## **Joint Meeting**



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Single-Dose, Bioequivalence, Rate of Absorption, and Food Effect Study of a New Paracetamol/Caffeine Formulation in Healthy Volunteers

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To determine the relative bioavailability and bioequivalence in fasted and semi-I fed states, and compare the rate and extent of absorption and food effect of two formulations of paracetamol + caffeine products: Panadol Extra (currently-marketed product) and Panadol Extra Advance. This study was designed as a single-center, open-label, randomized, single-dose, 4-way (2 formulations and 2 food states) crossover study. In each period, two caplets of either Extra Advance or current Extra, each totaling 1000 mg paracetamol + 130 mg caffeine, were orally administered. Thirty subjects were enrolled with all completing the study. Serial blood samples were collected at pre-dose until 10-hours post-dose. Plasma samples were assayed for paracetamol and caffeine concentration using HPLC/MS methods. Pharmacokinetic parameters were computed using a non-compartmental model. A linear mixed-effect model was used to analyze the logarithmically transformed  $AUC_{0-\infty}$ ,  $AUC_{0-t}$  and  $C_{max}$ as well as  $AUC_{0.30min}$  and  $AUC_{0.60min}$ .  $T_{max}$  was analyzed by a signed rank test on the within-subject differences. The new formulation was well tolerated by the subjects. For both paracetamol and caffeine, the 90% confidence intervals for the ratios of  $AUC_{0-\infty}$ ,  $AUC_{0-1}$ , and  $C_{max}$  for Extra Advance and current Extra, in both fasted and semi-fed states, all lied within the bioequivalence boundaries of [0.80, 1.25], except for paracetamol  $C_{max}$  in the fasted state, which was [1.11, 1.30] (mean ratio was 1.20). The new formulation showed significantly greater early absorption (AUC<sub>0-30min</sub> and AUC<sub>0-</sub>

 $_{60\text{min}}$ ) for both paracetamol and caffeine compared to Panadol Extra (P<0.0001) in both fasted and semi-fed states (ratios in the range of 1.4 to 7.7). The new formulation showed significantly shorter  $T_{\text{max}}$  for both paracetamol and caffeine (P<0.05), and paracetamol  $T_4$  (time to reach minimum therapeutic concentration in plasma of 4µg/ml) was twice as fast as Panadol Extra in both fasted and fed states. The new Panadol Extra Advnace formulation is bioequivalent to the currently marketed Panadol Extra formulation. Both paracetamol and caffeine are absorbed significantly faster with the new formulation compared to Panadol Extra.

## Biography

Dr. Dongzhou (Jeffery) Liu is working at GlaxoSmithKline as Medical Lead/Principal Clinical Investigator. Previously, he worked at Wyeth (now Pfizer) and Forest Labs with increasing responsibilities. His past 13 years' industry experiences include pharmaceutical, preclinical, and clinical development of medical products with making key contribution in launching 7 marketed Rx drug products. The areas of his expertise include ADME/PK/BE/BA study, PK/PD modeling & simulation, IVIVC/IVIE/IVMS, innovative drug design and delivery, Biopharmaceutical profiling. He obtained a PhD in Biochemistry, a MS in computer sciences, and a BS in Chemistry. He also obtained a EMBA. He has more than 50 publications and presented 20+ keynote speeches at global conferences. He is the lecture professor at SUNY-OId Westbury and Tianjin University School of Pharmacy. He is the members of NYAS, AAPS, ISSX, ACS, SAPA, etc.