The present studies were initiated to assess the abuse potential of buprenorphine in man. During the course of these studies, however, it became apparent that buprenorphine was a potent, long acting drug which suggested its possible utility as a maintenance drug in the treatment of opiate addiction and the studies were modified accordingly. It was thought that buprenorphine as a partial agonist of morphine with perhaps a greater affinity for the morphine receptor and a long duration of action would 1) be an effective blocker of morphine through the mechanism of cross tolerance and the mechanism of competitive dualism, 2) have some reinforcing effects, and 3) would produce only minimal physical dependence.

Three single dose studies were conducted. In each, drug effects were measured with change in pupillary diameter, subjects' and observers' single dose opiate questionnaires[6,12] and the subjective drug effects questionnaire[13] containing items from the MBG Scale and PCAG Scale and the LSD Specific Scale.

In the first study, subcutaneous buprenorphine, 0.2, 0.4 and 0.8 mg; subcutaneous morphine, 15 and 30 mg; and placebo were compared in 9 subjects utilizing the double blind crossover design. In these studies observations were made at 0.5, 1, 2, 3, 4, 5, 12, and 24 hours after drug administration. Buprenorphine produced typical morphine-like subjective effects and miosis but its effects were of slower onset than morphine and were longer lasting. There was a greater effect at 24 hours with all doses of buprenorphine than with the 30 mg dose of morphine. Subjects and observers identified buprenorphine predominantly as an opiate with a pattern of signs and symptoms similar to those for morphine. Because of the disparity in time action curves, dose response curves were constructed utilizing peak responses for each drug rather than total 5 hour scores. Buprenorphine produced dose-related increases in mean peak scores on miosis and all measures of morphine-like subjective effects and was estimated to be approximately 30 to 50 times more potent than morphine (Fig. 11). There is no evidence that buprenorphine produced elevations on the PCAG or LSD Scale scores greater than those produced by morphine (Figure 11). In these studies buprenorphine, like morphine, had emetic action but this emetic effect of buprenorphine would persist 8 to 12 hours after buprenorphine and was found disturbing by some of the subjects.

In the second study subcutaneous buprenorphine, 0.6 and 1.2 mg, and subcutaneous morphine, 20 and 40 mg, were compared to determine if the effects of buprenorphine plateaued on these measures as it did on certain measures in the non-tolerant, non-dependent chronic spinal dog.[16] On all measures the responses to 1.2 mg were less than responses to 40 mg of morphine. Relative potencies were obtained only on the miotic effects indicating again that buprenorphine was 1/25 to 1/30 as potent as