Dr. CROUT. They are intimately related, but different, and there are different standards that appropriately apply, depending on the kind of evidence you want in the two areas.

The issue of adequate well-controlled trials is paramount to a determination of effectiveness. The issue of adequate well-controlled trials is not paramount to a determination of safety.

We will take information related to safety anywhere we get it. It does not have to come out of well-controlled trials.

In looking at the two together, I agree with you the benefit-risk decision involves safety and effectiveness together.

Senator NELSON. It seems to me that we have got to be looking at it together.

Dr. CROUT. The benefit-risk decision requires they be looked at together.

Senator NELSON. But then you have to look at safety and efficacy. Everybody would agree that chloramphenicol is a very potent drug, very dangerous drug; however, according to the NAS/NRC study, it is indicated only when the patient is seriously ill, his life is threatened with disease, and no other antibiotic will work, so you have a case in which a drug, that everybody will say on its face is unsafe, but it is not unsafe in relationship to this patient, because the disease is a greater threat to his life. The incidence of aplastic anemia that may result from its use, in the one in 20,000, so you do have to look at both together, you agree with that?

Dr. CROUT. Absolutely.

Mr. MERRILL. I think what Dr. Crout is saying is just where we begin to work with DEA to build up our case, and the focus will be on the safety side of the equation, because it is that side of the balance which seems to have shifted since 1972.

Senator NELSON. All right.

It seems to me, with something as trivial as this class of drugs that you ought to be requiring some better evidence of efficacy over the long period. I should imagine that widespread street use would raise questions of safety.

Let me ask you another question. Dr. Henderson from Ottawa, who was on the Canadian panel that I mentioned before, testified that his panel recommended that the indication of obesity for this class of drugs be removed, and this was done. He also said that only in very limited cases, in treatment of obesity—I think that is a fair paraphrasing—would he give fenfluramine, because it was not addictive; that, in fact, lots of patients rejected it because they got upset stomachs or something else unpleasant; that there was no way that it would be abused; and in limited situations, he did use fenfluramine.

Have there been any studies done to compare the effectiveness of fenfluramine vis-a-vis the amphetamine congeners to see how effective fenfluramine is?

Dr. CROUT. There are studies comparing a variety of anorectics, one with the other.

Senator NELSON. They are underway now?

Dr. CROUT. No, they are done.

One of the purposes of the anorectic review in 1972 was to look at all of those studies simultaneously, and when you put them all