EPA.

February 14, 1977

(of TSCA)

Administrator
Environmental Protection Agency
401 M Street, South West
Washington, D.C. 20460

Subject: CFR parts 700-701/ESCA.

Dear Mr. Administrator,

These comments concern the draft for rules, dated February 4, 1977: general provisions and inventory reporting requirements, part 700-701, Toxic Substances Control Act.

These remarks are addressed principally to page 22, paragraph 2, that appeared to give manufacturers, in the name of the protection of confidential information, inwarranted and unlimited latitude in withholding information necessary for the assessment of potential risks of chemical introduced into commerce. This would frustrate one of the principal objectives of the Toxic Substances Control Act.

I refer specifically to Proposed Section 701.6 which would require the submission only of "a proposed name for the chemical substance which is as generic as necessary"; (2) a list of the elements of the chemical substance and its molecular weight; and (3) a relevant bibliography. The critical point is that the name "which is as generic as necessary", together with a mere listing of the elements of the substance are totally inadequate to permit an appraisal of the potential toxicity of the candidate substance. In fact, item 3 is inconsistent with the latitude of the former requirements since it is difficult to see how there can be any literature on the substance which has not identified it to a closer specification than the aforeset requirements.

It is true that a list of the constituent elements would be almost satisfactory if we are concerned only with inorganic substances: salts, minerals, and so forth. Even here, there are exceptions but the rule would be that one could usually predict the toxicity of an inorganic substance from its elemental composition.

When we come to organic molecules, the situation is totally transformed. The actual chemical and biological behavior of that organic substance (i.e. one containing carbon and other atoms) is almost totally dependent on the precise arrangement and configuration of these atoms, the matter in which they are interconnected. For example, as illustrated in the enclosed reprint publication, as simple a substance as phenol - which contains only 6 carbon atoms and 1 oxygen - comprises 2,237 possible isomers, each one of which has its own distinctive potential for biological and chemical behavior! Many common organic molecules have 10 or 12 or even 20 carbon atoms, and here the number of possible isomers is so large as to tax even our fastest computers, namely in the millions or billions!

over

RE DENDRAL

To illustrate the problem in another way, beta-propiolactone, $C_3H_4O_2$ is a relatively simple organic molecule which happens to have been already identified as a dangerous occupational carcinogen. But there are several other molecules having exactly the same elemental composition, for example acrylic acid which occurs naturally in fried foods. This is just to illustrate how the provision of less than all available structural information would frustrate one's efforts to make reasonable priority assessments of possible sources of environmental toxicity. Any larger molecule that included $C_3H_4O_2$ in its elemental composition might be potentially regarded as a derivative of beta-propiolactone than in the absence of other information would have to be subject to suspicious inquiry, so the whole process would become a meaningless ritual.

It is manifest that the TSCA embraces a profound conflict between established property rights in trade secrets and the public interest in improving the safety of the environment. It is even possible that the courts may hold that this is an unconstitutional infringement on those rights. However, I believe that it would be preferable to discover the proper lawful boundaries to define these conflicting claims than to proceed with a system that manifestly fails to meet the Congresses intentions and objectives, still imposes substantial economic burdens on the chemical industry, and seems to offer some unsubstantiated coloration of environmental protection.

I hope that other means can be found to protect the valid interests of the several parties in this conflict without deveiving ourselves or the public. about its substance.

On page 21 there is reference to the exclusion of impurities not deliberately present in the chemical reaction sequence. While it will be practically impossible to ascertain all impurities present in commercially practical preperations it is manifestly true that such impurities may be far more important as potential health hazards than the primary substances. We all know the well known example of the unfortunate impact of trace amounts of tetrachlorbenzodioxine in preparations derived from the relatively inoccuous trichlorophenol. When such information is known to the manufacturer or processor, surely this should also be brought to public attention.

Speaking as a research investigator I am gratified at the latitude which has been given with respect to small amounts of chemical substances required for research and testing and believe that the approach in this draft is indeed the most practical and workable one available without totally frustrating further investigation of chemicals in our environment.

Sincerely yours,

Joshua Lederberg
Professor of Genetics

JL/rr

P.S. One further comment on page 9 of the draft with respect to the handling of polymers. I would agree that the only practical approach to this problem at the present time is a classification in terms of the constituent monomers. And I would agree that some latitude with respect to minor components should also be entertained. However, in this circumstance one should distinguish between monomers which are related to one another as chemical homologs (the presence or absence of additional - CH_2 - residues, for example,) and which may therefore be expected to have similar biological effects, and minor components whose chemical and biological activity may be expected to be quite different. I would therefore propose that the 10% latitude be available only for such homologous monomers; monomers containing different functional groups should be registered at least down to the 1% level but future introductions involving substantial increases in such constituents should then be treated as new compositions.

Not all polymers can be treated in this way. After all, all of the diverse proteins of the human body including pharmacologically active hormones can be thought of as polymers of simple amino acids. In addition, the most dreaded toxins are likewise proteins of similar generic composition. Separate provision should therefore be made for polymers which might reasonably be expected to have unique biological activity along the lines of these considerations. It may not be necessary to issue final regulations at this time since the great majority of the applications of such materials will probably be in the realm of food additives, medical devices, or otherwise within FDA jurisdiction. However, note should be taken of this possible exception in order to anticipate future developments.