In conclusion, we fully endorse the well established medical principle that care should be exercised in the use of any drug during pregnancy.

Sincerely yours,

J. RALPH FOWLER, M.D.
Medical Director,
J. B. Roerig & Co.
JOHN L. WATTERS, M.D.
Medical Director,
Pfizer Laboratories.

THE STUART CO.,
DIVISION OF ATLAS CHEMICAL INDUSTRIES, INC.,
Pasadena, Calif., May 10, 1966.

DEAR DOCTOR: We have just been advised by the Food and Drug Administration of conclusions reached by that agency concerning the teratogenicity of buclizine in rats. FDA has decided that buclizine should be contraindicated for use in early pregnancy. Recent data, including animal experiments still in progress in our Bio-Medical Research Laboratories, indicate that buclizine (an active ingredient in Bucladin and Softran) induces a teratogenic response in rats when administered at dosage levels substantially higher than the maximum recommended dose for humans. These findings are at variance with earlier experiments in mice and rats performed by others which disclosed no indication of teratogenicity at high dosage levels. We accept the FDA decision in this matter even though our own animal experiments are still inconclusive and we have not had an opportunity to examine the data or reports upon which the agency's decision is based.

We have been requested to add the following caution to the labeling for Bucladin and Softran:

CONTRAINDICATIONS

Buclizine, when administered to the pregnant rat, induced fetal abnormalities at doses above the human therapeutic range. Clinical data are not adequate to establish non-teratogenicity in early pregnancy. Until such data are available, buclizine is contraindicated for use in early pregnancy.

Since the nausea and vomiting of pregnancy (an indication for Bucladin) are not usually of a critical nature and can generally be controlled by other means, it does not seem feasible to conduct extensive clinical experimentation in women in early pregnancy to establish beyond doubt the non-teratogenicity of buclizine.

Bucladin was introduced in 1957. In this period of almost nine years, there have been no reports received by Stuart of human malformations in which it could be established that buclizine was the causative agent. Because of this extensive history of use in pregnancy without demonstrated teratogenic effect, there does not appear to be reasonable cause for concern among your pregnant patients who have taken Bucladin or Softran.

The Stuart Company will continue to make Bucladin and Softran available on prescription for use by your patients when indicated at any time except during early pregnancy.

Sincerely yours,

R. J. KROENERT, *General Manager.*

CHAS. PFIZER & CO., INC.,
New York, N.Y., April 27, 1966.

DEAR DOCTOR: The purpose of this letter is to request that you promptly destroy all samples of our Pfizer Laboratories and J. B. Roerig divisions, which are in your possession. We make this request because we have detected some instances of mislabeling of drug samples which were packaged and labeled for us by outside suppliers.

This request is made because we fully share with you the high degree of importance attaching to the integrity of any drug sample given to a patient. We have every confidence that our request will meet with your sympathetic understanding, and your aquiescence to our request.

It is important to emphasize that the instances of sample mix-ups that we have discovered all involve samples packaged by outside suppliers which we and other pharmaceutical manufacturers use from time to time for this purpose. We realize that you have no way of knowing which of the samples you have were