by the Bureau of Medicine's staff and then subsequently discussed with the firm. The firm had themselves prepared another draft so that actually the preparation was bilateral in this case.

Senator NELSON. What is the normal practice?

Dr. LEY. The normal practice, Senator, is for the firm to initiate the labeling change.

Senator NELSON. And if my recollection is correct, the firm prepares the labeling and at some stage the FDA reviews it, but ordinarily the FDA does not approve it prior to its being used?

Dr. LEY. That is correct, Senator.

Senator NELSON. In this particular case your department——

Dr. LEY. May I make one minor correction?

Senator NELSON. Yes, sir.

Dr. LEY. The labeling must be approved by FDA before it is used to accompany packages of the drug.

Senator NELSON. What about the indications and precautions and description of uses that are put in advertising?

Dr. LEY. The advertising claims and promotional claims need not be precleared by the FDA. However, they are based on labeling which is, and must be cleared by the agency before the labeling may be used as a basis for the advertisement or promotion.

Senator NELSON. Referring to that aspect of the advertising which lists the warnings and the precautions, does that have prior approval?

Dr. LEY. The body of information from which the warnings and precautions in an advertisement comes must have approval. Recent ads and the only current ad for this product features the entire package insert language for warnings and precautions.

Senator NELSON. On chloramphenicol, you mean?

Dr. LEY. Yes, sir.

Senator NELSON. Is this a special case?

Dr. LEY. This as it has evolved is a special case. With other drugs the manufacturer may prepare a brief summary which summarizes information in the package insert. That was not done in the case of this drug in any of the advertisements that were created after the committee hearing last year.

Senator NELSON. What about other ads where they are, of course, required to insert a warning and the precautions. Is that the language of the manufacturer, or is it language specifically approved by the FDA for all drugs?

Dr. LEY. In the case where specific warning statements are featured in the package insert and reproduced in the advertisements, that language must be approved by the agency.

Senator NELSON. But if they write an advertisement, do they have to include the warnings and precautions as are included in the package insert?

Dr. LEY. They must include these.

Senator NELSON. You may proceed.

Dr. LEY. The revised labeling included a carefully worded indications section expressed in restrictive terms. It included an estimate of the incidence of fatal aplastic anemia, based on a report made January 1, 1967, by the California Medical Association and State department of public health. It also states the desirability of hospitalizing patients being treated with chloramphenicol to facilitate observation during therapy.