

23 June 1966

Leonard A. Sagan, M.D.
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 Division of Biology and Medicine
 U.S. Atomic Energy Commission
 Washington, D. C. 20545

Dear Dr. Sagan:

This is in response to your request for comments on Dr. Sweet's proposal.

As you are aware, Dr. Sweet has managed to maintain a hope for the eventual success of neutron capture therapy throughout all of its ups and downs, particularly when others have been ready to write it off as a lost cause. I suppose that part of the reason for this is that his nearness to the problem, in seeing relatively large numbers of patients for whom all other modes of therapy are at least equally unsatisfactory, makes him correspondingly more aware of the importance of keeping on trying. This does not mean that I think he would persist in this line if the accumulated evidence sufficed to convince the standard objective observer that the cause were hopeless. I do not think that such is the case, but only that he may give more weight than others to leads that are at all promising.

It has more or less been agreed upon that the principal problems in NCT are those of depth dose ratios and clearance of the target compound from the blood (assuming that preferential uptake in the tumor and other prerequisite criteria are also satisfactorily met). The first of these problems has largely been met by the work of R. Fairchild and others in modifying the neutron beam spectrum. Even here, however, there remains considerable room for further improvement and there is a need for documentation of the dose patterns for various geometries and special conditions. The search for suitable labeled compounds is a much more difficult problem for many reasons, including the lack of a theoretical basis for predicting the relative merits of the various possibilities and the complexity of the testing procedures required for screening possible compounds.

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Dr. Sweet's group is probably the most active, though certainly not the only, group involved in the search for a suitable target compound. In particular, Dr. Frigerio has recently indicated some progress along this line in animal tests, but I have no information as to whether quantities sufficient for trials in patients are available or whether any such trials are scheduled. Dr. Sweet's proposal to continue work on the sulfhydryl-boron compounds sounds at least as promising as any other line that I have heard of. The proposal indicates a highly critical attitude, as shown by the investigation of the details of the distribution with respect to the capillary walls. (Incidentally, Fairchild has just completed a manuscript on an improved technique for determining the histological distribution of boron-10 using the autoradiographic method. The chief contribution is a procedure for reducing the background, a problem that has precluded studies of low concentrations.) The biologically-active compounds are also clearly possibilities and deserve investigation. I feel more pessimistic about the possibilities of the antigen approach, largely because of the large molecular weights involved, with the concomitant difficulty of their carrying enough boron atoms with them. However, it's not clearly impossible, and there may be a bonus in the intimate proximity to vital intracellular structures.

In summary, I offer the opinion that the proposed investigations have sufficient merit to justify their continued support. There is enough evidence to show that possibilities do remain in some lines and it is too early to say that some of the untested lines can be dismissed.

I am assuming that there is no question about the theoretical and dosimetric aspects of the proposal. Dr. Brownell is a recognized authority in these fields and can bring an unusual combination of talent and experience to bear on the problems to be investigated.

It was not feasible to follow your suggestions to have Fairchild review the proposal, but he is quite familiar with the MGH group's work, and I am sure that he would concur in the opinion that the proposals for dosimetry are sound and that they can be expected to be pursued at a high level of competence.

Sincerely yours,

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