REPORT OF UNTOWARD / ADVERSE EFFECTS OR REACTIONS

DATE: 3/21/95 PROTOCOL NUMBER: .92-54-50-01

PROTOCOL TITLE: A Randomized Clinical Trial of Leuprolide Depot plus Estrogen-Progestin 'Add-back' Therapy for-Leiomyomata Uteri

PRINCIPAL INVESTIGATOR: Andrew J. Friedman, M.D.

PHYSICIAN INVOLVED, IF ANY: N/A

PREVIOUSLY REPORTED: NO X YES - TO WHOM:

SUBMIT A COFY **OF** THE ABOVE **REPORT WITB THIS** NOTICE)

DATE AND TIME OF EVENT: 3/17/95

LOCATION: Ms. Kuha's place of employment

SUBJECT'S NAME: Donna Kuha BWH CHART NO: 086-47-86-9

SPECIFIC CIRCUMSTANCES Of EVENT:

Ms. Kuha has been involved in this randomized clinical trial for 6 months. During the first 3 months, Ms. Kuha was treated with Leuprolide Depot, 3.75 mg intramuscularly every 4 weeks plus elemental calcium, 1200 mg daily. During the latter 3 months of her involvement in the study, she continued on these two medications with the addition of Premarin (either 0.3 or 0.65 mg daily) plus Provera, 2.5 mg daily. Her 6-month visit was on March 9, 1995. On March 17, 1995, she was found either unconscious or semi-conscious at her place of work and was taken to the hospital. It was discovered that she had suffered a large left middle cerebral artery stroke with presenting symptoms of global aphasia and right hemiparesis. Dr. Suzanne Westbrook is her attending physician. Non-invasive studies to-date (patient is still hospitalized) have revealed a patent ductus arteriosis. She has a regular sinus rhythm, no evidence of carotid disease or lower extremity blood clots that have been identified at this time. To my knowledge, there are no published reports of stroke on patients with Leuprolide therapy. The doses of Premarin and Provera used are typical doses used for postmenopausal women. The patient was involved in the study as a medical treatment for uterine fibroids.

Andrew J. Friedman, M.D.

SIGNATURE OF PRINCIPAL INVESTIGATOR

AJF/ms

cc: Gerald Weisberg, M.D., Medical Director. TAP Pharmaceuticals. Inc., 2355 Waukegan Road, Deerfield, Illinois 60015

Dr. Sobel, Director, Division of Endocrinology and Metabolism. Center for Drug Evaluation and Research, HFD-5510, 5600 Fishers Lane, Rockville, Maryland 20857

'THIS REPORT IS TO BE USED AS NOTICE BY AN INVESTIGATOR FOR SPECIFIC CIRCUMSTANCES INVOLVING UNTOWARD EFFECTS OR REACTIONS UNDER AN APPROVED PROTOCOL.

rev. 1/93