PROGRAM ADVISORY COMMITTEE ON THE HUMAN GENOME

FIRST MEETING

January 3 and 4, 1989

Building 31, C Wing, Conference Room 6
National Institutes of Health
Bethesda, MD

MINUTES

The first meeting of the Program Advisory Committee on the Human Genome took place on January 3 and 4, 1989, in Bethesda, MD. The following Committee members attended:

Norton D. Zinder, Ph.D., Chairman
Elke Jordan, Ph.D., Executive Secretary
Bruce M. Alberts, Ph.D.
David Botstein, Ph.D.
Jaime G. Carbonell, Ph.D.
Joseph L. Goldstein, M.D.
Leroy E. Hood, Ph.D.
Victor A. McKusick, M.D.
Maynard V. Olson, Ph.D.
Mark L. Pearson, Ph.D.
Cecil B. Pickett, Ph.D.
Phillip A. Sharp, Ph.D.
Nancy S. Wexler, Ph.D.

The following liaison members also attended:

George F. Cahill, Jr., M.D.
C. Thomas Caskey, M.D., F.A.C.P.
Mary E. Clutter, Ph.D.
Robert M. Faust, Ph.D.
Benjamin J. Barnhardt, Ph.D.

Drs. Goldstein and Clutter were unable to attend the second day of the meeting. The Committee roster and lists of speakers and others who attended are attached to these minutes.

DAY 1

Dr. James B. Wyngaarden, Director of the National Institutes of Health (NIH), began the meeting with an overview of the history of NIH's role in genetics research. He noted that NIH has invested in this type of research for several decades, by sponsoring intramural programs as well as by providing resources to the extramural scientific world. Dr. Wyngaarden reported that, in FY 1988, Congress awarded NIH the sum of $17.2 million to conduct research on the mapping and sequencing of the human genome. Following this appropriation, NIH

held a major retreat in Reston, VA, to discuss the project and determine the role NIH would play. Dr. Wyngaarden summarized the meeting's accomplishments, one of which was the creation of the Office of Human Genome Research within the Office of the Director, NIH. In addition, the meeting defined four sub-areas of the human genome project: improvement of information management, improvement of methodology, mapping of the genome, and determination of the nucleotide sequence.

Next, Dr. Wyngaarden delivered the charge to the Program Advisory Committee. He stated that the Committee is empowered to advise NIH on all aspects of the human genome project, including new technologies, new directions, training needs, etc. In addition, the Committee will be expected to assist in preparing a plan for the human genome project, which is due to be submitted to Congress in early 1990. In discussing the definition and boundaries of the project, Dr. Wyngaarden noted that virtually all Institutes of the NIH are involved in research that interacts with this program. He stated that the Office of Human Genome Research does not wish to usurp projects that have been undertaken by individual Institutes; rather, it seeks to coordinate efforts into a cohesive plan and to determine what can be done differently.

Dr. Norton D. Zinder, of The Rockefeller University, began his remarks by noting that this meeting marked the formal beginning of the NIH human genome project. He stated that obtaining the sequence of the human genome is "a priceless endeavor" and that the project will be endless: Once the sequencing has been completed, the information must be used, and the applications are almost limitless.

Dr. Zinder proceeded to set the dates for future Committee meetings. The next meeting will be held on June 19-20, 1989, and the following meeting will take place on December 4-5, 1989. The latter meeting will include discussion of the report to be submitted to Congress by March 1990.

Dr. James D. Watson, Associate Director for Human Genome Research, NIH, discussed the background and goals of the human genome project. He stated his intention to complete the project "as fast as possible within a reasonable cost." He estimated that approximately 15 to 20 years would be required to complete the entire project but that important results are likely to be produced within the next 5 years.

Dr. Watson discussed coordination of projects under the program. He felt that small laboratories consisting of 5 to 10 scientists working on special projects will probably not be sufficient to achieve program goals. Larger groups--even centers--may be necessary. Decisions about which laboratories should be encouraged to grow larger will have to be made, and this is an area in which the Office of Human Genome Research and the Program Advisory Committee must become involved.

Dr. Watson stated his belief that the human genome project must be run by the scientific community. He urged the Committee members to travel and get to know the laboratories that will be doing the work rather than simply reading their proposals. Dr. Watson also emphasized that the Advisory Committee was not convened to ratify decisions that had already been made; rather, the Committee will make decisions that will influence the direction of the program at NIH.

Dr. Elke Jordan, Director of the Office of Human Genome Research, NIH, described the function of the Office and discussed its interaction with other groups. She announced the creation of the NIH Coordinating Committee on the Human Genome, which consists of representatives from the Institutes of NIH that are involved in genome-related research (i.e., almost all the Institutes). The Coordinating Committee will facilitate communication between the Institutes and the Office of Human Genome Research. In addition, Dr. Jordan discussed the collaboration between NIH and the U.S. Department of Energy (DOE), which has been established through a Memorandum of Understanding (MOU) between the two agencies. The Health and Environmental Research Advisory Committee (HERAC) of DOE and the Program Advisory Committee of NIH will form subcommittees that will meet jointly to fulfill the requirements of the MOU.

Dr. Jordan also stated that the Office of Human Genome Research will interact with the Human Genome Organization (HUGO) to facilitate coordination of genome research internationally. She noted that representatives from other countries involved in this type of research may be invited to future Committee meetings to provide updates on their activities.

Following this presentation, Dr. Ruth Kirschstein summarized ongoing research on the human genome that is sponsored by the National Institute of General Medical Sciences (NIGMS). She described two NIH-wide program announcements, issued in May 1987, entitled "New Approaches to the Analysis of Complex Genomes" and "Computer-Based Representation and Analysis of Molecular Biology Data." Initially, solicitations sought applications involving development of methods to fragment, purify, and clone large segments of DNA; to develop ordered sets of such fragments; to explore better ways of sequencing the fragments in order to expand the genetic and physical maps of the human and other genomes; and to conduct computational analyses of data. Dr. Kirschstein also discussed the Request for Applications (RFA), published in October 1987, for research initiatives involving the human genome and those of model organisms (yeast, *Drosophila*, the mouse, and *Caenorhabditis*). She noted that two special study sections had been created to review the applications submitted by the scientific community.

Dr. Kirschstein reported that 63 grants were funded in FY 1988. The largest number of these grants involved technology development and instrumentation, and 23 were specifically related to the human genome. Dr. Kirschstein estimated that approximately $12 million will be available in FY 1989 for new research and that approximately 30 to 40 additional grants will be funded.

Dr. Irene Eckstrand of NIGMS described the Institute's plans to sponsor meetings and workshops, including the Human Gene Mapping Workshop, which is to be held June 10-17, 1989, in New Haven, CT. She also reported that NIGMS, DOE, and Howard Hughes Medical Institute will cosponsor a series of meetings on data management for physical mapping information. These meetings will deal with nomenclature, software, and data base management.

Dr. Eckstrand stated that NIGMS also plans to facilitate collaborations among investigators working on similar projects in order to improve communication and to design networks for data transfer and analysis. With these goals in mind, NIGMS will sponsor a meeting in March 1989 of approximately 25 investigators who are working on chromosome 11. In the fall of 1989, a meeting will be held to address strategies and technologies for DNA sequence determination.

During discussion of these presentations, Dr. Kirschstein stated that NIGMS had used the FY 1988 and FY 1989 funds primarily for research projects and had not allocated funds directly for training, although research grants supported training indirectly. Dr. Kirschstein also commented that NIGMS was able to provide funds for equipment needs in the scientific community but that authority for construction was not available.

Dr. Donald A.B. Lindberg provided background on the National Library of Medicine (NLM) and discussed NLM's plans to augment existing resources by developing factual data bases, particularly for microbiology and biotechnology. He described a new information model whereby data reside where they have been created, and users access the data through networks. He noted that NLM plans an active role in managing such networks. Dr. Lindberg also stated that NLM has recently funded projects on information processing and will continue to support this type of research in 1989. In addition, he mentioned that NLM has funded training grants in medical informatics for the last 20 years.

Dr. Lindberg reported that the National Center for Biotechnology Information has been established at NLM and is funded at $8 million per year. He stated that the Committee's input on optimal ways to use the Center will be sought.

Dr. Daniel R. Masys presented further detail on NLM's biotechnology information program, which focuses on problems specific to automated information systems, e.g., nonstandard vocabularies, structures, and searching methods. He stated that the National Center for Biotechnology Information has been charged with the following tasks:

- To design, develop, implement, and manage automated information systems for human molecular biology, biochemistry, and genetics;

- To perform research in advanced methods of computer-based information processing capable of representing and analyzing the vast number of biologically important molecules and compounds;

- To enable use of the systems and methods developed; and

- To coordinate international gathering of biotechnology information.

Dr. Masys summarized NLM-supported projects that have been ongoing for the last several years in the following areas:

- Development of new data bases and enhancement of existing ones, e.g., through the design of linkage schemes;

- Improvement of information retrieval and analysis; and

- Communication, including sponsorship of meetings and workshops on computational biology, e.g., the Macromolecules, Genes, and Computers Workshop to be held in the summer of 1989.

During discussion of issues surrounding the design of information systems, several participants cautioned against overstandardization in the organization of data from areas of research that are highly experimental. Dr. Masys stated

that input from the Committee would be important in making decisions about the types of data bases that should be supported (e.g., Are separate data bases for nucleic acids and proteins necessary, or would it be advantageous to combine them?). Dr. Lindberg noted that outreach is an area of major concern at NLM, and ways of educating the scientific community about available resources are being explored.

Dr. James C. Cassatt described the NIGMS-funded GenBank, a data base that contains not only sequence information but also bibliographic data and biological information pertaining to the sequences. GenBank currently contains more than 22,000 entries comprising approximately 24,000,000 base pairs, and data are available online as well as on magnetic tapes, floppy disks, and CD-ROM. GenBank also collaborates with other nucleic acid sequence data bases--the European Molecular Biology Laboratory (EMBL) in Heidelberg and the DNA Data Bank of Japan.

Dr. Cassatt stated that future challenges include insuring that GenBank data are complete and up to date. He emphasized the importance of timely data entry and reported that a user-friendly program to facilitate data entry will be available to the research community in 2 months. In addition, journals that publish sequence information will be asked to require authors to enter their data into GenBank upon acceptance of their manuscripts.

During the discussion period, several participants stressed that the Committee should work on ways to encourage investigators to enter their data into appropriate data bases quickly.

Dr. Delbert H. Dayton described the Repository of Human DNA Probes and Libraries, which is funded jointly by the National Institute of Child Health and Human Development and the Division of Research Resources (DRR). The Repository, an international facility that has served 2,667 users, provides for the reliable exchange of cloned human DNA and the distribution of chromosome-specific libraries. The American Type Culture Collection (ATCC), which operates the Repository, accepts DNA relevant to human genetic disease and focuses on genes, clones that identify restriction fragment length polymorphisms (RFLPs), and segments of importance in genetic linkage analysis. The ATCC collects well-characterized probes from investigators, expands and verifies the probes, and stores multiple samples that are distributed to interested investigators upon request. The ATCC currently receives probes at the rate of 300 per year and expects to distribute libraries at the rate of 1,000 per year by the 5th year of the contract. Probes that are likely to be heavily requested are identified through contacts with the Human Gene Mapping Library at Yale University and the Human Gene Mapping Workshops.

Following this presentation, several participants commented on the changing technology for the production of cloned DNA and noted that the ATCC will have to keep pace with these changes. Dr. Dayton stated that initial efforts to explore automation of procedures are already under way.

Dr. Caroline H. Holloway provided an overview of the Protein Identification Resource (PIR). This data base, funded by the DRR's Biomedical Research Technology Program (BRTP), collects information on protein sequences and facilitates the identification of unknown proteins. In addition, protein and nucleic acid information can be correlated, allowing the identification of

proteins based on nucleic acid sequence. Online data bases also include GenBank and EMBL. PIR is located at the National Biomedical Research Foundation at Georgetown University and has 126 universities and nonprofit organizations signed up as online users. Dr. Holloway noted that the grant that supports PIR will terminate at the same time as the GenBank contract terminates, which provides an opportunity for making decisions about collaboration between these two data bases.

Next, Dr. Holloway summarized the status of Bionet, also funded by the BRTP, which allows users access to a number of biological sequence data bases, including GenBank and PIR; software tools; and an electronic bulletin board. Bionet is operated by Intelligenetics in Mountain View, CA, and there are 867 users who subscribe.

During the discussion period, several participants noted that DRR's experience with centers should be valuable to the Committee in its efforts to determine the requirements for centers in the human genome project. There was also discussion of the differences among the grant, contract, and cooperative agreement mechanisms at NIH. Dr. Katherine L. Bick, of the Office of Extramural Research, NIH, provided clarification of these differences.

Dr. Judith Greenberg described the activities of the Human Genetic Mutant Cell Repository, an NIGMS-funded repository at the Coriell Institute for Medical Research in Camden, NJ. The Repository, also known as the Cell Bank, provides high-quality, well-characterized, contaminant-free cultures of cell lines from individuals with genetic disorders and from normal individuals. The Repository contains 4,500 cell lines, primarily fibroblasts and lymphoblasts, representing a variety of monogenic and multifactorial disorders. Chromosomal abnormalities such as duplications and deletions are also represented as well as hybridomas and myelomas. Gene mapping accounts for 12 percent of the Repository's utilization, while other utilization includes studies on the following: regulation of gene expression, cell physiology, mutagenesis, carcinogenesis, DNA synthesis and repair, and pharmacology.

Dr. Greenberg reported that, in January 1989, NIGMS awarded the Coriell Institute for Medical Research a 5-year, $5.7-million contract to continue operation of the Repository. The Repository will undertake additional activities under the new contract. For example, it will make DNA preparations from selected cell lines for distribution to investigators, which will enable distribution of DNA from somatic cell hybrids.

Following this presentation, the desirability of duplication between the Repository's pedigrees and those maintained by the Centre d'Étude du Polymorphisme Humain (CEPH) was proposed as an item for the Program Advisory Committee's consideration, given that linkage mapping is a high priority in the human genome project.

The meeting continued with an overview of genome activities in agencies other than NIH. Dr. Benjamin J. Barnhardt provided background on DOE's Human Genome Initiative, which has been undertaken to expand DOE's ability to investigate the health effects of radiation and energy-related chemicals. He stated that DOE's Human Genome Initiative encompasses three major objectives: development of resources, including overlapping sets of cloned DNA fragments prepared as

cosmids and yeast inserts; development of new mapping and sequencing technologies; and development of data base management systems, techniques for automated input of DNA sequences, and computational tools for analysis.

Dr. Barnhardt stated that DOE's intramural effort in the Human Genome Initiative is largely represented by three national laboratories: the Lawrence Berkeley Laboratory and the Los Alamos National Laboratory, which have been designated as human genome centers, and the Lawrence Livermore National Laboratory. Dr. Barnhardt highlighted other DOE-supported activities, including preparation of chromosome-specific libraries for ATCC, involvement in the National Gene Library Project, and partial support of GenBank. He stated that future goals of the Human Genome Initiative are to complete construction of linearly ordered DNA clones for chromosomes that have already been started and to initiate the construction of such clones for additional chromosomes.

During the discussion period, Dr. Barnhardt noted that DOE does not fund training directly but that the human genome centers provide training indirectly. He also described ongoing efforts at Los Alamos National Laboratory to promote technology transfer to the private sector.

Dr. George F. Cahill, Jr., summarized the genome-related activities of the Howard Hughes Medical Institute (HHMI). He stated that HHMI spends approximately $40 million per year to support investigators involved in genetics research, including those working on *Drosophila* genetics. In addition, the Institute provides support for medical students in research as well as for doctoral trainees.

Dr. Cahill stated that HHMI also funds genome resources at approximately $3.5 million per year, including the Human Genome Mapping Library (HGML), the CEPH data base, and the Online Mendelian Inheritance in Man data base, among others. HHMI plans to investigate methods of making these data bases compatible with each other. Dr. Cahill remarked that HHMI will rely heavily on recommendations from the Program Advisory Committee regarding other areas of the human genome effort that need support.

Following this presentation, several participants reiterated the importance of designing data bases that can intercommunicate. They stressed that the Committee should play a role in developing guidelines that will minimize incompatibility in future data bases.

Next, Dr. John C. Wooley described the National Science Foundation's (NSF's) support for projects focused on infrastructure in genetics, for which $50 million will be spent in FY 1989. He discussed five broad areas of special interest to NSF: instrument development, particularly during early stages; provision of instrumentation and facilities for genetic research; software development; basic genetic research (primarily on nonhuman organisms); and biological data bases. Specific NSF activities have included funding, in FY 1989, of a science and technology center dedicated to new technologies for DNA and protein chemistry. NSF is also involved in development of new software and algorithms for data base searching and development of special purpose hardware to increase the speed of biological data base searches. NSF has also collaborated with NIH to provide biomedical scientists access to resources at the NSF Advanced Computing Centers (Supercomputer

Centers). In addition, Dr. Wooley mentioned NSF's interest in the use of new technologies to advance research on corn and other agricultural plants and reported that NSF currently supports an RFLP effort in maize for $300,000 per year.

Dr. Wooley stated that NSF is committed to technology transfer and to maintaining a "pipeline" of future scientists. Funds that support the biological research centers and the science and technology centers will also support multidisciplinary and interdisciplinary training activities at these facilities.

Discussion focused on specific details related to the science and technology center that was recently funded. Dr. Zinder noted that the administrative organization of the center may serve as a paradigm for future centers that may be established by the human genome program. The question of how to evaluate the progress of such centers was raised, and Dr. Wooley stated that the peer review system would play an important role in this area.

Dr. Robert M. Faust discussed the U.S. Department of Agriculture's (USDA's) interest in the human genome effort. He stated that USDA considers mapping of plant genomes a high priority and funds mapping studies on corn and soybeans at $750,000. He also summarized recent advances in plant genetic research: Construction of RFLP marker genes has begun for corn, tomatoes, cabbage, and other crop plants; researchers have mapped three genes that control drought tolerance, five genes that have a major impact on flavor in tomatoes, and three genes involved with insect resistance in tomatoes; and a group of genes influencing yield in corn has been identified. Dr. Faust commented that USDA is interested in the human genome project primarily because of the technology that may result.

Dr. Faust also discussed the USDA Plant Genome Research Conference, which was convened in December 1988 to plan an initiative for mapping and sequencing the genomes of plants important to agriculture and forestry. Dr. Faust noted that the report developed at this conference is still in the draft stage; however, it mentioned development of a foundation of knowledge for plant science research as one of the initiative's goals. In addition, the draft report identified several criteria for selecting plants to map and sequence, including the following: Economic impact and domestic importance, maximum information transfer to other plant species, and provision of basic and fundamental insight. The draft report also mentioned features that should be incorporated in a national information network to support plant genome research: The network should be user friendly; should allow for all types of maps, quantitative information, and raw data; should be kept current through frequent updates and include a mechanism for data validation; and should be free or relatively inexpensive to users. Participants at the conference also recommended that an Office for Plant Genome Research be created at USDA to coordinate the Department's activities with other genome-related projects, such as the human genome program at NIH.

During the discussion period, several participants commented that USDA could aid the human genome effort by conducting mapping and sequencing of the genomes of agriculturally important organisms for comparative purposes.

The final segment of the first day of the meeting focused on international activities. Dr. Victor A. McKusick described the Human Genome Organization (HUGO), which was established in 1988 to facilitate international collaboration in the mapping and sequencing of the human genome. HUGO will also coordinate the efforts of investigators involved in mapping and those who work on sequencing and cloning. In addition, HUGO will coordinate research among investigators working on different species. Dr. McKusick stated that HUGO receives partial funding from HHMI but hopes to obtain multigovernmental as well as private funding.

Dr. McKusick reported that HUGO plans a wide variety of activities, ranging from international training programs to development of guidelines on ethical, social, legal, and commercial issues surrounding the human genome project. It will arrange for the exchange of data, samples, and technology relevant to genomic research and will assist in the organization and funding of the Human Gene Mapping Workshops.

There was brief discussion regarding inclusion of Third World countries in HUGO. Dr. Watson felt that, in order to keep costs down, representation in HUGO should be limited to countries that are actually doing the mapping and sequencing, rather than those interested only in the results. The Committee members stated that anyone who wishes to should be able to contribute to the human genome project.

Dr. Maynard V. Olson discussed Japan's endeavors in the area of human genome research. He reported that the Japanese have focused heavily on sequencing projects, in contrast to the approach generally taken in the United States, which is to concentrate on linkage and physical mapping, with a phase-in of sequencing as technological improvements materialize. Specifically, Japanese researchers have completed the sequence of chloroplast DNA and are currently coordinating a major effort to sequence the *E. coli* genome.

Dr. Olson noted that the interagency coordination situation in Japan is very complex, with various ministries, including the agriculture, education, and technology ministries, involved in mapping and sequencing projects. Nevertheless, Japan's hierarchal system lends itself to concentration on programmatic goals. He suggested that observation of Japan's coordination strategies may provide insights relevant to management of the human genome program in the United States.

During the discussion following this presentation, one participant noted that another aspect of Japan's management strategy has been successful coordination between academic and industrial laboratories, particularly with regard to data base management and software development.

Dr. Mark L. Pearson summarized the United Kingdom's activities in the area of technology development. He reported that British scientists have developed new techniques for the detection of sequence polymorphisms, i.e., polymorphisms between restriction sites. In addition, they have developed microsequencing methods for determining sequences at the end of restriction fragments, making it possible to generate large amounts of information that can facilitate the ordered overlapping of DNA sequences. In an effort to develop megabase-scale sequencing methods, British scientists are employing transputer technology as well as parallel processing methods that can handle

large blocks of sequences. Dr. Pearson also discussed the United Kingdom's large-scale mapping and sequencing projects, which have focused on the human genes CF, NF, and HD; viral genomes, including cytomegalovirus; plants, including *Arabidopsis*; and bacteria.

There was brief discussion following this presentation, during which the participants reiterated the need for international cooperation and sharing of data. They predicted a major role for HUGO in facilitating international communication and planning in genomic research.

Dr. Peter L. Pearson provided background on the European Economic Community's (EEC's) Predictive Medicine Program, which is planning a human genome analysis component. He reported that a working group consisting of two representatives from each of EEC's member states has been created to develop the program. This group has since been divided into the following six study groups: physical mapping, genetic mapping, advanced technologies, data base management, ethics, and training. He noted that EEC's human genome program plans to offer training fellowships that will allow less technologically advanced European countries to participate in and benefit from the program.

Dr. Pearson stated that the European approach to organization of the human genome effort involves coordination among laboratories through a network, rather than consolidation of projects in centers. It is anticipated that CEPH will form the center of the network, with which 20 European laboratories will be affiliated. Dr. Pearson also noted that a shared-costs financing arrangement will exist between EEC and laboratories that wish to participate in its human genome program.

During the discussion period, Dr. Pearson stated that coordination of effort among numerous laboratories would not preclude the possibility of two laboratories' working on the same task; in fact, he felt that a certain amount of overlap would be desirable.

There followed a general discussion of the first day's presentations. In an attempt to define the extent of interfacing activities that would be appropriate between the human genome program in the United States and similar programs in other countries, Dr. McKusick stated that the most important aspect of this interface will be exchange of data and biological resources. Such exchange would enable investigators to work more efficiently and would help to minimize duplication of effort.

Several participants sought clarification on the extent to which NIH plans to support human genome research abroad. Dr. Jordan responded by stating that NIH accepts applications for funding from foreign sources and has recently funded two foreign projects. Dr. C. Thomas Caskey commented that it is too early to contemplate major foreign funding and that resources must be kept within the United States until the U.S. program is well established. However, he stated that a small amount of money for "people movement" and collaboration between research groups would go a long way toward promoting cooperation and communication and, hence, acceleration of research.

Dr. David Botstein remarked that a spin-off of the U.S. human genome program is the long-term benefit that will be provided by the training component. A group of well-educated scientists will be poised to make use of the advances

and discoveries that result from the program. Dr. Olson concurred with the emphasis on human resources and stated that failure to address this issue adequately will lead to an "obsolete scientific personnel situation" in the future. He also cautioned against viewing acquisition of a data base containing the complete sequence of the human genome as the end point of the program. He stated that obtaining a reference sequence of the human genome will elevate the analysis of primary sequence data to a much more prominent position in biology, and predicted that state-of-the-art capability in this activity will be a prerequisite to being broadly competitive in basic research and biotechnology.

Dr. Zinder agreed with these comments and reiterated his earlier statement that sequencing of the human genome will be an "endless adventure." Following these remarks, he adjourned the first day of the meeting.

DAY 2

Dr. Zinder began the second day of the meeting by emphasizing the importance of the Advisory Committee to the human genome program. Next, he invited discussion of the biological scope of the program. The participants discussed the value of studying the genomes of model organisms at length. They agreed that the Committee should encourage such research for a number of reasons, e.g., advancement of sequencing technology and elucidation of the meaning of sequence information. They agreed in general that efforts should concentrate on five or six model organisms, preferably those for which genetic and physical mapping already have a strong start; however, several of the participants cautioned against a rigid definition of which organisms should be studied.

Dr. Watson raised the issue of the extent to which research in medical genetics should be supported by the human genome program. Dr. McKusick commented that the program is not capable of funding studies of all diseases with a substantial genetic factor. He felt that program support, at this stage, should be limited to studies on mapping of diseases that are both prevalent and caused by single-gene mutations. Several participants felt that projects in other diseases could qualify for program funding if they included the potential for technological or methodological advancement.

In terms of the technical scope of the program, the participants felt that the Committee should focus heavily on development of new technology and on making resources more available to the scientific community. Dr. Caskey emphasized the need to encourage investigation of the use of molecular biological tools in the field of cytogenetics.

The need for construction of new research space, particularly in connection with the establishment of centers, was discussed, and it was strongly urged that the Office of Human Genome Research should seek authorization to fund such construction.

Training was emphasized as an area in need of immediate attention, since the lead time required for setting up programs is likely to be lengthy. Several participants stressed the need for a forum in which students trained in technology-related disciplines, e.g., computer science, could receive training in biology, which would allow development of technological advances focused on

biological applications. Dr. Luther S. Williams of NIGMS announced that the Institute has recently launched a new training program in biotechnology that will employ an interdisciplinary, collaborative format.

Following this discussion, a working group on training was proposed, with Dr. Joseph L. Goldstein (chairman) and Dr. Leroy E. Hood as members.

Discussion moved to the topic of program management, and the advantages and disadvantages surrounding the creation of centers were debated. Dr. Olson commented that, since the Committee would not be able to micromanage numerous genome-related projects conducted by individual grantees, establishment of centers would probably be the best way to achieve programmatic goals. However, he stressed that such centers should be small and somewhat redundant in their activities, so that competition among them would insure progress. Dr. Phillip A. Sharp also supported the development of centers and noted that, in addition to providing a stimulating environment that promotes interaction among individuals, centers also provide a focus for attracting new resources.

Other issues raised in relation to centers were center-based training activities and industry participation. Dr. Zinder then proposed a working group on centers, with Dr. Phillip A. Sharp (chairman), Dr. Maynard V. Olson, and Dr. Cecil B. Pickett as members.

There was further discussion on program management, during which Dr. Watson stated that the relationship between the Office of Human Genome Research and NIGMS must be close and friendly but that the power to shape the human genome program through funding decisions should reside with the Office and its Advisory Committee. Dr. Kirschstein assured Dr. Watson and the Committee that NIGMS stood ready to assist them in achieving program goals and would carry out their decisions.

Next, Dr. Zinder moved to the topic of ethics. He estimated that, because of the high visibility of the human genome program and its potential impact on issues such as abortion and genetic screening, considerable program resources would be allocated for ethics-related work. He noted that the working group on ethics would become an important interface between the program and the public. Following these comments, he asked Dr. Nancy S. Wexler to chair the working group on ethics and also requested that Dr. Victor A. McKusick serve on this group.

Finally, a working group on data bases, which would examine extant data bases, formulate strategies for maximizing their usefulness, and examine the need for new data bases, was proposed. Dr. David Botstein was named chairman of this group. Drs. Jaime G. Carbonell and Mark L. Pearson were also appointed to this group, and Dr. George F. Cahill, Jr., was invited to serve *ex officio*.

After thanking the Committee members and the participants for their assistance in the preliminary efforts to launch the human genome project, Dr. Zinder adjourned the meeting.

I hereby certify that, to the best of my knowledge, the minutes and attachments are accurate and complete[1].

Norton D. Zinder, Ph.D.
Chairman

Elke Jordan, Ph.D.
Executive Secretary

[1] These minutes will be formally considered by the Committee at its next meeting, and any corrections or notations will be incorporated in the minutes of that meeting.

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ON THE HUMAN GENOME

January 3 and 4, 1989

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January 3 and 4, 1989

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January 3 and 4, 1989

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