cycline became available and, in 1952, tetracline—that is the basic chemical entity of both oxytetracycline and chlortetracycline—came into use. In 1959, demethylchlortetracycline became available for general use.

The tetracyclines are effective against rickettsia, a number of gram-negative and gram-positive bacteria, and the agents responsible for lymphogranuloma venereum, inclusion conjunctivitis and psittacosis. These are somewhat exotic diseases, but nevertheless represent, in large portions of the southern United States for the first two, and across the whole country for the last, significant disease problems in this United States.

The tetracyclines, because they were active against some types of infections, therefore became known as broad spectrum antibiotics. Although claims have been made for the superiority of some tetracyclines over others, their chemical, antimicrobial, pharmacological, and therapeutic properties are, with some exceptions, very much alike.

Senator NELSON. You say claims have been made for the superiority of some tetracyclines over others. What are you referring to?

Dr. LEY. Mr. Chairman, in the differences among tetracyclines the spectrum of activity is essentially identical for all. There are differences in performance and absorption and in the amount of tetracycline required to produce a given blood level among the various chemical manipulations of the tetracycline complex. So that the differences are chiefly in the mode or quantity of administration, so that with one product you may be able to maintain blood level after starting therapy by taking only one tablet a day, whereas with another product you may have to take several tablets or capsules several times a day to achieve the same blood levels.

Senator NELSON. Are they compounded in different ways with a specific purpose in mind?

Dr. LEY. No. The tetracyclines as a group have only excipients or inactive materials compounded with them, as we have discussed so far in the testimony. There are differences in the formulations, but these differences have no relationship in general to the way the product performs.

Senator NELSON. So in terms of the production of the drug, that is, the combining of excipients, this isn't done for the specific purpose of reaching a certain blood level at a certain time to meet a certain disease circumstance, and another one compounded in a different way to sustain a different blood level at a different time for a different disease situation, you are not saying that?

Dr. LEY. No, Senator. The changes in formulation that are characteristic of this group of drugs considered so far are simply changes that have been established by the various manufacturers to either stimulate killing or to provide greater stability for the active material in the capsule.

Senator NELSON. And your conclusion is that, with some exceptions, they are very much alike. What kind of exceptions are you referring to?

Dr. LEY. The exceptions are essentially all in the area of dosages required to achieve a given blood level. In terms of therapeutic response they are identical.