March 17, 1967

Dr. Walter W. Stiern
212 Goodman Street
Bakersfield, California

Dear Dr. Stiern:

My tardiness in responding to your letter of October 17 should not be taken as a measure of my appreciation for the very insightful interest that you have taken in the problem of the utilization of animals for medical research purposes. Your letter has made a very accurate paraphrase of my own views as to the positive value of the replacement of street animals by breeding programs for these purposes. However, many of my colleagues have pointed out that the sudden imposition of serious restrictions on the use of impounded strays would impose a very serious burden on their research budgets at a time when the National Institutes of Health and other agencies are undergoing a de facto retrenchment. The too sudden imposition of restrictions could therefore have a very deleterious effect on the progress of medical research. If, however, the state were to pass a law with a realistic deadline, perhaps some five years hence, for the full implementation of a transition to calculated breeding programs, this might provide the necessary leverage to augment the necessary research funds.

Fortunately, a recent article in Medical World News helps to put the whole problem in reasonable perspective, and if these figures are reliable, the substitution of scientifically bred animals for the dogs and cats now used in medical laboratories would involve an increased national expenditure of certainly not more than $10 million. This figure in relation to our whole budget for medical research would certainly be a very positive investment to quiet the absolutely pointless antagonism between pet lovers and medical researchers.

The same article also reviews one of the more positive programs under NIH support at the University of Oregon for the breeding of special strains of dogs for laboratory purposes. I would also refer to Dr. Shannon's testimony before the Magnuson committee last summer, and I believe he will have copies not only of his testimony, but of other information from the National Institutes of Health, relating to some of your questions.

Some of my colleagues have been particularly critical of my recommendations if they were to enforce the use of pure-bred animals for so-called acute experiments. Until there has been more experience than has been possible in the past on the use of such animals, it is difficult to evaluate the positive advantages. However, I find it very difficult to believe that the expected

reproducibility of experimental results with carefully bred strains can fail to compensate for the additional cost of such animals, not to mention the other factors of improved previous care that you mention in your own letter. Of course, it would be important to take the views of acute-experimenting physiologists into account in any legislation that you may adopt.

Perhaps I should clarify that my use of the phrase "pure-bred" may not be the best recommendation from a strictly technical standpoint. There are many reasons to believe that first generation hybrids between two highly inbred strains will furnish the most vigorous and most uniform material for laboratory purposes, in exactly the same way that such hybrid corn is one of our most important agricultural commodities. The important thing is the reproducibility of the genotype, which is very well achieved in such F_1 hybrids. In general, highly inbred strains themselves may not be as vigorous as hybrid offspring. There is also some evidence to indicate that they may be developmentally somewhat more unstable, despite their uniform genotype. An excellent review of pharmacogenetics has geen published recently by Hans Meier, "Experimental Pharmocogenetics", Academic Press, New York. This is full of extremely useful information about the special properites of pure-bred strains.

To recapitulate, since so little work has been done so far on the establishment of properly bred strains of larger animals, my arguments must be based on general theoretical principles and on our experience in other fields of agriculture and animal husbandry. The results in these fields have, however, been so rewarding that I feel there can be little doubt about the validity of the conclusion about the absolute superiority of scientifically designed breeds for any kind of experimentation. You will, I trust, take note of some of the difficulties that I have mentioned that arise from too sudden an imposition of new restrictions. It might be more appropriate to establish a new era in animal experimentation by the use of positive measures, i.e., subsidies or tax relief in connection with research and testing programs that make a contribution to the use and development of such animal strains.

It will be very gratifying if the state of California could take special leadership in this field.

Yours cordially,

Joshua Lederberg
Professor of Genetics

P.S. The more I think of it the less importance I would attach to the distinction between acute and chronic experimentation as a criterion for the benefits of genetic uniformity in the animals used. However, many acute experiments involve the response of only a single tissue, i.e., smooth muscle, or heart, or voluntary muscle, and these are perhaps less likely to show obvious variation under genetic control than responses which depend on complicated metabolic relationships of an intact animal.

I would like to give some further thought to other positive measures that the State might take to encourage animal breeding programs. I believe it would be very profitable if you were to consult the chairman of the Departments of Genetics and Animal Husbandry at the University of California at Davis, and especially Professor Michael Lerner at the Department of Genetics at Berkeley.