pretend to include all the specifications and tests that a highly skilled, conscientions manufacturer requires his product to meet before he will put his name on it.

Mr. Chairman, the chart which I have here (chart #1 attached) provides a dramatic illustration of the potency of some of the pharmaceuticals manufactured today and the importance of pharmaceutical know-how in manufacturing and quality control technology. It shows the proportionately small amount of drug that is contained in 100 tablets of this product. This small amount of drug creates a serious problem—that of making certain that each tablet in the batch contains exactly the correct fractional amount of the total quantity of drug used. This requires technological and control know-how. Furthermore, if an error occurs during manufacture and some tablets have too little drug while others have too much, the consequences to the patient could be serious—yet the cause of the error could not be identified by USP or NF tests. In other words, unless quality and uniformity are built into the batch, laboratory tests may very well not reveal the defect, nor can all the testing in the world of the batch after it is made instill quality into the batch.

The fact is that the detailed specifications needed to produce a quality drug product under good control procedures are so extensive and so all-encompassing as to defy inclusion in compendia of any sort. Quality control measures, records and reports used in leading drug firms for each batch of even the simplest drug product are massive. These begin with the raw materials and end with the consumption of the product. Details of the manufacturing and control procedures utilized for only a few products of a capable manufacturer would constitute a book in itself.

What I am saying is that conformance to compendial standards like those of the USP and NF, while of unquestioned importance, represents only part of the story. Total quality control involves much more. Mr. Chairman, with your kind permission I would like to call your attention to chart #2 (copy attached) to demonstrate what quality control is, what it does, and how it does it.

We all know that safety and effectiveness of a drug product are determined by well-designed, properly controlled and correctly executed clinical tests. Such tests are run by the manufacturer on one, sometimes two, but rarely, on more than two, batches of the product.

Having proved the safety and effectiveness of the product, we must ask ourselves this question: "To what facts are the product's safety and effectiveness due?"

I have indicated the five factors on chart #2. First, the specific COMPONENTS used—drug and non-drug components. Let me state, Mr. Chairman, that contrary to common belief, the drug component in most tablet products comprises less than 10% of the makeup of the tablet and that the number of components other than the drug may vary from two or three to as many as twenty or more.

The capable manufacturer makes sure that components all have pertinent, significant specifications and that these are in writing; that the components are purchased only from known, reputable vendors; that written, detailed instructions describing the manner and method of sampling incoming shipments of components exist and are followed; that all analytical test methods are written, are complete, up-to-date, available to the analysts, and are followed for establishing compliance with the written specifications. For example, an apparently trivial characteristic such as particle size of a component, whether the component is the active drug or not, may very well be a significant specification for which a test may be required prior to approving it for use in manufacturing a batch of the drug product.

The second factor is the formula. Neither the USP nor the NF lists the formula of the products contained therein and for good reason as we shall see later. The formula must list each component and the amount that is to be used. The master formula should be checked by no fewer than two capable, competent people, independently and individually, for correctness. Each batch formula derived from this master formula is produced by a process which assures against errors in transcribing, so that each batch formula will have to be correct if the master formula itself is correct.

The third factor is the Manufacturing (or Compounding) Procedure. Now, again, these are written, extremely exacting, detailed descriptions of every step of the manufacturing operation, including directions denoting the specific type of equipment to be used in each instance.

Fourth, are the various Analytical Tests, Inspections and Checks that must be carried out at certain stages during manufacture of the batch. These are in-process controls and they are important; they must be written, they must be detailed; there must be a lot of know-how in deriving the tests, inspections and checks to be followed at the various stages of the manufacturing operation—