Chapter 6

Organization of Projects

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"Organization is a means to an end rather than an end in itself. Such structure is a prerequisite to organizational health; but it is not health itself. The test of a health business is not the beauty, clarity, or perfection of its organization structure. **It is the performance of people. "**

Peter Drucker,
Management: Tasks, Responsibilities, Practices
(New York: Harper & Row, ***1974),*** p. 602.

ADMINISTRATIVE STRUCTURES

Chapter 5 presented the history, current involvement, and future plans of the many government and nongovernment parties interested in genome research. This chapter assumes the continued interest and participation of the current actors, and it discusses the options for organizing those actors at the Federal level.

A properly designed administrative or organizational structure for genome projects is important. As form so perfectly matches function in DNA, so the organizational form of the project should match its function and goals. These include rapid accumulation of knowledge about the genome, efficient storage and distribution of that information, and conversion of this knowledge into productive theories, tools, reference materials, and medicines. The political consequences of a poorly administered group of projects are not only failure to achieve potential intellectual and economic contributions, but also negative impacts on the organization and funding of other scientific investigations. A genome project blueprint cannot be drawn without taking into consideration the abutting structures as well as the internal constraints.

Three major funding agencies must be included in any consideration of organizational design: the National Institutes of Health (NIH), the Department of Energy (DOE), and the National Science Foundation (NSF). Nongovernmental bodies such as the National Academy of Sciences (NAS) and the Howard Hughes Medical Institute (HHMI) are already participating in organizational and advisory roles, and commercial firms anxious for sequencing technology and data seek input as well.

There are at least five possible administrative structures a human genome project could develop:

- ***One agency—a*** project performed exclusively by one of the expert agencies.
- ***Single-agency*** leadership—a project in which Congress would designate one agency to coordinate and oversee the research.
- Interagenccv ***agreement and consultation—a*** cooperative project among the agencies in which no additional authority structure would be created.
- ***Interagency task force—a*** project in which a committee with the authority to direct research planning among the agencies would be chartered.
- ***Consortium-a*** project in which the private sector as well as the Federal Government would plan research, with possible cofund - ing from the corporate partners.

The first alternative, a project organized and executed solely by one agency, may be dismissed as unnecessary and politically unworkable. A single-agency project could only result from cutting out others, and several agencies have already made substantial investments in genome research and related technologies. Further, the current genome infrastructure, including GenBank" and DNA clone repositories, is already interagency.

The other four proposals have unique strengths and weaknesses. For any of them to be successful, however, the administrative structure must at least organize communications at the scientific, interagency, and international levels. At most, it should be capable of planning a research program

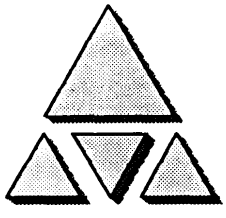
involving many partners and funding them accordingly. Congressional decisions on the organizational structure can be based on perceptions of the necessary patterns of authority, of quality and scope of experience in research and development, and of fiscal and economic priorities.

Single-Agency Leadership

One possible beginning for genome projects would be the designation by Congress of a lead agency to coordinate ongoing activities in various agencies (see figure 6-l). This option was the one favored by a majority of those on the National Research Council committee that issued a report on mapping and sequencing the human genome (18). The strengths of this organizational option derive from its clear designation of authority. Such leadership can be dynamic, and research would follow the theme established by the lead agency. A lead agency, and thus a lead administrator, focuses the project in all its aspects: It provides a communications link among researchers, domestic and foreign; a contact for media; and a target of criticism and politicking. Drawbacks to designating a lead agency are the possibility of incomplete commitment by the lead agency and the potential inability of the lead agency to command the resources of other agencies effectively. Choosing this option would necessarily entail choosing which agency should lead,

Among NIH, DOE, and NSF–the three funding agencies—NIH and DOE are the most appropriate candidates to lead a genome project, NSF is an unlikely leader because its mandate excludes the investigation of human health and disease, the ultimate focus of the projects. Further, a large-scale operation conducted by NSF would inevitably detract from other research of which NSF may be the sole patron. Such a loss would occur in each of the funding agencies involved, but NSF may be most sensitive because it funds much less biology than NIH, and the research it supports is more basic as a rule than that supported by DOE or NIH (30). NSF can contribute to genome projects by stimulating interest in automation and robotics (which it has done), in animal models of human disease (by gathering animal and microorganism sequence data for comparison), and in instrumentation (through its biology centers).

Figure 6-1 .—Lead Agency



Choosing between NIH and DOE is troublesome because these agencies have complementary strengths and weaknesses. The project would have a different face with different leadership.

Because of its mandate to support investigations to improve the Nation's health, NIH dominates biomedical research. The institutes spent an estimated $313 million in 1987 for projects that involved mapping or sequencing, over $90 million of which funded projects to characterize the human genome (13,15). NIH has conducted, funded, and administered genetics research expertly for years, and the institutes would seem to be a natural home for genome projects. The theme of an NIH-led project would likely be a renewed commitment to the peer review system and to small, or cottage industry, science, with some added attention to the research infrastructure.

One great strength of NIH is its decentralized administration: Quality projects uninteresting to one institute may well be funded by another. This flexibility is achieved at a cost, however. Critics have scrutinized this process and concluded that, among other faults, it cannot support a large, directed project (28). NIH leadership can have difficulty imposing the priority decisions needed for a concerted effort. A distinction is often made between the operating styles of NIH and NASA (the National Aeronautics and Space Administration), with NASA having much greater central authority and NIH exemplifying a decentralized process for setting priorities. To manage some of the proposed genome projects, mechanisms beyond NIH's standard researcher-riginated format may be required. This could "require a change in NIH's philosophical outlook and its approach)" according to George Cahill of HHMI (23).

NIH could conduct a directed research program, It has done so in the past for the study of particular diseases (e.g., polio and cancer) and is now doing so for AIDS. While NIH has not previously mounted a major project to develop a set of tools for biology (as mapping and sequencing projects are often characterized), it has the funding mechanisms and expertise necessary to do so. The mapping and sequencing projects have been described as a library of information awaiting translation, and NIH administers the National Library of Medicine (see ch. 5). To facilitate special genome projects, NIH has created new study sections to review grants that focus on methods; NIH could also convene a new scientific advisory body in an existing institute to direct a focused project, set aside funds for special projects in one or more institutes, and begin new centers or multidisciplinary programs analogous to existing ones. It already has a multi-institute coordinating body to develop special initiatives like those announced in May and October 1987 for analyzing complex genomes and for informatics in molecular biology. NIH is currently in the process of establishing a mechanism for obtaining outside advice.

The high capital needs in some areas, the diverse expertise (extending beyond biomedical research) needed on some research teams, and the standardized and repetitive work of mapping and sequencing may render small research groups unable or unwilling to do such work (8). Experience at the National Cancer Institute with the Special Virus Cancer Program has suggested that the standard grant mechanism is insufficient for such tasks as the production of standardized tools, the distribution of clinical materials, and the increased coordination of investigators (33). If the institutes were to assign high priority to genome projects, those projects could conflict with other major research efforts, for example research on AIDS. Some persons, among them Ruth Kirschstein, Director of the National Institute of General Medical Sciences, have questioned whether "it would be appropriate to have a specifically targeted program that would compete with all the extraordinarily important programs NIH funds" (23). The danger is that a targeted program would become an instead-of program rather than an in-addition. to program, as was the case with the Special Virus Cancer Program (33).

As a lead agency, DOE would endow the genome project with different characteristics of organization and expertise. DOE has long supported research on human mutations and DNA damage and repair through the Office of Health and Environmental Research. The mission of OHER is to understand the effects of radiation and other means of energy generation on human health and the environment. OHER views ignorance of the genome and the inability to sequence and analyze DNA rapidly as major limitations on its research. As NIH might emphasize the human disease aspects of genome research, DOE would emphasize the investigation of mutagenesis and other areas closely related to OHER's mission. Critics have characterized OHER's rationale as "clearly impractical" (17) and "forced and . . . disingenuous" (30). But because of OHER's interest in human genetic material, DOE already has established expertise in crucial technologies such as automated chromosome and cell sorting, and in the computer storage of genetic data. DOE believes that, through its national laboratory structure, it should develop methods and tools useful to the entire commu - nity of molecular biologists (27).

The strengths and weaknesses of DOE are largely complementary to those of NIH. DOE's strength is its familiarity with the administration of focused research programs, It manages many large facilities for research in physics and chemistry—such as accelerators for high-energy physics—and the scientists whom DOE funds in these areas are among the best in the world. DOE also maintains excellent computing resources. Yet DOE does not have the same stature within the community of molecular biologists that NIH does (11,16,24,30).

The national laboratories have long provided services to the community of molecular biologists that are not provided by other agencies. The national laboratories have pioneered many high-technology instruments useful in biology: zonal centrifuges, high-pressure liquid chromatography, fluorescence-activated cell sorters, and chromosome sorting. Teams at national laboratories have prepared sets of DNA clones from individual human chromosomes, and current mapping projects are logical extensions of this work. Even though the national laboratories are not renowned for

their expertise in molecular biology, some of the technology, analytical software, and new methods that need to be developed will not be in biological disciplines—they will involve engineering, physics, and mathematics, all areas of acknowledged national laboratory expertise.

DOE enjoys the reputation of being a proficient organizer of projects among government, university, and industry researchers. As an agency, it is experienced in managing large projects and disbursing large sums of money, extramurally to universities and research centers and intramurally to the national laboratories. Critics fear that, if DOE assumes leadership of genome projects, its bias toward central management will corrupt research and stifle the more traditional, perhaps more creative, cottage industry approach.

DOE's review process for genome projects would involve prospective and retrospective peer review. The degree of scrutiny is not likely to differ substantially from that at NIH. Funding through DOE would be less likely to sap other biomedical funds, but other biological research programs at DOE could suffer. Designating DOE as the lead agency would give the organizational lead to an agency that supports only a small fraction of related research and thus only a small fraction of the user community. Having DOE administratively lead all genome projects could prove unmanageable in the long term.

The controversy over which agency should lead —DOE or NIH—may be misguided. Each agency has a role to play, and discussion should focus instead on how to encourage cooperation and to ensure that the research program of one agency does not inhibit that of the other. One observer has asserted that a major directed program at NIH alone would soon be politically incorporated into the overall NIH budget and would thereafter displace untargeted research. The corollary is that "DOE could find the leadership excellence more easily than NIH could provide the budgetary insulation" (14). Nonetheless, NIH is the logical choice for lead agency if Congress chooses to designate one—its mission is most directly affected, and the scientific community now supported by NIH is by far the largest of the intended beneficiaries of genome projects. If NIH leads, then the expertise and multidisciplinary research already supported by NSF and DOE should be explicitly taken into account in future planning. Difficulties in designating a lead agency are discussed under options for action by Congress in chapter 1.

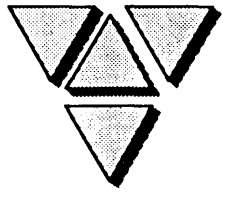
Interagency Agreement and Consultation

The lack of a lead agency implies no favored research strategy or funding mechanism, but a balanced program to take advantage of NIH, DOE, NSF, and other agencies' strengths. Agencies could be left to themselves to cooperate and communicate among themselves and with other interested organizations in the United States and abroad (see figure 6-2). A group of agency principals–agreed to by the agencies or under the Office of Science and Technology Policy—could meet to achieve these goals and exchange details of research directions and developments.

An interagency agreement and consultation framework eschews any formal creation of authority and relies on the good will of the participants to exchange information freely. Such an arrangement allows each agency autonomous, and presumably efficient, use of its resources and permits each agency to address those research topics most closely associated with its institutional interest. Interest may not always correspond to expertise, however, and it may conflict with or overlap other agencies' programs. This would act against one ostensible goal of the cooperative effort—to streamline projects by eliminating unnecessary duplication of research. An informal or ad hoc framework may also be inappropriate for very expensive, long-term projects because evolving and potentially diverging priorities may diminish rapport among the agencies.

A communications and consultation committee could be responsible for these cooperative, com-

Figure 6-2.—interagency Agreement and Consultation



munications, and streamlining functions, but the institutional focus would be scattered and the project would exist without clear leadership. Although in the best scenario such a committee would be completely abreast of all the domestic research, it might be too diffuse a body to support international organization of a project.

Decentralized authority is not without benefits, however, for pluralism of funding sources and flexible, decentralized organization are strengths of American science. Genome projects may be compelling enough to turn the organizational gears without creating a special bureaucracy for the task. A cooperative effort also permits a flexible mix of funding options, and each agency would retain control over its research planning.

The subcommittee on the human genome of the Biotechnology Working Group of the Domestic Policy Council acted as "a mechanism for exchanging information . . . [with] the right people at the right level," according to David Kingsbury of NSF (23). This coordinating group will now be located under a life sciences committee at the Office of Science and Technology Policy. Such a group of government administrators facilitates interagency communication but may not address other needs. A purely government body is open to the criticism that scientists and not government administrators must provide direction or at least participate directly in planning (31). This conflict is similar to that found in creating an advisory body, which generally reflects the question of how much influence scientists should have on the science policy process (discussed below).

The merit of informal agreement and consultation is that each agency would have the flexibility to follow its own research agenda. Agreement and consultation would not require legislation by Congress and would make interagency cooperation a matter of congressional oversight. A disadvantage is that flexibility maybe achieved at the cost of clear authority and accountability. Further, there might be no mechanism for resolving conflicts among agencies. The appropriateness of informal interagency cooperation turns on a judgment of which is more efficient—a directed and planned effort or a pluralistic and decentralized process.

Interagency Task Force

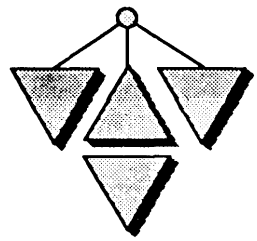
A genome initiative might require more active leadership than that described above. An interagency task force dedicated to pursuing the genome project and wielding some authority over funding and research might provide such leadership (see figure 6-3).

The task force could be constituted much like an interagency committee, with principals from the participating agencies; however, the task force would possess authority in certain areas, such as gathering of information from participating agencies, preparation of reports, formulation of recommendations, and interagency planning. It could design and direct a genome project, drawing on each of the participating organizations (see box 6-A).

A task force would be much like a lead agency in its ability to draw the attention of foreign researchers, the media, and domestic political interests. And like a lead agency, the task force would present a central character—its chairperson —who would act as spokesperson for the project. If the chairperson of the task force were selected from the agency representatives, however, the appointment would likely carry with it the same kind of political difficulties as selecting a lead agency.

Establishing a functional authority may require substantial political investment, but the cost of subsequent decisions is negligible because they can be immediate and final. With a committee authorized only to facilitate communication, a dilemma in the assignment of a particular research project, for example, could be costly in any number of ways, from the time it takes to reach a cooperative solution to the money required to duplicate the research should no equitable distribution

Figure 6-3.—interagency Task Force



Box 6-A.—Acid Precipitation Task Force

The Acid Precipitation Act of 1980 (Public Law 96-294), Title VII of the Energy Security Act, established a lo-year program to reduce or eliminate the sources of acid precipitation. To implement this program, Congress mandated the formation of the Acid Precipitation Task Force, composed of members from the national energy laboratories, the agencies, and four presidential appointees, and chaired jointly by representatives from the National Oceanic and Atmospheric Administration (NOAA), the U.S. Department of Agriculture (USDA), and the Environmental Protection Agency (EPA). The task force is thus a truly interagency body, drawing on a variety of agency expertise for leadership.

The legislative history describes the task force as being charged with preparing a comprehensive research plan, to include individual research, economic assessment, Federal coordination, international cooperation, and management requirements. The comprehensive plan is implemented and managed by the task force. The Acid Precipitation Task Force could thus serve as a model for an interagency task force dedicated to genome projects.

In 1985, representatives from the various agencies signed a memorandum of understanding that fixed the structure for administering the act. The memorandum assigns authority and responsibility to: 1) a Joint Chairs Council, consisting of principals from USDA, DOE, EPA, NOAA, the Department of the Interior, and the Council for Environmental Quality, and responsible for approving the annual research program and the corresponding portions of the budgets of the participating agencies; 2) the task force, to review the annual research program and budget and to provide advice and recommendations to the council; 3) the Director of Research (appointed by the Joint Chairs Council), to formulate the research program and budget; 4) the Interagency Scientific Committee and the Interagency Policy Committee, consisting of senior scientific and policy executives, respectively, from the agencies, to advise and recommend; 5) an External Scientific Review Panel; 6) 'the Office of the Director of Research, consisting of scientists and support staff; and 7) research task groups, each under the lead of a specific agency, to develop a research plan and budget for a particular task.

Shortly after the 1985 reorganization, the General Accounting Office reviewed the program at the request of Congress, because management changes and delays in reporting had become constant. The General Accounting Office's recommendations are more functional than structural, and they relate to the difficulty of issuing public reports under great scientific uncertainty. The almost intractable nature of some of the acid precipitation problems is apparently issue-specific and not related to the organization of the project.

The authority under the new organization is significantly vested in the Joint Chairs Council, the Director of Research, and divided between a scientific column and a policy column, The fine structure is fascinating: It attempts to permit each participanting agency to retain authority over its research expertise by creating research task groups. For example, Interior is responsible for monitoring deposition, NOAA for atmospheric processes, and DOE for emissions and control technology. In genome projects, distribution according to expertise would have NIH focus on mapping techniques and biological technologies, and DOE focus on automation and robotics and computation. This could be useful as long as it did not assign tasks to the wrong agency and did not inhibit flexible interagency planning for areas of legitimate overlap. The agencies participating in the Acid Precipitation Task Force are working on a scale similar in magnitude to that of a genome project; from fiscal years 1982 to 1987, the agencies spent just over $300 million for acid precipitation research.

The joint chair arrangement, among NIH, DOE, and NSF in a genome project, would represent a smooth distribution of authority. The appointment of a director of research might prove the only bone of contention, as the selection might imply what style of research—small-group science v. Big Science—is to be funded. The Acid Precipitation Task Force also balances the concerns of policy specialists with those of scientists and seeks the input of nonagency scientists as well (it does neglect nonagency policy specialists, however). This interagency task force approach attempts to combine the dynamic properties of an authoritative leader with the efficiency of agencies pursuing their own research expertise.

SOLIRCE: Office of Technology Assessment, 1987, based in part on U.S. Congress, General Accounting Office, *Acid Rain: Delays and Management Changes in the Federal Research Program,* GAO Pub. RCED-87-89 (Washington, DC: GAO, 1987).

be achieved. A task force or lead agency could eliminate some of this cost.

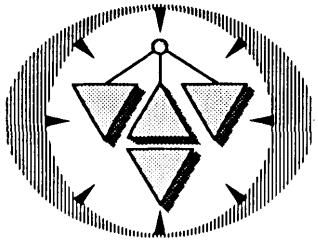
A task force may not be able to match efficiency in decision making with efficiency in administering the agencies' resources. Its recommendations could be ignored by agencies, or it could prove an obstruction or source of delays. A task force is a bureaucratic solution, identifying a person or group with the goal of genome analysis and building upon the existing authority structure. Such authority may be necessary to direct research and provide a focus for international communications, but it adds another layer to the bureaucracy that separates the administrators of science from the investigators.

Consortium

Like the task force approach, a consortium would involve the creation of a new authoritative entity. Unlike the organizational structures discussed previously, however, this approach would require the active participation of private firms (see figure 6-4). The introduction of this new factor complicates the staging of a genome project.

The typical consortium is a close working association between a university research group and one or more private firms interested in the pursuit and economic development of that research. Government involvement in consortia is often limited to financial support during the initial stages of basic research, while industry waits to fund the development stage. State government is frequently more active than Federal, because the projects are perceived to be closely linked to local economic development (see box 6-B).

Figure 6-4.—Consortium



A consortium of universities, businesses, and government is directed toward several mutually enriching goals: strengthening universities, stimulating (competitive) economic growth, engaging in basic research, creating generic technologies, and developing and delivering specific products (6). These goals correspond to those of some genome projects, which some persons hope will maintain America's competitive position in biotechnology against challenges from Asia and Europe. Genome projects would, for example, seek both to create generic biotechnology tools (such as techniques for handling very large DNA fragments, detecting very small amounts of DNA, and designing software for analysis) and to develop specific products (such as vectors for cloning DNA or automated DNA sequencers). Such results would benefit university researchers and corporate investors alike.

The question of setting the research agenda (in other instances the responsibility of the individuals conducting the research and the agencies funding it or of the task force established to oversee it) is complicated by private firms' need to emphasize technology development and not necessarily free inquiry. Profit-seeking firms often have shorter-term goals than are practical for the support of basic research and therefore focus on the development of short-term technologies over long-term ones. Not all industries have a short-term perspective, however: Pharmaceutical firms are accustomed to basic research and long-term payoffs—investments requiring more than a decade to bear fruit.

A private emphasis on development is closely associated with the effective transfer of technology into the marketplace. A consortium would no doubt speed technology transfer to participating firms, but firms might suppress the spread of scientific information to protect their investment (5). The phenomenon of sitting on data is not restricted to industry—academic scientists may delay dissemination of information in order to consolidate results for their own financial or reputational benefit (12)—but proprietary interest will not help the free exchange of data. Thus, the question of proprietary rights versus information in the public domain is a sticky one for

genome projects, where a naturally occurring DNA sequence can translate into a muhi-million-dollar product. Thus the presence of commercial firms in academia is two-sided: Goals of technology transfer and economic development may be more easily reached, but the control exerted by industry over the planning of the research agenda and the dissemination of results might be too self-interested. Concern that the economic aspirations of private firms might corrupt the atmosphere of academia may be overstated now, since only a few businesses have shown any interest in the genome project; but the possibilities of reaping economic benefits, especially in the current environment of international competitiveness, are likely to attract more private sector involvement in the future.

Box 6-B.—Midwest Plant Biotechnology Consortium

Representing a large number of university, industry, and government partners, the Midwest Plant Biotechnology Consortium is an experiment in basic research and technology transfer among agricultural sectors. Its purpose is to increase the competitiveness of American agriculture and agribusiness through the development of basic plant biotechnology research.

The idea for the consortium began at DOE's Argonne National Laboratory (ANL), which has a historical research interest in photochemistry and photosynthesis. ANL determined that a coordinated program in plant science could contribute to biotechnology applications of interest to both industry and government agencies.

When ANL invited participation from universities and industry, it specified a number of principles that would guide the consortium. The continued importance of both industrial and scientific peer review processes was stressed, and the intellectual property rights were established from the outset. ANL also emphasized the regional nature of the consortium, encouraging the participation of Midwest institutions to investigate for Midwest agribusiness. Aside from these initial guidelines, the original organization of the consortium remained informal until recently, when it sought incorporation as a 501(c)(3) (tax-exempt) corporation and developed a more formal budget process.

Government interest in the consortium comes from those agencies involved in the genome discussion—DOE, NSF, and NIH—with the addition of USDA. A secretariat operates the consortium, determining policy and procedure with informal involvement of government officials. More formal arrangements may be possible in the future. An executive board of corporate and university officers oversees the technical and administrative operations. A number of research topic subgroups (e.g., plant growth, pesticides-herbicides) also exists, and the primary interaction for technology transfer occurs at this level.

The consortium solves the problem of research direction by a two-tiered system: The industrial partners first select proposals on the basis of commercial potential, and then a peer review system selects on the basis of technical merit. The consortium expects the Federal Government (with some State funds) to support research through the initial stages, that is, until the industrial partners can see around the development corner to a commercial application. Research proposals developed as part of the consortium will be subjected to normal competitive grant review at the Federal agencies. Industry would then fund the final steps.

Organizationally, the Midwest Plant Biotechnology Consortium offers a number of useful parallels to a genome project. The Federal agencies overlap similarly, as does DOE's attempt to link the research program to related research at the national laboratories. Intellectual property rights are sensitive in both projects; the consortium provided from the outset that each research participant would retain rights according to institutional policy and that the industrial participants would have the right to first disclosure, The consortium retains the integrity of the peer review system while allowing industry to set some of its own research priorities based on commercial potential. The parallels break down where some of the short-term commercial interest in a genome project focuses on automated tools and machinery in addition to the results of biotechnical manipulation. Funding for the consortium is also considerably less than what is expected to be necessary for a genome project.

SOURCE" Office of Technology Assessment, 1987

If consortia related to one or more genome projects are formed, several issues will have to be resolved. First, terms of participation must enable a broad spectrum of private firms to participate. Small firms with limited resources have had difficulty, for example, in paying entry fees to some biotechnology consortia (22). And nonprofit organizations, which must make their information available on a nondiscriminatory basis under U.S. tax laws, might have difficulty in participating if there are preferential terms for industrial partners.

Discussion

None of the four workable administrative structures—the lead agency approach, which requires a choice between DOE and NIH; the cooperative approach, which requires no new legislation; the task force, which creates a formal authority; or the consortium, which adds a dose of private sector assistance—is static. Administrative forms may overlap: For example, the consortium may require a lead agency, or the cooperative effort may create consortia or task forces to attain specific objectives. The administrative structure at the national level does require explicit choices, however. Congressional action will vary according to the option chosen. Interagency agreement and consultation would require no new legislation, only oversight. Designation of a lead agency, establishment of a task force, or creation of a single national consortium would require new legislation.

Administration of genome projects will require monitoring of some central services and facilities, some services and functions performed at centers, and many grants to small groups. This raises several concerns about communication among agencies and among the scientists whose work they support. The diffusion of research among a large number of groups complicates communication, but it permits the most flexible organization of research; the investigator may be as focused or interdisciplinary as the research demands. A reduction in the number of groups reduces the difficulty of communication but limits the number of people trying wholly new approaches to the scientific or technical objective. The pace of innovation may be directly proportional to the number of groups: A commitment to a single center or institute might fix the relevant technology prematurely. When innovation is less important than production, then specialized facilities are logical because they simplify the organization of work. Problems of communication for centrally administered projects are of a different variety. Often the most difficult problem is ensuring that services are appropriate and tailored to the needs of those using them. Different genome projects will have different modes of communication. Projects that rely on many small groups will need communication networks or frequent meetings of scientists; central services will require feedback from user communities.

ADVISORY STRUCTURE

Second to the administrative structure in organizational hierarchy, though not in importance, is the structure of an appropriate advisory body or bodies. Agencies supporting genome projects will benefit from tapping the academic and industrial sectors for the requisite expert wisdom. Similarly, academia and industry wish to ensure their input into the decision-making process and to exercise some control over the research that affects their livelihood. The responsibilities, composition, structure, and funding of advisory groups then become issues.

Responsibilities

The primary responsibility of the independent advisory board (or boards) would be to follow the research plan and budget envisioned by the agencies, task force, or consortium and to make recommendations where appropriate. Such recommendations might include identification of promising research initiatives in need of funding or oversight of standards necessary to ensure quality control. The board could be granted budget authority to enact these recommendations, or its

role could be strictly advisory. Consideration of broad overarching issues–such as the ethical implications of using some newly developed technologies or the economic benefits of targeted technology development-could also be a function of the board.

The advisory board would naturally have a reporting duty: to the participating agencies, to Congress, to the public, and perhaps to the international community of scientists. The advisory board would be an organ of communication among the agencies, supplementing their informal direct contact. Congress would probably want to be kept abreast of research progress and could require periodic assessments in order to plan genome projects and other research initiatives. Annual or biannual reporting to Congress on progress and the distribution of funds could be fit into the budget process, for this will be one way in which genome projects are held accountable to the taxpayers. The executive branch could be kept up to date by the advisory board or through the Office of Science and Technology Policy. An advisory board not composed entirely of Federal officers would fall under the Federal Advisory Committee Act (Public Law 92-463). Pursuant to the act, the advisory board's meetings and papers must be open to the public. The advisory board could also be the contact for international communication.

Composition

An advisory board would require members with varied backgrounds. Scientists with experience in the planning of mapping and sequencing work would be needed for technical advice. Scientists with database expertise would also be required, as the storage and dissemination of the project's information is as central as the generation of it. Scientists could be chosen from universities, industry, and federally supported laboratories. Choosing the board involves the same issues as the consortium decision: how much influence development- and profit-minded industry experts should have on the project. One suggestion, from an industrial association, is to set up an advisory board with 50 percent university, 30 percent government, and 20 percent industry representatives (9). This would in fact be an extension of current practice, as university and industry representatives often work together productively. The selection of scientists from abroad to serve on the advisory board, perhaps as nonvoting members, would help it assume an international role.

Since the project's impact would extend into general science policy, economic competitiveness, medical care delivery, and the like, experts from such fields might be included. The board might want, for example, to ensure that other areas of biomedical research do not suffer from a drain of funds or personnel, and policy experts and economists would be helpful in this. Lawyers might be necessary to address questions of intellectual property. Ethicists might be included to help the board address such issues as confidentiality of data on research subjects or whether to investigate the chromosome containing disease gene A before that containing disease gene B. Representatives of interested private philanthropies, particularly those supporting research in human genetics, might also be included, An advisory board would logically include at least a representative of the Howard Hughes Medical Institute, as it funds a substantial portion of genome projects.

Structure and Funding

Scientists and nonscientists could serve together on a single advisory body or on separate bodies. The choice will influence the method of research planning and science policy formation: In a single body, the procedure is multifaceted but essentially unitary; in separate bodies, the procedure is separated into scientific and policy components. Another possible division of advisors would be government representatives on one panel and private representatives, from academia, industry, and other backgrounds, on another.

Appointments to a policy board could be made by the President, with the advice and consent of the Senate. The choice of members could be assigned to a nongovernmental body, such as the National Academy of Sciences, to ensure the board's independence and its technical competence. As an alternative, the task of selection could be delegated to the Office of Technology Assessment.

BIG SCIENCE v. SMALL-GROUP SCIENCE

The likelihood that Big Science will invade molecular biology has often been cited in opposition to a concerted government program of genome projects. Small science is largely conceived and executed by a principal investigator directing a small laboratory group funded by a grant. Big Science can refer to many things. It can mean large and expensive facilities. It can refer to large, multidisciplinary team efforts that entail cooperative planning and therefore require individual scientists to sacrifice some freedom in choosing goals and methods. Or it can refer to bureaucratic central management by government administrators. These different meanings have been intermingled in the emotionally charged debate about genome projects. (For further insight into that debate, see box 6-C.)

Three lines of argument have been made against conducting molecular biology research on one of these Big Science models: style, efficiency, and political interference.

Displacement of Higher-Priority Science

Some scientists worry that a major Federal program to map the human genome and sequence a significant portion of it would detract from the conduct of more important science (2)3)20). The argument is that special appropriations for human genome projects could well go to projects that do not present the most immediate obstacles to scientific progress and might supplant funds that would be allocated differently by the peer review processes of scientific agencies. If genome projects were not of the same scientific caliber as projects in other areas of science, agencies would nonetheless be precluded from reassigning those funds.

Other scientists argue that some genome projects do not lend themselves easily to current review procedures and merit a special effort (7,10, 19,25,30). Genome projects will involve not only science, they say, but also technology development and production. Some aver that existing peer review committees give short shrift to projects intended to develop methodology (as opposed to answering a scientific question) and tend to underfund shared research resources. They believe that the value of genome projects warrants a special effort, including new peer review committees and increased resources for a research infrastructure.

A related issue concerns the details of funding mechanisms. Those who believe strongly in the superiority of investigator-initiated small-group research urge caution in supporting large projects that are administered by institutions rather than individuals. The agencies most directly involved—namely, NIH and DOE—are adopting policies that answer both arguments by promising to use a system of peer review that gives the scientific community substantial power to direct genome projects but that differs from current peer review by adding new review groups to focus on component genome projects.

Style and Efficiency

Some scientists have objected to a Big Science approach to genome projects because it goes against the tradition of science as a cottage industry conducted by small, largely autonomous groups. The underlying assumption is that Big Science management would undercut the motivation and circumscribe the freedom of investigators by making them beholden to administrators in a scientific bureaucracy. Yet team effort is likely to be cheaper and faster in the long run for genome projects that focus on developing instruments or producing maps. It would be unwise and wasteful to shun all projects that do not conform to the small-group mode. One science administrator advised scientists that:

> . . . insofar as what they do is part of the war against human suffering, their desires and tastes are not all that matter. Biomedical science is not done, or, more important, is not supported by the public, simply because it gives intense satisfaction to the dedicated and successful biomedical researcher (32).

Large and expensive projects must meet certain criteria, otherwise they could indeed supplant other research. They must meet needs that cannot be met by small-group research (e.g., produc-

Box 6-C.—Quotes on Genome Controversies

Proposals for genoxne projects, particularly sequencing the human genome, have provoked considerable controversy among luminaries in molecular biology and related disciplines. The following quotations illustrate the liveliness of the debate over the past 2 years.

"Sequencing the human genome is like pursuing the holy grail." Walter Gilbert, Harvard University, at several national meetings, March 1986 to August 1987.

"[sequencing the genome now] is like Lewis and Clark going to the Pacific one millimeter at a time. If they had done that, they would still be looking." David Botstein, Whitehead Institute, Cold Spring Harbor Symposium on the Molecular Biology of ***Homo sapiens,*** June 1986.

"Humans deserve a genetic linkage map. It is part of the description of ***Homo sapiens .***" Raymond White, Howard Hughes Medical Institute, University of Utah, in ***Science*** **233:158, 1986.**

"The idea is gaining momentum. I shiver at the thought." David Baltimore, Director, Whitehead Institute, in ***Science*** 232:1600, 1986.

"Of course we are interested in having the sequence, but the important question is the route we take to getting it. " Maxine Singer, Director, Carnegie Institution of Washington, in ***Science*** 232:1600, 1986.

"Sequencing the human genome would be about as useful as translating the complete works of Shakespeare into cuneiform, but not quite as feasible or as easy to interpret. " James Walsh, University of Arizona, and Jon Marks, University of California, Davis, in ***Nature 322:590, 1986.***

"I believe such a conclusion [against special efforts to sequence the human genomel represents a failure of vision, an unwarranted fear of (not very) 'big' science ." Robert Sinsheimer, University of California, Santa Cruz, in ***Science*** 233:1246, 1986.

"My plea is simply that we think about this project in light of what we already know about eukaryotic genetics and not set in motion a scientifically ill-advised Juggernaut." Joseph Gall, Carnegie Institution of Washington, in ***Science*** **233:1368, 1986.**

"Too bad that it needs such fancy wrappings to attract public attention for an obvious good. " Joshua Lederberg, "The Gift Wrapped Gene, " in ***The Scientist, Nov.*** 17, 1986, p. 12.

"The sequence will give us a new window into human biology." Renatto Dulbecco, Salk Institute, interview with OTA staff member, January 1987.

"Of course, if you have the clones, you're going to want to sequence them. The question is which ones to do first. I think it is scientifically arrogant to prejudge what will be important and what will not." Paul Berg, Stanford University, interview with OTA staff member, January 1987.

"I'm surprised consenting adults have been caught in public talking about it [sequencing the genome] . . . it makes no sense." Robert Weinberg, Whitehead Institute, in ***The New Scientist,*** Mar. 5, **1987,** p. **35.**

"The sequence of the human genome would be perhaps the most powerful tool ever developed to explore the mysteries of human development and disease." Leroy Hood and Lloyd Smith, California Institute of Technology, in ***Issues in Science and Technology*** **3:37, 1987.**

"The main reason that research in other species is so strongly supported by Congress is its applicability to human beings. Therefore, the obvious answer as to whether the human genome should be sequenced is 'Yes. Why do you ask?' " Daniel Koshland, Editor, Science 236:505, 1987.

"The real problem that faces us is not the cost of the Human Genome Program, but how to get it going, seeing both that the right people are in charge and that they work under an administrative umbrella that will not tolerate uncritical thinking and so will never promise more than the facts warrant." James D. Watson, ***Director's Report,*** Cold Spring Harbor Laboratories, September 1987.

"We will see a new dawn of understanding about evolution and human origins, and totally new approaches to old scientific questions." Allan Wilson, University of California, Berkeley, at a symposium for the director, National Institutes of Health, Nov. 3, 1987.

tion, service, or targeted technology development). They must not merely be useful, but fill critical resource gaps as well (4). These criteria are likely to be met by many databases, repositories, and mapping projects. They have not yet been met by proposals to sequence the entire human genome.

Some argue that, while it may appear that certain projects are best conducted by large, multidisciplinary teams, in the long run science progresses faster if large, targeted projects are not begun (20). That is, small-group science is so much more productive in the long run that attempts to direct science will inevitably go astray.

Similar debates preceded the approval of costly projects in other fields. Construction of cyclotrons and other particle accelerators was resisted by many physicists in the 1930s IHeilbron and Kevles, see app. A], and space-based instruments were opposed by many astronomers in the 1960s (26). Yet these facilities permitted scientific advances that would otherwise have been impossible, and they were (and are) most often used by small research groups. The issue is not that expensive facilities should not be built, but that they should address critical needs and be carefully planned.

Politicization

One way in which concerted projects are believed to drift into inefficiency is through political interference. This can be on a small scale (haggling that impedes progress among members of a research team) or a large scale (e.g., pork barrel science at the national level), One scientist has observed, “a megaproject like sequencing the human genome is certain to increase the political control over scientific decisionmaking” (3), and the American Society for Biochemistry and Molecular Biology warns against ‘(the establishment of one or a few large centers that are designed to map and/or sequence the human genome” (1). Large research institutions can drift once their missions have been accomplished, and it can be difficult to close down unproductive efforts (32).

Molecular biology has been remarkably productive for three decades without the management style of Big Science. In the recent inventory of 275 Big Science facilities compiled by the House Committee on Science and Technology, none was biological (29). Yet some human genome projects, for example developing new instruments or pooling results from many different groups, will require multidisciplinary teams concentrating on a technical problem. This situation is analogous in many ways to the situations faced earlier by other sciences in their transition to Big Science IHeilbron and Kevles, see app. A] (32). It is difficult to imagine, for example, automating the steps in cloning DNA, sequencing it, or mapping it without combining optics, chemistry, physics, engineering, and electronics. If the end products of genome projects—materials and information—are to be reliable and used internationally, there must be quality control and standardization.

Clearly, some important functions require central coordination or multidisciplinary team research, although not necessarily centralized administration; some tasks cannot be forced into the mold of small-group science. Technological developments will determine the pace and extent to which Big Science becomes part of biological research. The question will be how to decide which projects merit special effort and which do not. Decisions of several types will be necessary in conducting genome projects. The advantages of decentralized planning must be balanced against the need for some centralized resources. The importance of mapping, sequencing, and technology development must be compared to other research and services. Such decisions will require an administrative structure to make them.

Biomedical investigations are now, and in the foreseeable future will continue to be, conducted primarily by small groups, although Big Science facilities and services can amplify and complement them. Small groups will remain the principal means of studying physiology and disease. When new institutions are created for elements of human genome projects, special attention must be paid to making results useful to small scientific groups. It would be ironic if genome projects starved small-group research efforts in order to create new tools.

The costs of database, repository, and map projects are not large relative to the costs of other biomedical research, so planned projects are un-

likely to have any measurable adverse impact on other research. Moreover, genome projects intended to bolster the research infrastructure should free funds for new work by making research faster and less costly. If genome projects threaten the health of small-group biomedical research, then genome projects should take a back seat.

SUMMARY

The Howard Hughes Medical Institute recently issued a short report on efforts to map the human genome; it observed:

> The sooner the entire genome is mapped and sequenced once and for all, the sooner scientists can get on with the real work of human biology: understanding what the genes do (2 I).

Databases and repositories must be centrally administered, although not necessarily centrally located, in order to be widely accessible. Technology will most likely determine whether and when large facilities and coordinated administration are necessary to conduct genome projects. If large facilities prove to be more efficient, this will not necessarily be incompatible with research by small groups; it could in fact enhance it. If, however, large facilities and centrally organized research programs threaten the lifeblood of biomedical research—investigator-initiated grants—then the projects should be reevaluated and, if necessary, cut back.

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