with respect to raw material components, intermediates, and at the finished product stage.

Finally, we come to what can be called Other In-Process Controls, one important function of which is to assure that all of the preceding four factors were, in fact, operative and correctly so. Thus the required records, reports, data, signatures, analytical and inspection test results on each batch would comprise an important segment of this factor.

Now, Mr. Chairman, let us assume that we have confirmed the safety and effectiveness of one or, at most, two or three batches of the product. However, when we get down to the matter of day-to-day, batch-to-batch production of the product, we obviously cannot clinically test each batch before releasing it to the marketplace. Such tests are extremely time-consuming and costly. Yet we must be sure that each batch is the clinical counterpart of the prototype batch(es).

Here, Mr. Chairman, is where the capably exercised Quality Control function comes into play. Quality control, by *locking into* each batch manufactured subsequently to the clinically tested, prototype batch(es) the five factors responsible for the product's safety and effectiveness, *services as a substitute for the clinical tests on a batch-to-batch basis!*

In other words, Mr. Chairman, quality control must be visualized as a chain, as shown in chart #3 (copy (copy attached). Thus, the manufacturer who has capably applied the chain throughout the batch's manufacture can be reasonably certain that compliance with the laboratory test results at the end of the manufacturing operation assures the safety and therapeutic effectiveness of the batch. However—*and this is important*—laboratory test results obtained on a sample of a batch or a shipment of tablets, without knowledge as to whether the quality control chain was applied at all or how effectively, may not be at all significant in evaluating the safety and therapeutic effectiveness of the batch or shipment.

Dr. Lueck will present specific evidence to support the inadequacy of apparent compliance with typical laboratory specifications to assure therapeutic performance. In other words, generic equivalency does not necessarily connote therapeutic equivalency.

The importance of particle form and size in antibiotics, like chloramphenicol, and in sulfadiazine and the anti-fungal agents, come to mind. Variability in response to different formulations of the blood anti-coagulant 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.

A few examples of the steps over and above standard procedures or official standards taken by a quality manufacturer to improve his product and distinguish it from competing products are the following:

(a) To lessen pain on injection. As you know, the injection of some drugs is painful. We are constantly striving to lessen such pain and some of us have learned that by the addition of certain ingredients we can produce a product that causes less pain on injection. This does not happen by accident.

(b) To produce medications, particularly injections, which lessen the liability of allergic reactions, which are sometimes not just troublesome but, on occasion, fatal. Much can be done to exclude as far as possible ingredients suspected of causing such reactions. Again, such procedures are sometimes costly, but the manufacturer who values his identity and reputation will constantly strive to attain higher levels of purity. The manufacturer who is interested only in "generic equivalency" may not.

(c) To produce more prompt solution in the stomach and absorption in the blood where this is desired. Variations in manufacturing procedures, differences in the crystal structure or particle size of the active ingredient and its purity, differences in the combination of non-drug components—all may affect the time necessary for the drug to dissolve in the gastrointestinal tract and may distinguish one product from another. Such differences can have a crucial effect on the therapeutic efficacy of the product.

(d) To retard solution in the stomach of a drug that is better absorbed in the intestinal tract, or which performs its function better if it is gradually released. All this is, and can be, influenced by different methods of compounding the product, or (if a tablet) by a different coating, or by the addition of other non-drug ingredients.