have to be constantly alert but it has nothing to do per se, in my judgment, with the development of a pricing policy.

Senator NELSON. How many drugs have involved a bioavailability problem of consequence?

Dr. EDWARDS. If you don't mind, I would like to have Dr. Jennings address himself to that.

Dr. JENNINGS. I am not sure I can give you an exact figure, Mr. Chairman. I would say the number is within the range of a dozen —that is, where a problem has been identified under the rather strict criteria that we use to define generic inequivalence—that is, the same drug, the same dosage form, the same potency, and purported to have the same effect.

I think the problem of bioavailability is like any other problem of quality control. It requires on the part of the industry and the regulatory agency constant vigilance. We are apt to find different product effects from time to time and this is the whole reason for our system of surveillance and inspections and sample analysis.

Over the past several years I think we have become more sophisticated with respect to questions that relate to bioavailability and generic equivalence, the problems of dissolution and absorption, crystalization, and all that sort of thing.

There have been problems. There was a problem with chloramphenicol a couple of years ago that you are very familiar with, a problem which was resolved successfully. The smaller manufacturers, as you recall, after having the deficiency brought to their attention, by making a few changes in formula, were able to produce a product that was comparable to the originally approved product.

We more recently had a problem with digoxin and I think this one illustrates the growing sophistication on the part of the industry and the agency. Here the problem seemed to be related to the dissolution rate and there is good correlation between the dissolution time of the tablet and the amount of the drug that became biologically available. As a result of this finding, the USP has added a dissolution rate to their specifications and I feel this is the proper approach to the question of bioavailability—that is, one of quality control, including new and more sophisticated specifications as we become more and more familiar with the various aspects that contribute to problems of bioavailability.

Senator NELSON. Well, the record will speak for itself, but if I recall the testimony of the FDA on this issue, its position is that with respect to drugs which are composed of the same compound, in the same dosage form, meeting USP standards, the question of bioavailability is—these are my words—relatively insignificant in the whole drug picture.

Would you agree or disagree with that?

Dr. JENNINGS. Yes, sir, that is our opinion.

Senator NELSON. Let me turn to another issue. Yesterday I raised it with the Veterans Administration, though it is more properly within HEW. That was the question of the drug Aldomet.

That is the drug alpha-methyl DOPA, an antihypertensive.