The CHAIRMAN. I am sure you are aware that the general position of the last four Food and Drug Administration Commissioners, plus a long line of distinguished clinicians, who have testified for several years before the committee has been that if the drugs in the marketplace meet compendial standards, they are therapeutically equivalent. That is kind of a rough generalization. Do you quarrel with that?

Mr. TRYGSTAD. Yes; I do not think that is correct at all. There are a number of studies that have been made to show that there are differences in bioavailability among many drug products. Also differences in therapeutic performance. I think the OTA report pointed this out, and I think we should get beyond simply the first sentence.

The CHAIRMAN. Well, the OTA report on page 22, however, is quite clear in support of the generalization I just made. The report says:

> Many, many drugs are given in thoroughly standard doses with little regard to the body size of the patient or the titration of the dosage to exactly the desired therapeutic effect. Such practice reflects the fact that for many drugs there is a wide margin between the concentration of the drug in the body and body fluids needed to produce the desired therapeutic effect and the concentration at which undesirable toxic effects begin to appear. Thus the standard dose is usually one that will produce in the vast majority of patients a concentration in the blood level well above the levels needed for therapeutic effect without reaching unacceptable levels of toxicity.
>
> Clearly under such circumstances a wide range in bioavailability could be tolerated without hazard of therapeutic failure.

So the authority you cite generally supports the generalization that I just made.

Mr. TRYGSTAD. Well, first of all there are other points made in the OTA report that I would like to get back to, but I think this is a rather interesting statement they have made there. It has some rather peculiar logic. What they are saying is that it really does not make any difference—say you take a 10-grain tablet, and it really does not make any difference with many of them if 1 grain gets into the system and works or 9 grains get into the system and work.

Now, if that same logic were to be applied to a dosage form of a product, you would say that even though this product is claimed to be a 5-grain tablet, it really does not make any difference whether there is one grain in it or 10 grains in it.

The CHAIRMAN. If one grain will accomplish the same therapeutic effects, it really does not make any difference if there is not a toxicity question, does it?

Mr. TRYGSTAD. That is correct if all of that is true, but I cannot imagine the Food and Drug Administration's allowing a product on the market that is labeled to have a content of five grains and letting one go by that has only one, or it maybe has nine grains in it.

Now, you are really talking about the same thing. If a patient takes a tablet, and he only gets the availability in his system of a grain of it or nine grains of it, it is practically the same thing as saying it does not make any difference if the labeled amount is in the product, or if it varies in any amount from one to nine grains.