Donald S. Fredrickson. "An overview of the role of NIH and other Federal Agencies in the conduct of research with recombinant dna." in National Academy of Sciences (U.S.), Research with recombinant DNA/G: an Academy forum, March 7-9,1977. NLM Call number QU 58 745r 1977. location: **dna\dna77\forums**

This forum was organized by Robert R. White with David Hamburg as co-chair. The invited speakers included: Daniel Koshland, John Abelson, Maxine Singer, Daniel Callahan, Erwin Chargaff, David Nathans, Alexander Rich, Paul Berg, Robert L. Sinsheimer, FRancisco Ayala, Sir JOhn Kendrew, Stephan Toulmin, BRuce Dull, Bernard Davis, Delbert Barth, Anothony Mazzocchi, Irving S. Johnson, Ruth Hubbard, Raymond C. Valentine, Ethan R. Signer, DAvid Baltimore, JOhnathjan Beckwith, Roger G. Noll and Paul A. Thomas, with a summary by Tracy M. Sonneborn, and final comments by Donald Kennedy (then FDA Commissioner). The were many commentators from the floor, including Jeremy Rifkin (with his chorus of girls decked out in placards "I will not be cloned") and Francis Simring, my nemesis from the Friends of the Earth.

Professor Bengt Gustaffson of the Karolinska much later told me that he was there and that when I got up to say what the government was and would do, that "It was like the Romans".

I did not feel like Hannibal or Pontius at this hearing--yet I left some impression that we were in control of the situation. Even Mrs. Simring was not too critical of us:

Francine Simring: I would like to congratulate the NIH and Dr. Fredrickson on the wonderful job they have done of disseminating materials, transcripts, and Xeroxs to all interested parties... many nations are looking to the United States for leadership ...(the IAC listed registration of such research with a national registry.) However there is a parenthetical opening for indusrtry that read as follows: "Subject to appropriate safeguards to protect proprietary interests."...

Fredrickson: Thank you, Mrs. Simring. I'm glad to meet you, even at this distance, and I hope to close the gap between us...

Later Kennedy commented on the IAC process.

Participants - last pages

DSFredrickson
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Dr. Fredrickson
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NIH Forum '77.

PROBLEMS OF CONTROL AND REGULATION.

AN OVERVIEW OF THE ROLE OF NIH AND OTHER FEDERAL AGENCIES IN THE CONDUCT OF RESEARCH WITH RECOMBINANT DNA

Donald S. Fredrickson

Director, National Institutes of Health

I am very grateful for the opportunity to summarize something about the government process in this matter which you have been discussing throughout this Forum.

Governments in general, and the federal government in particular, entered the matter of recombinant DNA research several years ago when, after Asilomar as you recall, one of the recommendations of the scientists was that the NIH form a committee that might begin to set up guidelines to establish strict conditions for the conduct of research that involved the use and production of recombinant DNA molecules. These guidelines were developed by a recombinant DNA committee, and after extensive scientific and public review the NIH released them on June 23, 1976.

The provisions were designed to afford protection with a wide margin of safety to workers and to the environment. The NIH guidelines were published in the *Federal Register* on July 7, 1976, for public comment.

In September the NIH also filed a draft environmental impact statement on the guidelines for public comment, and the final NIH environmental impact statement we expect to be published shortly. As many of you are aware, in August 1976, a volume was published by the NIH that contains the transcript of a public hearing held on the guidelines as

well as all correspondence received by my office on this matter prior to the release of the guidelines in June. And there will be a subsequent publication of all correspondence and many other related documents to continue this complete public record of government action in regard to recombinant DNA research.

By the time the environmental impact statement had been issued and the guidelines released, it was already apparent that the international community of science had come to agreement that recombinant DNA techniques should be used only with a common set of standards across the world. The question was how to bring this about. And as matters of this sort are often settled, first the boundaries of activity were restricted to those maximum ones in which the law can be operable across a population, and hence most countries settled down to attempt to enter this second phase for themselves before seeking further international comity and conformity with particular standards.

At the time the NIH guidelines were released there was convened by the Secretary of Health, Education, and Welfare an Interagency Committee on Recombinant DNA Research. The committee was formed with the approval of the President, and at the Secretary's request I have served as chairman.

Now, this Interagency Committee is composed of representatives of the federal departments and agencies that do several things. One component is made up of those agencies that support or conduct recombinant DNA research, or may do so in the future. Another group includes the representatives of all the federal departments and agencies that have present or possibly potential regulatory authority in this area. And to these are added a number of other departments, such as the State Department, the Department of Justice, and others that have particular interest in the general aspects of the committee's affairs. There are approximately twenty-five member agencies that make up this committee.

The mandate of the Interagency Committee is to review the nature and scope, particularly of the federal activities, relating to recombinant DNA research. Second, the committee was directed to determine the extent to which the NIH guidelines may currently be applied to research in both the public and the private sectors. It was to recommend, if appropriate, legislative or executive actions necessary to ensure compliance with the standards set for this research, and to provide for the full communication and necessary exchange of information on recombinant DNA research programs and activities throughout the federal sector.

The Interagency Committee held its first full meeting last November, and during that month it had a second meeting. The first of those meetings was held on November 4 and was devoted to a review of the development of the NIH guidelines for research involving recombinant DNA molecules. At the same meeting the committee also reviewed *in extenso* international activities relative to this same matter. I will not repeat that review, because I understand you are to have a report of a workshop which will summarize it for you in much greater detail than I can now. But the committee was fully aware of activities relative to this matter not only in this country but abroad.

At the meeting of the committee held on November 23, the federal research agencies then discussed their activities and possible roles in the implementation of the NIH guidelines. All of the research agencies endorsed the NIH guidelines to cover the recombinant DNA research that they conducted or funded. Three agencies of the federal government are now supporting research that involves the use of these techniques, the NIH, the National Science Foundation, and the Department of Agriculture. The Department of Defense, NASA, and the Energy Research and Development Administration are not at present conducting such research, but agreed to use the NIH guidelines to govern future research should they undertake it.

In that November 23 meeting the federal regulatory agencies also reported on their regulatory functions. Following that lengthy review a special subcommittee was set up to analyze the relevant statutory authorities for the possible regulation of recombinant DNA research. All regulatory agencies were represented on that subcommittee, and their representatives were assisted by attorneys from their offices of general counsel.

The subcommittee was charged to find out whether existing legislative authority would permit the regulation of all recombinant DNA research in the United States, whether it was funded by the government or not, and to seek out whether or not those existing legislative authorities would include at least the following requirements perceived by the committee to be important: review of such research before it is undertaken by an institutional biohazards committee; compliance with physical and biological standards and prohibitions in the NIH guidelines; registration of such research in a national registry; and enforcement of the above requirements through monitoring, inspection, and some sanctions.

It was the conclusion of this subcommittee after extensive review that present law permits imposition of some of the desired requirements on much recombinant DNA laboratory research, but no single legal authority or combination of them currently exists that would clearly cover all research or other uses of recombinant DNA techniques and meet all the other requirements. The committee examined, first of all, the Occupational Safety and Health Act, and found that while OSHA has broad authority it has limited access to many of the laboratories, and it does not cover self-employed persons. The Environmental Protection Agency under the Toxic Substances Control Act is directed to control chemicals that may present an unreasonable risk of injury to the health or the environment. The subcommittee found that probably most recombinant DNA molecules could come under the definition of chemicals; however, Section 5 of the Toxic Substances Act explicitly exempts registration of chemical substances used in small quantities for the purposes of scientific experimentation or analysis. The latter exemption represents the most serious deficiency in the authorities of that act for the purposes of regulating the use and production of recombinant DNA molecules.

The Hazardous Materials Transportation Act was also examined. It gives the Department of Transportation and the Center for Disease Control in Atlanta considerable authority over interstate shipment of hazardous

materials but, indeed, there were many aspects of this act which are wanting in regard to regulation of recombinant DNA research.

The Environmental Defense Fund, in November of 1976 petitioned the DHEW to regulate recombinant DNA research under Section 361 of the Public Health Service Act, and this petition was filed with the Interagency Committee for its consideration. Under this section the authorities are restricted to organisms that are communicable and cause human disease. To use Section 361 for regulatory authority one would have to assume that recombinant DNA research may cause human diseases and that these may be communicable. Further, Section 361 does not apply to plants or animals or the general environment. It was the conclusion of the committee that Section 361 lacks the requisite authorities.

The same is true of Section 353 of the Public Health Service Act. This applies to clinical laboratories, but it is not considered to be applicable to research laboratories.

Many other authorities, particularly of the EPA and of other agencies including the Food and Drug Administration, were examined, as were the powers of the Department of Agriculture, whose authorities were found applicable solely to nonhuman life and plants.

In summary, the Interagency Committee concluded that no single authority or combination of authorities currently exists that could clearly reach all recombinant DNA research in a manner that the committee deemed was appropriate. It was agreed that regulatory actions could be taken under existing authorities, but that they would be in considerable jeopardy of legal challenge.

The full committee then adopted the report of the subcommittee, agreeing with its conclusion about existing authority. It then turned its attention to examining possible new legislation. In considering elements for new legislation the committee reviewed federal, state, and local actions and activities that bear on the regulation of DNA research. In addition to activities in municipalities such as Cambridge, it received a report from the New York State Attorney General's Environmental Health Bureau for State Regulation, which made certain recommendations for regulation in New York State. The committee was aware of the hearings in the California legislature, and it also was able to examine legislation now submitted to the Congress, specifically Senate Bill 621, the DNA Research Act of 1977, introduced by Senator Dale Bumpers, and the companion measure introduced into the House by Mr. Ottinger.

The committee also had available to it comments elicited by its various members from a number of persons whose opinions were sought concerning questions relative to legislation. These sources included agricultural scientists, biomedical scientists, environmentalists, and leaders from labor unions and private industry. In the light of this background the committee has been considering in its most recent meetings what should be the elements of new legislation that might cover the regulation of the use and production of recombinant DNA molecules. It has had to consider issues of definition, the question of registration of all activities, and the question of whether licensure might be an effective part of a regulatory process, and it has dealt strongly with

aspects of interagency cooperation. It also has had to deal with the difference or the distinction between research and commercial use of recombinant DNA products, particularly because many commercial aspects are clearly covered by existing legislation or authority invested in the Environmental Protection Agency and the Food and Drug Administration. It has also had to contend with the fact that the NIH is not a regulatory agency and that it has no intention of becoming one, and that it would be inappropriate for NIH to assume inspection and enforcement authorities when it has participated in standards setting.

The Interagency Committee meets again tomorrow. We expect and hope that it may produce an interim report dealing with some recommendations with respect to legislation within a week. Then the committee will turn to other agenda relative to this problem, and at some point will probably self-destruct when it has carried out fully the terms of its mandate.

In brief, there is a strong and active focus within the executive branch to formulate recommendations to help set federal standards, which I think to be very much needed, with regard to the regulation of the use and production of recombinant DNA molecules. The task has not been simple. The committee has recognized its responsibility to protect fully the public interest. It recognizes that recombinant DNA activities can pose some threat to workers, to the general population, to the environment, and also to a creative and responsible scientific apparatus. Thus, the task of recommending appropriate, effective, and reasonable legislation for regulation of this activity is a matter of very grave concern.

DISCUSSION

NORTON ZINDER, Rockefeller University: I would like to support, and I am surprised that I am going to do so, the idea of having legislation, federal legislation, with regard to recombinant DNA research. The proliferation of local option with different guidelines in different states and different cities can only lead to a situation of chaos, confusion, and ultimately to hypocrisy amongst the scientists involved. I strongly plead that the government move ahead on this as rapidly as possible.

FREDRICKSON: Thank you, Dr. Zinder.

AL PLUMMER, retired civil engineer: I am neither for nor against rapid research in recombinant DNA. I am here to learn what the facts are so as a private citizen I can choose sides when it becomes appropriate. I have listened to 85 percent of the discussion, and so far I have not been able to identify who in the federal government is responsible for bringing together in one comprehensive document all the history, facts, alternative pathways, along with calculations, as best they can be made, of benefits and costs and the environmental impacts of this

problem. In other words, who is doing the planning that will point out where we are going so that we as private citizens can make intelligent decisions? Is there a group planning what kind of a program would be appropriate for the nation as a whole? I understand you are dealing with regulation and setting standards, and that is fine, but it doesn't really attack the problem of where we are going with this. Is it good? Is it bad? What are the problems? Can you tell me who is going to come up with a document?

FREDRICKSON: Yes, Mr. Plummer. First of all, several documents have already been issued which may be helpful to you. I referred to two of them. One is the NIH preparation of the history relative to its guidelines. The second is the environmental impact statement issued relative to its guidelines. The Interagency Committee now contains all the elements of the federal supporters and conductors of this research, and probably they are responsible for at least 90 percent of the research that is doubtless going on at the present time in this country. They will be reporting to the Secretary of Health, Education, and Welfare, in whose office now, as this matter ascends higher up in the Department, will be the next focus for disseminating and developing some of the considerations that you represent. A third focus will open up next week when the Congress of the United States will, I think, have the first of a number of hearings on this whole matter of recombinant DNA research. I believe that there are several committee hearings that are scheduled or are about to be, which will deal not only with the matter of legislation, but also the general aspects of the recombinant DNA research. Finally, we have been this week, and I expect to return to, the Appropriations Committee in the House, and the Senate next week, where we have also been answering a number of questions of the kind that you have posed.

PLUMMER: Well, my basic statement is that it is fragmented and it isn't pulled together in such a way that we can quietly analyze it and come to conclusions. As a result I see in this meeting that the opponents and proponents are polarizing and that will lead to emotional situations, and it will get more and more difficult to resolve unless we get the facts all laid out.

DAVID O. KRASSIK, Engineering and Applied Science, UCLA: I am interested in learning more about how one has established the adequacy of the current NIH guidelines. My background is not biology or biochemistry, and I have been listening to try to keep the words *vector*, *phage*, and so forth apart in my mind.

I did go to the containment workshop last night and there tried to find out whether there exist documents that would give details on the efficacy of physical containment and biological containment, but I was told no. I must confess, I was a little surprised at what seemed to be the relative ineffectiveness of P1 to P3 containment, assuming that there is a risk, and I have to rely on my medical and biological colleagues to tell me that.

With regard to the biological containment, again, one hears numbers of large factors, but again, there are uncertainties. So as I listened I found in my own mind no way of knowing as a result of these few days how the guidelines were arrived at, how the kinds of questions raised by Dr. Sinsheimer here at the Forum yesterday and previously have been dealt with or are being dealt with in deciding that these guidelines are adequate, that they are not too strict or not strict enough.

FREDRICKSON: Have you had opportunity to read the NIH guidelines, their appendixes, and all of the comments relative to them?

KRASSIK: Yes, I have, but with my limited background I could only digest part of it.

FREDRICKSON: If you will give us your name at the NIH one of the documents that will be very helpful to you is the revised or final environmental impact draft statement, which has addressed in detail comments of the kind and questions of the kind that you have raised. The development of both the guidelines in their final form and the environmental impact statement have involved an exchange of correspondence and a full attention to a wide range of public comment, each of which has been addressed in the revised document.

FRANCINE SIMRING, Friends of the Earth: I would like to congratulate the NIH and Dr. Fredrickson on the wonderful job they have done of disseminating materials, transcripts, and Xeroxes to all interested parties. And in the interest of expanding the accuracy, I want to make three short additions to what was said by Dr. Fredrickson.

You mentioned, I believe, that all correspondence was included in the yellow volume of August. I believe we would have to make that "some" correspondence in the interest of accuracy.

You mentioned that the nations settled down by themselves to do their guidelines. A few did, but for the most part in the correspondence that I read, many nations wrote to state they are looking to the United States for leadership, and will follow the U.S. guidelines when they are published. In the light of this afternoon's press conference, I think that is particularly important.

The last point that I would like to make is that Dr. Fredrickson mentioned that the Interagency Committee listed registration of such research with a national registry. However, there is a parenthetical opening for industry that reads as follows: "Subject to appropriate safeguards to protect proprietary interests," which means that they might not have to register their projects.

FREDRICKSON: Thank you, Mrs. Simring. I am glad to meet you even at this distance, and I hope to close the gap between us.

Indeed, the volume that I referred to does refer only to correspondence relative to the guidelines. Many of the subsequent letters we

have received will have a broader base because more action has occurred since that time. There will be another issuance. I know that some of your correspondence will also appear there.

With respect to extension of the U.S. guidelines, it is true that there are other countries that are using them, as well as the United Kingdom guidelines. You will hear more about that, I am sure, in the final description.

With respect to the matter of registration and the issue of proprietary information, this is certainly one matter which the Interagency Committee is discussing and will grapple with completely, you can be sure.

AUDIENCE: Dr. Fredrickson, like many people I am beginning to share a mania against federal intrusion into so many aspects, and I think it is rare and unique for the American scientific community to actually invite a federal incursion. Yet, with so many recent experiences, occupational safety and health and what have you, it has been proven that the federal government is probably the least adept. I am happy to see that you are working with the Hill on legislation, but you just mentioned that the NIH doesn't have or want enforcement authority regarding this work. Who would the legislation give it to? HEW? Federal bureaucrats? Who is going to monitor it? I assume that there will be legislation, but I hate to see an element of control removed from the scientific community, and I wonder who they will award it to.

FREDRICKSON: I am not sure to whom it will be awarded either. But you can be sure that this is a matter which the committee is now actively considering and will deal with in its report.