General HAYES. Not necessarily.

Senator NELSON. What do they do to the tablet to keep it from falling apart? What tests have been made to show that the tablet still retains its biologic availability?

General HAYES. That is another part of this also. I took the mechanical aspect for simplicity because it is dose-related. If you have a bottle of powder that is 100 tablets as it started, you don't know what you have for a dosage. On the other hand, we do have problems of extremes of temperature and you can imagine what the temperature, for instance, is in the storage depot at Cam Ranh Bay in Vietnam as opposed to the more ideal circumstances in a stateside drugstore. So we have to assure that the potency is not affected by the extremes of temperature, even if the tablet stays in one piece through all of this mechanical manhandling. So we have these two problems.

Senator NELSON. So you are saying that in a substantial number of the drugs that you buy and send overseas, their compositions differ somehow? Is that what you are saying? Not just packaging. It is a question of compounding, putting the compound together in a different form or making a tablet that somehow or another has a different physical characteristic and still retains its therapeutic value?

General HAYES. Mr. Feinberg will pick up now.

Mr. FEINBERG. Mr. Nelson, we require as a result of the conditions of temperature and long storage, as described by General Hayes, we introduced standards which are guided toward assuring that if material does or is subjected to these conditions, that they would still be suitable for use at the time that they ultimately have to be used. And some examples—water content in tablets. Tablets are made generally with granulations where syrup is added or water is added and depending upon the amount of water or moisture that remains in that tablet, and you do have some, will determine with some items, many items, whether hydrolysis will take place, whether the molecule will split up and whether you are going to have a suitable product after it is subjected to these various conditions.

So we would require in fact a tablet with a lower moisture content.

Now, when you get to that point, you have to consider tablet hardness. It may be so hard that it won't disintegrate. So we have to introduce sometimes varying limits for disintegration or for dissolution.

We have had in the past experiences dealing with excessive breakage because the tablets or the products are handled the way they have to be handled. We have in some instances bioavailability tests where you test in advance to determine whether the tablets will hold up under these conditions. And then wherever we can, we have what we call accelerated aging tests where we subject these same products to some higher temperature, like 120 degrees for 2 weeks, sometimes varying from that, and attempt to establish whether the material will hold up under those circumstances in the laboratory because if it doesn't do it in the laboratory, it certainly will not hold up in the field.

Now, when we do establish these kinds of information, we then include them as a requirement of the specification.