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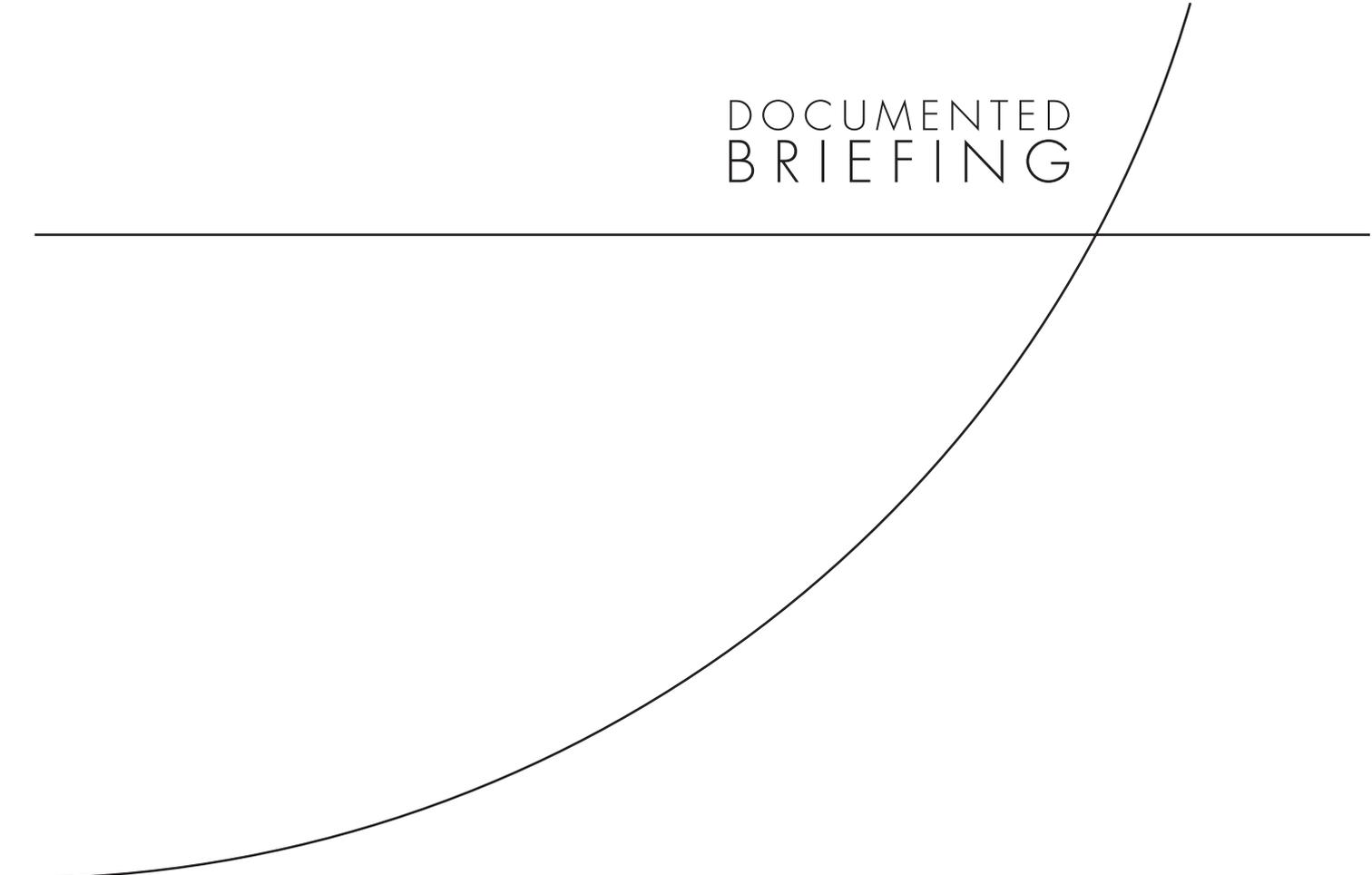
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DOCUMENTED
BRIEFING

Health and Medical Research in the United States

Observatory on Health Research
Systems

Miriam Shergold

The research described in this report was prepared as part of RAND Europe's Health Research System Observatory Documented Briefing series, funded by the English Department of Health.

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Preface

This documented briefing provides an overview of health and medical research in the United States. The report is part of a series of country-specific reports available from RAND Europe's Health Research System Observatory, funded by the English Department of Health.

The report is divided into three parts. In the first part, the *Structure of the U.S. Health Research System*, including funding sources, sectors performing health and medical research, and health research priority setting, is presented. The second part, *Processes and Performance of the U.S. Health Research System*, focuses on the types of funding available and how funding activities are conducted, and provides exemplars of the system's performance. The third part presents an *Outlook* and considers current and emerging health research issues in the United States.

The report is based on desk-based document review and will be updated on a regular basis. It does not attempt to discuss current policy options, or make recommendations for future strategy. The report will be of interest to government officials dealing with health and medical research policy, medical research councils, health and medical research charities, public and private institutions engaged in health research, and researchers.

The use of \$ throughout this report stands for U.S. dollars, unless stated otherwise.

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Summary

Summary: Key Points

- The United States holds a premier position in funding and conducting health R&D
- Key players among funders are industry and the NIH
- Industry and NIH strive to optimise investments through governance arrangements and funding policies that reflect the respective priorities of profitability and public health improvements
- Following a surge in funding at the turn of the millennium, recent years have seen budgets stagnate
- Funding shortages, ethical restrictions, and immigration hurdles threaten the United States' traditional ability to attract, develop, and retain world-class research capacity

The United States is the world leader in health research in terms of total investment, as well as investment in proportion to overall health spending. In the decade leading up to 2003, investment almost doubled to \$94.3 billion (0.86% of GDP²), representing 5.6 percent of total health spending. The country hosts a range of world-class public and non-profit research institutions that attract international talent and recognition. At the same time, it is a hub for industrial R&D in pharmacology, biotechnology, and medical devices: in 2003, 70 percent of the global drug development pipeline belonged to companies headquartered in the United States. Health R&D has traditionally benefited from support from both leading political parties.

Due to the scale of R&D activities in the United States, even funders that compare to large investors in other research intensive countries are dwarfed by the system's principal players: industry and the publicly funded National Institutes of Health (NIH). Together, these key players provide over 80 percent of all support of health research in the country.

The large budgets handled by businesses and the NIH pose a significant strategic challenge to the organisations' leaders. This is addressed by governance structures that reflect the respective aims of generating profits for shareholders and supporting research excellence in the service of public health. Both private and public funders have formulated strategic

² Percentage of gross domestic product (GDP) statistics are calculated using OECD Statistics: GDP, Annual in millions Current Prices (National Currency). <http://stats.oecd.org>

priorities to guide their funding policy. This is exemplified by the NIH Roadmap for Medical Research, which identifies key prerequisites for effective future investigation, and companies' decisions to focus on specific therapeutic areas or rates of return.

Following a period of rapid growth up to 2003, during which the NIH budget doubled, funding levels have stagnated, a trend also noticeable in for-profit investment. Influenced by competing public demands, such as public resources needed for disaster relief, this development has led to grave concerns among researchers. In particular, it has become increasingly difficult for young researchers to obtain support. Research advocacy representatives also argue that diminished investment will result in higher health costs in the future.

There is concern that young researchers' difficulties in obtaining support to develop their career and investigations will undermine recent years' successes in fostering a new generation of promising scientists. Researchers also warn that more cumbersome immigration procedures and ethically motivated restrictions on research, for example on research with stem cells, are affecting the United States' traditional status as a researcher magnet.

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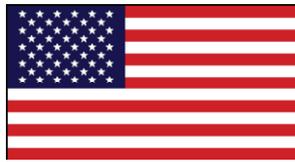
Abbreviations and terms

BIO	Biotechnology Industry Organization
DHHS	Department of Health and Human Services
FY	Fiscal year
GDP	Gross domestic product
NIH	National Institutes of Health
PhRMA	Pharmaceutical Research and Manufacturers of America

Introduction

Health and Medical Research in the United States

International Observatory on Health Research Systems



Miriam Shergold

July 2007

It is difficult to imagine the face and pace of contemporary biomedical research without the role played by the United States in investigation, training, and investment. All these activities take place in a setting that has its roots in history, and continues to evolve, shaped by cultural and political influences. As in other countries, public and private investors need to meet the challenge of making optimum use of resources in the face of virtually unlimited scientific possibilities, while also fostering the workforce required for progress in biomedical discovery.

This briefing provides a brief overview of the health research system of the United States. The first section introduces the structural framework of institutions and funding streams within which health research takes place. The second section describes key aspects of the activities and strategies of the system's key players, and outlines wider developments influencing the current outlook for biomedical science and scientists in the country.

Structure of the U.S. Health Research System

Funders of Biomedical Research

- Federal government
 - National Institutes of Health
 - Other departments and agencies (defense, agriculture)
 - National Science Foundation
- State and local governments
- Industry
 - Pharmaceutical
 - Biotechnology
 - Medical devices
- Foundations/charities
- Medical research organisations
- Disease-focused organisations
- Universities and colleges

Money for biomedical research in the United States comes from various public and private sources.

Public funds are allocated at the federal government level, as well as by state and local governments. Principal recipients of federal funding are the National Institutes of Health (NIH) via the Department of Health and Human Services (DHHS), as well as the Department of Defense, the Department of Agriculture, and the National Science Foundation, whose remit includes the support of research into biological sciences. Smaller amounts of public funding go to biomedical research at a range of other federal departments and agencies, such as the Department of Veteran Affairs and the Environmental Protection Agency (Connelly and Propst, 2006; National Science Foundation Division of Science Resource Statistics, 2006; Center for the Health Care Professions, 1995). On a much more modest scale compared to the federal level, state and local governments support research in their areas, and in accordance with their own specific priorities, as exemplified by stem-cell-research initiatives in California.

Industry represents a large, but also highly diversified, source of investment. Businesses engaging in biomedical research fall into, and sometimes straddle, the basic categories of drug development, biotechnology, and medical technology. There is great variety in the age, size, and profitability of individual businesses, with pharmaceutical giants like Pfizer acting alongside small biotechnology start-ups financed by venture capital.

Private funds also form the financial basis of not-for-profit organisations dedicated to progress in health intervention. These include foundations by wealthy individuals, often created through legacies, although the largest current funder is the Bill and Melinda Gates Foundation (The Foundation Center, 2006, 2007). As funders of investigations across a range of areas, and in external research settings, such foundations are complemented by the privately endowed research organisations, such as the Howard Hughes Medical Institute, and disease-focused organisations such as the American Cancer Society (Moses, Their, and Matheson, 2005; Institute of Medicine, 1999).

Finally, state and private universities and colleges invest their own institutional funds into biomedical research. This investment forms part of a portfolio of funding sources that also includes investment from industry, state and local governments, and private endowments.

Key Players

Industry and the NIH support over 80% of health research in the United States, creating a considerable gap between their investment and the sums invested by other sponsors.

Funder	Expenditure in 2003 (\$ billion)	Share of overall funding
Industry	54.1	57%
NIH	26.4	28%
State and local	4.3	4%
Private non-profit	2.5	3%

Source: Moses, Dorsey, et al. (2005)

Because the United States is both a large country and a premier location for biomedical research, in absolute terms, even some of its smaller funders are very significant compared to investors in other nations. For example, in 2003, the Bill and Melinda Gates Foundation alone gave \$236 million to health research, but the investment of all private not-for-profit funders taken together only amounted to about 3 percent of overall national funding (Moses, Dorsey, et al., 2005).

However, such private funding is important beyond the relative sums involved. Foundations are able to invest into areas not otherwise covered because they are, for example, commercially unattractive (e.g. malaria), politically controversial (e.g. contraceptives), or high risk (e.g. untried researchers, novel methods) (Center for the Health Care Professions, 1995).

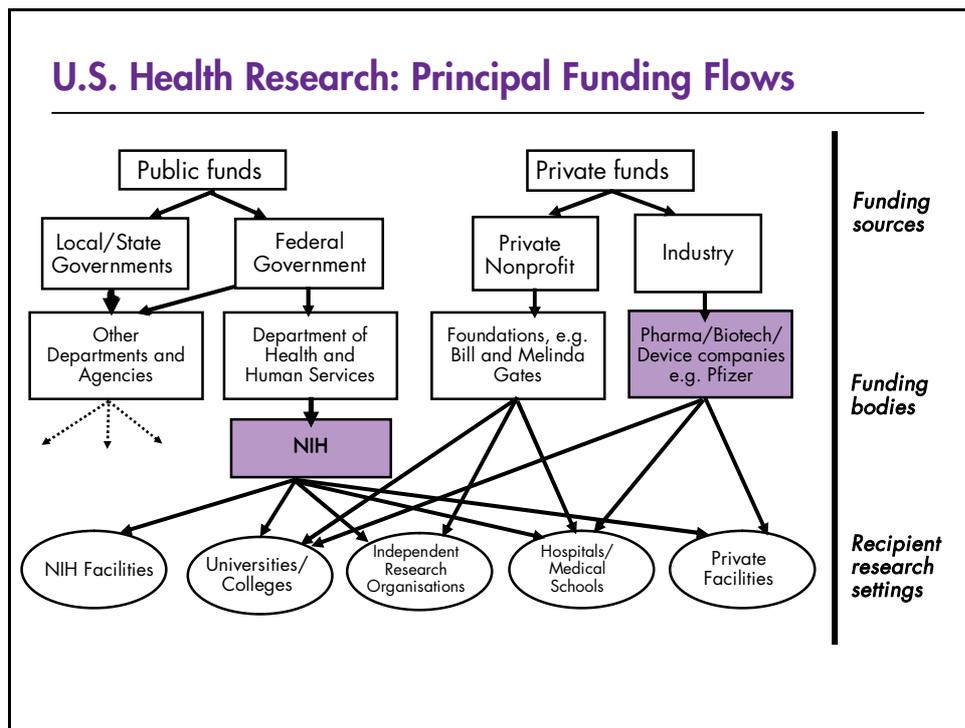
The concept of ‘key players’ therefore needs to be taken in a strictly relative, national, and financial sense. Within this context, however, contrasts in importance are stark. Industry is the undisputable leader, providing over half of overall funding, with an investment of \$54.1 billion (0.50% of GDP) in 2003 and \$61.1 billion (0.49% of GDP) in 2005. The next biggest funder is the NIH, with a budget of \$26.4 billion (0.24% of GDP) in 2003 and \$28.6 billion (0.23% of GDP) in 2005 (Moses, Dorsey, et al., 2005; Connelly and Propst, 2006).

Industry’s share of overall funding remained relatively constant at 56 percent to 61 percent between 1994 and 2003. However, there were notable differences in growth rates between

the three subsectors, with medical devices (264 percent) far outstripping pharmaceuticals (89 percent) and biotechnology (98 percent) (Moses, Dorsey, et al., 2005).³

Following the 1999–2003 growth period in the public and private sectors, during which the NIH budget doubled, spending in both sectors slowed down. The year 2005 saw an overall increase of health-related research funding of 2.2 percent, which fell below Biomedical Research and Development Price Index of 5.5 percent (Connelly and Propst, 2006).

³ BIO, “Biotechnology Industry Facts,” <http://www.bio.org/speeches/pubs/er/statistics.asp> (as of March 29, 2007).



Funding for biomedical research in the United States originates from public and private sources. Public funding, which is ultimately provided by the taxpayer, can be divided into federal and state funds. Private funding is provided by individuals, either as legacies, donations to not-for-profit organisations, or investment in commercial companies.

In the public sector, funds for biomedical research are distributed by local, state, and federal authorities to a range of departments and agencies. However, the most important funding flow is that from the federal government to the NIH.

Federal investment in health-related research is determined by the priorities of the federal R&D strategy, as well as the budget. The President prepares the budget assisted by the White House Office of Management and Budget, which receives budget requests from candidate recipients, such as the NIH. The budget is then submitted to Congress, both houses of which operate specialised committees on science and on appropriations (i.e. dedication of funds to a specific purpose). In designing the federal R&D strategy, the President is advised by his own Office of Science and Technology, leading figures from academia and industry serving on the President’s Committee of Advisors and Technology, and the heads of relevant agencies, which constitute the National Science and Technology Council (Organisation of Economic Co-operation and Development, 2005).

The agreed appropriations are channelled through the major federal departments engaged in R&D. Funds for the NIH are initially received by the DHHS. The NIH in turn allocates support to various intramural and extramural recipients in accordance with scientific merit and strategic priorities.

There is great variation in models for giving privately to biomedical research without expectation of a financial return, ranging from small donations to disease-focused charities

to substantial support to existing foundations or the creation of a new foundation, for example in the context of a legacy. Typically, such foundations invest the proceeds of their capital according to priorities set by their governing boards. Most often, the recipients are external research settings, such as universities. However, some foundations, such as the Howard Hughes Medical Institute, operate their own facilities.⁴

Private funds invested for financial gain go to businesses of varying size and maturity depending on the funds and willingness to take risk of the investor. Channels for investment include private equity, publicly listed shares, and venture capital funds. Businesses may operate their own private research facilities, but are not cut off from the rest of the active biomedical research sector. Depending on their own resources and requirements, they invest in researchers in public settings (e.g. Ph.D. students in academia). Conversely, they also receive public funds (e.g. NIH support for work on 'orphan' areas in which the company has expertise), but no commercial incentives for investigation.

⁴ The Foundation Center, "Foundations and Their Role in Philanthropy," [free online training resource], http://foundationcenter.org/getstarted/training/online/free_ftrip_detail.jhtml (as of March 19, 2007).

Industry: Mission

Investment in and conduct of health research by industry is driven by the aims of:

- Generating profits; and, within this framework,
- Improving health outcomes

‘Industry’ is an umbrella term for a highly diverse group of for-profit organisations. As such, industry cannot speak with one voice. However, trade associations and advocacy bodies provide an approximation to that voice. In biomedical research, the key bodies are the Pharmaceutical Research and Manufacturers of America (PhRMA), the Biotechnology Industry Organization (BIO), and the Medical Device Manufacturers’ Association.

To sustain their activities, grow, and satisfy their investors, businesses need to make a profit. Companies engaging in biomedical R&D are no exception to this rule, although making money from health care is often regarded as more controversial than other industry activities.

In their mission statements, the above-mentioned representative bodies strongly emphasise their research effort, dedicated staff, and key contribution to advances in treatments. For example, BIO proposes to “expand the boundaries of science to benefit mankind by providing better healthcare” and PhRMA defines its mission as “helping people live longer, healthier lives around the world” (PhRMA, 2006).⁵

The U.S. industry’s investment in biomedical research is of great significance indeed, and improved health outcomes are doubtlessly motivating for industry researchers. However, as the choice of areas of investigation is inseparable from financial considerations, research efforts are not in proportion to the actual burden of specific conditions. For example, anti-obesity drugs have commanded significantly more attention than anti-malaria drugs.

⁵ BIO, <http://www.bio.org> (as of March 29, 2007); and PhRMA, <http://www.phrma.org> (as of March 29, 2007).

Industry: Governance

Governance structures vary depending on the nature, size, and history of individual companies, with the principal models of:

- Public companies
- Privately owned companies

Strategic decisions are made by the Company Board

- Executive directors representing the management
- Non-executive directors representing investors' interests

As has already been emphasised, 'industry' as a key player in R&D comprises a diverse group of organisations, ranging from pharmaceutical companies over a century old to last week's biotechnology start ups. These organisations work with budgets and workforces of very different sizes. However, these companies share basic governance structures as either public or privately owned companies.

The equity of privately owned companies is typically owned by a small number of investors and cannot be easily bought and sold. These investors are deemed to be financially informed and consequently the regulations governing private companies are less stringent than those of publicly owned companies. Public companies have a wide shareholder base and shares can be freely traded; hence tighter regulations are required to ensure fair and equal access to information that could affect the value of the company. For example, public companies must report financial results every three months, which is not required of private companies.

Both types of companies are governed by a board that is responsible for all strategic decisions, as well as oversight of the internal running of the business. In many large companies, board members form committees dedicated to specific purposes, such as audits or corporate governance. The members are chosen to represent the interests of the management and investors. In publicly funded companies, there is often a clearly defined split between the executive directors, who are responsible for the management of the firm, and non-executive directors who reflect the interests of the shareholders. This clarity in roles is often less well defined in private companies. For example, in publicly funded companies, there is an expectation that different individuals will perform the role of the chairman and chief executive, a situation less likely to occur in private companies.

NIH: Mission



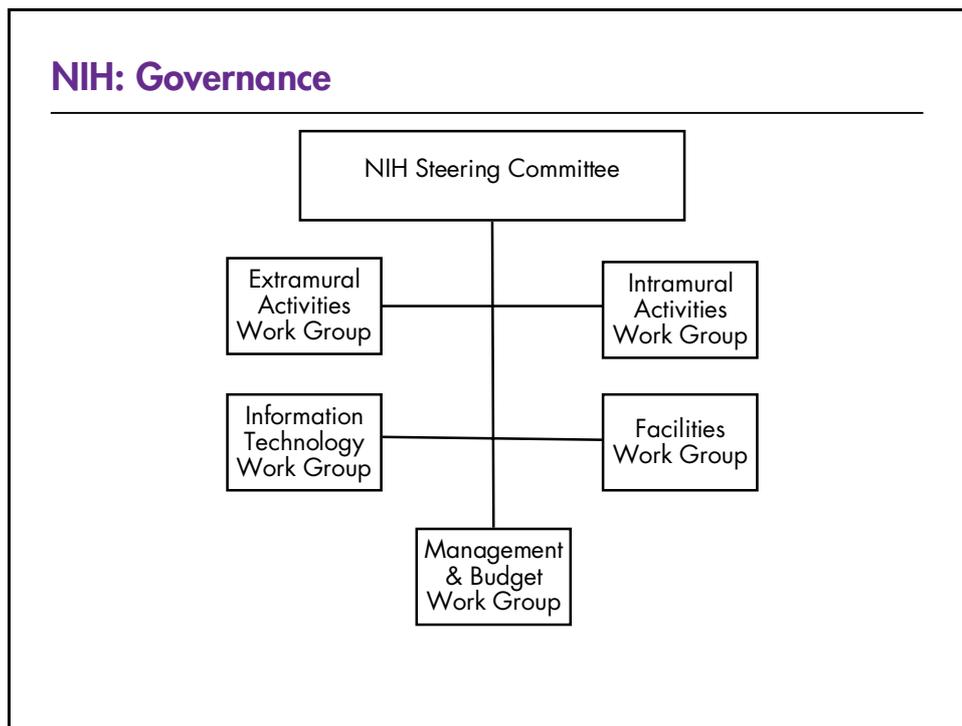
Source: NIH

Science in pursuit of fundamental knowledge about the nature and behavior of living systems and the application of that knowledge to extend healthy life and reduce the burdens of illness and disability.

The NIH is heir to a tradition of publicly funded health research in the United States that goes back to the late 19th century, when a laboratory was set up at the Marine Service Hospital, a precursor of the U.S. Public Health Service. Focused from the start on benefiting public health, researchers at this and subsequent facilities worked to combat major infectious and contagious diseases, such as cholera.

Today, the NIH is dedicated to basic and applied research across a broad range of health-related fields, within intramural and extramural facilities, with its own institutes and centres specialising in specific diseases (e.g. National Cancer Institute), organs (e.g. National Eye Institute), population groups (National Institute of Child Health and Human Development), and several other categories. At the same time, the organisation pursues the application and dissemination of its discoveries—“translating new knowledge into tangible benefits for the American people”, as recently summarised by the organisation’s current director, Elias A. Zerhouni.

To demonstrate its success in delivering its mission, NIH quotes the example of its research into coronary heart disease as having helped to prevent about 1 million early deaths per year, producing an economic return of \$2.6 trillion at an average investment of \$3.70 per American per year (Zerhouni, 2007).



Given the NIH's role as an investor of over \$28 billion (0.23% of GDP) into a plethora of intramural and extramural research activities every year, the running of the NIH presents a complex challenge. Key agents of central leadership are the NIH Steering Committee, and the Office of the Director.

The NIH Steering Committee serves to ensure that the organisation is working to fulfil its mission by addressing corporate concerns other than the setting of scientific priorities. In doing so, it is supported by several permanent groups, as well as ad-hoc groups established as required. For example, the (permanent) Extramural Activities Work Group considers all issues pertaining to extramural research and training; it also oversees peer review at the NIH and recommends budget allocations for the Center for Scientific Review.

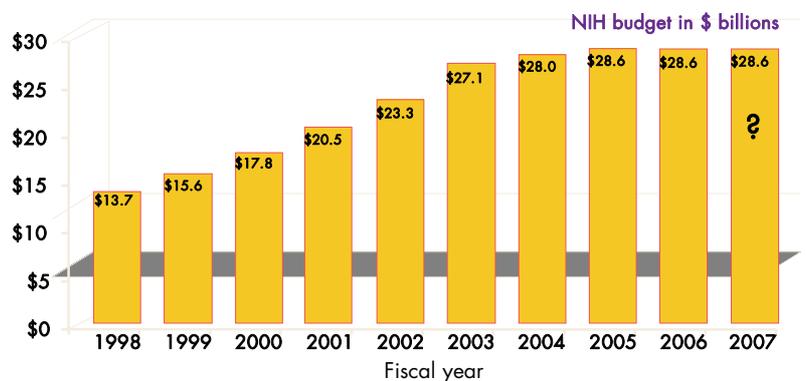
The NIH Director provides leadership to individual Institutes and Centers, as well as across the organisation. In doing so, he is supported by his own immediate office as well as a range of specialised staff offices and program offices. He is also advised by external advisory groups staffed by experts and members of the public, and the federal government through the DHHS and Congress. The director in turn advises the President on his annual NIH budget request to Congress.⁶

⁶ DHHS, NIH, "Role of the NIH Director," <http://www.nih.gov/about/leadership.htm#role> (as of March 19, 2007).

Processes and Performance of the U.S. Health Research System

Context of the Health Research System

- United States takes pride in being the 'biomedical research engine of the world'.
- Biomedical research is backed by both leading political parties.
- Funding for NIH doubled between 1998 and 2003, but subsequently slowed down due to competing demands, such as Homeland Security and disaster relief after hurricane Katrina.



The United States plays in a league of its own in terms of the funds available for health research and the volume of research activities. In the decade leading up to 2003, total investment in biomedical research almost doubled to \$94.3 billion (0.86% of GDP), outstripping growth in other research-intensive countries, none of which could equal the 5.6 percent of total U.S. health spending dedicated to biomedical research in 2003. In the same year, 70 percent of the global drug development pipeline belonged to companies headquartered in the United States (Moses, Dorsey, et al., 2005).

From 1999, buoyed by all-party and patient-advocacy-group support for research into emerging health issues, and funds from private and public sources, academic research institutions poured an unparalleled amount of resources into new research facilities and the training of scientists. It is estimated that whereas \$3.2 billion went to infrastructure from 1990 to 1997, investment rose to \$15 billion between 1998 and 2007 (Zerhouni, 2006a; Koizumi, 2006). In the words of the NIH Director, Elias Zerhouni, the resulting blossoming of investigation and young talent is "just what the nation wants and needs" (Zerhouni, 2006a).

However, there is widespread concern that the momentum gathered will be lost due to current funding shortages. At the NIH, the previous 'fat year' budgets were committed to projects due to run for several years, leaving little room for manoeuvre when, after 2003, NIH budget growth dropped below biomedical research inflation due to competing

national demands, such as hurricane Katrina and Homeland Security. The NIH is therefore finding it difficult to support the further careers of all the promising scientists that emerged from the previous surge in infrastructure investment. Similar trends in funding can be observed in industrial and philanthropic research funding, which have been suggested to receive important stimuli from NIH investment. It is estimated that as a result, the portion each of 'health dollar' invested in research has decreased from 5.8 cents in 2004 to 5.5 cents in 2005 (Connelly and Propst, 2006; Cohen, Nelson, and Walsh, 2002).

Industry: Priorities

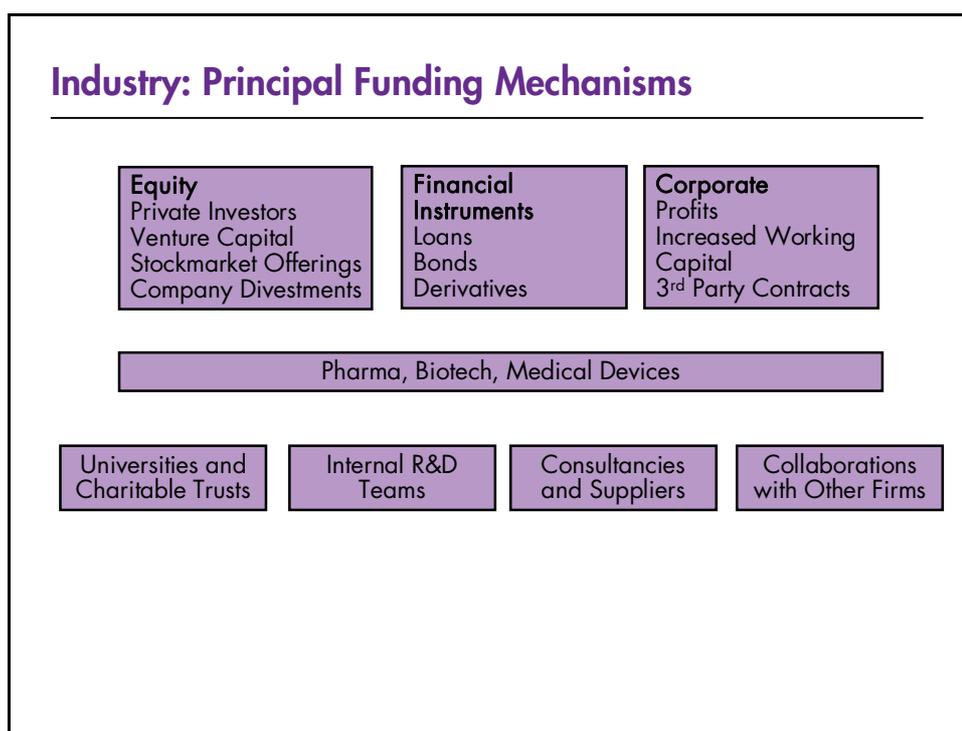
Investment is driven by the aims of:

- Maximising profits and sales
- Receiving a rate of return commensurate with business model
- Focusing on key therapeutic areas
- Finding differentiated medical outcomes
- Maintaining a well-stocked product pipeline
- Maximising patent lifetimes

As outlined earlier, industry research activities are driven by the key objective of generating an attractive financial return. Optimisation of profits and sales is therefore a top priority. This priority is often coupled with the expectation of a minimum margin for products, prompting established pharmaceutical manufacturers to divest themselves of lower-growth, lower-rate-of-return products. Recently, this dynamic was exemplified by Roche's sale of its over-the-counter drugs to Bayer, or Abbot Pharmaceutical's sale of its diagnostic instrument business to General Electric. Optimisation strategies common to all industry sectors include geographical expansion, increases in prices or volume, heightened productivity, as well as mergers and acquisitions.

In tandem with these financial considerations, companies also focus on specific therapeutic areas. For example, Pfizer recently re-organised its R&D groups around nine broad therapeutic areas, such as oncology, infectious diseases, and pain. At the same time, the company emphasises its comprehensive portfolio of medicines under development, highlighting the priority of ensuring future growth through a pipeline of products that will deliver effective improvements on existing drugs (Pfizer, 2006).

Pharmaceutical, biotechnology, and medical device companies all pursue the priority of maximising the lifetime of the patents they own. Such maximisation is achieved by bringing a product to market as quickly as possible after filing the patent, or modifying the product to file a new patent.

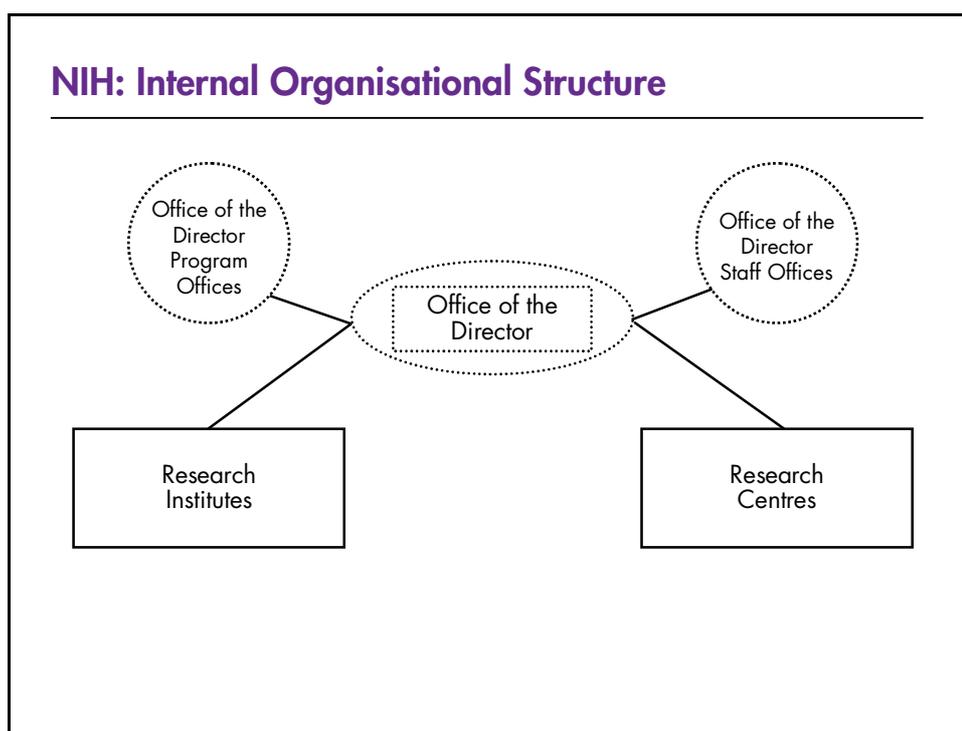


It is estimated that it costs an average of \$800 million and takes 90 months to bring a drug from Phase I (testing the safety of the drug in a small group of people) to market. Over half of this figure is the cost of capital needed to finance the R&D over this period. Only 21 percent of drugs that begin human testing are finally approved. However, the returns of successful products can be very high, with some 'blockbuster' drugs earning their developers \$100 million or more per month of exclusivity (DiMasi, Hansen, and Giabowski, 2003).

Multinational pharmaceutical companies are able to fund development costs through existing drug sales, managing their cash flow, or raising money in the equity or capital markets. They may also divest non-core businesses to fund further development, or to provide capital for their own acquisitions. Start-up companies raise funds through venture capital, public offerings on a stock exchange, or entering into collaborative arrangements with larger companies.

The funds raised from these diverse sources then support planned R&D activities. Depending on factors such as size and infrastructure of the company, in-house capacity, and nature of the investigations, these activities can take place within different institutional settings. Large companies like AstraZeneca have traditionally had their own laboratories and scientific staff, allowing maximum control over ownership, confidentiality, and planning. However, rather than carrying out the complete R&D cycle in-house, it is becoming increasingly common for large pharmaceutical companies to license compounds researched by biotechnology firms, and to subcontract clinical trials (Barton, Emanuel, 2005).

In the highly specialised, high value environment of biomedical R&D, all players may also seek out expertise available from scientists in academia, consultancies, and independent research institutes, as well as outsourcing certain aspects of development to specialised suppliers.



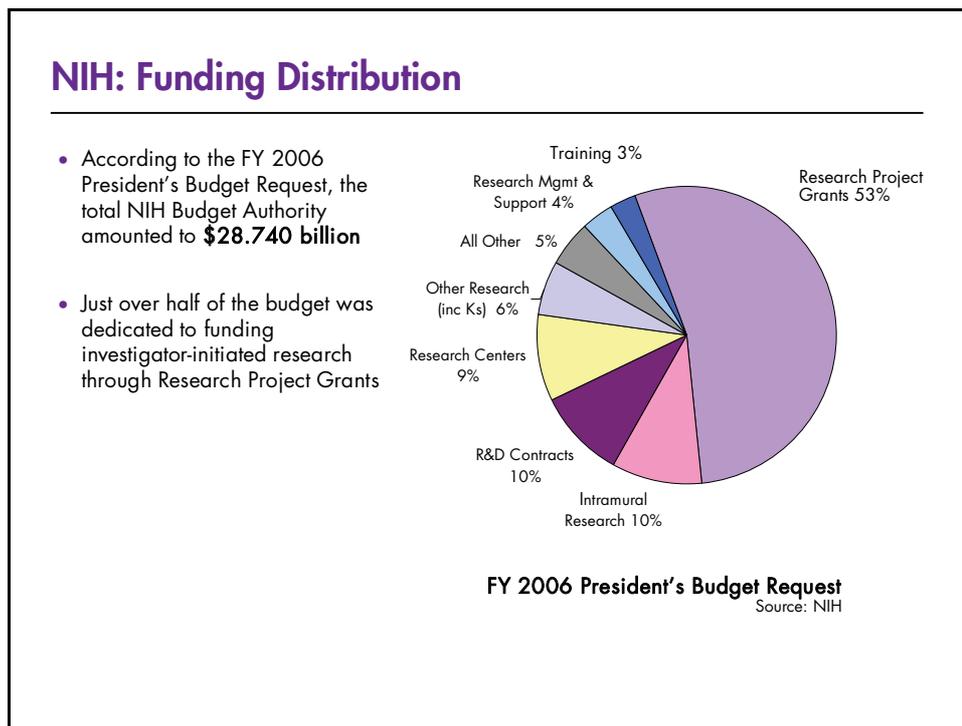
The Office of the Director of the NIH oversees the running of all parts of the organisation, both in scientific and in administrative terms. At its core, the Immediate Office of the Director provides a focal point for the policy development, coordination, and planning necessitated by NIH's large and diverse portfolio of activities. As already described in the outline of the NIH governance structure, in his leadership role, the director liaises with the heads of the individual institutes, as well as with external advisors and the U.S. government.

The size and complexity of the organisation and related administrative and strategic tasks requires a specialised support structure, which is provided by the program offices and staff offices that report to the director. Program offices serve as focal points for cross-NIH research activities relevant to a wider theme. For example, the Office of Behavioral and Social Science Research seeks to "stimulate behavioral and social science research throughout NIH and to integrate these areas of research more fully into others of the NIH health research enterprise".⁷ Staff offices concern themselves with overarching planning, policy, and personnel issues. For example, they include the offices of Extramural and of Intramural Research, as well as the Office of Portfolio Analysis and Strategic Analysis, and the NIH Ethics Office.

Intramural Research is organised in the NIH's 27 Institutes and Centers, each of which was created by the U.S. Congress. Most of these are located on the NIH campus in Bethesda, Maryland, and the surrounding areas. Institutes and Centers focus on subject

⁷ Office of Behavioral and Social Science Research, NIH, <http://obssr.od.nih.gov/content> (as of March 29, 2007).

areas such as organs, diseases, or developmental stages, but also include cross-cutting resource institutions like the National Library of Medicine. Institutes and Centers are headed by directors who report to the NIH Director.



The NIH supports more than 212,000 scientists at over 2,800 research universities, medical schools, teaching hospitals, independent research institutions, and businesses throughout the United States and abroad (Ad Hoc Group for Medical Research Funding, 2005).⁸ The principal recipients of its budget, which stood at \$28.6 billion (0.23% of GDP) in 2006, are extramural researchers, who claim 85 percent of resources. Of the remaining funds, 10 percent are distributed to intramural researchers, and 5 percent go to internal facilities, management, and administration (Koizumi, 2006).

Extramural research funding is principally awarded through Research Project Grants to individual researchers in open competition. Individual funding decisions are made on the basis of peer review of the grant applications submitted. Due to a surge in applications following an increase in research capacity on the one hand, and limited resources for new projects on the other hand, the average success rate for applications now stands at less than one in five, down from one in three at the turn of the millennium (Zerhouni, 2006a; Koizumi, 2006).

The distribution of the resources available changes with national priorities, which in turn depend on recent events and experiences. For example, the share of funding allocated to R&D contracts to purchase equipment and services from external organisations doubled to \$2.8 billion between fiscal years 2001 and 2004, as anthrax attacks and fear of terrorist acts made biodefence a top NIH priority. Further growth in investment is expected due to contracts for genetic research. Similarly, the relative importance of support for

⁸ NIH, "About NIH," <http://www.nih.gov/about/> (as of March 28, 2007).

interdisciplinary research through Research Center Grants, which currently command 10 percent of the budget, has grown over the past decade (Koizumi, 2006).

NIH: Principal Types of Grants Awarded

- **Research Project Grants** and multi-project **Program Project Grants** for investigator-initiated research, awarded across all types of organisations on behalf of the investigator.
- **Research Center Grants** to support long-term multidisciplinary research at extramural research institutions.
- **Other Research Grants** including support career development, specialised education, cooperative clinical research, and infrastructure.
- **National Research Service Awards** to institutions and individuals to develop research capacity, especially in areas of national need.
- **Research and Development Contracts** with non-profit and commercial organisations to further insights into the research area of the awarding Institute or Center.

With a share of over half of the total NIH budget, project grants represent the organisation's most important funding vehicle across the whole gamut of basic and applied research. Sought by and focused on individual researchers, but formally awarded to the investigator's institution, they represent a potential source of funding for all public and private research settings. Awards are made on the basis of peer review, either in open competition or in the context of a multifaceted programme aimed at a common theme, such as 'age-related changes in tissue function: underlying biological mechanisms'. In addition, NIH offers a range of specialised project-focused awards, such as Small Grants for short-term and pilot projects.

Research Center Grants help extramural institutions to carry out long-term and multi-disciplinary programs of research, support the development of research resources, and encourage the development of products, techniques, processes, methods, and practices. There are five types of centre: Specialized Comprehensive Centers, devoted to the basic to clinical investigation of a specific medical problem; General Clinical Research Centers, where new insights can be rapidly transferred to the bedside; Biotechnology Research Centers, enabling NIH investigators to make joint use of instrumentation and technology inaccessible in conventional settings; Comparative Medicine Centers, which provide resources for research with animal models; and Research Centers in Minority Institutions, which serve to boost the competitiveness of predominantly minority academic research settings.

Other Research Grants provide support for various causes including capacity building, and infrastructure development, such as Research Career Programs (K Awards) to facilitate outstanding young investigators' transition to senior positions, and the Cancer Education Program.

Ruth L. Kirschstein National Research Service Awards form part of NIH's efforts to replenish and develop the national workforce in health research, especially in areas of identified national need. Funds are provided for stipends, training programmes, travel, and fees.

R&D Contracts allow Institutes and Centers to tap into expertise and technology available from external, non-profit organisations to further their own investigations. Contracts are awarded through a Request for Proposals or a sealed Invitation for Bids outlining the awarding body's specific requirements (Ad Hoc Group for Medical Research Funding, 2005). Under the Small Business Innovation Research programme, the NIH, like other federal agencies, is required to set aside 2.5 percent of its extramural budget to enable U.S. small businesses to engage in research or R&D with potential for commercialisation.⁹

⁹ Public Law 97-219, Small Business Innovation Development Act of 1982; Public Law 102-564, Small Business Research and Development Enhancement Act; Public Law 106-554, Small Business Reauthorization Act of 2000.

NIH: Priorities – The NIH Roadmap for Medical Research

- Framework of cross-NIH initiatives to meet demands on 21st century health research, developed by NIH leaders and stakeholders
- Three broad portfolio themes
 - New Pathways to Discovery
 - Research Teams of the Future
 - Re-engineering the Clinical Research Enterprise
- FY 2006 budget of \$329 million (1.2% of the total NIH budget)

The NIH Roadmap for Medical Research defines overarching goals and priorities for the organisation as a whole, with the aim of ensuring optimum quality and relevance of its work in the 21st century. It has been described as a framework, but also a vision, for an institution able to produce a maximum of tangible health benefits by choosing wisely amongst a wealth of research opportunities, and pursuing this research effectively and efficiently (Zerhouni, 2006b).

Drawn up in 2002/2003 with input by leading figures from academia, industry, government, health-care providers, and the public, the Roadmap identifies three broad themes for boosting “the resources and technologies needed for 21st century biomedical science”:

- New Pathways to Discovery supports research into biological systems and the development of biomedical tools to advance the scientific community’s understanding of the molecular processes underlying disease.
- Research Teams of the Future stimulates the creativity and collaboration by supporting interdisciplinary work, high-risk projects, and public–private partnerships.
- Re-engineering the Clinical Research Enterprise encompasses initiatives to enhance clinical research, for example by harmonising regulations, and developing new diagnostic tools, and establishing new centres for academic clinical research.

Funds for Roadmap-related projects are contributed by all parts of the NIH as a “collective venture space of resources for shared needs”. In the fiscal year 2006, these resources amounted to \$329 million, or 1.2 percent of the total NIH budget (NIH, 2006; Koizumi,

2006). The Roadmap is managed by the Office of Portfolio Analysis and Strategic Initiatives, which is also in charge of co-ordinating other innovative trans-NIH initiatives.

NIH: Minority Research

- National Center on Minority Health and Health Disparities
- Trans-NIH initiatives
- Institute-specific funding programmes
 - Research into disease among health disparity populations
 - Infrastructure and faculty career development
 - Education and engagement of minority populations



Source: NIH

As part of its mission to improve the health of people in the United States, NIH needs to account both for the requirements and the contributions of ethnic minorities. Members of these minorities suffer from a profound disparity in health status compared to the population as a whole; and within biomedical science, certain communities—African Americans, Hispanics, Native Americans, Alaskan natives, Native Hawaiians, and Pacific Islanders—are underrepresented.

The NIH has devised a range of structures and initiatives to respond to this situation. A dedicated Office of Research on Minority Health was established in 1990, followed by the creation of a National Center on Minority Health and Health Disparities ten years later. Over this period, research programmes run by the Office examined common conditions as well as specific interventions in minority populations (e.g. in the areas chronic kidney disease and infant mortality). At the same time, the Office reviewed and promoted research training programmes for minority researchers across NIH. The promotion of an integrated research agenda and capacity building remain key objectives of the National Center on Minority Health and Health Disparities.¹⁰

Within other Institutes and Centers, research on and by minorities is coordinated through dedicated teams and programmes. In particular, the Division of Minority Opportunities in Research at the National Institute of the General Medical Sciences administers various funds for different stages of career development for minority scientists across the NIH; and the National Center for Research Resources operates a Research Centers in Minority

¹⁰ National Center on Minority Health and Health Disparities, “What We Do,” http://ncmhd.nih.gov/about_ncmhd/what.asp (as of March 30, 2007).

Institutions Program to develop research capacity and infrastructure that colleges and universities offering doctorates in health sciences.¹¹ Several other Institutes also offer their own programmes. Most of these are aimed at investigators, but also support public education and engagement activities.¹²

¹¹ National Center for Research Resources, NIH, "Research Infrastructure," http://www.ncrr.nih.gov/resinfra/ri_rcmi.asp (as of March 30, 2007).

¹² Office of Extramural Research, NIH, "NIH Initiatives for Underrepresented Minority Investigators," <http://grants2.nih.gov/grants/policy/emprograms/overview/minority.htm> (as of March 30, 2007).

NIH: Additional Activities

- The Evaluation Branch conducts in-house evaluations, advises on evaluation proposals and funding, develops a database of all past evaluations and best practices, tracks outcomes, and scrutinises NIH initiatives.
- Several Institutes jointly operate a funding programme on the Dissemination and Implementation Research in Health
- The Peer Review Advisory Council, established in 2005, advises the NIH Directorate on all procedures and policies related to the process of peer review.
- The NIH also directly works to educate the public on health issues, e.g. via comprehensive information on its Web site.

In line with its remit to invest federal resources to improve health outcomes for the nation, the NIH engages in a range of activities to improve its internal processes and help the public to benefit from its research.

The NIH Evaluation Branch tracks the outcomes of NIH initiatives through in-house evaluations, and advises on evaluation proposals and funding. All past evaluations and insights into best practice are being captured in a database. Staff at the Evaluation Branch liaise with evaluators throughout the NIH, as well as within the DHHS.¹³

As the allocation of NIH resources pivots on the assessment of grant applications by extramural experts, the process and quality of peer review is of great importance to the organisation. The Peer Review Advisory Council, established in 2005, advises the NIH Directorate on all procedures and policies related to the process and evaluation of peer reviews at the NIH Center for Scientific Review as well as the NIH Institutes and Centers.¹⁴

To ensure that scientific discovery leads to tangible benefits for patients, the NIH facilitates translation, dissemination, and diffusion. Some funding is earmarked for research into the relevant mechanisms, with several Institutes jointly operating a Dissemination and Implementation Research in Health grants programme (DHHS, 2006). The organisation also directly works to educate the public on health issues. The

¹³ Office of Portfolio Analysis and Strategic Initiatives, NIH (2007), "Evaluation Branch: About the Evaluation Branch," <http://opasi.nih.gov/desa/eb/about.asp> (as of March 28, 2007).

¹⁴ Office of Extramural Research, NIH (2007), "Peer Review Advisory Committee (PRAC)," <http://grants2.nih.gov/grants/peer/prac/index.htm> (as of March 28, 2007).

NIH Web site offers advice on a healthy lifestyle as well as information on a comprehensive range of conditions and related research. Members of the public can also access information via condition-specific information lines.

NIH: Handling of Indirect Costs

- NIH provides funds in accordance with the indirect cost rate negotiated with each individual organisation.
- Indirect Cost Rate Agreements with commercial organisations are negotiated annually on the basis of Indirect Cost Rate Proposals.
- Indirect Cost Rate Agreements with public and non-profit organisations are negotiated by the DHHS.

As in other countries, research in the United States is associated with direct costs, such as researchers' salaries and materials, and indirect costs, such as fringe benefits for employees, facility depreciation, and general administration. The NIH recognises that grantees require both types of costs to be covered, but also expects other interested parties, such as the government or industry, to pay their 'fair share' of indirect costs (Bishop, 2006).

However, the NIH operates no universal formula on how such costs should be distributed. Rather, various factors, such as size and location, determine the indirect cost rate used with any given partner. Indirect cost rates reflect the ratio between the total of indirect costs and an equitable direct cost base, and are negotiated through individual Indirect Cost Rate Agreements on the basis of the partner organisation's fiscal year.¹⁵

Commercial organisations that intend to conduct research with NIH funding are required to submit an Indirect Cost Rate Proposal to the Indirect Cost Branch of NIH's Division of Financial Advisory Services. By contrast, indirect cost rates for universities, hospitals, non-profit organisations, and local governments are negotiated by the Division of Cost Allocation of the DHHS.

¹⁵ Office of Acquisitions Management and Policy, NIH, "Frequently Asked Questions: Indirect Costs," <http://ocm.od.nih.gov/dfas/faqIndirectCosts.asp> (as of March 30, 2007).

Outlook

Outlook: Supply of Research Capacity

- U.S. research institutions attract gifted investigators from around the world.
- There is a better than ever supply of young researchers in biomedicine.

However...

- Research capacity is biased towards the coastlines and lakes area, leaving a central 'biomedical gap' where young researchers find it difficult to fund their research
- It is increasingly difficult for junior investigators to obtain research funding and develop their careers.
- U.S. regulations in controversial areas, such as stem-cell research, may result in a brain drain to more supportive countries.
- Involved and 'unfriendly' visa granting processes may affect future recruitment of international researchers.

As a country with a history of vigorous financial and political support for research and development, as well as being home to elite academic institutions and leading biomedical businesses, the United States has been a magnet for talented researchers worldwide. Currently, more than half of U.S. postdoctorate researchers are from abroad (Weissmann, 2006). Increased funding around the turn of the millennium has enabled U.S. institutions to train an unparalleled number of young scientists for a career in research. Nevertheless, the outlook for U.S. research capacity is not universally considered as idyllic.

The geographical distribution of scientific activity is heavily biased towards the coastlines and lakes area, leaving a central 'biomedical gap' where scientific capacity is low and young scientists find it particularly difficult to fund their research (Mervis, 2001).

More critically, looking at the nationwide picture, the slowdown of public and private investment into biomedical research in recent years has led to a mismatch between the emerging scientific workforce and resources to allow this group to develop their careers and investigations. The NIH's new Pathway to Independence programme and career support by individual Institutes and Centers aim to provide some relief to talented junior scientists affected by this crisis. However, many others face an uncertain future (Zerhouni, 2006a; Mervis, 2006).

There is also concern that politics may affect the country's appeal as a place to conduct research. Restrictions on cutting-edge research deemed unethical, such as work with stem cells, have already encouraged some scientists to seek out more permissive settings abroad,

and others may follow (Watt, 2006). Similarly, international scientists could be put off relocating to U.S. institutions by invasive or hostile treatment by the U.S. immigration authorities in the post-9/11 climate (Brumfiel, 2003; Teich, White, 2006).

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