Mr. GORDON. The reason I asked this question is, I am just wondering if these are patented drugs, that is, not the original ones, but the modifications. As I understand it, a patent cannot be issued on an invention or discovery which would be obvious to a person skilled in the art.

Dr. FREEDMAN. Well, the phenothiazine nucleus, if I recall, was an antihelmentic, it was used against parasites. So that it is sort of common in itself. The butyrophenones which he mentioned are an entirely different molecular structure. Before a rearrangement can become a drug many biological tests must be made to arrive at a safe phenothiazine. I am not an expert on this. So you will get no more information. I don't know about patents.

Senator NELSON. Please proceed.

Dr. PILLARD. I am continuing the quote here at the bottom of page 2. This is from the Davis review:

We selected the studies which were methodologically best. They indicated that chlorpromazine, perphenazine, trifluprομazine, fluphenazine (Prolixin), trifluoperazine (Stelazine), prochlorperazine and thioridazine (Mellaril) were about equally effective * * *

The overall therapeutic equivalence of these phenothiazines is a generally accepted fact.

It is also true, however, that patients will vary somewhat in their response to these drugs; at times a patient who is doing poorly on one will seem to improve on another. If this sort of differential response could be predicted it would be good to know because each patient could be assigned the drug most effective against his particular symptoms. Can we identify constellations of symptoms or subtypes of schizophrenia each of which is most appropriately treated by a different phenothiazine? Galbrecht and Klett addressed themselves to this question by studying 310 schizophrenics randomly given one of three different phenothiazines. They used a method of computerized data analysis which would discover whether different types of patients were responding systematically to one drug or another. They conclude: "results from the present study failed to support the hypothesis that those patients who received their drug of choice (a computer's choice—not the patient's) would respond more favorably than those randomly assigned to the other drug—*in no case was evidence of differential drug action obtained*" (my italics).

Senator NELSON. They found that each of them was equally efficacious?

Dr. PILLARD. Right.

Senator NELSON. Did they find any differences in side effects?

Dr. PILLARD. They didn't report on that. In the sense that side effects might have influenced the main therapeutic effect, I presume they didn't, because they reported that they were equally efficacious.

This is an impressive statement, since Galbrecht and Klett are experienced researchers using the newest methods of data collection and analysis. Hollister, in a recent review of psychotropic drug treatment cites no research which contradicts Galbrecht and Klett's conclusion.

Evidence such as this, which never finds its way into pharmaceutical advertising, suggests that there is no way at present to predict the