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Dear Irving,

Thanks for sending me the letter you sent to Genetics. You are, of course, free to offer your opinions on the matter and they will certainly contribute to the value of the "debate". But I do want to take this opportunity, in private, to tell you my views about what you wrote.

I've learned a great many things by being involved in this business but particularly intriguing and dismaying has been the way people have reacted to the publication of the letter. There were those who saw our action as having been "defeatist", "irresponsible" and "threatening to the future of basic research" etc; others have seen it as "courageous", "selfless", "responsible" and "reflecting a new awareness of the social responsibility of science". Clearly the nature of the response depended on whose "ox was being gored"!

In a way it's no different than any other issue. Traditionally those who perceive a threat or are themselves threatened by a particular proposal predict repression, a halt to progress and even doom as an inevitable outcome of the proposed action. One has only to listen to the various contending sides in the public debate on environmental pollution, nuclear power plants, oil drilling and exploration, or closer to home, the monitoring and control of drug research and marketing. In a way your arguments sound to me to be those of the "ox" who's being gored. The power and pharmaceutical lobbies when faced with public and governmental supervision of their activities counter with the argument that supervision or regulation is not needed, that their motives and methods are clean, and that progress would be impeded. In effect their plea is we know best so let's not "rock the boat". In all the years we have talked, I've never heard you defend that position so I'm puzzled why you adopt that stance now; is it because now the questioning has come closer to home?

I know you've had more first-hand experience with how the human experimentation review boards work but surely you can't be an advocate of doing away with all regulations or requirements for review in human experimentation. And surely, Irv, you can't be

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naive enough to believe that if it were left to the best intentions of physician experimenters that the interests and well being of the patient or subject would be meticulously guarded? The fact that the system is not ideal and has excesses does not, it seems to me, mitigate against trying to improve the system. Ideally, the impediments put in the way of the investigator should be minimal and primarily those that can protect the individual against the careless or irresponsible experimenter. The alternative of doing away with the system entirely and relying on each investigator to embrace the credo you suggested on page three seems to me ludicrous and unrealistic. (If all people were like you, I'd accept that as being all that is necessary, but there are few Irving Crawfords and unfortunately for many the temptation to do the "big experiment" is overpowering. And would you accept the same assurances from the pharmaceutical industry?)

Now a word about your scientific arguments. What do you suppose is your batting average in correctly predicting the outcome of a new experimental program? Twenty five percent? Fifty percent? Even ninety percent? I dare say that most of us would think that if our predictions or models were correct a third of the time, we'd be doing very well indeed. So, what happens if your estimate of the hazard is wrong and maybe grossly wrong. What degree of risk in being wrong and thereby being confronted with an unforeseen consequence are you willing to accept?: In experiments carried out by others and by yourself?: Is a risk of 0.1 for some deleterious consequences acceptable? (I recall how concerned people were when Pauling was estimating that nuclear bomb testing in the atmosphere was increasing the risk of leukemia by fractions of a percent and how the military and their supporters told us the probabilities were so small and the potential benefits to our security were so great.) With what assurance can you say that SV40 or adeno; herpes virus genes have ever occurred in combination with PSC101 or colE1 or λ phage DNA? And if they had, how do the conditions that led to their elimination compare to those in our environment today? Is it possible that the selections being put on those molecules by the experimenter are very different than those encountered by the 1 in 10^{10} spontaneously generated hybrids? You may be unimpressed by the argument that E. coli can be made into a malevolent agent and you may suspect that E. coli is so feeble that it would have a tough time surviving in the real world of the intestine but You could be wrong! In fact just as wrong as we were in the past when our equally dogmatic statements turned out to be inoperative because we lacked certain information.

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The meeting that was proposed to discuss these matters will bring together people who have what information is available, to determine what we know and don't know and how we can get the relevant information and, equally, important, what do we do in the meantime.

I believe that some prudent thought and action beforehand is better than a policy of sticking our collective heads in the sand, uttering some pious thoughts about let's all be responsible and assuming it will be so, and then all commiserating together later. We surely don't need a repeat of the thalidomide experience or of the consequences of indiscriminate use of DDT. Maybe a little care before we leap would pay off in the long run.

With best regards to Edna,
Sincerely,

PB:af