



## Evaluation of a Proprietary Algorithm to Provide a Clinical Adjunct to Predicting Dose Compliance

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### Introduction

▶ This study evaluated and modified the expected ranges (Enu) for Hydrocodone (HC) used by the Proprietary Algorithm with a urine immunoassay (FPIA) at three doses of HC using steady states urine samples.

▶ The Proprietary Algorithm is an adjunct to clinical assessment to determine whether patients are taking opiates and other medications as prescribed.

▶ It monitors patient compliance for a given dose of medication by determining a normalized urine medication concentration (Pnu) by modifying the Fluorescence Polarization Immunoassay (FPIA) response using the patient's sex, height, weight, and the specimen's pH and Specific Gravity (SG)

▶ The calculated urinary parameter, the Pnu, is compared with an expected normalized medication concentration range (Enu)

### Methods

▶ A prospective study of twenty (20) healthy naltrexone-blocked males and females were dosed every 6 hours to steady state ( 5 half-lives, approximately 1.5 days) on HC doses equivalent to 20, 60 and 120 mg per day. Urine samples were collected one hour before and after the last dose at each dose level.

### Methods

▶ The patients' normalized urine medications (HC) concentration (Pnu) was derived from the FPIA response and modifications based on the urine's specific gravity, pH, and the patient's sex, height, and weight. Naltrexone did not interfere with the FPIA measurement of the HC response

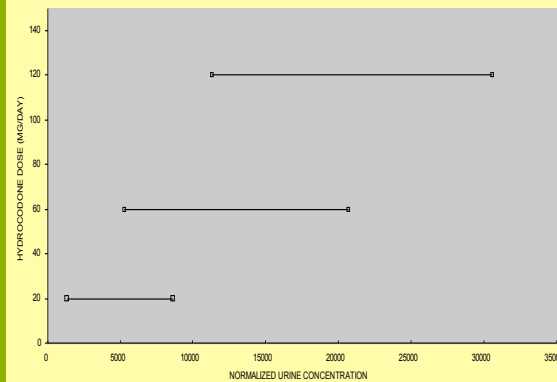
▶ Normalized concentrations (Pnu) were divided by the dose in mg and a log transformation was made prior to analysis. Results were compared among doses and subjects and no differences were found for these factors, therefore the overall mean and standard deviation of the 120 data points were used for calculation of limits on a per mg basis..

### Results

▶ Demographics: Twenty healthy volunteers (three female and 17 male) each received varying doses of HC and fixed doses of naltrexone according to the study protocol. These subjects ranged in age from 18 to 36 (mean = 23) and averaged 70.5 inches in height and 178 pounds in weight. Four were of Asian ethnicity and the remainder were Caucasian.

▶ The data derived from the study were used to establish 95% confidence limit of expected ranges (95% CLR) of values for average compliant individuals over the dosing tested (Enu).

Normal Ranges – Refractive Urine Concentration by dose with 95% Confidence Interval



### Discussion

▶ The results demonstrated a large degree of variability in HC metabolism and elimination for each dose level.

▶ This cohort of patients had large number of specific gravities (SG) < 1.004 contributing to difficulty in normalization of data.

▶ There may have been a greater percentage of SG<1.004 in the study as compared to clinical experience due to subjects hydrating in anticipation of scheduled urine sampling.

### Conclusion

▶ Data collected at a specified dose at steady state can be evaluated against the ranges derived in this study to determine with 95% confidence that compliant values fall in these ranges.

▶ The ranges do overlap for some doses but not for others.

▶ Discrimination between doses may be possible with methods to further decrease the variability of the adjustments.