annual Federal Service Pharmaceutical Seminar here in Washington, on November 10, last year—Dr. Meyers made this statement:

It also becomes important to establish the reproducibility of the dosage form of a drug from batch to batch if the clinical studies are not to be biased by an unknown variable.

He says:

A break in the control procedure—

This is specifically an endorsement of what I have just presented—

A break in the control procedures may be just as disastrous as the occurrence of unexpected toxicity.

Then finally—and I quote directly from his talk—

Evidence establishing the safety and effectiveness of one or more batches of a drug under investigation has no significance—

What he means is a drug product—

with respect to the safety of subsequent batches of the drug unless they can be shown to be the same as to identity, strength, quality, purity, with the batches studied.

Dr. Meyers, more recently in an appearance on November 28, at the APhA, Academy of Pharmaceutical Science—made this statement:

The active ingredient in a dosage form of a drug is probably not the sole determinant of its pharmacological effectiveness.

And Dr. Meyers also said that the physiological response may be a function of the formulations of the dosage as well as the active component.

Here is a very significant comment from this very experienced man in the Food and Drug Administration:

Regulations and guidance do not establish product quality. Assurance of product quality begins in exploratory research when the future product is nothing more than a gleam in the chemist's eye.

Mr. Chairman, what I am trying to portray in this chart, and with additive comments, is that generic equivalency does not necessarily denote therapeutic equivalency. I am reading from page 7:

The importance of particle form and size in antibiotics, like chloramphenicol, and in sulfadiazine and the anti-fungal agents, comes to mind. Variability in response to different formulations of the blood anticoagulant tablet, bishydroxycoumarin, are so significant that the choice of manufacturer source is clearly as important as the choice of the agent itself. The fineness of the drug in the tablet and how well the drug particle size is controlled by one manufacturing source as compared to another may very well determine whether dangerous clotting is prevented or serious internal bleeding occurs after ingestion of the usual dose. There are many examples of this sort.

Mr. Chairman, I have a notebook here which contains 211 references, which relate directly to this matter of pharmacological equivalency, to the science of biopharmaceutics, which seeks to explore the ways by which physical and chemical differences in the drug and nondrug components in drug products can affect the therapeutic safety and effectiveness of the drug products.

Now, the question has been raised, or the statement has been made