In the advertisement, we listed 21 studies comprising the total published "Deprol" literature containing data on *non-psychotic* depressions. While the ad does not reflect the fact, data from these studies were *excluded* in whole or in part if—

(*a*) the diagnosis was not entirely clear;

(*b*) the recommended maximum dose of 6 "Deprol" tablets per day was exceeded;

(*c*) other psychotropic drugs or electroshock were part of therapy.

Moderate, marked, excellent, and complete responses were counted as favorable, while mild, fair, slight, and no responses were counted as unfavorable.

Using the above criteria, the final number of patients included was 323 selected from ten of the 21 listed studies. Nine of the ten studies were uncontrolled, and most patients in the ten studies concomitantly received informal or structured psychotherapy. The reported therapeutic results (ranging from 0% in a study with two non-psychotic depressed patients, through 64% in a study with 53 such patients, to 90% in two studies with 38 and 41 such patients respectively) also include, to an undetermined degree, placebo responses and spontaneous remissions known to occur in the therapy of neurotic depression.

The factors noted above represent problems that exist in working with any literature and are present in some "Miltown" advertisements carrying the theme "one of a series". In order to avoid any misunderstanding, we have discontinued the use of these "Miltown" advertisements as well as the described "Deprol" advertisement.

Sincerely,

WALLACE PHARMACEUTICALS.

DEPARTMENT OF HEALTH, EDUCATION, AND WELFARE,
FOOD AND DRUG ADMINISTRATION,
Washington, D.C., March 15, 1967.

IMPORTANT PRESCRIBING INFORMATION

DEAR DOCTOR: The association of ulcerative stenotic lesions of the small bowel with the use of coated tablets of potassium chloride alone or combined with thiazide diuretics has been generally recognized by the medical community.

In March 1965 a warning paragraph was placed in the labeling of coated potassium chloride products, including those combined with thiazides, and of the thiazides themselves, pointing out this hazard. Since that time there has been a decline in the number of reported cases of this lesion.

That the hazard still exists is shown by the 75 cases reported to have occurred since the warning was issued. Of these, 63 were associated with the combined thiazide-potassium chloride products, 6 with thiazide where coated potassium chloride tablets were administered separately, and 6 with thiazide where it is not known if potassium chloride tablets were administered. Of the cases reported, 54 involved surgery, 51 of which were associated with the combination preparations. Among these cases, 12 deaths were reported, but as yet a definite causal relationship to the medication has not been established. Current data provide neither a determination of the frequency of occurrence of the lesion, nor conclusive evidence of a dose-related effect. Animal studies do suggest that the important etiologic factor is a high concentration of potassium chloride in contact with the mucosa. All the thiazide-potassium preparations are capable of causing the lesion in the monkey.

In view of this, the Food and Drug Administration has directed the manufacturers of thiazide-potassium chloride preparations to limit the indications for use in the package insert and other labeling to the following:

(Trade Name-Generic Name) is indicated for Thiazide-Responsive Edema of Cardiac, Rental or Hepatic failure, chronic steroid administration, and for hypertension, but only where development of even a mild degree of Hypokalemia might have serious consequences.

Note: (Trade Name-Generic Name) in the recommended dosage may not alone provide sufficient potassium to prevent hypokalemia in chronic Diuresis. (Trade Name-Generic Name) should never be used for the treatment of Hypokalemia.

We have further directed that the package insert and other labeling for potassium-thiazide preparations which also contain reserpine or rauwolfia be similarly revised. These preparations will be limited in their indications to the