summary" relating to side effects, warnings and contraindications. The following important ideas relating to patient safety which are set out in the approved NDA labeling were not expressed in the "brief summary" part of the advertisement:

a. "Severe depression is a contraindication to the use of reserpine."

b. "If progressive increases in serum nitrogen (BUN, NPN, creatinine) occur, therapy should be discontinued.

c. "If patients are to undergo elective surgery requiring general anesthesia, reserpine should be discontinued at least 2 weeks beforehand."

d. "This drug should be used cautiously in hypertensive patients with renal insufficiency, particularly if such patients are digitalized."

e. "If there is evidence of myocardial irritability (extrasystoles, bigeminy or AV block), reduce the dose or discontinue SALUTENSIN regardless of whether the patient is on digitalis."

f. "Caution is also necessary when conditions exist which are known to alter serum electrolyte concentrations, e.g. vomiting and diarrhea."

g. "Decreases in serum potassium are more apt to occur in cases of fluid retention caused by hepatic cirrhosis and steroid administration."

h. "Increases in excretion [of sodium and chloride caused by hydroflumethiazide] may produce alterations in the concentrations or serum electrolytes resulting in hypochloremia, hypocloremic alkalosis, hyponatremia or hypokalemia." (The ads statement, "alteration in electrolyte balance . . . may occur" does not make it clear that sodium and chloride might be reduced to levels below normal and that there is a possibility of a serious clinical condition).

i. "Rarely, it may be necessary to stop thiazide therapy before hypokalemia can be alleviated."

j. "In states of pre-coma of hepatic origin, thiazide diuretics may precipitate coma."

The promotional text of the advertisement contains faulty and misleading representations as follows:

a. The claims that the use of Salutensin will "get blood pressure down sooner" and that use of Salutensin will yield "more successful management of hypertension," than "just thiazide-reserpine" have not been approved for labeling, nor is there evidence in the New Drug Application to support them.

b. Referring to the combination of thiazide, reserpine and protoveratrine-A the ad states: "Clinically, the advantages of such a combination have been summed up as follows: The concomitant use of reserpine and the thiazides and veratrum has greatly widened the therapeutic and toxic range, making veratrum more effective and simple to administer * * * It is unfortunate that more physicians do not take advantage of veratrum, thiazide, and reserpine to lower the arterial pressure simply, effectively and without side effects." The ad uses reference #2 (Finnerty) for the two-sentence statement quoted above. Such statement is objectionable for the following reasons:

(1) The reader is led to believe that Finnerty used proteveratrum A in his study. In fact, he prescribed Veriloid (alkavervir) and Unitensin (cryptenamine). (Protoveratrine A is a purified single alkaloid isolated from Veratrum album. Alkavervir is a partially purified extract containing a mixture of alkaloids, obtained from Veratrum *viride*. Cryptenamine is an alkaloid derived from an extract of Veratrum *viride*.)

(2) The ad misleads by quoting Finnerty out of context. The reader is led to believe that the author was advising the reader that the combination of veratrum, reserpine and thiazide lowers blood pressure, effectively and without side effect when a "simple" dosage schedule, supposedly like the one Bristol recommends, is followed. A review of Finnerty's article showed this not to be the case, for in the several sentences located between the two sentences quoted, the author gives these detailed instructions: the patient should eat at the same time every day; the patient should not eat for two hours after taking veratrum; a good beginning dosage of veratrum is 2 mg. three times a day, e.g., after breakfast, mid-afternoon and at bedtime, and then gradually increased over a period of two to three weeks—up to but not exceeding 4 mg. three times a day.

Also related to the problem of effectiveness and safety are the author's statements, elsewhere in his article, that the "thiazide" (chlorthalidone—which, incidentally, is not a thiazide) component of his combination therapy was given in a single 50 mg. daily dose (note that the recommended dosage range for the hydroflumethiazide in Salutensin is higher and the schedule permits the dose