals, balance trade in seafood, and compete technologically in aquaculture which is a rapidly growing sector worldwide; (3) upgrade technology in the seafood processing industry in order to meet foreign competition in quality, safety, and productivity and to help the industry meet increasingly stringent environmental regulation, and (4) provide a sound scientific understanding of the dynamics of fish populations in order to manage fisheries for optimal protection and economic benefit.

"Biotechnology for the 21st Century", the recent report of the Federal Coordinating Council on Science, Engineering, and Technology shows that out of the $3.8 billion federal investment in biotechnological research only a little over one percent is in support of marine biotechnology. The report states, "The majority of plant and invertebrate animal phyla on Earth are either exclusively or predominantly marine. ... They often exhibit processes and produce

substances with no terrestrial counterparts. Many of these marine organisms are so poorly understood that they have yet to be fully described and named. The open ocean is home to a vast array of photosynthetic plants, bacteria, and other microorganisms whose poorly understood metabolic activity is vital to the Earth's well-being and can be exploited for useful purposes. ... the breadth of research opportunities ... cannot be addressed adequately with current levels of investment."

Why in FY 1994?

NOAA has identified the urgency to rebuild and better manage the Nation's fisheries as one of its primary strategic goals. Improved techniques in fisheries that provide more accurate and timely information is essential for rational management of fisheries, therefore NOAA's investment in biotechnologies for fisheries applications should be considered high priority in order to accomplish this goal. The stage has recently been set for collaborative efforts and developments between NOAA, academia, and international marine science communities to conduct coordinated research for better understanding biophysical processes that affect the recruitment of economically important fisheries. In addition, the Department of Commerce is focussing on program priorities stressing economic growth and job creation. Now is the time to provide incentives to the marine science community to work together in the development of biotechnologies which can promote commercial development and enhance fisheries science. For example, although aquacultural production in the United States is growing, it is not keeping pace with that in Europe and Asia, where it is being developed aggressively.

Why NOAA?

This initiative speaks directly to the Department of Commerce's efforts to stress economic growth and job creation through:

- promoting entrepreneurship to increase new business formation and make new jobs,
- facilitating industrial and governmental efforts to improve the quality of American products and services, and
- pursuing a linked and balanced approach to meeting the Nation's environmental and economic competitiveness goals.

It also addresses previously stated goals of the Department of Commerce:

- to enhance human resources through greater educational opportunities,
- to speed up the commercialization of new technologies.
- to promote international trade in a global economy,
- to promote the expansion of industrial R&D and accelerate the commercial application of new technologies, and
- to support balanced management of the oceanic and atmospheric environment.

NOAA is responsible for managing the Nation's living marine resources and is the international leader in science for rational management and assessment of them. NOAA through the National Sea Grant College Program is mandated to develop living marine resources and has made itself a leader in research supporting marine biotechnology. NOAA has a continuing obligation to the Nation to encourage and sponsor the development of biotechnologies that enhance fisheries science and marine economic development. NOAA's current and planned research is complementary to that of other federal agencies whose primary efforts in marine biotechnology and in application of molecular techniques to addressing marine issues are characterized by the following:

National Science Foundation - basic research for the purpose of enhancing knowledge of biological processes in the ocean and marine environmental processes; role of marine plankton in carbon and nutrient cycling.

Office Naval Research - fundamental research on the role of microorganisms in oceanic processes, on understanding and controlling biological processes

affecting operations of ships, and on bioprocessing for naval applications.

National Institutes of Health - development of marine natural products for treatment of cancer and AIDS; development of culture and genetic enhancement techniques for marine species useful as models in physiological and toxicological research.

Department of Agriculture - research in support of aquaculture of fresh water fishes.

Food and Drug Administration - testing of seafood for safety, verifying effectiveness of and developing new methods for determining safety.

Department of Energy - basic research on microbiological processes in coastal environments.

The academic research role is distinct from industrial efforts. Except in the area of seafood science, academic research starts at a more fundamental level. It spawns ideas and new approaches for the commercial sector. For example, in regard to marine natural products, academic scientists determine structures of native molecules which may serve as templates for testing and structural modification by industry. Industry must develop economic methods for large-scale synthesis or biological production of compounds of commercial importance. Pharmaceutical houses also must conduct the extensive toxicological and clinical research and testing required by FDA. Academicians can elucidate biosynthetic pathways and natural functions related to novel drug candidates and isolate related enzymes which represent receptors related to drug action. Knowledge of these enzymes can lead to an understanding of drug action at the molecular level and stimulate new lines of industrial effort.

In seafood science and technology the boundaries between industry and academe are not precise. However, most of the 1600 seafood processors in the United States are small operations - less than $2,000,000 in annual sales. Few have research components; they have few, if any, technical experts on their staffs. Thus, government and academe play an essential role in research and technical assistance for this industry.

What Actions are Proposed?

The National Marine Fisheries Service and the National Sea Grant College Program will initiate or expand research in support of marine biotechnology and its applications in fisheries science and management in the following areas of need and opportunity:

• **Molecular genetics and genetic diversity.** The development of new industrial products and processes based on exploiting the biochemical processes of marine organisms - marine biotechnology for the 21st century - depends on fundamental advances in science that will provide the basis for genetic engineering of plants, animals, and microorganisms. Thus, basic research will be directed to developing DNA technology for manipulating, introducing, and expressing genes in aquacultural food species (finfish, crustaceans, and mollusks) as well as species with potential for use either in producing chemical products or in industrial processing - lower invertebrates, macroalgae, bacteria, and cyanobacteria. These advances will provide strains that grow faster, have higher efficiency in food conversion, produce higher proportions of muscle or desirable compounds, synthesize metabolites at greater rates, or catabolize waste materials or toxic effluents more efficiently. Among the advancements needed are (1) determining mechanisms by which gene expression is regulated, (2) developing methods by which foreign genes and additional copies of natural genes can be added to genomes of marine species, (3) developing techniques for transferring gene clusters responsible the synthesis of useful secondary metabolites. For development of ideally protective fisheries management schemes it will be necessary to continue development and to apply technology for unequivocal discrimination between fish species and strains and for determining the degree of genetic diversity within species.

- **Growth and production of aquatic species.** A range of biological and engineering research is needed to develop and improve technology for aquaculture in the U.S. and to develop a competitive position with respect to other countries. Research is needed (1) to provide for completion of the entire life cycle of marine aquacultural species in captivity, (2) to control and synchronize reproductive and growth cycles, (3) to make gene probes and compound probes for highly sensitive assessing of endocrine activity, (4) to develop gene probes and other molecular assays for detecting and measuring pathogenic viruses and bacteria, (5) to develop vaccines and other measures for controlling disease and parasites, (6) to improve technology for production and handling of larvae in hatcheries, (7) to define nutritional

requirements and to improve nutritional value of live feeds, and (8) to define ecological factors affecting production in polyculture systems and in open ponds.

- **Bio-organic chemistry and pharmacology.** A spectrum of biochemical and biological research will be conducted in this category. It will focus on (1) determining the structures of novel lipids and other unique small molecules, (2) isolating, identifying, and determining function of enzymes controlling important processes, (3) isolating and identifying bioactive secondary metabolites, (4) determining the process and site of action of novel substances that elicit physiological responses in ways different from standard drugs and industrial chemicals, (5) defining pharmacophores through molecular structure, synthesis, and computer modelling, (6) determining role of bioactive natural products in cellular processes, (7) defining properties of marine materials, particularly biopolymers, as a basis for industrial use, (8) defining biosynthetic pathways producing useful metabolites, (9) developing methods for manipulating materials into new forms, and (10) developing modified prototype materials.

- **Cell and tissues culture, bioreaction, and bioprocessing.** This research includes basic physiology and nutrition of marine microorganisms and cells of higher organisms that will provide the scientific base for their use in controlled systems for producing commercial substances. The research will focus on (1) determining nutritional and environmental controls on metabolism, especially secondary metabolism, (2) determining relationships between symbionts in production of metabolites, (3) developing techniques for giving halophytic plants useful agricultural properties or properties of value in restoring degraded environments (4) determining factors that promote production of useful materials and (5) developing biochemical engineering technology for use of saline organisms in bioreactors and photo-bioreactors. For example, basic advancements are needed for developing technology to use culture cells of macroalgae in bioreactors to produce useful biochemicals such as enzymes, pharmaceuticals, and agrichemicals.

- **Technology for seafood processing and other water-dependent industries.** The seafood processing industry is now facing serious problems in meeting increasingly stringent environmental regulations; economic technology is not available for water treatment and recycling and other functions in closed system aquaculture. Research is needed (1) to develop methods and technology for biological filtration and water reuse, (2) to define chemical, physical, and biological factors influencing water quality

and develop methods, including biological pre-conditioning, for their control, (3) to develop and improve methods for effluent control and biological treatment of wastes, (4) to develop approaches to recovery of byproducts, such as enzymes and functional proteins, from seafood processing wastes, (5) to consistently produce, store, and transport seafood of high organoleptic and microbial quality, (6) to develop reliable and economic methods for shellfish depuration, and (7) to develop and improve technology for preventing economic fraud through dishonest substitution of species.

- **Fish species and stocks.** Improved techniques for rapid species and stock identification and assessment are crucial to the rebuilding and better management of the Nation's wild stock fisheries. Research will focus on (1) precise techniques to replace old, meristic techniques in identification of species and stocks, (2) techniques for distinguishing wild from cultured species or stocks in the market for enforcement purposes, (3) techniques (e.g., mitochondrial DNA) for verifying species identity in the marketplace to prevent product substitution and mislabelling.

- **Recruitment processes and ecological relationships.** Improved molecular techniques are needed for measuring biological parameters and determining biological processes and ecological relationships that bear on fishery management decisions, development of alternative strategies, and interpretation of the effects of anthropogenic perturbations, such as pollution and harvesting, on important species. Predator-prey relationships and growth and maturation of populations are of particular importance. Specifically, the research will focus in part on (1) techniques (e.g., RNA-DNA condition index) for measuring factors associated with recruitment, (2) techniques for identification of prey, and (3) techniques (e.g., stable isotopic) for investigating the long-term historical changes in ecosystem trophic structure.

What Will It Cost?

(dollars in millions)

Major Actions	FTE [1]	Amount
Molecular genetics	2.0	2.0
Fish Growth	0.0	1.5
Bio-organic chemistry	0.0	1.5
Cell culture, bioreaction	0.0	0.8
Seafood technology	0.0	1.2
Fish identification	5.0	1.5
Eco-relationships	4.0	1.5
Total Request for FY 1994	11.0	10.0

[1] 1 FTE OAR
10 FTE NMFS

What Are the Benefits?

- New types of industrial materials and processes and new approaches to use of living marine resources.
- New companies to manufacture or biologically produce marine products.
- Increased food supply and economic competitiveness through aquaculture.
- New jobs in aquaculture and other bioindustries.
- Improved efficiency and competitiveness in seafood processing and higher quality seafood.
- Environmentally compatible technology for waste management in aquaculture and processing seafood.
- Human resources for careers in high technology.
- Improved management of fish stocks.
- Increased and better prediction of resource levels available to the fishing industry.

Outyear Funding Levels

(dollars in thousands)

Major Components	FY 1994	FY 1995	FY 1996	FY 1997	FY 1998	FY 94–98
Molecular Genetics	$2,000	$2,000	$2,100	$2,200	$1,900	$10,200
Fish Growth	$1,500	$1,500	$2,000	$2,500	$1,900	$9,400
Bio-organic Chemistry	$1,500	$2,000	$2,000	$2,100	$1,000	$8,600
Cell Culture, Bioreaction	$800	$1,000	$1,500	$1,000	$1,000	$5,300
Seafood Technology	$1,200	$1,500	$1,500	$1,800	$1,200	$5,500
Fish Identification	$1,500	$1,600	$1,700	$1,800	$500	$7,100
Ecosystem Relationships	$1,500	$1,600	$1,700	$1,800	$500	$7,100
Total Request	$10,000	$11,200	$12,500	$13,200	$8,000	$54,100

APPENDIX I

Examples of Important Advancements

Research in the National Oceanic & Atmospheric Administration has developed -

> **science and technology for synchronizing spawning of abalone** and controlling settlement of their larvae so that hatcheries could be developed for these mollusks which now are cultured commercially in California.

> much of the science and production technology on which a **new industry in aquaculture of hybrid stripped bass** is burgeoning. Annual production is now over 1,000,000 pounds with over 10 producers in the mid-Atlantic region.

> a **fast-growing, more attractive hard shell clam which** is the basis of a $7 million aquacultural development in South Carolina.

> a triploid oyster that makes possible a yearround rather than a seasonal oyster industry and contributed to the **revival and stabilization of the oyster industry on the West Coast.**

> the science and **technology for controlled farming of seaweeds** that produce industrial polymers. The polymer carrageenan from production of these farms is the basis of $100's of millions of industrial products (Carrageenan replaces fat for juiciness in McDonald's McLean burgers.)

> two "all-fish" expression vectors that will be useful in **genetic engineering of fish** and made generic contributions to DNA technology, e.g., showed the B-actin gene of carp to be nearly identical to the B-actin gene of mice and set the stage for using fertilized fish eggs for research that cost about $3 each instead of transgenic mice embryos that cost $300 to $3000 each.

> technology for determining and controlling molecular weight in **production of chitosan** from shellfish wastes, for producing microcrystalline chitosan, and for extruding it in fibers that can be woven. Research has shown that treatment of wheat seeds with chitosan protects resultant plants from disease and increases wheat production by up to 10% and that there is a spectrum of other uses for chitosan. These developments were a basis of **Inside R&D's** forecast that chitin/chitosan sale would increase to near $2 billion over the next few years.

> **vaccines for two major microbial diseases of salmon.** Preliminary field tests show them to be effective. This research sets the stage for commercial development of more effective and inexpensive vaccines and will contribute significantly to the economic

viability of trout and salmon farming.

> a rapid enzyme-linked immunosorbent assay (**ELISA**) **for the detection of** **Vibrio cholerae** in oysters. It can be applied to a spectrum of homogenized samples. A commercial firm has adapted this technology to produce a small hand-held kit into which a dipstick, previously exposed to sample, can be inserted. A squeeze of the fingers exposes the sample to diagnostic reagents. Within ten minutes a positive sample produces a color reaction discernable to the naked eye. The company is sending millions of these kits to Peru and other places in South American where they will be used to help combat an epidemic of cholera. The cholera bacterium has been identified in Gulf of Mexico waters; thus,the new assay is expected to help keep only safe shellfish in commercial trade.

> an inexpensive biochemical "dip-stick", monoclonal antibody **assay for ciquatoxin** which is a major problem in finfish from tropical areas. The corresponding disease ciguatera is one of the primary diseases associated with seafood. The invention is a compact, portable test kit used to test flesh near the gills of fish. Hawaii Chemtect International, Inc. will produce the assay kits commercially.

This research identified -

> representatives of **a new class of anti-inflammatory agent** that is the basis of over $10,000,000 in R&D investment at Allergan, Inc. which is developing a drug to combat psoriasis.

> new chemical and pharmacological classes of anti-inflammatory agents that are the basis of major R&D by **a new company Osteoarthritis Sciences, Inc.** that will be working with Massachusetts General Hospital.

> the **first human hormone, a potent immunohormone, from a plant source.** Determined the biosynthetic pathway for this hormone in an alga and showed it to be one of a whole class of algal products that are active in the biochemical pathways controlling inflammation and other disease states in humans.

FY 1994 Budget Initiative

Marine Biotechnology

For

Economic Development

FUNDING ALTERNATIVES

National Oceanic and Atmospheric Administration
U.S. Department of Commerce

Interpreting the Alternatives

Budget Alternative 1 - Full Request
$10.0 million in FY 1994

Even budget Alternative 1 would provide the basis for only preliminary research in some of the research areas covered by the initiative. (The initiative was put forward first at the $20 million level.) Because the range of species, problems, and opportunities is so broad in research geared to applying biotechnological techniques in fisheries management and to exploiting marine biological products and processes in high technology, funding at this level should be increased sharply in succeeding years.

Budget Alternative 2
$7.9 million in FY 1994

At this budget level initiating research to investigate the implications of genetic diversity in fisheries management would be delayed until fiscal year 1995. Assessing genetic changes in fish stocks from environmental perturbations would be delayed and efforts to use molecular techniques in sorting variables controlling trophic structures would be cut back.

Alternative Funding Levels

(In millions of dollars)

Major Components	Alternative 1						Alternative 2						Alternative 3					
	94	95	96	97	98	94-98	94	95	96	97	98	94-98	94	95	96	97	98	94-98
Molecular Genetics	2.0	2.0	2.1	2.2	1.9	10.2	1.0	2.0	2.0	2.1	2.2	9.6						
Fish Growth	1.5	1.5	2.0	2.5	1.9	9.4	1.5	1.5	2.0	2.5	2.5	10.0						
Bio-organic Chemistry	1.5	2.0	2.0	2.1	1.0	8.6	1.5	2.0	2.0	2.1	2.2	9.8						
Bioreaction	0.8	1.0	1.5	1.0	1.0	5.3	0.8	1.0	1.5	1.0	2.5	6.8						
Seafood Technology	1.2	1.5	1.5	1.8	1.2	5.5	1.2	1.5	1.5	1.5	1.8	7.2						
Fish Identification	1.5	1.6	1.7	1.8	0.5	7.1	0.9	1.5	1.6	1.7	1.8	7.5						
Ecosystem Studies	1.5	1.6	1.7	1.8	0.5	7.1	1.0	1.5	1.6	1.7	1.8	7.6						

Alternative Funding Levels

Major Actions	1	2
Molecular Genetics	•	O
Fish Growth	•	•
Bio-organic Chemistry	•	•
Bioreaction	•	•
Seafood Technology	•	•
Fish Identification	•	O
Ecosystem Studies	•	O

Full Implementation •
Partial Implementation O
No Implementation

Alternative Funding Levels

Outcomes and Products	1	2	3
Molecular Genetics	1998	1999	
Fish Growth	1996	1997	
Bio-organic Chemistry	1997	1997	
Bioreaction	1998	1998	
Seafood Technology	1997	1998	
Fish Identification	1995	1995	
Ecosystem Studies	1997	1997	

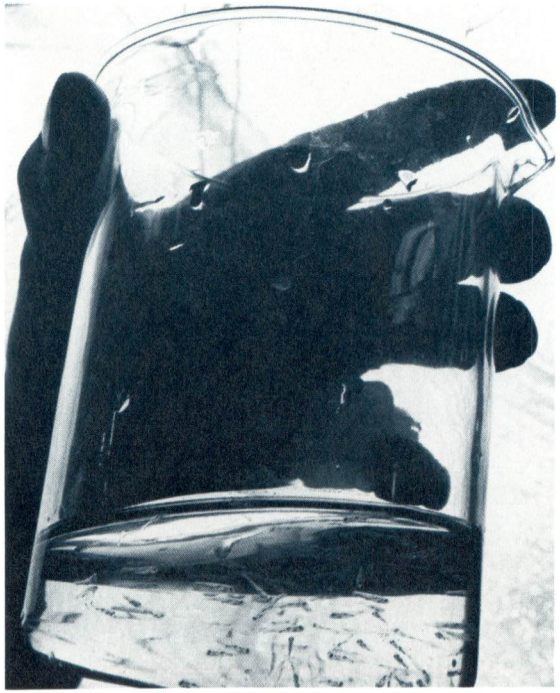
A SEA GRANT INITIATIVE

MARINE BIOTECHNOLOGY

Competing in the 21st Century

Contents

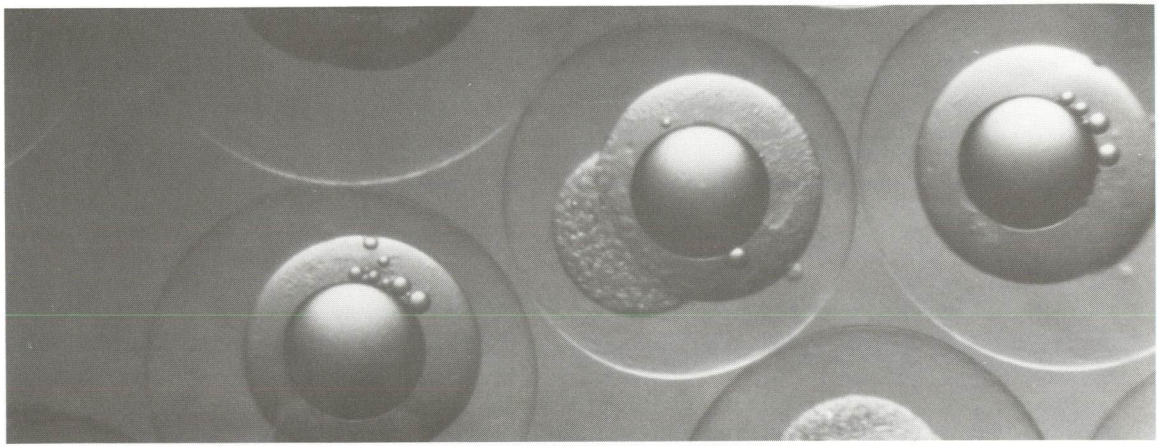
MARINE BIOTECHNOLOGY
Competing in the 21st Century



"A revolution in the ocean sciences has begun, with the application of the modern tools of biotechnology, molecular and cellular biology to marine organisms and ecosystems. The change is expected to be fundamental in nature, exponential in pace and unprecedented in its scientific and economic impact. . .within a decade, quantum leaps will have been made, not just in the amount of knowledge, but in the types of insights into the fundamental and longstanding problems of ocean sciences. . . ."

— *National Science Foundation*
1990

Marine Biotechnology
Research, Competitiveness and Technology Transfer

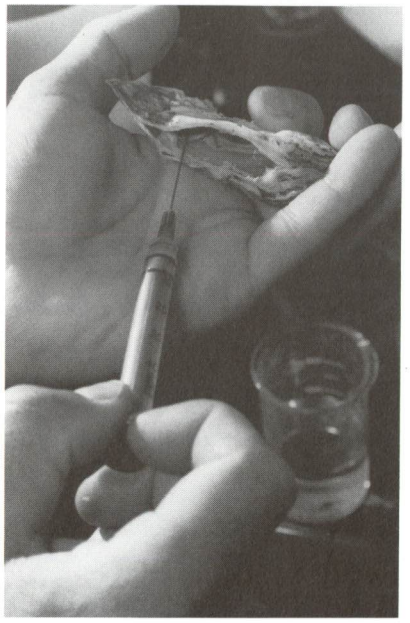


The United States has an important lead in the rapidly burgeoning field of marine biotechnology. But the country stands to lose its lead to other nations, which are aggressively pursuing new technologies.

For millennia the oceans have been a source of food, minerals and other natural products. But as population and human needs continue to increase, so too do the pressures on those resources. If we as a nation are to meet these growing needs, if we are to take advantage of the bounty the oceans offer, if we are to protect the viability of our coastal environments, we must commit ourselves to a national program that will build on our current scientific achievements and develop national expertise for the future.

No element of science and technology can match the potential of molecular biology and biotechnology to transform the lives of people around the world. While powerful molecular technologies already are being applied to the study of marine organisms, we have hardly begun to take advantage of their potential. To meet this challenge, research communities, government agencies and the private sector must interact more effectively. Current efforts simply are not adequate: the United States has no national program in *marine* biotechnology. It is only through a comprehensive plan that we will be able to meet the technological challenge at home and competition from abroad.

Economics of Biotechnology — Challenge and Competition



The public sector in the United States has provided less than $50 million annually for research and development in marine biotechnology; in Japan, that figure is between $900 million and $1 billion. Over the next ten years, for example, the Japanese Ministry of International Trade and Industry will bring an additional $200 million to the field and will support the creation of two centers of marine biotechnology, reflecting its assessment of marine biotechnology as the "the greatest remaining technological and industrial frontier." The United States, while assisting other governments in building capabilities in marine biotechnology, has only scattered efforts supporting research and development.

A national vision for development of marine biotechnology will lead to applications useful to many industries and, ultimately, the American consumer and world markets.[1] It will reverse the current trend where products from marine microbiology are already being imported into this country from abroad, further eroding the country's trade deficit.

Achievements and Potential

Since 1983, limited public funding of marine biotechnology has still resulted in more than 170 United States patents. Sea Grant programs across the nation have been instrumental in helping to support developments such as new classes of anti-inflammatory agents that have become the basis of major investment by the pharmaceutical industry, vaccines that combat major microbial diseases of salmon and a new assay that a commercial firm has used to produce a kit for rapid detection of contaminated seafood.

To exploit the unlimited possibilities that aquatic organisms have for protecting public health, for restoring degraded ecosystems, for improving seafood production and safety and for developing an array of new products, Sea Grant proposes an initiative with clear national goals that will help guide marine biotechnology in the United States.

[1] Biotechnology for the 21st Century. 1992. Federal Coordinating Council for Science, Engineering and Technology, Washington, D.C.

Marine Biotechnology in the United States

The United States is the current world leader in research expertise in marine biotechnology. However, our leadership faces stiff competition from other countries that are moving ahead with strong national investment and planning. Focused research in marine biotechnology in concert with commercial development offers the promise of economic and social opportunities: it will lead to new industries and new jobs; it will help upgrade and advance higher education to meet United States needs in an increasingly technical and competitive world. It will assist in reversing our trade deficit, which in seafood alone is $2.4 billion dollars a year, second only to petroleum; it will lead to new international markets and overall economic development.

A national commitment to research and development in marine biotechnology will also help us respond to the critical needs of society; it will:

- Open new avenues for monitoring health and treating disease
- Provide innovative techniques to restore and protect aquatic ecosystems
- Increase the food supply through aquaculture
- Enhance seafood safety and quality
- Develop new types and sources of industrial materials and processes
- Expand knowledge of biological and geochemical processes in the world ocean

This document describes the framework for initiating this important and exciting program in marine biotechnology. Three broad elements — Molecular Frontiers in the Ocean Sciences, Applications of Marine Biotechnology, and Marine Biotechnology and Society — encompass the range of research, application and education needed to exploit this new technology and ensure its wise use. Each element, in turn, includes examples of significant advancements to date and outlines directions for future research and development in this challenging field.

Marine biotechnology has made an auspicious beginning — this Sea Grant initiative gives the United States a means to chart a course through the 90s and into the 21st century.

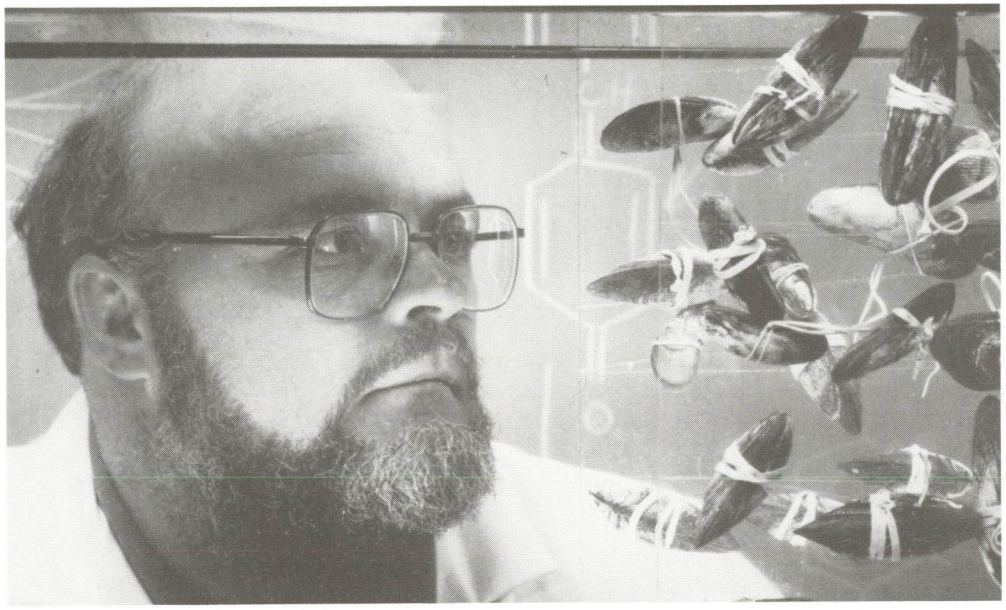
Sea Grant: The Nation's Marine Research Network

For more than a quarter century, the National Sea Grant College Program has promoted excellence in marine research and outreach. Sea Grant operates through twenty-nine coastal programs and numerous discrete inland projects, involving hundreds of universities, scientists, educators and students. During the past two decades, Sea Grant has provided benefits to resource management agencies and to a range of marine-related industries — to those in commercial and recreational fishing, aquaculture, shipping, mining, boating, seafood processing and biotechnology.

Productive research in support of marine biotechnology has been well underway in Sea Grant programs around the country. Despite modest funding, this effort represents a core of experience for the nationally coordinated initiative.

The key to the Sea Grant concept is partnership. One-third of each Sea Grant program's funds must come from nonfederal sources, from state or private funds. Federal funds, provided through the National Oceanic and Atmospheric Administration (NOAA), often serve as a catalyst, helping to mobilize support for important marine-related research and education activities. Sea Grant, then, provides an excellent mechanism for pursuing coordinated efforts, where corporate and other support can be joined with state and federal monies to fund research, technology transfer and scale-up activities.

As the outreach arm of NOAA, Sea Grant provides a link to academia, business and industry, other federal agencies, including the Environmental Protection Agency, the National Science Foundation, the National Institutes of Health, Departments of Agriculture, Interior and Defense, and the general public.



Sea Grant and Marine Biotechnology

Productive research in support of marine biotechnology has been well underway in Sea Grant programs around the country. Despite modest funding, this effort represents a core of experience for the nationally coordinated initiative in marine biotechnology that Sea Grant now proposes. Sea Grant programs have developed an effective managerial infrastructure with a strong track record and are clearly capable of directing a major national initiative. In addition, Sea Grant is the only agency in the marine sector with experience in outreach programs targeted to the transfer of marine science and technology and to the improvement of education in aquatic sciences.

Sea Grant has demonstrated experience in integrating public policy considerations into multi-disciplinary research and education programs. Part of Sea Grant's primary mission includes working together with federal and state agencies and other organizations, public and private, to consider critical marine-related issues. New developments in molecular biology — and their commercial application — will have significant ethical, ecological and economic implications. Sea Grant programs have a strong record of approaching such issues, helping to bring together expertise from across disciplines to foster balanced analyses and workable solutions.

The Need to Act Now

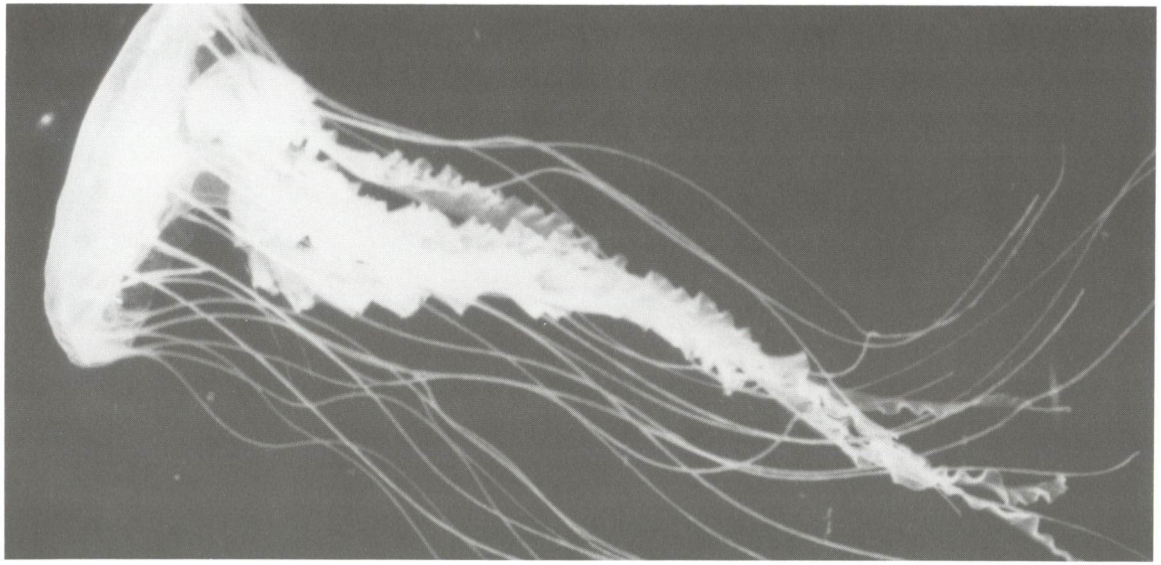
Marine biotechnology has the potential to develop rapidly — and to provide major economic returns to the nation. To take advantage of this opportunity, however, we must have an aggressive program of marine biotechnology research and development that draws on cutting-edge science underway in laboratories around the country. We must encourage and support multi-disciplinary research and ensure rapid technol-

ogy transfer. We must actively plan for partnerships with industry and commercial enterprise, and facilitate efficient technology transfer. Most importantly, we must train the next generation of scientists and technologists or risk losing the slim competitive edge we now have.

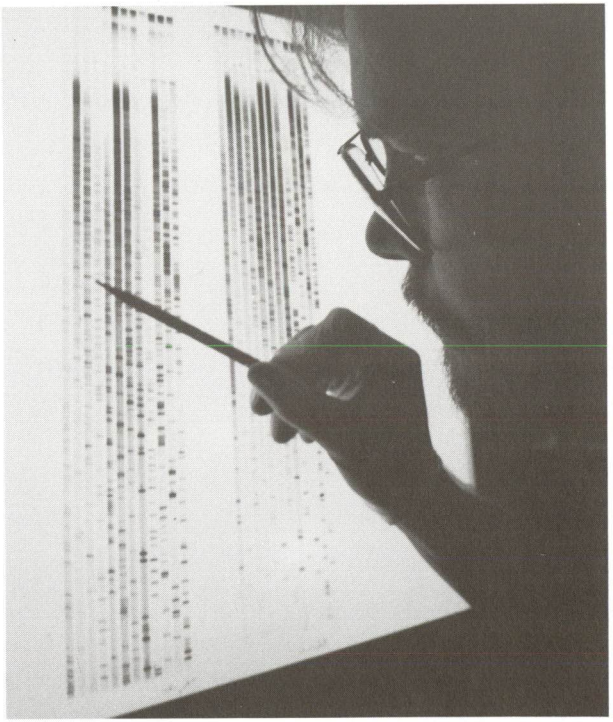
To assure the relevance of program elements, a focused initiative, open to researchers throughout the nation, will be guided by an advisory panel of academic and industrial scientists, economists and managers and will build upon the ideas and recommendations in the Biotechnology Research Initiative put forward by the Federal Coordinating Council on Science, Engineering and Technology, under the guidance of the President's science advisor.

The United States has an important lead in the rapidly burgeoning field of marine biotechnology. But as has happened with other emerging technologies, the country stands to lose its lead to other nations, most notably Japan, which are aggressively pursuing new technologies. By strengthening its leadership role now, the United States can help assure its competitive position as the stage is set for the next century.

A national initiative in marine biotechnology will fund the best science throughout the nation, to exploit this new technology.



Molecular Genetics



Knowledge of the genetics of marine organisms will yield important information about their phylogeny, evolution, disease, symbiosis, ecological adaptation and physiology. This information will improve our ability to understand and manage complex ecosystems. Also, information gained about simpler organisms such as bacteria, algae or invertebrates will give us insights into the functioning of more complex mammalian systems.

The introduction of foreign genetic material into organisms and genetic manipulation to induce sterile, polyploid or hybrid stocks has been accomplished with a few marine species. In some cases, these results have been immediately applied in commercial aquaculture. These methodologies can also be used in the management and enhancement of wild stocks. For example, genetic markers can be used to differentiate various strains, or to separate hatchery from wild populations. Examination of DNA has shown that some fish and shellfish populations consist of various substocks, often with differing abilities to adapt to environmental stresses. This observation suggests that genetic engineering could be used to improve survival and productivity of cultured stocks.

Marine viruses, recently shown to infect many phytoplankton and bacteria, are thought to play a major role in plankton dynamics. They may also provide a means for incorporating foreign genetic material into marine algae, which have proved resistant to genetic engineering, but which have great potential as sources of new chemicals and materials.

THE CHALLENGE

Determine the Molecular Genetics of Aquatic Organisms:

- *Identify the basis for unique adaptations*
- *Characterize environmental factors controlling gene expression*
- *Use aquatic organisms as molecular models*
- *Develop new techniques in molecular biology*

Exciting new areas of research in this promising field include:

- Certain Antarctic fish produce novel glycoproteins which inhibit ice crystal growth in their tissues; use of molecular techniques may permit their large-scale production for research and practical application. It may be possible to transfer the genes coding for this natural antifreeze to other species in order to improve their growth and survival in cold environments.

- The unique physiology of hydrothermal vent organisms — in particular their adaptation to life at high pressures, high hydrogen sulfide content and at temperatures which would denature most proteins — is receiving deserved attention. Molecular genetic methods are being used to clone the genes of barophilic (high-pressure) bacteria with the goal of studying the mechanisms of pressure control on gene expression.

- DNA-fingerprinting techniques demonstrated that traditional stock assessments of Atlantic salmon were erroneous, resulting in a large share of valuable United States stocks being given over to European fishing interests.

- Basic studies of fish gene expression have shown that carp contain many genes similar to those of mice. This has led to the use of fertilized transgenic fish eggs as a substitute for transgenic mouse embryos in genetic studies, with considerable savings in cost and handling effort.

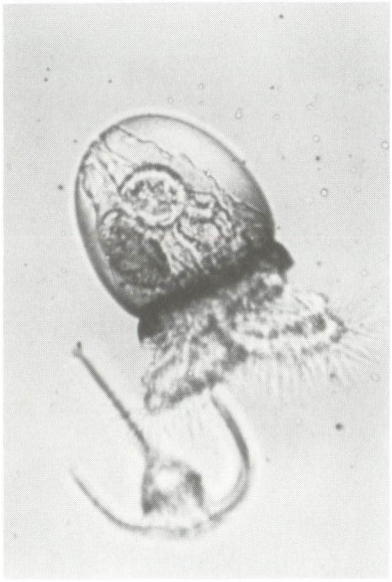
Bio-Organic Chemistry and Pharmacology

While the number of truly novel chemicals from terrestrial plants and microbial fermentation has declined, marine natural products chemists have shown that almost every class of marine organism elaborates a wide variety of molecules with unique structural features. Pharmacologists, physiologists and biochemists have demonstrated that many of these novel marine products modify fundamental life processes in ways suggesting biomedical applications. These molecules can serve as leads to guide the pharmaceutical and chemical industries in developing new products.

Because marine species may have evolved the production of chemicals for protection against predation, infection and competition, some of these chemicals are proving useful in agricultural and medical applications. By determining the biochemical pathways by which these compounds are produced — and the environmental or physiological triggers controlling their production — techniques of enhanced commercial production can be developed.

Ground-breaking discoveries in marine chemistry, pharmacology and biotechnology will provide essential help that the American pharmaceutical industry needs in its efforts to cure intractable forms of cancer, inflammation, arthritis and viral infections. New classes of marine invertebrates and microorganisms are needed as a source of medicinal, agricultural and industrial agents; in particular, bacterial symbionts (now known to be the source of many novel marine compounds) hold a tremendous potential for biotechnological exploitation. Further examination of molecular systematics and biogeography of compound-producing organisms can greatly improve the search for new sources.

New fermentation and related production technologies must be developed which



apply to marine bacteria, fungi and related species. Such advances will make possible further research on how drugs work and will provide new leads to bio-organic chemists studying the structure and production pathways of these materials. New approaches in defining molecular structure, including the use of powerful new computer techniques, will lead to synthesis of marine-derived drugs and will offer new potential solutions to production of larger quantities of rare drugs. Genetic engineering — the transfer of genes encoding for synthesis of the compound of interest into more manageable organisms —holds particular promise for mass production.

Recent developments include:

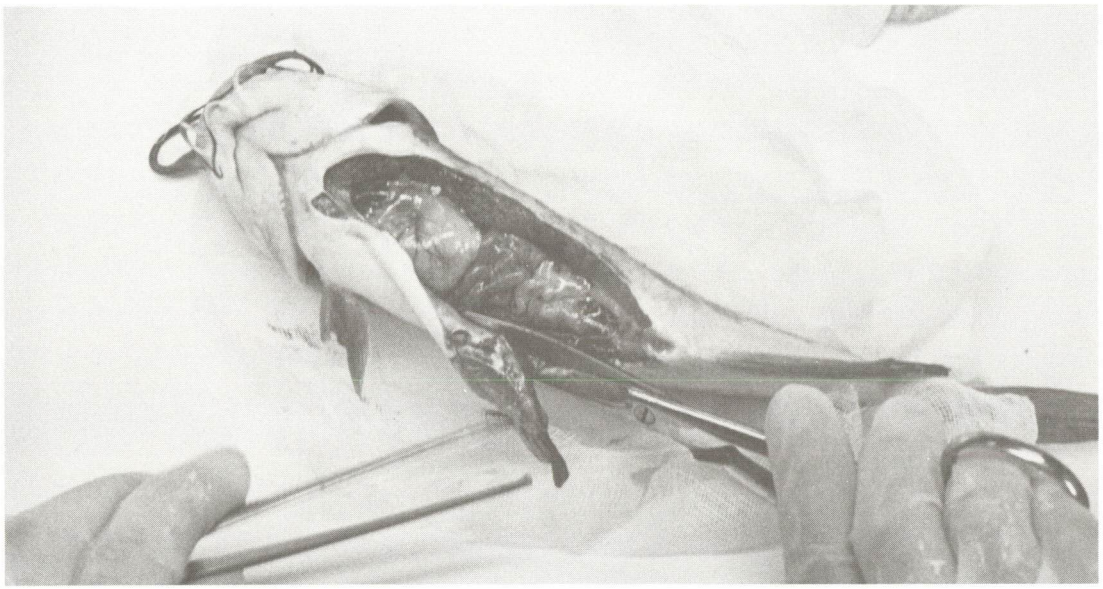
- Manoalide, an anti-inflammatory and analgesic agent isolated from a Pacific sponge, is now in clinical trials. Its action differs from that of standard drugs and it appears free of the side-effects of steroids.
- A substance isolated from shark cartilage inhibits blood supply to tumors, thus restricting their growth. Bryozoans and tunicates have also yielded novel compounds with highly specific antitumor activity; some are now undergoing clinical trials.
- Halenquinone, isolated from a sponge, is a powerful new antibiotic, while didemnin, from a tunicate, exhibits antiviral and anticancer activity.
- Extracts of a sponge have yielded a potent insecticide; especially interesting is the finding that this compound may actually be produced by a bacterium living in the sponge. Accumulating evidence suggests bacteria as the source of many bioactive marine chemicals such as tetrodotoxin.

THE CHALLENGE

Discover New Bioactive Materials:

- ***Identify new sources of drugs***
- ***Determine biosynthetic pathways***
- ***Define structure of marine-derived drugs***
- ***Characterize drug-receptor interactions***
- ***Define molecular mechanisms of action***

Immunobiology and Pathology



Animals and plants in the marine environment are subject to disease, parasitism and tissue pathologies such as tumors. And as with terrestrial species, these pathologies may be due to microbial agents or to environmental stress. The ecological or economic impacts of these diseases can be costly. For example, a probable virus has been implicated in the recent massive die-off of the black sea urchin, *Diadema*, in the Caribbean; grazing of fouling algae by this urchin is considered vital to coral reef health. Disease and parasites have brought about the virtual elimination of oyster populations in many areas, with corresponding economic and societal dislocations. Tumors in fish from coastal waters have been ascribed to exposure to toxic pollutants, though the exact mechanism of such impacts remains unclear. Determining the causes of these tumors, whether pollutants, infectious agents or other factors, will have a direct effect on public use and management of the resource. There is growing evidence that aquatic viruses, abundant in most systems, play a major role in the control of bacterial and algal populations. Infection by viruses thus may impact production and nutrient cycling, as well as plankton diversity and abundance.

The inability to culture many marine bacteria and viruses, or to elucidate the life cycles of parasites, hampers the diagnosis and treatment of disease. The immunological response of marine species, particularly invertebrates, to disease agents is not well-understood, nor is the impact of pollutants on the immune system. The aquatic environment itself makes the isolation, identification and quantification of potential disease

agents difficult. The techniques of marine molecular biology and biotechnology show tremendous promise for addressing these problems. Of particular importance would be the development of gene probes or immunochemical agents for disease diagnosis; establishment of fish and shellfish cell cultures to support basic research on the molecular basis of pathogenesis; production of vaccines by recombinant DNA technology; production of molecular probes or biomarkers for assessing effects of environmental stress on organisms; and determination of the relationship between environmental stress and disease resistance in fish and shellfish.

Recent examples of such advances are:

- The induction of specific enzymes in deep-sea fish, established using monoclonal antibody techniques, indicates biological changes due to anthropogenic chemicals are occurring even in the deep ocean. Molecular techniques have identified specific mutations, of uncertain cause, in critical genes associated with diseases such as cancer in fish.

- Gene probes have been developed for several viral diseases of shrimp. These have made possible the establishment of disease-free brood stock for United States shrimp hatcheries and will help prevent the loss of stocks during grow-out.

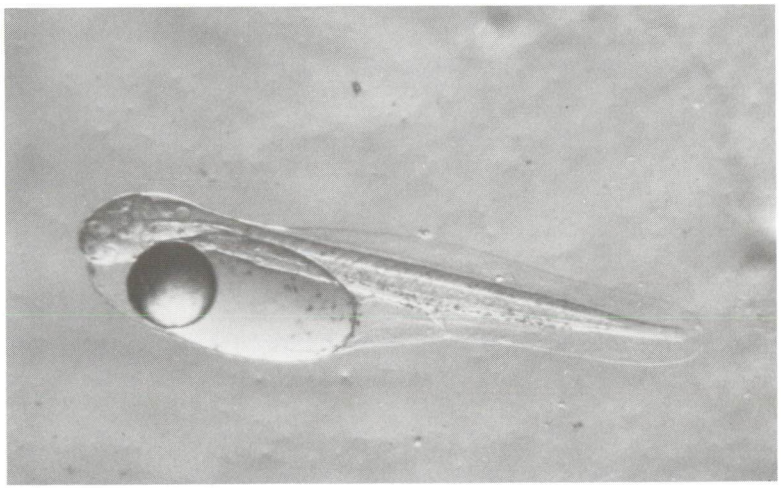
- Flow cytometry and specific immunological labeling are being employed to identify and enumerate pathogens, including cryptic life stages of parasites, in natural waters. Molecular probes are being developed to elucidate life cycles or identify alternate hosts of parasites which infect fish or shellfish.

THE CHALLENGE

Investigate Disease Processes:

- ***Use marine organisms as biomedical models***
- ***Develop new diagnostic techniques***
- ***Prevent and treat diseases in aquatic organisms***
- ***Determine the role of environmental stress on disease***
- ***Explore cell-to-cell recognition***

Endocrinology and Developmental and Reproductive Biology



Reproduction, development and growth in marine organisms, as in all animals, are regulated through the orderly release of hormones. These hormones are produced by the neuroendocrine system which integrates information from the genome and the environment. The central role of the neuroendocrine system in the regulation of growth and development can be exploited to generate the technology necessary for the efficient and reliable propagation of important food species. A knowledge of hormones and of endocrine regulation of growth can also be used to stimulate individual growth and improve productivity while reducing feed and other costs to the farmer; hormonal growth promoters of farm animals were among the first products of the biotechnology industry. For these same reasons, the application of cooperative research between endocrinology and molecular biology is critical if aquaculture is to significantly increase the food supply of both the nation and the world. A knowledge of hormone and gene interactions in the control of growth, reproduction and other aspects of physiology provides important new avenues for restoring populations of endangered species and in limiting populations of noxious organisms.

These approaches must be combined with a thorough understanding of the developmental biology of marine organisms. Many organisms pass through periods of development called critical periods in which mortality is high. While the factors involved in these critical periods remain largely undefined, they can have a strong negative impact on the economics of aquaculture and on the fisheries mitigation efforts of hatcheries. Characterizing the sources of such critical periods and overcoming their limits will provide essential tools in producing and growing many important marine organisms.

The intersection of endocrinology, molecular biology and developmental biology can provide still other important assets. Thus, research is essential not only in terms of developing useful products and technologies, but also in ensuring that they are applied responsibly.

Recent research areas include:

- Cloning of growth hormone and growth promoting factor genes of some commercially important fish has led to production of rapidly-growing stocks. Injections of growth hormone biosynthesized by bacteria containing this gene increase the growth rate of trout, while transgenic carp and catfish containing copies of this gene grow up to 50% faster than controls.

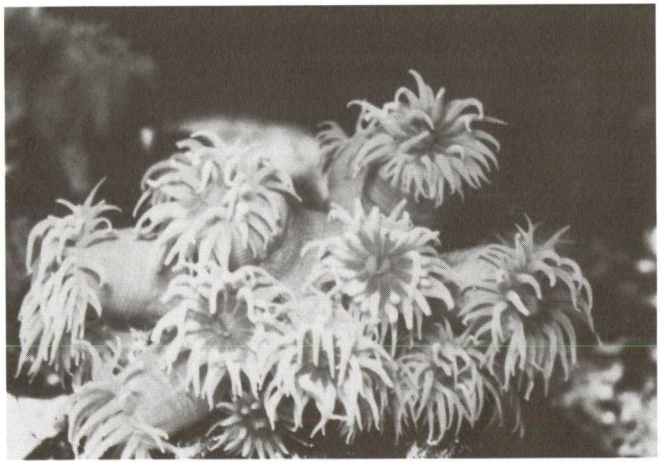
- Identification of factors controlling spawning and settlement of abalone and oysters has allowed synchronized spawning in captivity, leading to the development of commercial hatcheries for these valuable shellfish.
- Development of technologies for delivering growth hormones and gonadotropin-releasing hormone (GnRH) to fish in culture, either through micro-encapsulation or through implants, has made it possible to induce spawning in captive stocks.

THE CHALLENGE

Describe the Molecular Basis for Reproduction and Development:

- ***Identify genetic factors controlling reproduction***
- ***Discover biomedical uses for hormones of aquatic organisms***
- ***Identify internal factors directing growth and development***
- ***Uncover the molecular adaptive mechanisms of aquatic organisms***

Environmental and Evolutionary Biology



Rapid advances in marine biotechnology make it possible to answer some of the most intractable basic problems in modern biological oceanography. This was emphasized at a 1990 workshop supported by the National Science Foundation, the Office of Naval Research, and NOAA/Sea Grant, which concluded that "the impact of this new technology is similar to the impact of computer technology; both are completely revolutionizing the capability to address complex scientific issues." Marine biotechnology will provide ocean scientists with *a new means of knowing*, a new set of tools with which to examine basic ocean processes and to link these processes to the global ecosystem. Questions involving the distribution, characterization, recruitment and movements of marine organisms, their evolutions, adaptations, and interactions, and the elucidation of production, consumption and cycling rates are particularly amenable to biotechnological tools.

For example, the vast majority of micoorganisms in the oceans cannot be cultured, yet they play essential roles in the cycling and transformation of materials in the biosphere. Nucleic acid hybridization, monoclonal antibodies and other techniques of molecular genetics now are being used to characterize these cells and examine their activity.

This improved understanding will, in turn, enhance our ability to develop practical uses for the unique adaptations of marine organisms, to manage marine ecosystems and populations, and to restore impacted environments. However, significant barriers exist to the rapid incorporation of new technologies into the ocean sciences. Among these are the relatively small number of ocean scientists experienced in the tools of molecular biology and biotechnology, which emphasizes the need to incorporate training and interdisciplinary communication into any program in marine biotechnology.

Promising areas of research include:

- Use of gene probes to rapidly identify and enumerate marine organisms, particularly small but ecologically important forms such as phytoplankton and zooplankton. This work is currently extremely labor intensive, and can be a major bottleneck in oceanographic research.
- Investigation of harmful effects of the ozone "hole" in the Antarctic are being carried out by examination of DNA of marine organisms exposed to increased UV radiation. UV-tolerant forms are also being examined for potential natural sunscreens.
- Employing molecular techniques to examine symbiotic relationships between species, such as the identification of nitrogen-fixing symbionts, as well as the molecular and genetic basis which controls "self-recognition" of cells. The latter is important to questions such as coral bleaching (the expulsion of algal symbionts by stressed coral animals) and the infective mechanisms of certain protozoan parasites.

THE CHALLENGE

Explore Ecological and Evolutionary Processes:

- ***Determine ecosystem processes relating to environmental change***
- ***Characterize the phylogeny and evolution of marine organisms***
- ***Delineate stocks and natural populations***
- ***Clarify biogeography and biodiversity***
- ***Assess the ecological roles of microorganisms***

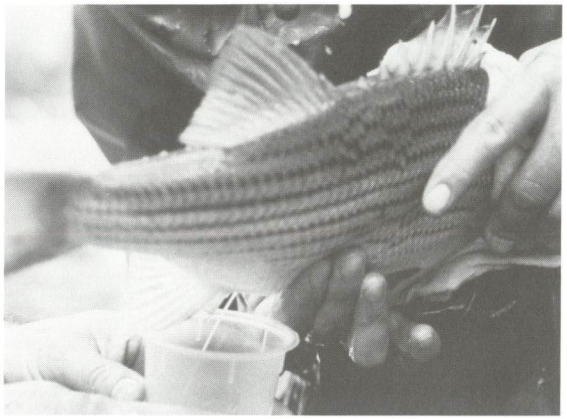
AQUACULTURE

Aquaculture is the growth of aquatic organisms in a controlled environment. Such environments may be bioreactors, open or closed raceways, ponds or natural bodies of water. The aim of such culture is to be able to produce items of economic import such as pharmaceutical agents, feed additives, isotopically enriched chemicals, polymers, lipids with petroleum potential and foodstuffs. The United States has a significant annual trade deficit in seafood, so increasing our nation's capability in aquaculture of food species would provide considerable economic benefit. There is also a growing market for production of ornamental fish, including captive breeding of tropical species now rare in their native countries. Economically viable aquaculture requires that the entire life cycle of a species be completed in captivity, yet many forms of potential importance do not reproduce under these conditions. Currently, fundamental research in physiology and endocrinology is directed primarily to understanding reproduction and growth of cultured species, and developing means for its control.

Other major areas of activity include research on means to increase the productivity or food value of the cultured species; drugs and vaccines to enhance immunity to disease or other stresses; genetic improvement of strains and identification of deleterious or desirable genes within stocks; vaccines, drugs and feeds tailored to specific species and means to increase the palatability, quality and safety of cultured food products.

Sea Grant has supported — and continues to support — groundbreaking research in aquaculture. Among recent accomplishments have been:

- Development of a triploid oyster that makes possible a year-round rather than



seasonal oyster production — this achievement has contributed greatly to the revival of the West Coast oyster industry.

- Use of DNA markers to differentiate between wild and hatchery-released stocks of fish, such as salmon, steelhead and striped bass, particularly in areas where wild, genetically-diverse stocks are threatened by habitat loss, overharvesting or competition from non-native species.
- Development of vaccines against two major diseases of salmon, IPN and IHN virus. This research sets the stage for commercial development of improved vaccines to increase survival in cultured trout and salmon.

THE CHALLENGE

Produce More and Healthier Seafood:

- *Enhance growth and productivity*
- *Control reproduction of cultured stocks*
- *Improve disease resistance and diagnosis*
- *Produce drugs and feeds tailored to each species*
- *Improve genetic makeup of strains*

Seafood Safety and Human Health

Fish and shellfish provide an important component to the global diet — in many countries, seafood represents the major (or only) source of protein for thousands of people. Population pressure and the need to maximize the global food supply will mean an increased reliance on seafood in the future. There are, however, obstacles to this goal. In many tropical areas, the presence of ciguatoxin in reef fish greatly limits utilization of this resource. Other naturally-occurring toxins, such as paralytic shellfish poisoning, may prevent consumption of shellfish over wide areas. Virulent pathogens can contaminate the seafood supply, putting large segments of the population at risk. Some of these disease organisms, such as *Vibrio cholerae,* are endemic to marine systems; others indicate contamination with human or animal wastes. The presence of chemical toxicants in fish or shellfish is an increasing problem in industrial societies. Transfer of products across national boundaries, and the relative lack of inspection and certification at most stages of harvest and processing makes the issue of seafood safety a growing concern worldwide.

Marine biotechnology can give us the capability to prevent or detect these problems, and to ameliorate their impact. Most importantly, it can help us answer questions about how these problems arise — what are the processes which lead to the contamination of reef fish with ciguatoxin, what ecological conditions favor the microorganisms which produce the toxin, and how can their presence be detected? What processes enable endemic species of bacteria to cause epidemics of acute disease? How are toxic chemicals made biologically available to fish and shellfish, and what metabolic processes lead to their accumulation in tissues of exposed organisms? What are the long-term human health impacts of prolonged exposure to these contaminants?

Because of the direct threat to human health, as well as the need for increasing the world's food supply, the issue of seafood safety is receiving considerable attention from scientists, policy makers and the public. The potential of marine biotechnology to address many of these issues is demonstrated by successes to date:

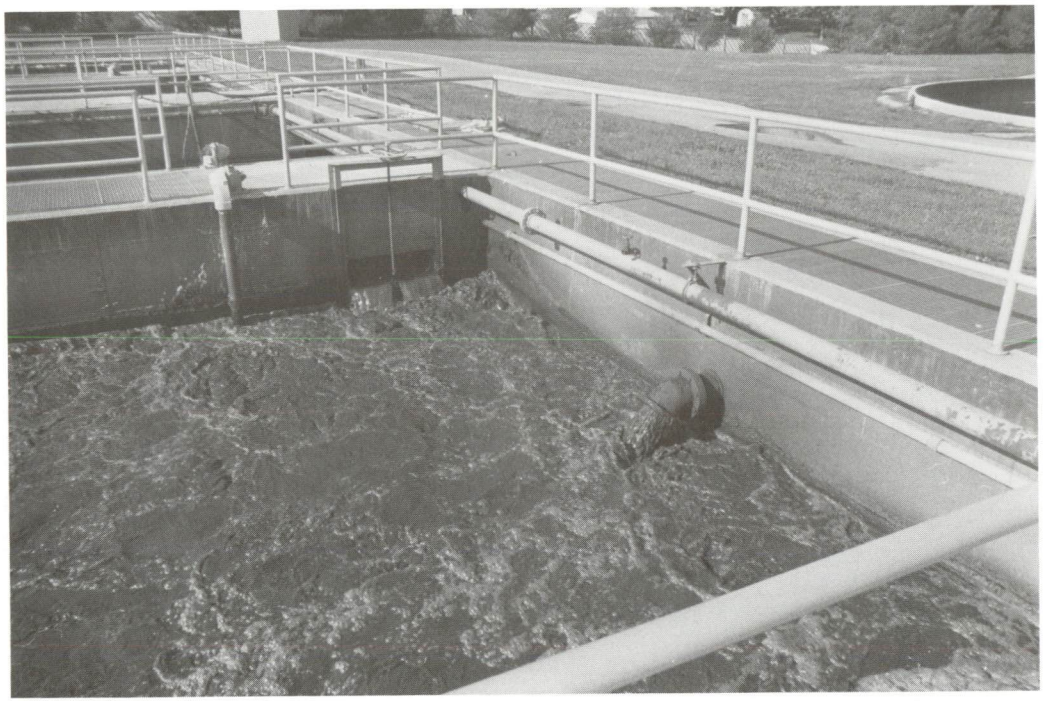
- Development of an inexpensive biochemical "dip-stick" monoclonal antibody assay for ciguatoxin, which can affect finfish from most tropical areas. This test kit is being produced commercially in Hawaii.
- Use of molecular techniques to elucidate the pathways leading to toxin formation by marine organisms, to chemically characterize these toxins and to determine the genetic coding governing their production.
- Development of a rapid enzyme-linked immunosorbant assay (ELISA) for *Vibrio cholerae* in oysters. A commercial firm has adapted this technology to produce a small hand-held kit for detection of contaminated seafood; millions of these kits will be sent to South America to help combat the cholera epidemic.

THE CHALLENGE

Safeguard Human Health:

- ***Detect contaminated seafood using rapid and sensitive methods***
- ***Characterize ecology of disease organisms***
- ***Improve depuration methods***
- ***Enhance shelf life of seafood***

Environmental Remediation



Marine organisms are also sources of novel bio-mediated pathways for processing and degrading a wide variety of natural and manmade substances. Degradation in aquatic environments by naturally occurring organisms or communities, or in bioreactors containing these organisms, offers potential for the disposal or cleanup of hazardous materials. In fact, waste processing in most modern sewage treatment facilities relies to a great extent on the manipulation of bacterial metabolism. Similarly, toxic industrial wastes or other effluents can be treated by properly selected aquatic microbes which have the capability (or have been genetically manipulated to acquire the capability) to break down these materials. Biosensors are being developed which use naturally-occurring marine proteins combined with information technology, for example, fiber optics and microcircuitry, to monitor for very low concentrations of toxicants.

Research is being initiated to identify the biochemical pathways of these processes, and to understand how these activities are distributed, regulated and maintained. There is a need to accelerate the search for naturally-occurring organisms which have the potential to degrade or process materials of interest — bacteria occurring near natural oil seeps — and to identify the genes responsible for these capabilities. Significant commercial potential for industrial use will follow, either by employing the original organisms or by inserting the appropriate genes into more traditional species.

A number of applications are already being developed which employ marine species, and others are being currently studied. These include:

- Oceanic bacteria have been discovered that directly oxidize and precipitate iron, manganese, cobalt, nickle and other valuable and strategic metals. The genes and enzymes of these bacteria may be the key to separating these metals from low-grade ores, bypassing more expensive and environmentally-damaging industrial processes now employed.
- Related to the above, bacteria have also been found that reverse these processes — that is, they can reduce or solubilize many metals (some toxic), and thus may be able to play a role in the remediation of pollution.
- In Israel, a new petroleum-emulsifying agent has been developed from marine bacteria. A multi-million dollar business now produces this material for use in the petroleum industry, with production licensed in over a dozen countries including the United States.
- Chitosan, a product extracted from shellfish waste, is being used to treat wheat seeds to reduce fungal infestation, with resultant increases in germination and ultimate yield (up to 10%). Many other applications of chitin and chitosan are currently under development, including medical materials; much of the original research in this material was supported by Sea Grant.
- A test plant employing naturally occurring bacteria which degrade phenols has demonstrated a 99% drop in the concentration of chlorinated phenols from 100 to 1 part per million in a bioreactor system. These procedures were tested successfully by the Environmental Protection Agency at a Superfund site, and two firms have contracted to use these procedures in commercial applications.

THE CHALLENGE

Protect and Restore the Aquatic Environment:

- ***Isolate or bioengineer organisms that degrade pollutants***
- ***Determine metabolic pathways to degrade hazardous substances***
- ***Develop processes to clean up waste streams***
- ***Design biological controls for nuisance species***

Biofilms and Corrosion

Biofouling and corrosion are major costs in commercial and U.S. Naval operations in marine environments. The occurrence of natural biofouling or corrosion-resistant substances has been demonstrated and these compounds merit intensive investigation at a molecular level to develop new methods for controlling these processes. Such approaches require an understanding of the attachment mechanisms of organisms that form biofilms, the growth of these films and how these processes influence fouling and the electrochemistry of corrosion.

There is an urgent need to develop newer, less toxic means of controlling biofouling of surfaces — both because of increasingly restrictive environmental regulations, such as the ban of tributyltin paints, and the current problems with exotic, invasive fouling organisms such as zebra mussels. Similarly, corrosion of marine materials can be intensified by microbial activity, and clarification of the biochemical and electrochemical pathways involved may allow control of these processes. Biofilms, and the invasion of tissues by surface-active bacteria, are also primarily involved in a number of human health problems, including dental caries, prosthesis septicemia and interstitial cystitis. There are also many potential benefits from a better understanding of biofilm formation, such as improved waste water treatment (trickling filter design), aquaculture (setting of oysters and other shellfish), agriculture and industry.

The naturally evolved chemicals which serve to reduce competition between surface-living organisms and bind organisms to surfaces under adverse adhesive conditions are potential areas for investigation, as are the cues which signal setting or metamorphosis in fouling macrofauna. These and other avenues are being pursued, including the following:

■ The organic matrix in oyster shell has been found to be a potent inhibitor of growth of crystalline calcium carbonate, the principal component of mineral scaling on marine surfaces. Synthetic substances modeled after this matrix also inhibit deposition of mineral scale. Research on the exact mechanisms involved is continuing while earlier results are being developed into commercial applications.

■ Recent developments in the study of bacterial exopolymers have shown that considerable differences exist in the metal-binding activity of these materials. This observation is now being expanded to look at the implications for corrosion of metal surfaces through enhanced microbial activity.

■ The observation of antagonistic interactions between closely related strains of film-forming bacteria, whereby one strain inhibits adhesion of the other clone, has led to the isolation of a material which shows a broad range of activity against film-forming bacteria and phytoplankton. This substance is now being further characterized and tested with Sea Grant support. It may have wide potential applications as a safer fouling-control agent.

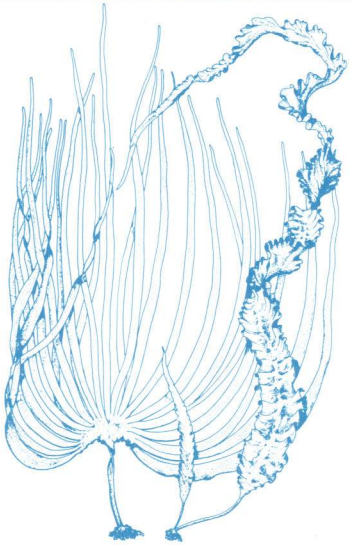
■ Bacterial biofilms promote the successful settling and metamorphosis of oyster larvae, and in fact these films produce DOPA-like substances which act as cues and inducers of settlement. Research in this area has led to the patenting of a product, derived from these substances, and its use in a number of oyster hatcheries to produce cultchless spat. DOPA proteins may have application as inhibitors of corrosion, as well.

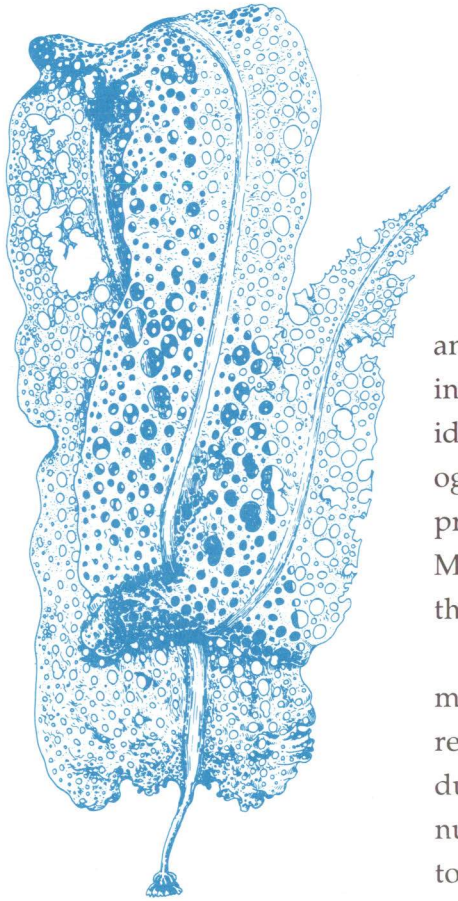
THE CHALLENGE

Reduce Fouling and Corrosion of Marine Structures:

- *Develop non-toxic fouling controls*
- *Determine the role of microorganisms in marine corrosion*
- *Describe molecular processes involved in fouling and corrosion*
- *Develop biomedical applications*

Biomaterials and Bioprocessing





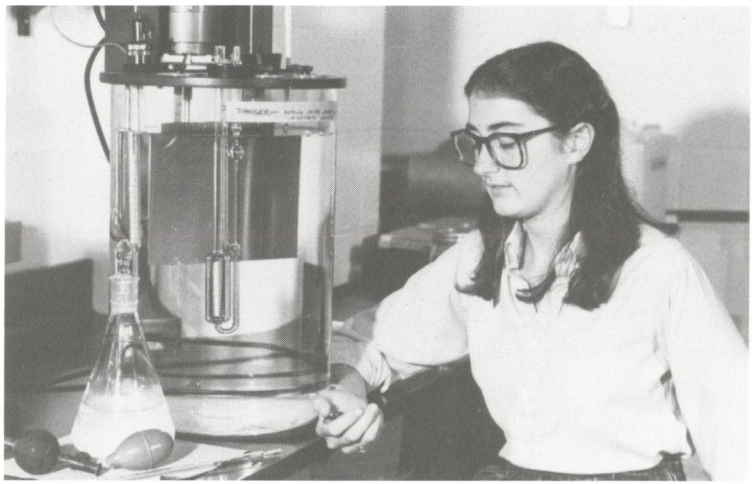
Marine organisms synthesize numerous chemicals with bioactive properties: metabolites, proteins, enzymes, polysaccharides, lipids and other materials which have direct application in health and life science. Determining the physiological and environmental role of many of these materials is likely to lead to new industrial processes and applications, for example, in bioremediation and in control of pests or diseases.

While most research on marine natural products has focused on identification, isolation and characterization and testing of the material for activity or utility, these are only the initial steps: elucidation of metabolic pathways by which materials are produced and identification of the genes responsible also will provide the bases for advanced technology, Because biosynthetic production, rather than extraction from the organisms, holds promise for more economical processes, this approach needs thorough exploration. Marine-derived polymers have potential application in a variety of products, among the most exciting being superconductors.

Photobioreaction may warrant attention both for production of energy and for material production. Light-harvesting chlorophyll and protein complexes can be reconstituted onto artificial membranes and are capable of collecting energy and transducing electrons with efficiencies comparable to photovoltaic cells. Under conditions of nutrient limitation, some microalgae produce hydrocarbons and lipids in quantities up to 65 percent of their dry weight. Application of DNA technology and other modern methods may provide economically viable approaches to exploring this biosynthetic capability.

For some applications, the quantities of materials required or the cost of obtaining them may limit — for a time — the commercialization of natural products. In these

cases, the study of models may reveal alternatives that are more cost-effective to produce than the naturally-derived materials, but which retain their desirable characteristics.



Related areas of marine biotechnology are already highly productive, and many new products are in use or in development. Among these are:

- Technology for the controlled farming of seaweed has allowed the production of biopolymers with many uses in industry. For example, carrageenan is widely used in the food and cosmetic industries and is the basis of hundreds of millions of dollars of commercial trade. Other algal polymers, such as agar and alginic acids, are also essential to a variety of biotechnological research and processing.
- Marine glues which adhere firmly underwater are being developed from the naturally-produced byssal glues of mussels. Such adhesives can be used in bone and teeth repair and may have other medical applications.
- Highly-charged oyster-shell proteins have been used as models to launch a new polymer technology. These new biodegradable and non-toxic compounds can be used to replace the hundreds of millions of pounds of non-degradable acrylic-based polymers employed annually as additives in detergents, dispersants and in other industrial applications.
- Marine biomass production as a source of energy or useful chemicals is now being studied; these investigations focus primarily on macroalgae but microalgae, marine grasses and marsh plants, are also potential sources. It may be possible, for example, to apply molecular genetic techniques and produce rapidly growing strains that are able to grow in normally unproductive saline soils, providing animal fodder, fuel or raw materials in marginal or degraded environments.

THE CHALLENGE

Exploit Marine Natural Products for Human Benefit:

- ***Develop sensors for continuous monitoring***
- ***Discover new prosthetic materials***
- ***Develop new uses for industrial byproducts***
- ***Use marine materials for novel applications***
- ***Engineer marine organisms for innovative industrial uses***

Policy and Public Responsibility

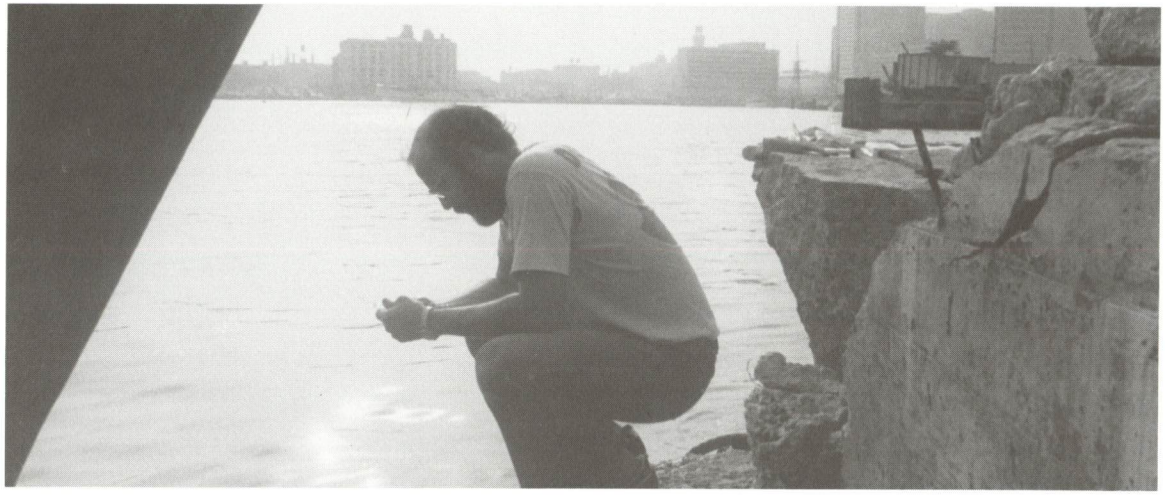
THE CHALLENGE

Promote Responsible Use of Marine Biotechnology:

- *Develop new approaches for establishing protocols*
- *Adopt policies to promote research and investment*
- *Encourage cooperative projects between institutions, agencies and governments*
- *Facilitate the transfer of information and technologies*

Biotechnology generally has engendered complex ethical, legal, political and social issues. As more and more research institutions use the advanced techniques of biotechnology in their work, as genetically engineered organisms are made ready for field testing, and as the products produced by genetically engineered organisms multiply in the market places, the number and complexity of public issues are certain to increase. Neither researchers nor their home institutions can ignore these issues or fail to become involved in the public debate that will influence how rules governing research and its applications are formulated and how funding for scientific activities is apportioned.

It is unclear to what extent marine biotechnology raises issues beyond those raised in other biotechnology fields. While the majority of products generated by marine biotechnology research may differ in kind and should pose few special problems to industries, regulatory agencies or the patent office, major differences are likely to be in regard to future field testing of genetically manipulated organisms. Since in the aquatic environment there are few natural barriers to prevent an organism from mov-



ing from one site to another, containing test organisms within one area becomes very difficult. Moreover, the transfer of genetic materials among organisms is problematical: for example, a recent discovery of vast numbers of viruses in ocean waters leaves open the question of whether introduced genes may be transferred from one species to another via virus vectors.

Marine biotechnology research, and the application of these results for public benefit, must include due consideration of ethical and regulatory issues. There will be the need to balance freedom to conduct research and to develop products with appropriate oversight and guidance. Existing policies, especially the protocols governing work in genetic engineering, will need to be adapted to guide research and development in marine biotechnology.

Economics of Marine Biotechnology

THE CHALLENGE

Evaluate Economic Benefit of Marine Biotechnology:

- *Perform cost-benefit analyses*
- *Evaluate economic potential of new products and processes*
- *Develop new markets for products*
- *Facilitate investment in marine biotechnology*
- *Provide guidance for new businesses and industries*

Marine biotechnology has received relatively scant attention in the United States, despite its obvious potential and despite the remarkable productivity that current research has demonstrated. It is unlikely that this level of achievement can be sustained if funding levels are not improved, and consistent support provided to research and development efforts.

Considering its potential, the present support for marine biotechnology is modest. Total research investment at academic and public institutions in the United States, excluding industry research, was approximately $44 million in 1991. Funding grew from $38 million in 1988 and is expected to reach $50 million by 1994. After adjusting for inflation, these figures represent no significant growth in investment for marine biotechnology research over this period.

Total support since 1984 for marine biotechnology research and development, exclusive of private sector investment, is estimated at $181 million. This support has resulted in 170 patents for funds expended to date, a large number of patents per research dollar given the academic orientation of most institutions which emphasize basic research.

With limited funding, marine biotechnology has been very successful in increasing our stock of economically important information. The ultimate value, however, will come from how this knowledge is applied to new product and process development. Although figures on overall value of marine biotechnology products are not available, there are estimates that on average the stock market value of a company increases by $810,000 with the awarding of a patent.

Education and Technology Transfer

Development of new methods, products and knowledge is only the first step; to be fully utilized, this new information must be transferred — to entrepreneurs, educators, institutions and industry. Formal mechanisms to disseminate research results, to instruct potential users, to facilitate the granting of patents and the licensing of products will facilitate this process. Sea Grant has a network of extension and communications personnel that could meet many of these needs. It is a base upon which to build additional efforts in technology transfer. This new direction will be both a challenge and an opportunity. Certainly expertise in many areas, such as intellectual property law, must be augmented. But the infrastructure is in place and needs no duplication.

Four major program elements are proposed:

- **Scientific Entrepreneurship**: Scientists need to learn the realities of the business world, and those involved in business must understand the principles of the scientific method. We will establish programs which emphasize cross-training, and which allow students from each discipline to become familiar with the approaches and needs of both fields.

- **Scientific Training:** A lack of trained personnel to drive the emerging marine biotechnology industry is one factor causing United States industrial growth to lag behind our foreign competitors. We will establish training programs to develop the

THE CHALLENGE

Develop Human Resources and New Partnerships:

- *Train scientists and technicians*
- *Educate the public*
- *Promote interdisciplinary activity*
- *Provide links between research and industry*
- *Develop protocols for technology transfer*

skills necessary for students at the college level, for faculty at colleges, universities and vocational institutions and for scientists in both industry and academia.

- **Public Awareness:** While marine biotechnology has great economic potential for this nation, it is essential that the public be informed about this science and feel comfortable with its use. The public awareness program will employ on-site training, seminars and production of teaching materials aimed at students from elementary grades to college, as well as the general public.

- **Minority Outreach Program:** The scientific and economic challenges of the next century will require action and input from our entire population. Demographic realities, as well as the moral imperative to share benefits of technological and economic progress with all segments of this society, mandate the increased involvement of women and minorities in science and industry. This program element will include a mentorship program to encourage students on an individual basis, and provide them with research experience in a supportive environment.

Sea Grant Institutions

Alaska Sea Grant College Program
University of Alaska

California Sea Grant College Program
University of California, San Diego

Southern California Sea Grant Program
University of Southern California

Connecticut Sea Grant College Program
University of Connecticut

Delaware Sea Grant College Program
University of Delaware

Florida Sea Grant College
University of Florida

Georgia Sea Grant College Program
University of Georgia

Hawaii Sea Grant College Program
University of Hawaii

Illinois-Indiana Sea Grant Program
University of Illinois

Louisiana Sea Grant College Program
Louisiana State University

Maine/New Hampshire Sea Grant
College Program
University of Maine
University of New Hampshire

Maryland Sea Grant College Program
University of Maryland System

Massachusetts Sea Grant College Program
Massachusetts Institute of Technology

Michigan Sea Grant College Program
University of Michigan

Minnesota Sea Grant Program
University of Minnesota

Mississippi/Alabama Sea Grant Consortium
University of Mississippi

New Jersey Marine Sciences Consortium
Rutgers University

New York Sea Grant Institute
State University of New York at Stony Brook

North Carolina Sea Grant College Program
North Carolina State University

Ohio Sea Grant College Program
The Ohio State University

Oregon Sea Grant College Program
Oregon State University

Puerto Rico Sea Grant College Program
University of Puerto Rico

Rhode Island Sea Grant College Program
University of Rhode Island

South Carolina Sea Grant Consortium
University of South Carolina

Texas Sea Grant College Program
Texas A&M University

Virginia Sea Grant College Program
University of Virginia

Washington Sea Grant College Program
University of Washington

Wisconsin Sea Grant Institute
University of Wisconsin

Woods Hole Oceanographic Institution Sea
Grant Program
Woods Hole Oceanographic Institution

For information about Sea Grant, contact:

National Sea Grant College Program
NOAA, Sea Grant, R/OR1
1335 East-West Highway
Silver Spring, Maryland 20910-3226

For further information on marine biotechnology, contact one of the following Sea Grant Programs:

California Sea Grant College
University of California, San Diego
La Jolla, California 92093-0232
(619) 534-4440

Maryland Sea Grant College
Taliaferro Hall, University of
Maryland
College Park, Maryland 20742
(301) 405-6371

Hawaii Sea Grant College Program
University of Hawaii
Honolulu, Hawaii 96822
(808) 956-7031

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"Document Control for Division of Life Sciences"

ACTION DOCUMENT NUMBER: 9203625

ATOR: 02 STATUS I DIRECTORATE STATUS C

****

M: CURIEN, Hubert: MINISTER OF SCIENCE, FRANCE

TO: DR. D.A. BROMLEY

DATE OF CORRESPONDENCE: 12/04/92

SUBJECT: HE IS FORWARDING THE NAME OF SOMEONE TO CONTRIBUTE TO OTA'S STUDY OF THE PATENTABILITY OF THE HUMAN GENOME.

****

DIRECTORATE ASSIGNED: LIFE SCIENCES

STAFF ASSIGNED: Clifford J. Gabriel

ACTION REQUIRED: AS NECESSARY

STAFF ACTION: AS NECESSARY

****

SENDER'S DUE DATE:

OSTP DUE DATE: 12/31/92 STAFF DUE DATE 12/31/92

DATE COMPLETED: DATE COMPLETED/DEPT: 12/23/92

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FILE: P-LIFE SCIENCES

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FILE: P-LIFE SCIENCES

CENTRAL FILES:

THE WHITE HOUSE

WASHINGTON

December 23, 1992

Dear Hubert Minister Curien:

Thank you for submitting the name of Monsieur Philippe Lazar as a potential French contact for the OTA project on patenting human DNA sequences. I have forwarded this information to Dr. Robyn Nashimi, OTA Project Director for this activity.

Sincerely yours,

Allan

D. Allan Bromley
The Assistant to the President
for
Science and Technology

The Honorable Hubert Curien
Minister of Research and Technology
1 rue Descartes
75005 Paris
France

Au meeting at Rambouillet was superb! Happy holidays and the very best for new years -

Allan

R E P U B L I Q U E F R A N Ç A I S E

3625

MINISTERE
DE LA RECHERCHE
ET DE L'ESPACE

LE MINISTRE

20752/C

Paris, le : 4 DEC. 1992

Dear Allan,

Thank you very much for the information you sent me in your letters dated October 5th and October 28th on the patentability of genome fragments.

As regard the study conducted by OTA, I recommend you to get in touch with :

Monsieur Philippe LAZAR
Directeur Général de l'Institut
National de la Santé et de la
Recherche médicale
101, rue de Tolbiac
75654 PARIS CEDEX 13
Tél. : 44 23 60 00

I look forward to meeting you soon in Rambouillet.

Hubert CURIEN

M. Allan BROMLEY
Assistant du Président
pour la science et la technologie
Maison Blanche
Hold Executive Office Bulding
WASHINGTON DC - 20106 USA

Mary

"Document Control for Division of Life Sciences"

TYPE: ACTION DOCUMENT NUMBER: 9203557
ORIGINATOR: 02 STATUS I DIRECTORATE STATUS C

****

FROM: LANG, Serge: YALE UNIVERSITY

TO: DR. D.A. BROMLEY

DATE OF CORRESPONDENCE: 11/30/92

SUBJECT: HE IS WRITING REGARDING THE HANDLING OF THE GALLO CASE.

****

DIRECTORATE ASSIGNED: LIFE SCIENCES

STAFF ASSIGNED: D.A. Henderson

ACTION REQUIRED: AS NECESSARY

STAFF ACTION: Necessary Action

****

SENDER'S DUE DATE:

OSTP DUE DATE: 12/23/92 STAFF DUE DATE 12/23/92
DATE COMPLETED: DATE COMPLETED/DEPT: 12/15/92

****

COPIES TO: D. Allan Bromley

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WHITE HOUSE TRACKING #: CONTACT PERSON:
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REMARKS: Response from OSTP would be inappropriate and not necessary, per DAH. Close out record.

OSTP RECEIVED: 12/09/92 DEPT RECEIVED: 12/14/92
FILE: P-LIFE SCIENCES

CENTRAL FILES:

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01. Letter w/ attachments	To: Distribution List From: Serge Lang Re: Handling of the Gallo Investigation (14 pp.)	11/30/92	(b)(7c), (b)(2)	

Collection:

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Office: Science and Technology Policy, Office of (OSTP)
Series: Bromley, D. Allan, Files
Subseries: General Science Files
WHORM Cat.:
File Location: Life Sciences: General [2 of 7] [1992]

Date Closed:	3/15/2010	**OA/ID Number:**	62038-006
FOIA/SYS Case #:	2005-0336-F	**Appeal Case #:**	
Re-review Case #:		**Appeal Disposition:**	
P-2/P-5 Review Case #:		**Disposition Date:**	
AR Case #:		**MR Case #:**	
AR Disposition:		**MR Disposition:**	
AR Disposition Date:		**MR Disposition Date:**	

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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

Medical Editor Axes Dingell's Remarks About Gallo

Two dreadnoughts accustomed to having their own way, *The New England Journal of Medicine* (NEJM) and Rep. John Dingell (D-Mich.), have been scrapping over the journal's insistence on deleting comments about the Gallo case from the published version of a lecture, "Misconduct in Medical Research," delivered last May by Dingell.

The Congressional flagellator of scientific ethics and the nation's leading medical journal are in dispute as a result of an invitation for Dingell to deliver the Shattuck Lecture at the annual meeting of the Massachusetts Medical Society, publisher of the NEJM. Jerome B. Kassirer, Editor of the *Journal*, nominated Dingell for the lecture, established in 1890, and usually published in the NEJM; and, ironically, it is Kassirer who insists on sanitizing Dingell's text, though the editor, in a post-lecture letter to Dingell, commented that "Your point of view, as espoused in the manuscript, is far more moderate than others have painted it...."

In the lecture, Dingell repeated his often-expressed assertion that the scientific community is reluctant to police itself against scientific misconduct, which, he said, robs the taxpayers and deprives legitimate scientists of support. Numerous incidents of scientific fabrication and plagiarism have been spotlighted by his Subcommittee on Oversight and Investigations, Dingell continued. In response, he said, his motives "have been misrepresented, particularly by persons who have everything to lose from the truth.... For a time, we were excoriated as a band of philistines incapable of understanding science and as a troop of inquisitors engaged in a senseless witch hunt." Dingell then summarized some of the more pungent investigations of recent times, including that of Robert C. Gallo, the NIH virologist, whose claimed roles in the identification of the AIDS virus and the development of the AIDS blood test have spawned nasty disputes and a long-running federal investigation.

About Gallo, the following is verbatim from Dingell's Shattuck Lecture text:

Finally, there is the matter of Dr. Robert C. Gallo, the NIH's world-famous AIDS researcher. Because the Subcommittee has not yet completed its investigation, I cannot tell you what our conclusion will be. I can say, however, that one of the things that puzzles and troubles us is the large number of unusual misunderstandings and coincidences in which Dr. Gallo appears to be entangled.

After Dr. Zaki Salahuddin, one of his longtime laboratory scientists, was convicted of a felony in connection with his activities at Dr. Gallo's laboratory, Dr. Gallo explained that he had been unaware of Dr. Salahuddin's activities. In short order, Dr. Prem Sarin, Dr. Gallo's Deputy Laboratory Chief, was indicted for activities unrelated to those of Dr. Salahuddin but also stemming from work at the laboratory. Dr. Gallo explained that he knew nothing of his Deputy Laboratory Chief's misconduct and that these two separate criminal cases involving his laboratory were unfortunate coincidences.

Then we learned that two human subjects described in an article coauthored in *The Lancet* by Dr. Gallo and French researcher Dr. Daniel Zagury had died, but that Dr. Gallo failed to report these deaths to NIH as required by grant regulations and erroneously reported in *The Lancet* that he had observed no adverse reactions in the human subjects. Dr. Gallo again had an explanation. He explained that the statement in *The Lancet* was an inadvertent error, and his failure to comply with NIH procedure was a result of his unfamiliarity with the regulations, despite some 20 years of employment at NIH.

More recently, in the controversy over the AIDS blood test, Dr. Gallo first stated that the virus he used was definitely different from that used by the competing French team. When genetic sequencing proved that the viruses were identical, Dr. Gallo suggested that the French must have taken his virus. When that claim was challenged, Dr. Gallo explained that there must have been an inadvertent contamination in his laboratory. Meanwhile, there were also questions about the cell-line in which Dr. Gallo grew his viruses. Initially, Dr. Gallo seemed to suggest that the cell-line was his own development. It eventually emerged that the cell-line belonged to Dr. Adi Gazdar, a researcher at another NIH institute. Dr. Gallo explained that this was a misunderstanding, that he never intended to deprive Dr. Gazdar of credit, but merely renamed the cell-line for convenience.

This is a deeply troubling case. An eminent scientist who heads one of the most important laboratories in the world is embroiled in so many instances of inadvertent errors, miscommunications, and unfortunate coincidences. We understand that the NIH itself receives millions of dollars each year in royalties from the blood test, but that should be no impediment to NIH's objectively assisting Dr. Gallo in resolving his difficulties.

In a letter to Dingell dated June 1 concerning publication of the lecture, NEJM Editor Kassirer stated, "As I mentioned to you immediately after the lecture, I have taken the liberty of deleting your comments about Robert Gallo. First, in all the others [cases described in the lecture], fraudulent material has been retracted in print. Second, the principal allegations against Gallo are based on apparent coincidences, misunderstandings, and inadvertent errors. While these allegations embellish the case you make, they have not been shown to constitute overt fraud. Third, the Gallo case has been exhaustively covered in *Science*, and repetition of these allegations seems superfluous." Referring to institutions criticized by Dingell in his discussion of scientific misconduct, Kassirer added: "In a spirit of fairness, I will be offering officials at Harvard, Tufts, MIT, Pittsburgh, and NIH an opportunity to submit short replies in the correspondence section that will appear in the same issue as your lecture."

Responding to Kassirer in a letter dated August 14, Dingell stated: "My understanding is that the printed lecture is supposed to reflect the lecture actually delivered, with only minor changes....I am concerned that your comments ... relative to the Gallo issue may reflect a misunderstanding of the facts and circumstances. For example, your statement that 'the principal allegations against Gallo are based on apparent coincidences, misunderstandings, and inadvertent errors' is erroneous; at most, one might say that 'the princi-

(Continued on Page 7)

. . . Kassirer Says Lawyers Advised Him to Edit Dingell

(Continued from Page 6)

pal allegations against Gallo are based on what Gallo *claims* are coincidences, misunderstandings, and inadvertent errors.' I have made some minor adjustments in the text to clarify the distinction," Dingell wrote, and then proceeded to another matter.

"Additionally," Dingell wrote, "your point that 'in all the others fraudulent material has been retracted in print' also appears to reflect a misimpression. In the Cleveland Clinic case [discussed in Dingell's lecture], no retraction has ever been printed, and in the [David] Baltimore case, Dr. Baltimore has recently expressed an intention to retract his retraction. On the other hand, there has been at least one significant printed retraction in the Gallo case. Dr. Gallo has retracted in print his initially vehement claim that his virus was independent of the Institut Pasteur's (although he continues to deny any wrongful intent in his appropriation of the Pasteur virus)."

Dingell conceded Kassirer's prerogative to edit the lecture, but noted that "I hope you would understand that I would want to reserve the option of writing a letter to the editor or otherwise expressing my disagreement." Noting Kassirer's invitation for responses to the published lecture to appear in the same issue, Dingell wrote that "my understanding is that the *Journal's* normal practice is to publish an article and then at some future point to publish responses together with the author's reply to the critiques."

In a response dated September 1, "enclosing our final revision," Kassirer stated, "you will note that I have deleted the material about Gallo as I described in my first letter. Because I had concerns about this part of your address from the beginning, I submitted it to the Massachusetts Medical Society's lawyers, and they concurred that it would be best from a legal standpoint to drop this section.... Needless to say, you would be free to submit a letter to the editor to protest this deletion." Kassirer added, "I have not sent a copy of your manuscript to any of the institutions named in your manuscript, and I will honor your request not to do so. We will, as you request, follow the normal practice of publishing the paper and then at a future time publish the responses along with your reply." If corrections and references are promptly supplied, he concluded, "we will have the lecture out before the end of the year."

The reported legal advice is puzzling, given that the Gallo controversies have long been on the public stage, including a Congressional hearing. In fact, virtually everything Dingell said about Gallo has previously appeared in print, as editor Kassirer noted in observing that "the case has been exhaustively covered in *Science*"—as well as, he might have added, in other publications.

In his bumbling venture into censorship, Kassirer has denied his readers the views of a Congressman with extensive power in biomedical affairs, and nourished Mr. Dingell's dark suspicions of establishment institutions.—DSG

Withdrawal/Redaction Sheet
(George Bush Library)

Document No. and Type	Subject/Title of Document	Date	Restriction	Class.
02. Cover sheet & Letter	To: Allan Bromley From: Kevin O'Neill Re: Assistance with securing work visa for client [personal information redacted] (2 pp.)	9/28/92	(b)(6)	

Collection:

Record Group: Bush Presidential Records
Office: Science and Technology Policy, Office of (OSTP)
Series: Bromley, D. Allan, Files
Subseries: General Science Files
WHORM Cat.:
File Location: Life Sciences: General [2 of 7] [1992]

Date Closed:	3/15/2010	**OA/ID Number:**	62038-006
FOIA/SYS Case #:	2005-0336-F	**Appeal Case #:**	
Re-review Case #:		**Appeal Disposition:**	
P-2/P-5 Review Case #:		**Disposition Date:**	
AR Case #:		**MR Case #:**	
AR Disposition:		**MR Disposition:**	
AR Disposition Date:		**MR Disposition Date:**	

RESTRICTION CODES

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

P-1 National Security Classified Information [(a)(1) of the PRA]
P-2 Relating to the appointment to Federal office [(a)(2) of the PRA]
P-3 Release would violate a Federal statute [(a)(3) of the PRA]
P-4 Release would disclose trade secrets or confidential commercial or financial information [(a)(4) of the PRA]
P-5 Release would disclose confidential advice between the President and his advisors, or between such advisors [a)(5) of the PRA]
P-6 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. Removed as a personal record misfile.

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

TYPE: ACTION DOCUMENT NUMBER: 9203477
ORIGINATOR: 02 STATUS I DIRECTORATE STATUS C
****

FROM: KELLOGG, DONNA J.: NORTHWESTERN UNIVERSITY MEDICAL SCHOOL

TO: DR. D.A. BROMLEY

DATE OF
CORRESPONDENCE: 11/12/92

SUBJECT: SOLICITS DAB'S ASSISTANCE IN ENSURING THE CONTINUED PARTICIPATION OF THE NATIONAL INSTITUTES OF HEALTH IN THE DEMONSTRATION PROJECT

****

DIRECTORATE ASSIGNED: LIFE SCIENCES

STAFF ASSIGNED:

ACTION REQUIRED: AS NECESSARY

STAFF ACTION:

****

SENDER'S DUE DATE:

OSTP DUE DATE: 12/07/92 STAFF DUE DATE

DATE COMPLETED: DATE COMPLETED/DEPT: 11/25/92

****

COPIES TO: D. Allan Bromley

****

WHITE HOUSE TRACKING #: CONTACT PERSON:

PHONE: EXT:

REMARKS: Dr. Raub sent a response, dated 11/25/92, to an identical letter, also dated 11/12/92, addressed to him from Kellogg; therefore, this has been handled for OSTP. Close out record.

OSTP RECEIVED: 11/20/92 DEPT RECEIVED: 12/01/92

FILE: P-LIFE SCIENCES

CENTRAL FILES:

Mary

EXECUTIVE OFFICE OF THE PRESIDENT
OFFICE OF SCIENCE AND TECHNOLOGY POLICY
WASHINGTON, D.C. 20506

November 25, 1992

Dear Ms. Kellogg:

Thank you for your letter to me regarding the decision by the National Institutes of Health (NIH) to discontinue its participation in one of the activities of the Federal Demonstration Project (FDP), i.e., the trial of a simplified application procedure for noncompeting continuation grants. Your disappointment at this turn of events is understandable, for the procedures by which agencies of the federal government handle noncompeting renewal awards undoubtedly include unnecessary and unproductive administrative requirements and therefore are an appropriate focus for an FDP initiative. Nevertheless, having discussed the matter at length with some of my NIH colleagues, I recognize that their decision, made in conjunction with higher-level officials of the Department of Health and Human Services (DHHS), has a strong supporting rationale.

As I understand the issue, the crux of the problem is that the streamlined FDP procedure for noncompeting renewals has failed to win strong support among the NIH funding units. My colleagues report widespread concern among program- and grants-management staff because the noncompeting renewal procedure now being tested does not generate all the information they believe they need to fulfill their stewardship responsibilities. This conclusion in turn has reinforced misgivings that senior DHHS policy officials have held since this particular trial first was proposed. Whereas many of us hoped that real-world experience with the streamlined procedure might allay the early concerns, the opposite has proved true.

Under the circumstances, with so many key staff at several different levels of DHHS disinclined to endorse the streamlined renewal process, I see no chance that the Department will adopt it as standard policy. Further pursuit of this particular FDP activity as currently designed therefore is likely to be an unproductive expenditure of energy, resources, time, and good will. Regrouping and reassessing the issue in the light of the concerns generated by the trial seems the better course.

I view this setback as unfortunate but far from lethal for FDP. The NIH decision neither tarnishes the other FDP achievements nor diminishes the importance of our fundamental goals. For my part, I will continue to be an advocate for FDP, as will many of my colleagues. That will include searching for a broadly acceptable way to address anew how we might make the noncompeting renewal process more efficient for both parties without an actual or perceived compromise of stewardship.

Sincerely yours,

William F. Raub

William F. Raub, Ph.D.
Special Assistant for Health Affairs

Ms. Donna J. Kellogg
Manager of Operations
Department of Cell, Molecular,
and Structural Biology
Northwestern University Medical School
303 East Chicago Avenue
Chicago, Illinois 60611-3008

Northwestern University Medical School

Department of Cell, Molecular,
and Structural Biology

Ward Building
303 East Chicago Avenue
Chicago, Illinois 60611-3008
(312) 503-8250
Fax (312) 503-7912/4516

November 12, 1992

D. Allen Bromley
Assistant to the President for Science and Technology
Old Executive Office Building
Room 358
1600 Pennsylvania Avenue, N.W.
Washington, DC 20500

Dear Mr. Bromely:

I write to solicit your assistance in ensuring the continued participation of the National Institutes of Health in the noncompeting continuation demonstration of the Federal Demonstration Project (FDP). The continuation of this demonstration, with full participation of the National Institutes of Health, is consistent with the President's January 28, 1992 Memorandum for Certain Department and Agency Heads on the subject of "Reducing the Burden of Government Regulations".

As you may know, the FDP was initiated in 1988 to help eliminate unnecessary administrative burdens on sponsored research and thereby enhance the research productivity of the United States. The noncompeting continuation pilot of the Federal Demonstration Project, initiated July 15, 1990, allowed participating federal agencies to issue out year funding commitments based upon an annual progress report. Some of the participating agencies, due to legal requirements or major procedural disruption, continued the requirement for a cover page. Other documentation was required only if significant changes occurred in the size or scope of a project.

A recent survey of the 1,092 researchers impacted by the noncompeting application process perhaps best demonstrates its importance. Overall, 1092 researchers reported time savings of 2.26 days under the noncompeting continuation demonstration of the FDP. Collectively, researchers saved 2464 days, with 90 percent of those days reinvested to scholarly activities. To provide another perspective on these "time reinvestments", it can be said that the study documents a total of 8.5 person-years of additional scholarly activities. Further applying these rates of return, it is possible to project that the overall additional investment in research activity made possible by FDP was roughly eighteen person years of research.

I appreciate your efforts in ensuring the continuation of this project of demonstrated importance to the academic community and the nation's research enterprise.

Sincerely,

Donna J. Kellogg
Manager of Operations

DJK:cb

"Document Control"

TYPE: INFORMATION DOCUMENT NUMBER: 9203493
ORIGINATOR: 02 STATUS C DIRECTORATE STATUS

****

FROM: STEWART, WILLIAM D.P.: CHIEF SCIENCE ADVISOR, UK

TO: DR. D.A. BROMLEY

DATE OF
CORRESPONDENCE: 11/09/92

SUBJECT: A THANK YOU FOR YOUR LETTER OF OCTOBER 27TH AND ASSURANCE THAT YOU WILL RECEIVE A COPY OF THE UK'S REGULATIONS ONCE FINALISED.

****

DIRECTORATE ASSIGNED: STAFF ASSIGNED:

ACTION REQUIRED: STAFF ACTION:

****

SENDER'S DUE DATE:

OSTP DUE DATE: STAFF DUE DATE
DATE COMPLETED: DATE COMPLETED/DEPT:

****

COPIES TO: D. Allan Bromley
LIFE SCIENCES
INTERNATIONAL/POLICY

****

WHITE HOUSE TRACKING #: CONTACT PERSON:
PHONE: EXT:

REMARKS:

OSTP RECEIVED: 12/02/92 DEPT RECEIVED:
FILE: P-LIFE SCIENCES

CENTRAL FILES:

3493

CABINET OFFICE
Office of Public Service and Science
OFFICE OF SCIENCE AND TECHNOLOGY
70 Whitehall, London SW1A 2AS
Telephone: 071-270 0259 Facsimile:071-270 0616

From the Chief Scientific Adviser and Head of Office
Professor William D. P. Stewart, FRS, FRSE

W0707

Dr Allan Bromley
Assistant to the President
for Science and Technology
The White House
Washington
USA

9 November 1992

Dear Allan,

Thank you for your letter of 27 October. I am pleased to hear that the US biotechnology regulatory oversight mechanisms are evolving to the risk-based philosophy established by the Office of Science and Technology Policy, and I am grateful to you for sending me a copy of their scope document.

As you noted, significant effort has been put into restructuring the UK GMO regulations and there is now a general consensus that previous concerns over the lack of clarity have been appropriately addressed. Although the regulations are process based, the EC regime makes provision for GMO products to be considered under product legislation once risk assessment procedures equivalent to that in the Deliberate Release Directive have been incorporated, and the UK will continue to pursue this policy.

I will ensure that you receive a copy of the UK's regulations once they have been finalised, and look forward to our continued efforts to work towards the international harmonization of biotechnology regulations.

Best wishes
yours ever
Bill.

PROFESSOR WILLIAM D P STEWART

"Document Control"

TYPE: ACTION DOCUMENT NUMBER: 9203526
ORIGINATOR: 02 STATUS I DIRECTORATE STATUS

****

FROM: IANNACCONE, Philip M.: NORTHWESTERN UNIVERSITY

TO: DR. D.A. BROMLEY

DATE OF
CORRESPONDENCE: 11/05/92

SUBJECT: HE IS WRITING TO SOLICIT DR. BROMLEY'S ASSISTANCE IN ENSURING THE CONTINUED PARTICIPATION OF THE NATIONAL INSTITUTES OF HEALTH IN THE FEDERAL DEMONSTRATION PROJECT.

****

DIRECTORATE ASSIGNED: LIFE SCIENCES

STAFF ASSIGNED:

ACTION REQUIRED: DIRECT REPLY

STAFF ACTION:

****

SENDER'S DUE DATE:

OSTP DUE DATE: 12/16/92 STAFF DUE DATE

DATE COMPLETED: DATE COMPLETED/DEPT:

****

COPIES TO: D. Allan Bromley

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WHITE HOUSE TRACKING #: CONTACT PERSON:

PHONE: EXT:

REMARKS:

OSTP RECEIVED: 12/02/92 DEPT RECEIVED:

FILE: P-LIFE SCIENCES

CENTRAL FILES:

3526

Northwestern University Medical School

Markey Program in
Developmental Biology

303 East Chicago Avenue
Chicago, Illinois 60611-3008
(312) 503-5232

Philip M. Iannaccone, MD, DPhil
Director

November 5, 1992

D. Allan Bromley
Assistant to the President for Science and Technology
Old Executive Office Building
Room 358
1600 Pennsylvania Avenue, N.W.
Washington, DC 20500

Dear Mr. Bromley,

I write to solicit your assistance in ensuring the continued participation of the National Institutes if Health in the noncompeting continuation demonstration of the Federal Demonstration Project (FDP). The continuation of the demonstration, with full participation of the National Institutes of Health, is consistent with the President's January 28, 1992 Memorandum for Certain Department and Agency Heads on the subject of "Reducing the Burden of Government Regulations".

As you may know, the FDP was initiated in 1988 to help eliminate unnecessary administrative burdens on sponsored research and thereby enhance the research productivity of the United States. The noncompeting agencies to issue out year funding commitments based upon annual progress report. Some of the participating agencies, due to legal requirements or major procedural disruption, continued the requirement for a cover page. Other documentation was required only if significant changes occurred in the size or scope of a project.

A recent survey of the 1,092 researchers impacted by the noncompeting application process perhaps best demonstrates its importance. Overall, 1,092 researchers reported time savings of 2.26 days under the noncompeting continuation demonstration of the FDP. Collectively, researchers saved 2464 days, with 90 percent of those days reinvested in scholarly activities. To provide another perspective on these "time reinvestments", it can be said that the study documents a total of 8.5 person-years of additional scholarly activities. Further applying these rates of return, it is possible to project that the overall additional investment in research activity made possible by FDP was roughly eighteen person years of research.

I appreciate your efforts in ensuring the continuation of this project of demonstrated importance to the academic community and the nation's research enterprise.

Sincerely,

Philip M. Iannaccone
Professor

PMI/sb

Mary

EXECUTIVE OFFICE OF THE PRESIDENT
OFFICE OF SCIENCE AND TECHNOLOGY POLICY
WASHINGTON, D.C. 20506

November 25, 1992

Dear Dr. Iannaccone:

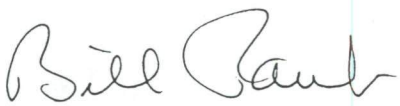
Thank you for your letter to me regarding the decision by the National Institutes of Health (NIH) to discontinue its participation in one of the activities of the Federal Demonstration Project (FDP), i.e.,the trial of a simplified application procedure for noncompeting continuation grants. Your disappointment at this turn of events is understandable, for the procedures by which agencies of the federal government handle noncompeting renewal awards undoubtedly include unnecessary and unproductive administrative requirements and therefore are an appropriate focus for an FDP initiative. Nevertheless, having discussed the matter at length with some of my NIH colleagues, I recognize that their decision, made in conjunction with higher-level officials of the Department of Health and Human Services (DHHS), has a strong supporting rationale.

As I understand the issue, the crux of the problem is that the streamlined FDP procedure for noncompeting renewals has failed to win strong support among the NIH funding units. My colleagues report widespread concern among program- and grants-management staff because the noncompeting renewal procedure now being tested does not generate all the information they believe they need to fulfill their stewardship responsibilities. This conclusion in turn has reinforced misgivings that senior DHHS policy officials have held since this particular trial first was proposed. Whereas many of us hoped that real-world experience with the streamlined procedure might allay the early concerns, the opposite has proved true.

Under the circumstances, with so many key staff at several different levels of DHHS disinclined to endorse the streamlined renewal process, I see no chance that the Department will adopt it as standard policy. Further pursuit of this particular FDP activity as currently designed therefore is likely to be an unproductive expenditure of energy, resources, time, and good will. Regrouping and reassessing the issue in the light of the concerns generated by the trial seems the better course.

I view this setback as unfortunate but far from lethal for FDP. The NIH decision neither tarnishes the other FDP achievements nor diminishes the importance of our fundamental goals. For my part, I will continue to be an advocate for FDP, as will many of my colleagues. That will include searching for a broadly acceptable way to address anew how we might make the noncompeting renewal process more efficient for both parties without an actual or perceived compromise of stewardship.

Sincerely yours,



William F. Raub, Ph.D.
Special Assistant for Health Affairs

Dr. Philip M. Iannaccone
Professor
Markey Program in Developmental
Biology
Northwestern University Medical School
303 East Chicago Avenue
Chicago, Illinois 60611-3008

"Document Control"

TYPE: INVITATION DOCUMENT NUMBER: 9203616
ORIGINATOR: 02 STATUS C DIRECTORATE STATUS
****

FROM: MORI, Wataru: COUNCIL FOR SCIENCE AND TECHNOLOGY, JAPAN

TO: DR. D.A. BROMLEY

DATE OF
CORRESPONDENCE: 11/14/92

SUBJECT: HE IS FORWARDING A COPY OF RTHEIR REPORT "GUIDELINES FOR RECOMBINANT DNA EXPERIMENT".

****

DIRECTORATE ASSIGNED:

STAFF ASSIGNED:

ACTION REQUIRED:

STAFF ACTION:

****

SENDER'S DUE DATE:

OSTP DUE DATE:

STAFF DUE DATE

DATE COMPLETED:

DATE COMPLETED/DEPT:

****

COPIES TO: D. Allan Bromley
LIFE SCIENCES

****

WHITE HOUSE TRACKING #:

CONTACT PERSON:

PHONE: EXT:

REMARKS: ENCLOSURES TO DAB.

OSTP RECEIVED: 12/07/92 DEPT RECEIVED:
FILE: P-LIFE SCIENCES

CENTRAL FILES:

3616

PRIME MINISTER'S
COUNCIL FOR SCIENCE AND TECHNOLOGY
Kasumigaseki 2/2/1, Chiyoda-ku, Tokyo, 100 JAPAN
Phone:(81)(3) 3581 1357, Fax:(81)(3) 3581 3079

November 14,1992

Dr. D. Allan Bromley
The Assistant to the President
for Science and Technology
The White House
Washington, D. C., USA

Dear Allan:

I am enclosing with this letter "Guidelines for Recombinant DNA Experiment", which has been translated into English recently. I hope it would be of use to you.

I am looking forward to seeing you again in December in France.

Sincerely yours,

Wataru

Wataru Mori
Member of
Council for Science and Technology

TYPE: ACTION DOCUMENT NUMBER: 9203623
ORIGINATOR: 02 STATUS I DIRECTORATE STATUS
****

FROM: RIESENHUBER, Heinz: MINISTER FOR SCIENCE AND TECHNOLOGY, GERMANY

TO: DR. D.A. BROMLEY

DATE OF CORRESPONDENCE: 11/02/92

SUBJECT: RE: THE PATENTABILITY OF GENOME SEQUENCES.

****

DIRECTORATE ASSIGNED: LIFE SCIENCES

STAFF ASSIGNED:

ACTION REQUIRED: AS NECESSARY

STAFF ACTION:

****

SENDER'S DUE DATE:

OSTP DUE DATE: 12/30/92

STAFF DUE DATE

DATE COMPLETED:

DATE COMPLETED/DEPT:

****

COPIES TO: D. Allan Bromley

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WHITE HOUSE TRACKING #:

CONTACT PERSON:

PHONE: EXT:

REMARKS:

OSTP RECEIVED: 12/17/92 DEPT RECEIVED: 12/23/92

FILE: P-LIFE SCIENCES

CENTRAL FILES:

Der Bundesminister
für Forschung und Technologie

5300 Bonn 2, November 26,1992

Heinemannstraße 2
Fernruf (02 28) 590 oder 59-
Teletex 22 83 628 = BMFTb

Dr. D. Allan Bromley
Assistant to the President
for Science and Technology
The White House

Washington D.C.
USA

Translation

Dear Allan:

Thank you very much for your letters of October 5 and 28, 1992.

I have noted with interest that the US Patent and Trademark Office does not permit patentability of genome sequences of unknown function. As you are aware, this attitude corresponds to my own opinion in the ongoing controversial discussion.

Thank you, too, for forwarding me the first project description. I eagerly await the study to be drawn up by the Congressional Office of Technology Assessment on the subject of the patentability of genome sequences. I would be very interested to learn more about this when we meet in Rambouillet. I consider it important that scientists from other countries also be involved in this study.

With regard to the question who can be called upon to contribute to this report on the German side, deliberations and discussions are still in progress.

As soon as a relevant decision has been taken you will be informed via the German Embassy in Washington of the names of the German experts selected.

Sincerely yours,

signed: Dr. Heinz Riesenhuber

Der Bundesminister
für Forschung und Technologie

5300 Bonn 2, 26.11.1992

Heinemannstraße 2
Fernruf (02 28) 590 oder 59-3407
Teletex 22 83 628 = BMFTb

Herrn
Dr. D. Allan Bromley
Assistent to the President
for Science and Technology
The White House

Washington D.C. / USA

Dear Allan,

vielen Dank für Ihre Briefe vom 5. und 28. Oktober 1992.

Ich habe mit Interesse davon Kenntnis genommen, daß das "Patent and Trademark Office" eine Patentierbarkeit von Gensequenzen unbekannter Zweckbestimmung ablehnt. Wie Sie wissen, entspricht dies auch meiner Auffassung in der kontrovers geführten Diskussion.

Ich danke Ihnen auch für die Übersendung der ersten Projektbeschreibung und sehe der Studie des "Congressional Office of Technology Assessment" zur Patentierbarkeit von Gensequenzen mit großem Interesse entgegen. Es würde mich freuen, bei unserem Treffen in Rambouillet näheres darüber zu hören. Ich halte es für wichtig, daß an dieser Untersuchung auch Wissenschaftler anderer Länder beteiligt werden.

Zu Ihrer Frage, wer auf deutscher Seite zu diesem Bericht beitragen kann, sind derzeit noch Überlegungen und Gespräche im Gange. Sobald eine Entscheidung getroffen ist, werden Ihnen die Namen der deutschen Experten über die Botschaft in Washington mitgeteilt.

Mit freundlichen Grüßen

Dr. Heinz Riesenhuber

THE WHITE HOUSE

WASHINGTON

December 23, 1992

Dear Minister Riesenhuber:

Your Science Counselor at the German Embassy in Washington, D.C., Dr. Klaus Schroeter, submitted the names of Professors Joseph Straus, and Walter Dorfler as potential German contacts for the OTA project on patenting human DNA sequences. Thank you for this information. I have forwarded this information to Dr. Robyn Nashimi, OTA Project Director for this activity.

Sincerely yours,

D. Allan Bromley
The Assistant to the President
for
Science and Technology

The Honorable Heinz Riesenhuber
Minister of Science and Technology
Federal Republic of Germany
5300 Bonn 2
Heinemannstrasse 2
Germany

Happy New Year!

TYPE: ACTION DOCUMENT NUMBER: 9203623
ORIGINATOR: 02 STATUS I DIRECTORATE STATUS
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FROM: RIESENHUBER, Heinz: MINISTER FOR SCIENCE AND TECHNOLOGY, GERMANY

TO: DR. D.A. BROMLEY

DATE OF CORRESPONDENCE: 11/02/92

SUBJECT: RE: THE PATENTABILITY OF GENOME SEQUENCES.

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DIRECTORATE ASSIGNED: LIFE SCIENCES

STAFF ASSIGNED:

ACTION REQUIRED: AS NECESSARY

STAFF ACTION:

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SENDER'S DUE DATE:

OSTP DUE DATE: 12/30/92

STAFF DUE DATE

DATE COMPLETED:

DATE COMPLETED/DEPT:

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COPIES TO: D. Allan Bromley

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PHONE: EXT:

REMARKS:

OSTP RECEIVED: 12/17/92 DEPT RECEIVED:

FILE: P-LIFE SCIENCES

CENTRAL FILES:

50

FAX:_____ MAIL: ✓

OSTP #:

Date of Correspondence: 11/x

Date of Receipt of Correspondence: 12/17

From: Dr Heinz Riesenhuber

Affiliation: Minister of S & T Germany

Subject: patentability of genome sequences

Action:
FYI:

Assign to: DLS

Due Date:

Copies to: Tom Ratchford, DAB

I think a fax of this is floating around

3625

FAX:_____ MAIL: ✓

OSTP #:

Date of Correspondence: 11/x

Date of Receipt of Correspondence: 12/17

From: Dr Heinz Riesenhuber

Affiliation: Minister of S & T Germany

Subject: patentability of genome sequences

Action:
FYI:

Assign to: DLS

Due Date:

Copies to: Tom Ratchford, DAB

I think a fax of this is floating around

Der Bundesminister
für Forschung und Technologie

5300 Bonn 2, November 26,1992

Heinemannstraße 2
Fernruf (02 28) 590 oder 59-
Teletex 22 83 628 = BMFTb

Dr. D. Allan Bromley
Assistant to the President
for Science and Technology
The White House

Washington D.C.
USA

Translation

Dear Allan:

Thank you very much for your letters of October 5 and 28, 1992.

I have noted with interest that the US Patent and Trademark Office does not permit patentability of genome sequences of unknown function. As you are aware, this attitude corresponds to my own opinion in the ongoing controversial discussion.

Thank you, too, for forwarding me the first project description. I eagerly await the study to be drawn up by the Congressional Office of Technology Assessment on the subject of the patentability of genome sequences. I would be very interested to learn more about this when we meet in Rambouillet. I consider it important that scientists from other countries also be involved in this study.

With regard to the question who can be called upon to contribute to this report on the German side, deliberations and discussions are still in progress.

As soon as a relevant decision has been taken you will be informed via the German Embassy in Washington of the names of the German experts selected.

Sincerely yours,

signed: Dr. Heinz Riesenhuber

Der Bundesminister
für Forschung und Technologie

5300 Bonn 2, 26.11.1992

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Herrn
Dr. D. Allan Bromley
Assistent to the President
for Science and Technology
The White House

Washington D.C. / USA

Dear Allan,

vielen Dank für Ihre Briefe vom 5. und 28. Oktober 1992.

Ich habe mit Interesse davon Kenntnis genommen, daß das "Patent and Trademark Office" eine Patentierbarkeit von Gensequenzen unbekannter Zweckbestimmung ablehnt. Wie Sie wissen, entspricht dies auch meiner Auffassung in der kontrovers geführten Diskussion.

Ich danke Ihnen auch für die Übersendung der ersten Projektbeschreibung und sehe der Studie des "Congressional Office of Technology Assessment" zur Patentierbarkeit von Gensequenzen mit großem Interesse entgegen. Es würde mich freuen, bei unserem Treffen in Rambouillet näheres darüber zu hören. Ich halte es für wichtig, daß an dieser Untersuchung auch Wissenschaftler anderer Länder beteiligt werden.

Zu Ihrer Frage, wer auf deutscher Seite zu diesem Bericht beitragen kann, sind derzeit noch Überlegungen und Gespräche im Gange. Sobald eine Entscheidung getroffen ist, werden Ihnen die Namen der deutschen Experten über die Botschaft in Washington mitgeteilt.

Mit freundlichen Grüßen

Dr. Heinz Riesenhuber

"Document Control"

TYPE: ACTION DOCUMENT NUMBER: 9203377
ORIGINATOR: 02 STATUS I DIRECTORATE STATUS

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FROM: PURSER, Ken: SOUTHERN CROSS CORPORATION

TO: DR. D.A. BROMLEY

DATE OF
CORRESPONDENCE: 10/29/92

SUBJECT: HE IS REQUESTING A CONTACT NAME AT THE NATIONAL CANCER INSTITUTE WHO WOULD BE ABLE TO GIVE HIM NAMES IN THE BIOMEDICAL FIELD TO COMMUNICATE WITH TO EXPLAIN AMS AND ITS POTENTIAL USES.

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DIRECTORATE ASSIGNED: LIFE SCIENCES

STAFF ASSIGNED:

ACTION REQUIRED: FOR DAB'S SIGNATURE

STAFF ACTION:

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SENDER'S DUE DATE:

OSTP DUE DATE: 11/16/92 STAFF DUE DATE
DATE COMPLETED: DATE COMPLETED/DEPT:

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COPIES TO: D. Allan Bromley

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WHITE HOUSE TRACKING #:

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REMARKS:

OSTP RECEIVED: 10/06/92 DEPT RECEIVED:
FILE: P-LIFE SCIENCES

CENTRAL FILES:

3377

Southern Cross Corporation
426C Boston Street
Topsfield, MA 01983, USA

October 29, 1992

Dr. D. Allan Bromley
Assistant to the President for Science & Technology
The White House
Pennsylvania Avenue
Washington, DC 20006

Dear Al:

I am sure you are aware of the work being done at Lawrence Livermore by John Vogel, Ken Turteltaub and their associates who are using ^{14}C Accelerator Mass Spectrometry to measure the concentration levels of potentially carcinogenic chemicals in animal organs when the ingested concentrations are close to actual human doses. Their measurements are in contrast to most laboratory studies where the ingested concentrations may be as much as 10^4 to 10^7 greater; any natural DNA repair mechanisms will probably be overwhelmed at these high concentrations.

I believe that the technique of AMS represents an important new resource for biomedical research and, although John Vogel and his colleagues are publishing and giving talks on the subject, I would like to augment their efforts by presentations to the biomedical community that would be slanted more towards educating existing ^{14}C users to the fundamental advantages of AMS for detecting long-lived isotopes. Unfortunately, the few interactions I have had to date with such audiences suggests a significant potential barrier exists between AMS and biomedicine and that education is needed to enhance coupling – probably by both parties!

The existing ^{14}C workers I have talked to usually start off believing that 10^6-fold enrichment will still be essential with AMS and they look at me skeptically when I tell them that to achieve an atom counting rate >3,000 ^{14}C events/second the tracer enrichment need be only 100 times above natural levels; also, that from a 100μg carbon sample this rate will be maintained for 15 minutes. Their eyes really roll when I point out that using AMS for ^{14}C detection the enrichments *cannot* be much greater than 1000 and, thus, the permanent disposal of waste becomes a low-cost non-issue: If one gram of 100-fold enriched waste is diluted with 100 grams of fuel oil the mixture can be incinerated to produce a

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concentration of ^{14}C radioactivity in the stack gasses not greater than that naturally present in the atmosphere. Communication is tough, however, and one listener left the meeting still talking about dpm!

While I am reluctant to ask, it would be helpful if you could suggest a contact at the National Cancer Institute, or elsewhere, who would be able to give me names in the biomedical field with whom I could communicate to explain AMS and its potential usefulness.

Other news: The AMS machine at Woods Hole is working well. It measures $^{14}C/^{12}C$ ratios with accuracies of $\approx$0.5% and runs unattended around the clock at an average rate of one sample per hour. The WHOI group is presently measuring about 1500 samples per year and only limitations in the throughput of their sample conversion lines are preventing WHOI from measuring the 4000/year they originally promised to the oceanographic community. I think they will soon have this bottle-neck eliminated. Accuracies of 0.2%, or better, can undoubtedly be achieved with modest effort if this becomes desirable. There will soon be copies of the system at Groningen, Kiel and perhaps Glascow. There are a bunch of others further out; Ted Litherland would like a second one at Toronto and is working on the funding.

As you know, Peter Rose, Geoff Ryding, Hilton Glavish and I were supported by Sumitomo Heavy Metals for over a year and worked with IMS in Vienna developing the design for an Ion Lithography tool. However, now that IBM, Toshiba, and Siemens have decided to use deep u.v. Optical Lithography for the 256-Megabit DRAM, the need for ion lithography seems to have moved into the next century. We are disappointed, but that is the luck of the game.

I plan to be in Washington during most of the week of December 7th and I wondered if it might be convenient to drop by and see you for a few minutes during one of the days of that week.

Best regards,

Ken Purser

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FAX: (508) 887 0031

"Document Control"

TYPE: ACTION
DOCUMENT NUMBER: 9203289
ORIGINATOR: 02
STATUS I
DIRECTORATE STATUS

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FROM: DAVIS, Bernard: HARVARD MEDICAL SCHOOL

TO: DR. D.A. BROMLEY

DATE OF CORRESPONDENCE: 10/17/92

SUBJECT: HE IS WRITING REGARDING THE VIEW OF BASIC RESEARCH VERSUS APPLIED RESEARCH.

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DIRECTORATE ASSIGNED: LIFE SCIENCES

STAFF ASSIGNED:

ACTION REQUIRED: AS/IF NECESSARY

STAFF ACTION:

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SENDER'S DUE DATE:

OSTP DUE DATE: 11/10/92

STAFF DUE DATE

DATE COMPLETED:

DATE COMPLETED/DEPT:

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COPIES TO: D. Allan Bromley

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REMARKS:

OSTP RECEIVED: 10/29/92

DEPT RECEIVED:

FILE: P-LIFE SCIENCES

CENTRAL FILES:

3289

BACTERIAL PHYSIOLOGY UNIT
HARVARD MEDICAL SCHOOL
25 SHATTUCK STREET
BOSTON, MASSACHUSETTS 02115
TELEPHONE: (617) 732-2022

Oct. 17, 1992.

Dr. D. Allan Bromley,
Office of Science and Technology Policy,
The White House,
Washington, DC.

Dear Dr. Bromley,

Last June you sent me a copy of your annual report to Congress, and I'm afraid I didn't get to read it until just now. I find it excellent, in content and style. And in a way I'm particularly happy to encounter it now, after seeing the stampede toward applied research by Healy, Massey, and George Brown. With such agreement it looks as though you will have a tough job defending basic research as the nourishing source of major breakthroughs, as you do so well in your report. I will take the liberty of passing on a suggestion that I have made for the ASBMB Public Affairs Advisory Committee, of which I am a member: that under Bill MacElroy the NSF installed a major program of applied research a couple of decades ago, called RANN, and it survived for only a few years.

I had already drafted an OpEd on Healy's strategic plan, and it is scheduled for the next week or two in the Wall Street Journal. I hope it will be possible to add to it references to your position and to the others that I have mentioned.

I believe it was Santayana who said that those who do not remember history are condemned to repeat it. But illustrating his point, I would guess that others probably had said the same thing earlier and he did not know it.

Sincerely,

Bernard D. Davis

"Document Control for Division of Life Sciences"

TYPE: ACTION DOCUMENT NUMBER: 9203290
ORIGINATOR: 02 STATUS I DIRECTORATE STATUS C

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FROM: HOSEY, M. Marlene: NORTHWESTERN UNIVERSITY MEDICAL SCHOOL

TO: DR. D.A. BROMLEY

DATE OF CORRESPONDENCE: 10/12/92

SUBJECT: SHE IS WRITING TO SOLICIT DR. BROMLEY'S ASSISTANCE IN ENSURING THE CONTINUED PARTICIPATION OF NIH IN THE FEDERAL DEMONSTRATION PROGRAM.

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DIRECTORATE ASSIGNED: LIFE SCIENCES

STAFF ASSIGNED: William Raub

ACTION REQUIRED: AS NECESSARY

STAFF ACTION: AS NECESSARY

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SENDER'S DUE DATE:

OSTP DUE DATE: 11/10/92 STAFF DUE DATE 11/16/92
DATE COMPLETED: DATE COMPLETED/DEPT: 11/25/92

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COPIES TO: D. Allan Bromley

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PHONE: EXT:

REMARKS: Dr. Raub responded to this letter as well as one addressed to him.

OSTP RECEIVED: 10/30/92 DEPT RECEIVED: 11/10/92
FILE: P-LIFE SCIENCES

CENTRAL FILES:

EXECUTIVE OFFICE OF THE PRESIDENT
OFFICE OF SCIENCE AND TECHNOLOGY POLICY
WASHINGTON, D.C. 20506

November 25, 1992

Dear Professor Hosey:

Thank you for your letters to Dr. D. Allan Bromley and me regarding the decision by the National Institutes of Health (NIH) to discontinue its participation in one of the activities of the Federal Demonstration Project (FDP), i.e.,the trial of a simplified application procedure for noncompeting continuation grants. Your disappointment at this turn of events is understandable, for the procedures by which agencies of the federal government handle noncompeting renewal awards undoubtedly include unnecessary and unproductive administrative requirements and therefore are an appropriate focus for an FDP initiative. Nevertheless, having discussed the matter at length with some of my NIH colleagues, I recognize that their decision, made in conjunction with higher-level officials of the Department of Health and Human Services (DHHS), has a strong supporting rationale.

As I understand the issue, the crux of the problem is that the streamlined FDP procedure for noncompeting renewals has failed to win strong support among the NIH funding units. My colleagues report widespread concern among program- and grants-management staff because the noncompeting renewal procedure now being tested does not generate all the information they believe they need to fulfill their stewardship responsibilities. This conclusion in turn has reinforced misgivings that senior DHHS policy officials have held since this particular trial first was proposed. Whereas many of us hoped that real-world experience with the streamlined procedure might allay the early concerns, the opposite has proved true.

Under the circumstances, with so many key staff at several different levels of DHHS disinclined to endorse the streamlined renewal process, I see no chance that the Department will adopt it as standard policy. Further pursuit of this particular FDP activity as currently designed therefore is likely to be an unproductive expenditure of energy, resources, time, and good will. Regrouping and reassessing the issue in the light of the concerns generated by the trial seems the better course.

I view this setback as unfortunate but far from lethal for FDP. The NIH decision neither tarnishes the other FDP achievements nor diminishes the importance of our fundamental goals. For my part, I will continue to be an advocate for FDP, as will many of my colleagues. That will include searching for a broadly acceptable way to address anew how we might make the noncompeting renewal process more efficient for both parties without an actual or perceived compromise of stewardship.

Sincerely yours,

Bill Raub

William F. Raub, Ph.D.
Special Assistant for Health Affairs

Professor M. Marlene Hosey
Department of Pharmacology
Northwestern University Medical School
303 East Chicago Avenue
Chicago, Illinois 60611-3008

3290

Northwestern University Medical School

Department of Pharmacology

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October 12, 1992

Mr. D. Allan Bromley
Assistant to the President for Science and Technology
Old Executive Office Building
Room 358
1600 Pennsylvania Avenue, N.W.
Washington, DC 20500

Dear Mr. Bromley:

I write to solicit your assistance in ensuring the continued participation of the National Institutes of Health in the noncompeting continuation demonstration of the Federal Demonstration Project (FDP). The continuation of this demonstration, with full participation of the National Institutes of Health, is consistent with the President's January 28, 1992 Memorandum for Certain Department and Agency Heads on the subject of "Reducing the Burden of Government Regulations".

As you may know, the FDP was initiated in 1988 to help eliminate unnecessary administrative burdens on sponsored research and thereby enhance the research productivity of the United States. The noncompeting continuation pilot of the Federal Demonstration Project, initiated July 15, 1990, allowed participating federal agencies to issue out year funding commitments based upon an annual progress report. Some of the participating agencies, due to legal requirements or major procedural disruption, continued the requirement for a cover page. Other documentation was required only if significant changes occurred in the size or scope of a project.

A recent survey of the 1,092 researchers impacted by the noncompeting application process perhaps best demonstrates its importance. Overall, 1,092 researchers reported time savings of 2.26 days under the noncompeting continuation demonstration of the FDP. Collectively, researchers saved 2464 days, with 90 percent of those days reinvested in scholarly activities. To provide another perspective on these "time reinvestments", it can be said that the study documents a total of 8.5 person-years of additional scholarly activities. Further

applying these rates of return, it is possible to project that the overall additional investment in research activity made possible by FDA was roughly eighteen person years of research.

I appreciate your efforts in ensuring the continuation of this project of demonstrated importance to the academic community and the nation's research enterprise.

Sincerely,

Marlene Hosey

M. Marlene Hosey
Professor

MMH/mcf

TYPE: ACTION DOCUMENT NUMBER: 9203123
ORIGINATOR: 02 STATUS I DIRECTORATE STATUS
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FROM: GOLDMAN, Robert D.: NORTHWESTERN UNIVERSITY MEDICAL SCHOOL

TO: DR. D.A. BROMLEY

DATE OF
CORRESPONDENCE: 10/12/92

SUBJECT: HE IS WRITING TO SOLICIT DR. BROMLEY'S SUPPORT TO ENSURE THE CONTINUED PARTICIPATION OF NIH IN THE FEDERAL DEMONSTRATION PROGRAM.

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DIRECTORATE ASSIGNED: LIFE SCIENCES
STAFF ASSIGNED:

ACTION REQUIRED: AS NECESSARY
STAFF ACTION:

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SENDER'S DUE DATE:
OSTP DUE DATE: 10/29/92
STAFF DUE DATE
DATE COMPLETED:
DATE COMPLETED/DEPT:

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COPIES TO: D. Allan Bromley

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PHONE: EXT:

REMARKS:

OSTP RECEIVED: 10/19/92 DEPT RECEIVED:
FILE: P-LIFE SCIENCES

CENTRAL FILES:

3123

Northwestern University Medical School

Department of Cell, Molecular,
and Structural Biology

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303 East Chicago Avenue
Chicago, Illinois 60611-3008
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Fax (312) 503-0954

Robert D. Goldman, PhD
Stephen Walter Ranson Professor
and Chairman

October 12, 1992

Dr. D. Allan Bromley
Assistant to the President for Science and Technology
Old Executive Office Building
Room 358
1600 Pennsylvania Avenue, N.W.
Washington, DC 20500

Dear Dr. Bromley:

As Chairman of a medical school basic science department and a National Institutes of Health (NIH) grantee, I wish to ask for your assistance in helping to make certain that the NIH is able to continue its participation in the non-competing continuation Federal Demonstration Project. The participation of the NIH in this demonstration is consistent with the President's January 28, 1992 Memorandum for Certain Department and Agency Heads aimed at "Reducing the Burden of Government Regulations".

I am certain that you know that this project which started in 1988, is aimed at the elimination of unnecessary administrative burdens on federally sponsored research. Through the elimination of these burdens, research productivity has risen over these past few years. In a recent survey, the 1,092 researchers participating in the project nationwide reported a time savings of 2.26 days during the preparation of non-competing renewal applications. Therefore on a collective basis at least 2,464 days were saved and at least 90% of the time saved was invested in scholarly pursuits. In other terms, this reinvestment of the time of researchers has amounted to 8.5 person years of additional scholarship for the nation.

Based on the above considerations, there is no doubt that the FDP has paid off tremendously and will continue to do so. Please help to make certain that the NIH continues to participate in this project.

Respectfully yours,

Robert D. Goldman

Robert D. Goldman

RDG/ld