Chronology of Major Events Associated with Formulation of Policy on Recombinant DNA Molecules

Other Than NIH Recombinant DNA Molecule Program Advisory Committee

A. June-September 1973. At the Gordon Research Conference on Nucleic Acids (July 11-15, 1973), the capability to perform recombinant DNA experiments became apparent and concern was expressed about the potential hazards of recombinant DNA molecules. Those in attendance voted to send a letter to Dr. Philip Handler, President of the National Academy of Sciences (NAS), and to Dr. John R. Hogness, President of the Institute of Medicine, NAS, and to publish the letter. The letter, signed by the Conference Co-Chairmen, Dr. Maxine Singer of NIH and Dr. Dieter Söll of Yale University, appeared in *Science*, 181, 1114, 1973, and suggested "that the Academies establish a study committee to consider this problem and to recommend specific actions or guidelines, should that seem appropriate."

B. July 1974. A Committee on Recombinant DNA Molecules[1] published a letter in *Science*, 185, 303, July 26, 1974; *Nature*, 250, 175, July 19, 1974; and *The Proceedings of the National Academy of Sciences*, 71, 2593, July 1974, which received substantial coverage in the press. This letter, entitled "Potential Biohazards of Recombinant DNA Molecules," proposed that:

> "First, and most important, that until the potential hazards of such recombinant DNA molecules have been better evaluated or until adequate methods are developed for preventing their spread, scientists throughout the world join with the members of this committee in voluntarily deferring . . . [certain] experiments . . . .
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> "Second, plans to link fragments of animal DNA's to bacterial plasmid DNA or bacteriophage DNA should be carefully weighed . . .
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> "Third, the Director of the National Institutes of Health is requested to give immediate consideration to establishing an advisory committee charged with (i) overseeing an experimental program to evaluate the potential biological and ecological hazards of the above types of recombinant DNA molecules; (ii) developing procedures which will minimize the spread of such molecules within human and other populations; and (iii) devising guidelines to be followed by investigators working with potentially hazardous recombinant DNA molecules.
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> "Fourth, an international meeting of involved scientists from all over the world should be convened early in the coming year to review scientific progress in this area and to further discuss appropriate ways to deal with the potential biohazards of recombinant DNA molecules."

C. January 1975. The Report of the Working Party on the Experimental Manipulation of the Genetic Composition of Micro-Organisms was presented to Parliament by the Secretary of State for Education and Science in the United Kingdom. This document, known as the "Ashby Report," described the advances in knowledge and possible benefits to society of experiments involving recombinant DNA molecules, and attempted to assess the hazards in the use of these techniques. The report concluded that many benefits can be expected from the use of these techniques, and that the potential hazards can be controlled by appropriate containment procedures. "Our verdict is that we can expect many benefits from using these techniques and, provided precautions are taken . . . the potential hazards need not cause public concern. So while we urge that possible hazards must always be borne in mind by those engaged in research, we also believe it important to stimulate lively enquiry into this field of research."

D. February 24-27, 1975. The International Conference on Recombinant DNA Molecules[2] took place at the Asilomar Conference Center, Pacific Grove, California. It was sponsored by the National Academy of Sciences; supported by the National Institutes of Health and the National Science Foundation; and attended by 150 people (including 52 foreign scientists from 15 countries, 16 representatives of the press, and 4 attorneys). The Conference reviewed scientific progress in research on recombinant DNA molecules and discussed ways to deal with the potential biohazards of the work. Participants at the Conference felt that work on construction of recombinant DNA molecules should proceed provided that appropriate biological and physical containment is utilized in the conduct of the experiments. The Conference made recommendations for matching levels of containment with levels of possible hazard for different types of experiments. Certain experiments were judged to pose such serious dangers that the Conference recommended they should not be undertaken at the present time.

A report on the Conference was submitted to the Assembly of Life Sciences, National Research Council, National Academy of Sciences, and approved by its Executive Committee on May 20, 1975. The summary statement of the report was published in *Science*, 188, 991, June 6, 1975; *Nature*, 225, 442, June 5, 1975; and *The Proceedings of the National Academy of Sciences*, 72, 1981, June 1975. The report noted that "in many countries steps are already being taken by national bodies to formulate codes of practice for the conduct of experiments with known or potential biohazard. Until these are established we urge individual scientists to use the proposals in this document as a guide."

E. July 24, 1975. The World Health Organization issued a press release indicating that "The Advisory Committee on Medical Research (ACMR), in a series of recommendations addressed to the Director-General of the World Health Organization, has decided to strongly support genetic studies involving the artificial recombination of DNA . . . . Although fully recognizing the possible risks involved in DNA recombination techniques,

the Committee felt that such risks can be minimized . . . . The continuation (under appropriate safeguards) of microbiological research, including genetic manipulation and cell fusion studies, is of the utmost importance for progress in medicine and public health."

F. December 1-3, 1975. A Workshop on "The Design and Testing of Safer Prokaryotic Vehicles and Bacterial Hosts for Research on Recombinant DNA Molecules" was held in La Jolla, California, supported by the National Institutes of Health. The consensus of the Workshop was that some hosts and vectors meeting requirements for a high level of biological containment, as demonstrated by tests in the laboratory, will be available in the near future.

2. NIH Recombinant DNA Molecule Program Advisory Committee

The National Institutes of Health Recombinant DNA Molecule Program Advisory Committee[3] was established on October 7, 1974, to advise the Secretary of Health, Education, and Welfare, the Assistant Secretary for Health, and the Director, NIH, "concerning a program for the evaluation of potential biological and ecological hazards of DNA recombinants of various types, for developing procedures which will minimize the spread of such molecules within human and other populations, and for devising guidelines to be followed by investigators working with potentially hazardous recombinants."

The first meeting was held on February 26, 1975, in San Francisco, immediately following the "Asilomar Conference." The Committee recommended that the NIH use the recommendations of the Asilomar Conference as guidelines for research until the Committee had an opportunity to elaborate more specific guidelines, and that NIH establish a newsletter for informal distribution of information.

At the second meeting, May 12-13, 1975, in Bethesda, Maryland, the Committee received a report on biohazard containment facilities in the United States, and reviewed a proposed NIH contract program for the construction and testing of safer hosts and vectors. A subcommittee, chaired by Dr. David Hogness, was appointed to draft guidelines for research involving recombinant DNA molecules, for discussion at the next meeting.

At the third meeting, July 18-19, 1975, in Woods Hole, Massachusetts, beginning with the draft guidelines prepared by the Hogness subcommittee, the Committee prepared proposed guidelines for research with recombinant DNA molecules.

Following this meeting, many letters were received that were critical of the guidelines. The majority felt the proposed guidelines were too lax, while others felt that they were too strict. All letters were reviewed by the Committee, and a new subcommittee, chaired by Dr. Elizabeth Kutter, was appointed to revise the guidelines.

The fourth Committee meeting was held on December 4-5, 1975, in La Jolla, California (immediately following the Workshop on Safer Prokaryotic Vehicles and Bacterial Hosts). For this meeting a "variorum edition" had been prepared, comparing line-for-line the "Hogness," "Woods Hole," and "Kutter" guidelines. The Committee went through these, voting item-by-item for their preference among these three variations, and, in many cases, adding new material. The result is the "Proposed Guidelines for Research Involving Recombinant DNA Molecules."

Prepared January 12, 1976

FOOTNOTES

1. The Committee on Recombinant DNA Molecules, Assembly of Life Sciences, National Research Council, National Academy of Sciences, "acting on behalf of and with the endorsement of the Assembly of Life Sciences of the National Research Council on this matter," were: Dr. Paul Berg, Stanford University Medical Center (Chairman); Dr. David Baltimore, Massachusetts Institute of Technology; Dr. Herbert Boyer, University of California Medical Center, San Francisco; Dr. Stanley N. Cohen, Dr. Ronald W. Davis, and Dr. David S. Hogness, Stanford University Medical Center; Dr. Daniel Nathans, Johns Hopkins University School of Medicine, Dr. Richard O. Roblin III, Harvard Medical School; Dr. James D. Watson, Harvard University; Dr. Sherman Weissman, Yale University; and Dr. Norton D. Zinder, Rockefeller University.

2. The organizing committee for the International Conference on Recombinant DNA Molecules was composed of: Dr. Paul Berg, Stanford University Medical Center (Chairman); Dr. David Baltimore, Massachusetts Institute of Technology; Dr. Sydney Brenner, Medical Research Council, Cambridge, England; Dr. Richard Roblin III, Harvard Medical School; and Dr. Maxine Singer, National Institutes of Health.

3. At its first meeting in February 1975, the Recombinant DNA Molecule Program Advisory Committee was composed of: Dr. DeWitt Stetten, Jr., National Institutes of Health (Chairman); Dr. Edward A. Adelberg, Yale University School of Medicine; Dr. Ernest H. Y. Chu, University of Michigan; Dr. Roy Curtiss III, University of Alabama Medical School; Dr. James E. Darnell, Rockefeller University; Dr. Stanley Falkow, University of Washington School of Medicine; Dr. Donald R. Helinski, University of California, San Diego; Dr. David S. Hogness, Stanford University; Dr. John W. Littlefield, Johns Hopkins Hospital; Dr. Jane K. Setlow, Brookhaven National Laboratory; Dr. Waclaw Szybalski, University of Wisconsin; Dr. Charles A. Thomas, Jr., Harvard Medical School; and Dr. William Gartland, Jr., National Institutes of Health (Executive Secretary). Subsequently, Dr. Elizabeth Kutter, Evergreen State College; Dr. Wallace Rowe, National Institutes of Health; and Dr. John Spizizen, Scripps Clinic and Research Foundation, joined the Committee.