

THE ROCKEFELLER UNIVERSITY

1230 YORK AVENUE

NEW YORK, NY 10021

JOSHUA LEDERBERG

PRESIDENT

2 July 1980

Dr. Nathaniel Barr  
U.S. Department of Energy  
OHER/EV E-201  
Washington, D.C. 20545

Dear Dr. Barr:

Thank you very much for sending me the application for a research grant from Dr. Richard Wilson. This work is the most cogent that I know directed towards the development of a comprehensive risk assessment model, the vulnerability of human populations to the health effects of various chemicals. Of particular importance is the systematic and comprehensive way in which information derived from laboratory studies on experimental animals and other test materials can be used to maximum advantage for unbiased predictions of their effects on the human. This is a matter of the highest national priority since policy choices having a profound effect on our energy, chemical, and general technological economy are so strongly influenced by concerns about adverse health effects. With the innumerable new chemical entities coming onto the market every year, and the indefinite proliferation of those that can be identified by sensitive analytical procedures in all of the environmental inputs to the human organism, it becomes a matter of compelling urgency to predict human effects from prior laboratory data. Especially important is the development of a cogent model for aggregating the first order effects of a variety of substances present at relatively low concentrations. Other considerations apply to various forms of radiation although here, more than for most chemicals, considerable information has also been obtained from known human exposures.

Besides the importance of these models for the estimation of human risk, the synoptic studies can also be expected to be most revealing where they focus attention on unusual discrepancies in the response of different species to a given chemical or in the performance of a given compound in a variety of assays which otherwise are generally highly correlated. For example, the characterization of compounds which have high mutagenic, but lower carcinogenic, activity, or vice versa, is one of our most important clues to the further specification of the biological mechanism of carcinogenesis. Discrepancies between species, or polymorphisms within them, can point the way to distinctive patterns of metabolism, or of cellular susceptibility to chemical entities, which again can shed important light on the fundamental biological processes. Thus these

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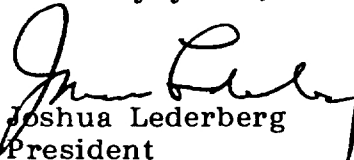
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studies overall have an important bearing not only on the optimal policies that can be derived from existing data from diverse sources; they can also be the most revealing pointers to new areas of investigation for the elucidation of basic mechanisms. Without more rationally oriented and comprehensive studies of this kind we can only be howling ourselves into a national or even global impasse in the policy choices for further development of energy resources as well as for technological advance in every field.

The outline of work presented by Professor Wilson is somewhat informal but this should not lead to any underestimation of the cogency of the thinking or of the energy and diligence that have been applied in data gathering. The publication "Interspecies Comparison of Carcinogenic Potency" is already a milestone in scientific basis of environmental policy, hopefully, an inspiration to many other investigators who until now have undertaken no more than a piecemeal examination of the potential horrors of individual substances. Whilst worst-case-oriented presentations may be a prudent policy for these matters taken one at a time, this can lead only to paralysis if applied consistently to the whole range of environmental inputs. All the more reason again for the essentiality of developing rigorous analytical methods for the aggregation of available data. Mandates imposed by TSCA and other important items of environmental legislation during the past decade can only be fulfilled by the further development, not only of individual mechanistic studies on particular substances, but also by the perfection of aggregative synoptic approaches of a kind presented here.

This work has my most enthusiastic endorsement and in my view should be supported as a matter of urgent national policy.

Sincerely yours,

  
Joshua Lederberg  
President