Letters

Microbial Containment

The *NIH [National Institutes of Health] Guidelines for Research Involving Recombinant DNA Molecules* define two general methods to reduce the hazards that might arise from the application of this technique. The first of these is called physical containment and is, in effect, the sum of all the physical and technical barriers that are designed to keep infectious materials confined to the laboratory. The second, which is called biological containment, is not truly a containment at all. It is the selection or construction of a host-vector system which has been so modified as to minimize its chances of survival should it escape from physical containment into the environment.

The long-awaited reports by Israel, Chan, Garon, Rowe, and Martin (2 Mar., pp. 883 and 887) have demonstrated a remarkable attenuation of the infectivity of polyoma virus DNA when it has been incorporated into either plasmid or phage DNA and inserted into *Escherichia coli* χ1776. These results would seem to indicate the existence of a third kind of containment, which for want of a better name is here called microbial containment. Microbial containment may be defined as the increment (or decrement) in safety which results when otherwise infectious DNA is spliced into a vector and this, in turn, is inserted into an appropriate microbial host. The studies with polyoma virus DNA reveal that this increment is large, possibly of the same order of magnitude as the increments in safety anticipated with approved physical and biological containment methods. It is suggested that, in future experimental designs, attention be paid not only to two but to three containments: physical, biological, and microbial. Only half in jest, it has been suggested that the safest way of handling infectious DNA materials in the future will be by the application of the recombinant DNA technique.

Certainly, extrapolation from these results must be cautious. As in the case of biological containment, where each candidate host-vector 2 system must be individually tested and proved, so in microbial containment each new situation must be separately tested. It is noteworthy, however, that contrary to the common experience wherein procedures deemed to be safe are found to be unsafe, in the present situation a procedure initially flagged as potentially dangerous has proved to the contrary to enhance safety. Let us rejoice!

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Grants: The Time Factor

In his editorial on the burden of competitive grants (16 Feb., p. 607), A. Carl Leopold suggests that now might be the moment to give thought to ways of reducing the time required to prepare (and review) research proposals.

Not a bad idea. And in fact the National Institutes of Health presently would like to encourage scientists to submit shorter and more cogent proposals. Peer review groups are, likewise, encouraged not to summarily reduce the tenure of meritorious proposals, but to allow those scientists to get down to the uninterrupted business of research as planned. Leopold's observation that currently a large number of proposals fail to obtain funding is related to the politics of national priorities rather than to review mechanisms.

However, even if research funds were unrealistically boundless, a wise researcher would still invest substantial time reviewing what has gone before and reflecting on what his or her own best approach ought to be. In facing the realities of time and support, and since neither will ever be open-ended, a major and systematic effort should continue to be made to help us all realize the best return on our finite dollars and years.

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I would like to respond to Leopold's perceptive editorial. Let me propose a specific reform that should retain the present system's most essential feature—accountability—yet greatly ease its burdens.

In brief, established investigators should compete on the basis of recent (say the past 5 years) accomplishments rather than proposals. For the investigator, it should be a reasonably simple task to collect a set of reprints and preprints and prepare a summary of their import. For the panels, it should be considerably easier to review accomplishments rather than promises.

Another very important advantage of an *accomplishment grant* system would be the encouragement of innovation. The investigator, not the panels, would judge the truly new and take the risks.

Under this proposed reform, the older *proposal grant* system would continue, but on a much reduced scale. It would be generally patronized only by beginning investigators, or by older ones who somehow needed a fresh start.

In addition to its apparent practicality, the spirit of this reform should appeal to a country weary of too much bureaucracy and too much regulation. It would be a move toward freer enterprise in research.

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Leopold's editorial brought a flash of enlightenment. The Egyptians had their pyramids, Roosevelt his WPA (Work Projects Administration), and we have the writing of grants.

The country has expensively educated more scientists than it feels it can employ as research scientists. The problem is not their salaries but the expense of their research.

How, then, can one occupy the time of these elegant intellectual athletes without permanently crippling their research abilities? How can they be kept in the "ready reserve," prepared to move into the breach if the nation decides it must catch up with Sputnik Russia or the war on cancer?

The solution is simple—let them write grant applications. They can think about research even if they can't actually perform it. It's a little like the draftees before World War II drilling with wooden rifles; but it is better than no drill at all.

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Szent-Györgyi's Research

In order to create a more complete picture of the situation described in the article "Albert Szent-Györgyi, electrons, and cancer" (News and Comment, 9 Feb., p. 522), I offer some additional information pertaining to this important problem. The author states that "nothing so far has been published about it [Szent-