tion know-how—a konw-how by one manufacturer to formulate in such a manner that the tablet not only disinitegrated but released its drug for absorption and a physiological response. What detrimental effect this lack of therapeutic response had on the patients in this report I do not know. I do know, however, this detrimental effect with respect to the case I was personally involved in and I might say that it was a serious one. A change from a trade name brand to a generic one did save this patient several dollars at a cost of permnent physical body damage.

One way of administering the large doses of p-aminosalicylic acid needed in the treatment of tuberculosis with minimum discomfort to the patient is to prepare granules with shellac or other coatings. Now the availability of the drug from shellac coated granules decreases with age of the granules and after some time the blood levels attained are usually below the minimum therapeutic concentration. Since there are no standards for such coatings it again should be obvious that various brands of coated PAS granules cannot be considered equivalent—equivalent only in the sense that these products may contain the same amount of the drug. But certainly not equivalent with respect to clinical efficacy.

The effect of dicalcium phosphate and other metallic salts in depressing tetracycline absorption is well known to members of the profession of pharmacy. Prior to the time that this effect was known, interchanging brands of tetracycline made large differences in blood levels and therapeutic effects obtained and was discouraged. Why? Here obviously the filler maateirals used had some marked effect on the product. Again we can ask ourselves this generic equivalent question. The products all contain tetracycline—why then should some inert excipient mateiral prevent us from making the statement that these products aren't generically equivalent.

I would like to digress here for a few moments and point out some research that my students and I have been engaged in at the College for the past several years. We, as pharmacists, have been extremely interested in this question of generic equivalency. The increasing number of reports dealing with the therapeutic discrepancies of a drug in tablet form prepared by various firms certainly suggested that all tablets containing a certain drug do not behave alike. It was our belief that these discrepancies must be due to more than just effects of disintegration times, method of manufacture, size of drug particle and so on. We felt that, since many of our drugs are complex sophisticated molecules containing many functional groups capable of undergoing interaction or reactions with the various fillers that these interactions or complexes would occur when a tablet was manufactured and compressed. Our research started out with dogs which have been reported to show these therapeutic discrepancies. I've already mentioned some of these, for example, diuril, tetracycline and prednisone.

We have, for the first time by chemical and spectrophotometric methods (10), been able to show that drugs, such as those I've mentioned, do undergo surface chemical reactions with the fillers or so-called inert materials used to prepare these tablets. For example, tetracycline reacts chemically with the surface of the insoluble dicalcium phosphate filler used in the manufacture of such tablets. Such a complex keeps the drug tightly bound so that it dissolves at such a slow rate that no therapeutic level is obtained for the necessary physiological response. Prednisone undergoes similar surface interactions with many of the common filler materials used in the manufacture of solid dosage forms. This prednisone-excipient or filler interaction would certainly account for the lack of therapeutic response I mentioned earlier. Diuril also undergoes this type of interaction.

Our research with these and many other drugs point out that this type of interaction is common and that it depends on what type of filler is used.

One then, in formulating a tablet, does so as to minimize this effect by a scientific approach to this selection of excipient material.

The drug manufacturer, striving for the highest quality in his products, not only recognizes that these undesirable drug-excipient complexes may exist and formulates in such a way as to avoid these but also sends the product to the clinic to be absolutely sure the drug does give the desired therapeutic response. This type of approach is not only expensive but one that is absolutely necessary from the patient's point of view.

Can the generic house formulate in this manner and still produce cheap therapeutically active drugs? Some in Washington unfortunately think so.

This problem of clinical or therapeutic efficacy of drug products is a question which all members of the health team must be concerned with now and not the