

November 15, 1971

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Dear Pete,

I have read over the CCD material (for which, thanks) and especially the Swedish remarks about the definition of toxins. (I had made the identical remarks, even including alcohol, in discussions with Jim Leonard at Geneva the summer before).

Dragging toxins in by the heels, as substances, and packaging them with the microbes, has complicated all the definitions - as we have discussed many times. Now the Swedes are creeping down the toxins alley to sneak in as much CW as possible. The mischief is not in the aim but in the ambiguities it leaves behind.

I agree that toxins should be described in terms of what is now conventionally classified that way. But we had better nail down an explicit definition in accordance therewith.

- A toxin is
- 1) a chemical substance
  - 2) of polymeric, high molecular weight composition
  - 3) known to science at least initially as a byproduct of the growth of a microorganism
  - 4) whose potential use, if any, in war depends on its toxicity\* to man, animals or crops.

This will relieve developments like that of penicillin (which was a military monopoly at first in World War I) or pyrethrin insecticides or algal foods or other microbial specialty products from being confused with toxins.

If one admits compounds like tetrodotoxin, you are well on the way to (unilateral) moratorium on the development of new CW agents, since the toxicologists can hardly ignore what has been learned of the molecular specificities of such compounds.

We may well wish to achieve such a moratorium but this is hardly the route of choice. Furthermore, it will place investigators of such compounds under a stigma of "working with BW", apart from the formal prohibitions of the treaty.

\* death damage or disease  
(would that cover a few gas-bone toxins?)

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There remains an insoluble problem of the synthetic analogues of bacterial toxins which are bound to become much better known in the next decade. (I foresee at least a tenfold "improvement" in toxicity by the discovery of the "active fragments" of the toxin molecules). There is no logical boundary between a simple derivative of a natural toxin, and a completely novel chemical compound discovered by rational application of the principles learned from the natural toxins. Finally, very active work on the synthesis of hormone-like proteins will undoubtedly uncover new agents of high potency with uses/abuses analogous to the insecticides/nerve-gases. Not that insulin is moderately toxic to normal people (at doses of some few mg.); other hormones are even more active. A synthetic insulin would readily be described as "toxin-like".

But we can do little better than assert the hope that we will have perfected better controls on CW before the potential confusions in this area become material. I do believe we should narrow the zone of possible confusion by an explicit definition of toxin as indicated above. There are many examples of a rapid loss of precision where concepts as opprobrious as war gas or toxins are involved. We may recall that the history of counting toxins ~~is~~<sup>as</sup> BW was to preserve the credibility of a moratorium on biological production and stockpiling.

Sincerely yours,

Joshua Lederberg  
Professor of Genetics

P.S. I hope the above comments are useful to you; but as I read them over, I couldn't help but think, "God save us from the specialists!" These details relate to side issues, and I am sure we have to work them over very carefully to avoid mischievous confusions later. Also, they represent what I may individually have to offer from my own expertise. But they are so unrelated to the real problems, the underlying issues. My paper for the Stanford journal which I sent you, also touches on the paradoxes of dealing with arms control in technical detail, and the eventual posture of suffering evil gladly that must emerge, I suppose, from compromising with the realities of the world.

Where I feel cut off from reality is in a need for empirical justification that a particular course of action -- unilateral restraints, or dotting all the i's and crossing the t's in contractual agreements, for example -- is going to make any important difference in the long run. Perhaps insofar as history all deals with non-reproducible situations, it would be self-illusory to look for much scientific reassurance, which nags at me when I create purely speculative anticipations of good or harm.

Anyhow I wanted to say that what any of us knows how to do very well, is not necessarily the same thing as what is most needed to advance the human condition; and it would be easy to fall into the trap of confusing the two.