# MEMORANDUM

DEPARTMENT OF HEALTH, EDUCATION, AND WELFARE
PUBLIC HEALTH SERVICE
NATIONAL INSTITUTES OF HEALTH
NATIONAL CANCER INSTITUTE

TO : Dr. James A. Duke, MPRL, USDA

DATE: March 13, 1979

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FROM : Dr. Matthew Suffness, PAPS, NPB

SUBJECT: GESOC - further clarification of purpose

I think I need to fill you and Rich Spjut in on a bit more of the rationale for GESOC and some of the things that are going on in the chemical end of things.

There is no doubt that further reports of active compounds are going to appear in the literature on genera on that list and that new antitumor agents are going to be discovered from some of these genera. However, further investigation of these genera by our program is not useful for the following reasons:

1. The types of compounds which are in these genera are predictable and have been extensively screened. None of the compounds show the kind of broad activity and therapeutic index which is necessary for further development. For example, 200 sesquiterpene lactones have been screened and, although most are cytotoxic, few have in vivo activity and the ones which do show only marginal activity in only one or two systems. Therefore, by eliminating genera where the activity is predictably due to such compounds some actives will be missed but these are useless anyway.

2. Many investigators take their leads from our program so that genera which are published as containing actives by our chemists are subsequently taken up by other chemists. By the time new compounds are isolated they are 5-10 years behind our program and I can't see why we need to concern ourselves with not finding every analog in a series of compounds which is not very good anyway.

3. Most of the compounds discovered in these genera are eventually acquired and screened in the NCI program through voluntary submissions of pure compounds either unsolicited or through our literature surveillance efforts.

4. As I see our program, the continuing study of genera which have produced active compounds of low interest is beating a dead horse. Certainly this will give us a higher number of active plants but we are not engaged in a numbers game. What the program needs to do is to find novel leads with high activity which have a chance of going somewhere and the chances of finding such leads in GESOC genera is negligible. The thrust of this program as envisioned

by NCI leaders and external review committees is for discovery of novel types of compounds with high in vivo activity and a broad spectrum of antitumor activity and there is no way I can justify plant collecting activities which are not in that direction.

5. The need for screening plants in families and genera new to the program is the best and maybe only way to meet the stated objectives and this is the reason for the push that John Douros and I have made in the past couple of years to get into new areas of the world for collection.

I hope this gives you a clearer view of what we are trying to do and why. I will be pleased to discuss this further with you at your convenience if you so desire.

Matthew Suffness

cc: Dr. Barclay
Mr. Spjut