The question of so-called "equivalency" arose the first time a drug product became available from more than one source.

To each new drug discovered (which already has a precise chemical name) a generic name or nonproprietary name is chosen as the common name for the drug. For example, "Prednisone" the generic name for the chemical compound 17,21-Dihydroxypregna-1,4-diene-3,11,20-trione. Upjohn's product of this chemical is Deltasone which is a trade name. Deltasone is a trade name for a finished dosage form containing this chemical or steroid.

This generic or common name is required by federal law. Now, while a generic name has nothing to do with the finished product or with the quality, somehow the expression "generic equivalent" has come to be used erroneously to imply equivalent quality, not only of the drug itself but of the dosage form.

A pharmaceutical company does not simply sell a drug in its basic chemical form. It sells one or more dosage forms of the drug. A compressed tablet of a given drug sold by company X is not necessarily equivalent to a compressed tablet sold by company Y in spite of the fact that each tablet contains the same active ingredient.

For purposes of this discussion, suppose you and I were asked to make an aspirin tablet—and to make ourselves as "equivalent" as possible we are told that we can use the same manufacturing equipment and the same lot of the pure aspirin or acetylsalicyclic acid chemical. Let us here also suppose that the two batches of tablets prepared are labelled A and B. The question we, as drug specialist should ask ourselves is—just how equivalent are the two lots of tablets? The only thing equivalent is that we both used the same aspirin chemical and the same manufacturing equipment—and it stops here. Not only will there be a significant difference in the excipients and fillers used by both of us since this choice is not part of any regulation but also to (a) the method used in preparing the granules prior to compression of the tablet, (b) the amount of pressure used in the tabletting operation, (c) the amount of aspirin in each tablet since decomposition of this chemical does occur during the manufacturing operation, and (d) the availability of the aspirin to the patient once taken.

I would, for the next few minutes, like to examine this "generic equivalent" term more closely by citing actual examples taken from clinical and pharmaceutical journals. But before I do let me quote from Dr. Nelson's and Levy's paper which appeared in the Journal of the American Medical Association (1) dealing with Pharmaceutical Formulations and Therapeutic Efficacy. They state that, and I quote, "Formulations of drugs into various dosage forms may modify profoundly the onset, intensity, and duration of physiologic response. It may also modify the correct dosage required by the patient, the incidence and intenstiy of side effects and the stability of the drug. Because of these modifications it is clear that in some cases choice of dosage form and manufacturer's brand may be as important as the choice of the actual therapeutic agent."

There are many factors which go into the manufacture of a quality and therapeutically active drug product. Dr. Max Sadove (2), a clinical researcher of the Veterans Hospital in Chicago, with some twenty years experience in drug evaluation lists some twenty-four factors. Time does not permit a discussion of all these, however, I would like to mention the more important ones—potency; compatability; purity; drug availability; drug solubility; effect of vehicle, base or other ingredients; quality of active ingredient; particle size; dissolution rate; stability; pH; and viscosity.

Differences in therapeutic efficacy among different generically equivalent dosage forms are often due to differences in the date at which the active ingredient or ingredients become available for absorption. This difference in the rate of absorption may greatly modify the onset, intensity and duration of the desired physiological response. Not only is this response modified but depending on the degree of absorption of the therapeutic agent from the dosage form, the incidence and intensity of side effects from the drug may also be altered. This difference in therapeutic efficacy may also be due to lack of stability, contamination and to sub-potent preparations. What I'm saying is simply this—the drug must be in solution and absorbed to be therapeutically effective. Factors then such as particle or crystal size, disintegration time, dissolution rate, etc., all have a tremendous bearing with respect to this absorption rate. Let me illustrate with some examples.

A European pharmaceutical firm (3) was asked to increase the physical size of their Dicumarol (bishydroxycoumarin) tablets to facilitate breaking the tablets for administration of half doses. This they did easily by just making the tablet larger. Patients who switched from the smaller tablets to the larger ones