STANFORD

20 April 1977

Hon. Daniel J. Flood
House Appropriations Subcommittee
Room 2358
Rayburn House Office Bldg.
Washington D.C., 20215

Re: Hearings on HEW/NIGMS appropns.

Dear Mr. Flood:

I appreciate the opportunity to forward some brief remarks for the record of your committee, though I regret it was not possible for me to come to Washington at this time to appear in person.

A considerable number of other people working in the scientific community have also, I understand, made submissions that may relieve me of the necessity to restate detailed justifications for the indispensable work of the NIGMS. In fact, I believe it is very well understood why there is a continuing need to support the basic scientific foundations of health research, at the same time that there is increasing impatience and impetus to demand practical improvements in the health of the public as evidence of the benefits of that investment. The more we know, and the closer we come to grips with a host of everyday problems, the more we realize our profound ignorance that impedes easy answers to them. Without the work funded by NIGMS there would be serious difficulties in accumulating the stock of fundamental knowledge that we still need, urgently and desperately, to be able to combat the natural imperatives of disease, aging and death.

This is, as you recognize from many years of experience and responsibility, the common wisdom about the importance of basic science; and I would be the last one to deprecate it. However, I am not sure it tells the whole story. In my own view, values that are at least as important as the 'accumulation of factual knowledge' are the maintenance of the critical scientific tradition within our medical schools and universities, and the training of younger workers within that tradition. Without it, we would soon revert to dogmatic recipes for the diagnosis and treatment of disease: the human penchant for easy answers to hard problems is very well illustrated by the market for nostrums and horoscopes, and before it adopted the scientific tradition, the medical profession itself was equally liable to irrational myths.

However, the NIGMS is charged with much more than maintaining the vitality of research in such basic sciences as biochemistry, genetics and cell biology. To fulfill its responsibility as a foundation-stone of the National Institutes of HEALTH, it must also work to sustain a continuum of expertise and concern about more practical problems that arise from the consideration of disease. There are not many administrative instruments to help support this function; and it comes about mainly as a side-effect: the medical school that has strong and well-supported research programs, and also effective clinical programs, may have the institutional strength and capability to develop that continuum from its own ethos and resources. This does happen, but one is obliged to say often in spite of, rather than in response to, official doctrine about the accountability of research projects one-by-one and year-by-year to the central administration. Exceptionally, efforts like the Genetics Research Centers and program-project grants do provide direct support to the integrity of that continuum. The project system is the basis of quality control and of the support of the creative initiative of individual scientists, and must continue to be the principal vehicle -- but for the reasons suggested perhaps not the only one -- for the identification and furtherance of the scientifically most promising efforts.

To insist on the fundamental importance of basic science is not to ignore the impatience for practical results that I mentioned earlier, and that we all know to be a political reality. I share that impatience, and wish I understood better ways to satisfy it more quickly. With all of the important and exciting promise of current findings in the biochemical genetics of man, I also realise that the scientific foundations of that effort were laid in 1941. That was the work of Beadle and Tatum on the 'Biochemical Genetics of Nutritional Mutants in the Red Bread Mold, Neurospora'. We can trace a direct line of intellectual and methodological connection for 35 years between those studies and our present glimmers of insight into the biochemical genetics of heart disease, and perhaps even of schizophrenia. Policy makers might well ask: is there no way that such an interval could be shortened; will we have to wait another 35 years before we can see the real fruits of that scientific breakthrough?

I am not sure that I know the best answers to such a question; I believe it is sometimes put forward quite mischievously or destructively, and often with disastrous remedies in mind -- akin to killing the goose that lays golden eggs. I do believe that it is time to ask it soberly and constructively as we seek to improve our long range policies for the support of research and the improvement of health. The one answer that I will defend right out is that our progress in dealing with such complex questions can be no better than the vitality of our institutions that have the responsibility of attacking them. In the system of grants to individual projects by annual appropriation, there is an assumption that these institutions, and the availability of creative workers can be taken for granted; that they will always be there to respond to a crash appropriation when a given need is perceived over some short period of time.

Policy makers who articulate this impatience must also be aware that other social imperatives are at cross-purposes with the most expeditious research effectiveness, particularly where human disease is directly involved. To a minor degree because of the substance of new restrictions intended to safeguard the rights of human subjects in experimentation, and to a major degree because of the enforcement bureaucracy needed to sustain those rights by prior authorization, such research is significantly impeded. Similar considerations apply to many other aspects of scientific accountability. I understand the weight of these extra-scientific considerations, and mention them only in the spirit of realism -- that we should all understand that the accumulation of regulatory controls on science imposes a substantial cost together with their intended social benefits. When we speak of human experimentation, however, self-imposed limitations within the traditional Hippocratic framework already account for the principal reason why such research is already far,far slower than studies on experimental organisms. At a time when patients presented with acute life-threatening disease, like infections for which there was no therapy, one still had to take substantial risks, in desperation, that could more rapidly advance clinical science. So we are also in a very real sense the victims of our own success, both on the ethical side, and in the light of the remaining health problems that we must give high priority today -- the pervasive chronic ills like atherosclerosis, diabetes, schizophrenia.

The recourse that is left to us is fundamental, or transparent model diseases, or on focussed fragments of some major health issues. The hope is -- the best we have -- that a really fundamental understanding of biological process may enable us to approach the clinical situation with clear understanding, and that this can take the place of ethically dubious trial-and-error study of human disease. This can be asserted conscientiously and humbly, while still recognizing that purely empirical research has dominated many of the useful medical breakthroughs of the past three decades -- the antibiotics being the outstanding example. Comparable opportunities simply do not present themselves in the same fashion at this stage of scientific and social history.

Having said all this, I believe there is much more that needs to be learned about the processes by which scientific discovery is itself accomplished, how that process might be improved in respect to the education of scientists, the tools with which they work, and the institutions and career-frameworks that guide their lives. Equal attention must be given to the quickest translation of such discoveries in the understanding and prevention, and failing that, the treatment of the ill health.

Realizing that there is ample room for improvement in all of our enterprises, the NIGMS stands as a central spearhead for the mobilization of scientific wisdom for health, and I believe it will continue to show similar leadership in the continued refinement of the forms by which social purposes and the creativity and ambitions of individual scientists can most harmoniously be consolidated.

Yours sincerely,

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Professor of Genetics