EXHIBIT E

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Digoxin recalls requested by FDA based on new dissolution requirements

The Food and Drug Administration has announced new, more stringent requirements for the manufacture of oral digoxin products. As a result, pharmacists should expect a recall of many digoxin tablets in the near future. Under the program, FDA will test individual batches for conformance with compendial standards, including dissolution. The FDA bases the new requirements on clinical data which show a significant correlation between *in vivo* bioavailability and *in vitro* dissolution rates. According to the FDA, the digoxin tablets that dissolved more rapidly demonstrated a higher bioavailability.

Because of the narrow margin between the therapeutic and toxic levels of digoxin and the potential for serious risk to cardiac patients using digoxin products which vary in bioavailability, the FDA has determined that immediate steps must be taken to assure improved uniformity of all digoxin products. This includes a recall of all digoxin products now on the market which do not meet the new requirements for *in vitro* dissolution rates.

The new dissolution requirements are based largely on a test procedure and specifications adopted in the Sixth USP Interim Revision Announcement of Nov. 15, 1973. Under the FDA requirements, the dissolution rate must always fall within a certain range; it is as unacceptable for a digoxin tablet to dissolve too rapidly as it is for the tablet to dissolve too slowly.

The FDA has stated that, as more definitive bioavailability data becomes available, still more stringent dissolution rate requirements may be set for digoxin.

Although complete information is not yet available on those manufacturers which will be requested by FDA to recall their digoxin, FDA initially has requested the following firms to recall certain lots of their digoxin products: Barr Laboratories, Inc. (lot 2221032); Blueline Chemical Company (lot 81335); Cord Laboratories, Inc. (lot 27781); Heather Drug Co. Inc. (lot 210073); E. W. Heun Company (lot MD578A); Kasco Efco Laboratories—E. Fougera and Company (lots 2087, 2635, 2768, 2819); Marshall Pharmaceutical Corporation (lots 7595, 7623); Parke Davis and Company (lot LG312A); Premo Pharmaceutical Laboratories, Inc. (lot B32817); Rexall Drug Company (lot D32014); and Stanley Drug Products, Inc. (lot 077306).

As noted in the Jan. 19 *Newsletter*, pharmacists should keep a record of the lot number and manufacturer's name of digoxin tablets dispensed to each patient in the event that the information is necessary for dosage adjustments of digoxin patients. FDA plans to advise practitioners of the changes in digoxin bioavailability resulting from product reformulations.

FDA is very apprehensive that patients now taking a digoxin product not conforming to the new requirements might now receive digoxin tablets of greater bioavailability and, hence, experience overdigitalization.

Needs of practitioners to highlight AGP sessions at 1974 APhA annual meeting

Effective communication with patients and prescribers and efficient management practices are both essential for a successful pharmacy practice, and the Academy of General Practice of Pharmacy has retained specialists in these fields for Academy sessions at the 1974 APhA Annual Meeting in Chicago.

Schmidt, Pryor and Company, a Kansas City management consultant firm, through a grant from the Upjohn Company, will present two sessions for practitioners, AGP President Donald O. Fedder announced after the Jan. 14-15 meeting of Academy Officers in Washington, D.C. The firm has had broad experience with pharmacists and other health care professionals.

Radioactive pharmaceuticals require special knowledge by pharmacists who handle them, and the Academy will attempt to serve the needs of these practitioners at the 1974 Annual Meeting by sponsoring a day-long symposium on the subject. The program will feature presentations on education, legal aspects, organization and operation of a nuclear pharmacy.

AGP Officers also approved preliminary plans for an all-day seminar on techniques of dosage form administration, to be co-sponsored by the Illinois Academy of Preceptors. The program, which will utilize pharmacists and nurses as instructors, will deal with such topics as rectal and vaginal dosage forms, oral liquids and solids, ophthalmics, otics, nasal preparations, pediatric dosage forms and injections.

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