United States Government **Department of Energy**

memorandum

DATE May 6, 1986

REPLY TO ATTN OF ER-70

SUBJECT Information on a Major New Initiative: Mapping and Sequencing the Human Genome

TO Alvin W. Trivelpiece, Director
Office of Energy Research

BACKGROUND:

In the early 1970's Walter Gilbert, a former Harvard University physics professor, and Fred Sanger, a Cambridge biochemist, developed important new approaches to DNA sequencing. The methods, which allow rapid determination of the information content of genes, have been a major impetus to the recent burgeoning of academic and commercial biotechnology, and led to Nobel Prizes for Gilbert and Sanger. Because sequencing touches virtually every aspect of modern molecular biology, and bears directly on central questions of heritable mutations, cancer, genetic disease, etc., considerable pressure exists to accelerate the rate at which genes are sequenced and precisely mapped onto chromosomes. At the present rate of sequencing, several hundred years will be required to obtain the full human genome; i.e., to obtain the sequence of every human gene.

In December 1985, I asked Dr. Mark Bitensky, a Los Alamos Senior Fellow to organize a workshop consisting of world leaders in molecular biology and medical genetics, drawn from universities, the private sector and the National Laboratories, to address a number of questions related to stimulating a major increase in the rate of mapping and sequencing human genes. Specifically, participants were asked to assess (i) the feasibility of sequencing the human genome by approximately the year 2000; (ii) the costs of such a venture; (iii) the desirability in terms of human health and national economic growth, and (iv) the nature of the role, if any, that the Department of Energy might play. An executive summary of the meeting, written by Dr. Bitensky, as well as the reports of the participants on which it is based, are attached.

DISCUSSION:

Virtual unanimity was reached on the following conclusions:

(1) Mapping and sequencing the human genome within the next 10-15 years is, under a reasonable set of assumptions, technically feasible, and would be a major achievement in the history of biology.

(2) Although the implications of such an accomplishment cannot be fully anticipated, the project will affect virtually every area of biomedical science, and a substantial number of major medical and basic research advances having important health and economic impacts are expected. For example, we can anticipate important advances in understanding genetic disease; in understanding at the deepest level, the variation in human susceptibility to environmental contaminants and other disease causing agents; in assessing the frequency and nature of heritable mutations; in the design of peptides and protein binding molecules for pharmaceuticals, disease prevention, etc. The participants noted that even a 1% impact on the nation's $400 billion per year health care budget would, within a year, more than return the estimated $1-2 billion cost of the project.

(3) The National Laboratories have a major role to play in a human genome project especially in its initial phases. The role derives in part from the fact that questions central to the OHER mission would become directly addressable; in part from current National Laboratory activities such as the GENBANK and GENE LIBRARY projects at Los Alamos and Livermore, which are the natural precursors of a genome project; and in part from the genome project's crucial dependence on new engineering and computational technologies whose development will require large interdisciplinary teams. The goal of the latter would be to increase sequencing speed by at least two orders of magnitude. This will require robotics development, image processing, physical analysis of separation processes and so forth, as well as various computational requirements including database restructuring, the development of advanced algorithms and analytical capabilities, and national networking with a dedicated supercomputer at the central node.

(4) The project would be national in scope, somewhat reminiscent of the effort that led to the conquest of space, but supported by multiple agencies, including the private sector, with one agency playing the lead, managerial role. International cooperation would be sought at the outset.

(5) The workshop participants were acutely aware of the need for innovations to effectively manage a project that would be far larger and far more interactive than any that has ever been attempted in the life sciences. The extensive experience of the Department of Energy in managing such projects is in distinct contrast to that of other agencies that would also support the genome project. For this, as well as the technical reasons indicated above, DOE is a natural organization to play the lead management role, at least in the initial phases of the project.

(6) An item for immediate action is the formation of a steering committee to provide guidance on scientific strategies and priorities, administrative structure, and organizational liaison.

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Attachments

cc: J. Decker, ER-2