

lots of the finished product were adjusted according to this specification; a crude method, indeed, in the light of present-day procedures. In the field of control of the quality of medicinal products, it can be likened to the first Wright brothers' flight as compared to present-day aviation.

Shortly thereafter, manufacturers of lesser quality products were forced, through the exercise of freedom of choice available to the prescribing physician to market standardized preparations. This, then, was the beginning of quality control.

Quality control is not a term that is exclusive to the pharmaceutical industry. Most major industries maintain extensive quality control departments. Their philosophy of quality control, however, is often based on one-hundred percent inspection of the finished product.

Inspection of every finished pharmaceutical product is not only impractical, but does not guarantee quality. Analysis is helpful, but cannot be done on *all* units of the product because it is destructive in nature and, of course, a one-hundred percent analysis would leave no product to administer to the patient.

Therefore, since inspection and analysis cannot alone assure quality in a product, a new approach to checking quality was born, the concept of control rather than analysis.

Control of the quality of a medicinal product is based on preventive measures. That is, the establishment of control procedures, methods, and systems involving all the components, the methods of manufacture, and the package and labeling of a product. These measures reduce or prevent errors or defects from entering into product, and thereby assures its quality.

Because of the advent of more and more complex pharmaceutical products with their diversified physiological actions, there has arisen a new concept in the realm of quality control—the theory and practice of “total quality control” as stated in the Principles of Total Quality Control recently adopted by the Pharmaceutical Manufacturers Association. A copy of this statement is attached as Exhibit A for inclusion in the record.

Guided by these principles, the function of the quality control division of a pharmaceutical company is to *coordinate, integrate, and provide an atmosphere within the company* for total quality control.

The term “quality” in a medicinal product can be defined as the assurance of safety, efficacy, and acceptability for the intended function of the product.

The product must be safe when used according to directions for the indications recommended. In other words, when the product is administered according to the directions on the labeling, using the recommended dosage, observing the cautions cited, and monitored by medical experts when needed, the product is considered to be safe within the framework of medical judgment.

The product must also be effective. It must do the job according to the claims which are made for it.

The efficacy of a product must be determined prior to the time of submission of a new drug application. The monitoring process, however, does not stop there. One aspect of total quality control requires that the effectiveness of a marketed product be under continuous surveillance. This is especially true in the area of individual patient responses, variations and tolerances, drug interaction, and long-term product stability.

The product must of course be acceptable. This refers, among other things, to the selection of the product form, such as a tablet, capsule or ampoule, etc. Packaging is also important. The package must preserve and protect the product, be clearly and accurately labeled, and be convenient to the physician and patient.

Mr. Chairman, now that we have briefly defined safety, efficacy, and acceptability, I would like to consider how these goals may be achieved in each product, batch after batch. We feel the first step of building quality into a product begins in the research or design phase.

Design Phase (Please refer to Addendum I)

It is in research that quality is designed into the product.

As indicated by my associates, a new drug substance is first studied extensively in animals to establish toxicity, safety, and pharmacological activity.

Chemists, bacteriologists, biologists, and pharmacists then design various dosage forms for the product. They establish standards of purity, methods of preparation, formulas, analytical specifications and collect stability data. In general, they find out all they can about the product prior to initiating clinical investigation studies concerning safety and efficacy in human subjects.