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Donald S. Fredrickson, M.D.
Director
National Institutes of Health
Bethesda, Maryland 20014

Dear Dr. Fredrickson:

I have been engaged in research in genetics, microbiology, molecular biology and the molecular basis of evolution throughout my scientific career and I feel that the time has come when I must express my views to you concerning recombinant DNA research and the present NIH Guidelines.

I am a microbiologist-molecular biologist by training, I taught medical microbiology for 3 1/2 years in a Medical School, and I have been awarded most of the major awards for outstanding research in microbiology that are given in this country (see attached summary of my career). I have heard much talk and have read many statements on both sides of the major issues involved in recombinant DNA research and have followed closely the stages in the drafting of the NIH Guidelines. I am personally familiar with the Guidelines and the concerns which have been expressed and in fact currently have several students engaged in P1-level research and one who is beginning a P2-level project of his own choosing with the DNA of a mold. The views I express below are my own but, based on my discussions with many other scientists, I believe that they are shared by the majority of informed scientists.

I feel comfortable in the knowledge that fellow scientists were the first to raise the question of whether there are conceivable hazards associated with some types of anticipated recombinant DNA research. However, I believe that the NIH Guidelines are unrealistic in that they legislate the existence of biological hazard where experience has taught us that hazards do not exist. My thoughts on possible hazards, my discussions with others, and my observations of the workers in my lab during the 6 months we have operated under the Guidelines have convinced me that it was an error in judgment - perhaps an overreaction to the unjustified concerns of few - to impose any

restrictions whatsoever on most work which is presently classified as P1 or P2-level research. It is unrealistic to ask scientists to follow unnecessarily strict procedural precautions in their research when, on the basis of the experience of years of research, they are convinced that no hazard exists. Most P1 and P2 level recombinant DNA research is not significantly distinguishable from genetic research performed over the past 30 years with viruses, bacteria, yeasts and molds. For us to consider it different is hypocrisy. To my knowledge there is not a single instance of the appearance of a novel pathogen from this prior genetic research.

The dangers which have been imagined by some are no greater, in my opinion, than the likelihood that laboratory mutants of common bacterial viruses such as ØX174 or P22, or a mutant fruitfly released into the environment, or a pot of soup allowed to spoil, will do us all in. Furthermore, there is no factual basis for the most serious theoretical objection that has been raised - the suggestion that there is a barrier between prokaryotes and eukaryotes preventing DNA interchange. This is a mystical view, pure and simple, and everything scientific we know about the basis of evolution suggests that prokaryotes and eukaryotes have exercised the ample opportunities they have had to exchange their DNA for millions of years. The recent discovery that at least some eukaryote genes are expressed in prokaryotes suggests that fundamental biological processes are quite similar in both groups of organisms. In addition, the existence of transmissible plasmids and transposable genetic elements in lower and higher organisms argues convincingly that nature has, for some time, practiced recombinant DNA techniques.

If one walks through the halls of any hospital the <u>real</u> concerns of humans become obvious. It is ironic that at the first time in the history of medical research when we have the capability of studying defective human genes, there is cry by a few to ban such research. In my view, the combined techniques of DNA cloning, restriction enzyme analysis and DNA sequencing are so powerful and of such immeasurable potential benefit with little or no conceivable risk, that it will become virtually impossible for any molecular biologist to avoid using them in his or her research; not to do so would seriously impair our ability to deal with many of the problems which face our society.

I therefore feel that it is extremely important that conceivable risks be assessed more realistically than they have, in proposing appropriate containment conditions. The present Guidelines ask scientists to discard what they believe as fact based on years of experience and training, and, in the absence of any new information or insights, to adopt an unrealistic and arbitrarily determined code of behavior. I feel compelled to urge as

strongly as I can that you reexamine the Guidelines and at a minimum recommend the removal of all restrictions and the requirement for certification, for all recombinant DNA research that is presently classified as P1, as well as recombinant DNA research involving the fusion of DNA of nonpathogenic microorganisms. Unless you do I fear that, by analogy, all biological research will shortly be judged potentially hazardous and will be subjected to progress-stifling controls. The Keene bill introduced in the California Assembly is a case in point and would in fact place strict controls on all biological research.

In my opinion, the NIH Guidelines and their requirement for project certification are already abridging our freedom of inquiry in the absence of any evidence of hazard and, therefore, are near-equivalent to book-burning episodes in the past.

I would appreciate it if you would transmit this letter to all individuals and government agencies concerned with the regulation of recombinant DNA research. I am circulating this letter to some of my colleagues throughout the country with the request that they express their views to you immediately.

Yours respectfully,

Charles Yanofsky

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Encl.

Charles Yanofsky

Born in New York City, April 17, 1925. Received the B.S. degree (Biochemistry) from the City College of New York in 1948. Received the M.S. and Ph.D. degrees (Microbiology) from Yale University in 1950 and 1951, respectively. Served with the Armed Forces of the United States 1944-1946.

Member of the following societies:

American Society of Microbiologists
Genetics Society of America
American Association for the Advancement of Science
Sigma Xi
American Society of Biological Chemists

Research and/or Professional Experience:

Professor, Department of Biological Sciences, Stanford University
1961 - present
Associate Professor, Department of Biological Sciences, Stanford University
1958-1961
Assistant Professor of Microbiology, Western Reserve University Medical School
1954-1958
Research Assistant in Microbiology, Yale University Medical School
1951-1953

Awards, Honors, and Service:

President, Genetics Society of America, 1969
Career Investigator of the American Heart Association, 1969-
Appointed Herzstein Professor of Biology, 1967

Elected to the American Academy of Arts and Sciences, 1964
Elected to the National Academy of Sciences, 1966

Lederle Medical Faculty Award, 1955-1957
Eli Lilly Award in Bacteriology, 1959
U. S. Steel Award in Molecular Biology, 1964
Howard Taylor Ricketts Award, 1966
Albert Lasker Award in Basic Medical Research, 1971
National Academy of Sciences Award in Microbiology, 1972
Townsend Harris Medal, CCNY, 1973
Louisa Gross Horwitz Prize, 1976