

(3) That two references, namely, a paper by L. B. Berman, M.D. et al., published in *Proc. Soc. Exp. Biol. Med.* 118: 333, 1965, and a paper by L. Bencomo, M.D. et al., published in *Cur. Therap. Res.* 7: 339, 1965, pertain to use of the drug when other diuretic regimens have failed when in fact the papers do not show that the patients in the studies were refractory to other diuretic therapy;

(4) That two references, namely a paper by D. E. Hutcheon, M.D. et al., published in *Arch. Int. Med.* 115: 542, 1965, and a paper by H. Kleinfelder, M.D. published in *German M. Month.* 8: 459, 1963, support the claim that natriuresis with furosemide far exceeds that of the thiazides and that there is no parallel increase in kaliuresis, but misleadingly fail to reveal that the papers also show that the 24-hour urinary potassium excretion is essentially no different with furosemide than with thiazide in most patients, and that potassium depletion and hypokalemia do occur with furosemide;

(5) That there is a "highly favorable urinary Na/K ratio" and "greatly enhanced Na, proportionately low increase in K excretion": but fail to present in fair balance (a) that there is almost always a marked increase in urinary potassium when furosemide is given as compared to potassium excretion with no diuretic, (b) that the 24-hour urinary potassium excretion is usually the same or greater with furosemide as compared with thiazide or mercurial diuretics, and (c) that notwithstanding the quoted claims, hypokalemia may develop during the use of furosemide;

(6) That data in graphic form obtained from two papers, namely, by R. J. Timmerman, M.D. published in *Curr. Therap. Res.* 6: 88, 1964 and by H. Kleinfelder, M.D. published in *German M. Month.* 8: 459, 1963, accurately reflect general experience concerning effectiveness of the drug but fail to reveal that the data are from studies conducted on only 15 patients in the former and four patients in the latter study;

(7) That furosemide is a "non-thiazide diuretic" but misleadingly fail to present at this point in fair balance that furosemide shares many important contraindications, warnings and side effects with the thiazides and in this important sense the two classes of compounds are quite similar; and

(8) In the advertisements in *Medical World News* of October 21, 1966, *Medical Economics* of October 31, 1966, and *MD Medical News Magazine* of November 1966, it is claimed that, "When the effects of Lasix (furosemide) and hydrochlorothiazide were compared over a 24-hour period, fluid output produced by Lasix (furosemide) was 200% greater, and sodium excretion was 167% greater," which claim is not a true statement in that the data in the paper by H. Kleinfelder, M.D. *German M. Month.* 8: 459, 1963, show that the correct percentages are 105% and 67%, respectively; and

(B) Each of the aforesaid advertisements suggest, contrary to the requirements of regulation 21 CFR 1.105(f) (1), uses for the drug that are not in the labeling accepted in the approved new drug application for the drug since the advertisements represent that the drug is for use in a variety of conditions "from the easy to control to the severe and thiazide refractory edemas . . ." and "Throughout the spectrum, from the mild to the most severe and refractory edema," which representations exceed the indications for use as specified in the labeling accepted in the approved new drug application.

4. That by reason of the foregoing, the aforesaid article is held illegally within the jurisdiction of this Court, and is liable to seizure and condemnation pursuant to the provisions of said Act, 21 U.S.C. 334.

Wherefore, plaintiff prays that process in due form of law according to the course of this Court in cases of actions in rem issue against the aforesaid article; that all persons having any interest therein be cited to appear herein and answer the aforesaid premises; that this Court decree the condemnation of the aforesaid article and grant plaintiff the costs of this proceeding against the claimant of the aforesaid article; that the aforesaid article be disposed of as this Court may direct pursuant to the provisions of said Act; and that plaintiff have such other and further relief as the case may require.

UNITED STATES OF AMERICA,
DREW J. T. O'KEEFE,
United States Attorney.

Assistant United States Attorney.