The point I am trying to get across is that one doesn't necessarily have to make a blanket statement that all fixed combinations are bad. It just so happens that many are. But on occasion one can find a combination that might be valuable. I think we ought to have an open mind and judge each on its merits.

There are two examples that I want to cite which are used particularly by the British in the underdeveloped areas of the world. Here there is a tremendous amount of tuberculosis. Instead of using just isonazid alone, which is the usual drug for tuberculosis, they also combine it with another material called thiacetazone.

These can be put in the same capsule, and the African or the Asian patient can take one capsule a day, rather than as we do in the United States, give them isoniazid and another drug, para-aminosalicylic acid, which has to be taken in huge quantities which are not acceptable in that part of the world.

Senator NELSON. I didn't understand what is not acceptable in that part of the world.

Dr. KUNIN. It requires about 12 grams a day of para-aminosalicylic acid. That means that if you are going to send a fellow off into the bush after he has been diagnosed as having tuberculosis, he would have to carry a bucket with it, and he probably won't take it. So in this part of the world a fixed combination of isoniazid and thiacetazone, as used by the British, seems to be reasonable for certain practical purposes.

This is currently of no great importance to the United States, I am just citing it as an example.

Senator NELSON. So it is not that it is the best way to administer a drug under the best circumstances, but that under the circumstances over there it is about the only way?

Dr. KUNIN. That is right.

All I am trying to say is that, as we review all of the combinations of antimicrobial agents used in the United States today, one cannot make a good case for their continued use. However, one should keep an open mind and say, if one can demonstrate the efficacy of a combination which is greater than any one of the ingredients, and which has some economic or sociological advantage, we should be prepared to accept that combination provided that the evidence for efficacy is presented. Our charge is efficacy. Here we find all of these compounds not to be effective as fixed combinations. But there may be some exceptions.

I want to keep the door open just a little bit.

Senator NELSON. If I understand what you are saying thus far, the panel has not reviewed any fixed combination that they felt met the statutory standard of efficacy.

Dr. KUNIN. That is right. We want to be prepared, however, for any new evidence that the companies may have, any new development that may occur, so that we don't become so fixed and inflexible that we cannot be prepared to accept new advances that might be of advantage.

Actually when the combinations first came out, there was some rationale, at least one could present points of view that seemed to be reasonable. I think one of the questions that may trouble you, Senator Nelson, is why do physicians continue to use these combinations even after so many years of condemnation by, you might say, the academic men of the community. The reason, I believe, is that in the very be-