of the diuretic to be given up to four times a day); that it was necessary to administer supplemental potassium to those digitalized patients who had been given a trial of other thiazides—other than chlorthalidone—to avoid arrhythmias, that a marked increase in toxic reactions occurs when more than 0.25 mg. of reserpine per day is administered (note that the dosage range recommended in the package insert for the reserpine component in Salutensin may be much higher than that recommended by Finnerty); that because mental depression from reserpine has resulted in suicides, monthly checkup is mandatory; that the combination of veratrum, thiazide and reserpine is indicated in moderately severe hypertension, and that he does not advocate the combination in mild or severe hypertension.

21 U.S.C. 352(f)(1) [*Reg. 1.106(b)(4)*]: Salutensin is a prescription drug within the meaning of 21 U.S.C. 353(b)(1)(C) in that it is limited to prescription use by its approved new drug application. Accordingly, since adequate directions for lay use cannot be written for a prescription drug, it is clear that the labeling for Salutensin here involved did not bear adequate directions for lay use as required by 21 U.S.C. 352(f)(1). Furthermore, the Salutensin involved here was not exempt from 21 U.S.C. 352(f)(1) as provided for by regulations 21 CFR 1.106(b) since it failed to comply with the condition for exemption set forth in subparagraph 4(i) of such regulations. This condition requires that any labeling of a prescription drug shall contain adequate information for use including indications, effects, dosages, routes, methods and frequency and duration of administration and any relevant hazards, contraindications, side effects and precautions under which practitioners licensed by law to administer the drug can use the drug safely and for the purpose for which it is intended and, if the drug is subject to 21 U.S.C. 355, the labeling providing such information shall be substantially the same as the labeling authorized by the approved new drug application for such drug.

In the case of Salutensin, examination of the Mailing Piece designated as "SH 3852 RV", which is labeling for the drug as described in regulations 21 CFR 1.105(1), has disclosed that such labeling is not substantially the same as that which is set forth in the approved new drug application for the drug.

1. This mailing piece deviates substantially from the approved package insert labeling by failing to disclose the following side effects, warnings and precautions:

a. Reduction of serum electrolyte concentrations may occur with Salutensin "resulting in hypochloremia, hypochloremis alkalosis, hyponatemia . . ." The warning in the mailing piece that "alterations in electrolyte balance . . . may occur" does not clearly inform the reader that the electrolytes, sodium and chloride, can be depressed below normal levels to cause these potentially serious clinical states.

b. "If indicated, potassium loss often may be easily replaced by including potassium-rich foods in the diet (tomato juice or orange juice or other citric juice, banana, etc.). Patients unable or unwilling to take fruit juice may be given potassium chloride 1 Cm 2 to 4 times daily by mouth. Rarely, it may be necessary to stop thiazide therapy before hypokalemia can be alleviated."

c. Some patients may have "insomnia" and "nightmares."

2. The promotional text of this mailing piece contains these faults:

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

b. This mailing piece also refers to the work by Finnerty (reference #2) in such manner as to mislead the reader.

c. The company's description of the work by Smith (reference #3) exaggerates a claim for efficacy yet fails to mention side effects reported by the author.

(1) The reader is not told that the subjects in this study were hospitalized and had an average age of 77 years. Without this information he is prevented from correctly evaluating the results of the author, and from posing the question of whether or not these patients could be expected to show similar blood pressure reductions on just one of the ingredients of Salutensin, i.e. the reserpine or the hydroflumethiazide.

(2) Further, the mailing piece fails to reveal that the physicians attending these patients were allowed to adjust the dosage of the drug within a range of 1 to 4 tablets daily. This information is clearly set out in the approved package insert. The failure to reveal this in the mailing piece is misleading because the