Testimony by David Baltimore for the Committee on Science and Technology, U.S. House of Representatives, Subcommittee on Science, Research and Technology, March 30, 1977

My name is David Baltimore. I am the American Cancer Society Research Professor of Microbiology at the Massachusetts Institute of Technology in Cambridge, Massachusetts. I was one of a group of scientists who, in 1974, first drew attention to the potential problems inherent in the manufacture and study of recombinant DNA molecules. Since that time I have been actively involved in discussions about the types of controls appropriate to this new methodology of modern biology.

Before considering the risks and benefits arising from recombinant DNA technology, I believe it is important to present the technique within its historical context. Modern biology has been a very productive science but has progressed much more rapidly in the study of bacteria than it has in the study of higher cells including those of human beings. Two considerations have led to the limited progress in higher cells: the large amount of genetic information in cells of higher organisms and the difficulty of carrying out genetic studies using higher organisms. Recombinant DNA technology has offered a partial solution to these problems of scale. The technology allows individual genes to be isolated away from all other genes and to be studied as independent entities. With this new technology, we have already gained new knowledge about the organization of the genetic material of higher cells and a treasure trove of new results can be expected as the technology receives wider

application.

Further knowledge of the organization and function of genes in higher cells is of critical importance to our understanding of disease. The diseases which now plague the American population are mainly diseases in which cells malfunction. We do not understand the basis of the malfunction in any of these diseases and our ability to prevent and treat the diseases is limited by our knowledge of them. Recombinant DNA technology is a new tool in the continuing battle against our ignorance of how higher cells carry out their basic functions. It joins an impressive array of techniques developed over the last thirty years which have allowed biologists to see deeper and deeper into the functioning of cells. The goal of modern biology is the understanding of normal and aberrant living processes. We are very far from that goal in almost all critical areas of human biology but recombinant DNA methods should speed our acquisition of knowledge.

The new knowledge which will be acquired about the functioning of human and other cells will bring with it new capabilities. Because we do not know the shape of that new knowledge it is impossible to specify what capabilities will be inherent in it. It is important to recognize that attempts to predict future developments in biology are severely limited by the meager knowledge we have of the biology of higher cells. Such terms as "genetic engineering" have little precise meaning because at present we can only use our imagination to guess the shape of the future and our imagination is extremely limited.

Benefits from Recombinant DNA Research

If we realize that recombinant DNA technology is only a tool of modern biology and is not a science in itself then we also will realize that recombinant DNA technology by itself offers no benefits. It is the totality of modern biology which offers possibilities of benefit for the future and recombinant DNA methods are one, albeit a critical one, of the tools that the modern biologist can use. So an analysis of the benefits to come from recombinant DNA is like an analysis in 1940 of the benefits that might derive from the electron microscope. When the electron microscope was developed its powers were speculative--today we know that it has been a critical element in our increased understanding of both normal and diseased tissues.

The appropriate question is not what are the benefits to come from recombinant DNA technology but what are the benefits to come from modern biology *in toto*. The Congress of the United States has for many years strongly supported the notion that basic research in biology will bring with it critical understanding of those diseases that plague the citizens of the United States. The Congress has funded research without requiring specific justification for why one type of research will be more beneficial than another. This was a very farsighted policy of the Congress because it represented an understanding that it is impossible to predict with precision where critical advances in modern science will arise. An investigator working on a worm or a fly may come across a principle which is central to all of life and often such a principle will be more evident in a simple system than it will be within the context

of the complicated biology of human beings. Biologists have devoted themselves to finding the truths of life and as part of that search biologists have developed the methods of recombinant DNA research which can allow modern biology to better attack problems of human cells.

What then are the benefits of basic research? They are, as they must be, entirely speculative. We believe that deeper knowledge of cancer will help to prevent it and cure it but we can not promise that that is true. We can, however, say with assurance that without new knowledge we will be extremely limited in our ability to prevent and cure cancer. It is very fashionable to say today that 80-90% of cancer has an environmental or life-style cause. From that fact certain scientists have made the facile conclusion that all we need do is search around in the environment and in our life-styles to find the causes of cancer and so to allow their eradication. One of the great men in the search for the causes of cancer has been Sir Richard Doll. In a recent article entitled "Strategy for Detection of Cancer Hazards in Man" he went through our present knowledge of the causes of human cancer and concluded "we cannot, of course, hope to detect hazards efficiently until we know how cancer is produced, so that a policy for detection must include the support of basic biological research. Success in this field is dependent on the development of ideas and is difficult to foster except by providing the conditions in which outstanding investigators are able to give free rein to their imagination." So the leading investigator of the causes of cancer believes that more basic research is necessary before those causes can be found. Recombinant DNA research is a critical

tool in the development of basic research knowledge which can help in the finding of new methods for prevention and cure of cancer.

You notice that I am not speculating about any precise benefits which could come from recombinant DNA work. It is the nature of basic research that we cannot know what it will find and therefore there is no way to precisely define the benefits it will bring. But if you believe, as I believe, that with knowledge comes new capabilities then basic biological research is likely to bring us new capabilities to handle the diseases which plague us.

Risks of Recombinant DNA Research

There are two basic types of risks which one must take into account in considering whether recombinant DNA techniques present a hazard. One is the risk of the misuse of the knowledge that can be provided by the techniques and the other is the risks of specific damage that can be produced by the use of the techniques themselves. I should like to deal with these two risks separately.

The possibility of misuse of the knowledge that can be derived from recombinant DNA research is a part of the general problem of the misuse of the techniques of modern biology. Two general categories of potential misuse are often distinguished: one is in the development of biological warfare weapons and the other is in the development of methods of genetic engineering. I believe that it is very important to strengthen the interpretation of the Biological Warfare Convention of 1975 which has been given by the Arms Control and Disarmament Agency. They have concluded that the Biological Warfare Convention bans the use of recombinant DNA techniques for the

development of biological weaponry and if that interpretation is internationally recognized it will go a long way towards preventing the use of recombinant DNA methods in the development of weapons.

"Genetic engineering" is a phrase which covers two types of possible activities. One is the use of genes to provide therapy for an individual who is suffering from a disease caused by a genetic defect. Such a procedure could lead to the amelioration of the symptoms of the disease but would not permanently alter the genetic pool of the human race. The other form of genetic engineering would be the replacement of genes in such a way that parents would now transmit new genes to their offspring. Both of these forms of genetic technology are still speculative potentials for the future but recombinant DNA methods have brought those possibilities closer to development. In a relatively short time it may be possible to consider gene therapy solutions to specific diseases but the permanent replacement of genes is probably in the far future. In either case, however, it is important to realize that recombinant DNA technology is not the same as genetic engineering. It is a tool which can bring closer the time when genetic engineering is a reality and is a problem that we must worry about. You will often hear critics argue that recombinant DNA work should be stopped because of its implications for genetic engineering. That is a possible strategy of social control but you must realize if recombinant DNA work were not allowed not only would genetic engineering be further in the future but also all benefits

that can derive from modern biology will be slower in coming.

The other type of potential risk that may be a consequence of the use of recombinant DNA methods would be a risk deriving from the production of harmful organisms during the conduct of recombinant DNA experiments. When I first participated in a public call for deep consideration of possible risks, I had serious fears about what types of hazards could occur if recombinant DNA methods were used without appropriate caution. Since that time I have listened to evolutionists and to infectious disease experts as well as to a range of critics who have presented scenarios of what kinds of dangers could be brought about by recombinant DNA work. I am today much less concerned about hazards than I was before I began to listen to the debates. I have heard, for instance, how rare it is for any organism to survive the rigors of the natural world. I have realized how unlikely it is that any gene added to an unfit microorganism might make that microorganism suddenly capable of monstrous doings. I have realized that for an organism to survive in the natural world its fitness must be constantly tested by battles with nature and that laboratory organisms are poorly suited to the natural world because they have not had to battle it. I have realized that single genes are not the determinants of disease but that a whole constellation of genes must be present for an organism to be considered dangerous. Only genes working together and selected together can make an organism into a serious determinant of disease. So I believe that the risks that are being discussed in the popular press are wildly overstated.

When we first drew attention to the potential hazards of recombinant DNA work, we could see three areas in which single genes might be dangerous. These included the acquisition by bacteria of resistance to clinically useful antibiotics, the insertion of toxin-producing genes into benign bacteria and the insertion into bacteria of genes that may be carried in cancer-causing viruses. I can now see that these were the appropriate areas of concern because these are situations in which single genes might be a danger. The NIH guidelines for research involving recombinant DNA molecules places these three types of experiments in either the category of banned experiments or of experiments to be done only under the highest containment conditions. The guidelines then grade as best they can other types of experiments associated with much lower likelihood of potential hazards. It is my belief that the biological and physical containment provided by the guidelines is sufficient to control hazards that have any vague likelihood of occurrence. Admittedly, no guidelines can give us 100% freedom from risk but that is not a criterion we ask of any aspect of our lives.

Conclusion

The public debate over recombinant DNA techniques has brought out very deep fears about the direction of modern biology. It is extremely important when such fears surface that a broad-ranging discussion takes place including both scientists and the public to air the fears and analyze their foundations. I believe that the public has been unduly alarmed by the dangers of recombinant DNA research and that this is liable to lead to a patchwork of regulations relating to such research in the various municipalities and

states across the country. In this situation I believe it is necessary for the federal government to step in and provide a defensible series of regulations which can allow the work to go forward under uniform conditions throughout the nation. It would be ridiculous, to me, to have more stringent regulations in one jurisdiction than in another, especially because the types of hazards about which one might worry can not be restricted by political boundaries.

There is one final distinction I consider very important. There are critics of recombinant DNA research who are attempting to stifle progress in all of modern biology. They are fearful of the consequences of modern biology, a fear which is generally directed toward "genetic engineering." To cut off a field of research because of fear of the possibilities inherent in knowledge would be a suicidal policy for a civilized country. While we should not blind ourselves to the dangers that can come from scientific advances, if we stifle research as a way of avoiding the dangers we will condemn ourselves to a life with both no new knowledge and no new capabilities.

It is critically important for this subcommittee and its parent committee to periodically assess the state of modern biology. Because it is a field that touches on basic elements of life it is a field with enormous potentials for both benefit and hazard. I trust, however, that you will be judicious in dealing with potential hazards so as not to stifle the development of knowledge which is prerequisite to new methods for dealing with disease.