

tion medically more desirable than lower, more prolonged, concentrations? The decision would be quite different in the case of an antibiotic in contrast with an antiepileptic preparation. What if by such criteria a generic formulation turns out to be biologically superior to the original proprietary? What if blood concentrations cannot be measured?

With some drugs, there are reasonably good analytical methods for biological assays, whereas for others a meaningful test is virtually impossible at this time. Consequently, the problem of the biological equivalence of drugs should be approached expectantly and progressively. Critical evidence of chemical and physical equivalence is the first order of business. Obviously, new drugs and accepted drugs of greatest pharmacodynamic action or therapeutic importance may additionally require careful biological scrutiny.

It would seem reasonable for the FDA to require that the generic manufacturer submit, in addition to evidence of chemical equivalence and purity, data on dissolution rate and data from other in vitro tests demonstrating equivalency. However, if there is evidence that in vitro evaluation or animal tests do not correlate well with pharmacodynamic effects in man, there may be need to resort to clinical tests. In this way, the principle of generic prescribing based on therapeutic equivalence may become acceptable to the medical profession and be supported by the pharmaceutical industry.

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Senator NELSON. I am puzzled about exactly what it means. The most distinguished pharmacologists in the country who have appeared before the committee have consistently taken the position that if the drug meets the USP and NF standards, they are equivalent. The only exception is that USP and NF may have missed something so that at some stage some excipient has a different effect from that of some other excipient for some reason or other. The testimony of the expert witnesses we have had is that the USP and NF standards are the best in the world, and for all practical purposes, drugs meeting their standards are equivalent. There are, I believe, about a half a dozen examples out of the thousands of drugs on the market which may meet USP standards and are not therapeutically equivalent.

That is the general position of Dr. Modell and a whole series of the most distinguished authorities in the country before this committee. Are you saying they are wrong?

Mr. STATLER. No, sir. We, in fact, use those sources and those references as a means for determining the drugs to be used in the VA, but there is a divergence of opinion among clinical pharmacologists as to the efficacy of certain equivalence of chemical drugs.

This is, of course, what we have alluded to. There are problems. Our physicians in our hospitals do weigh their clinical experience on the use on patients and do find from time to time that certain drugs do provide response to a better degree than others.

Senator NELSON. We have had testimonials like yours, but we have yet to have scientific evidence submitted. It is strange that in the 31½ years of our hearings we have not had any scientific evidence to show that where two drugs meet USP standards, the same compound, and yet they are not therapeutically equivalent. Do you have any clinical studies that demonstrate that? We wish that somebody would submit them if they are available, because we have not any yet.