

# 5<sup>th</sup> World Congress on **Bioavailability and Bioequivalence** Pharmaceutical R&D Summit

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## **The effect of stomach pH on the bioavailability of weakly basic oncology drugs and formulations options to reduce exposure variability**

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Some weakly basic drugs have relatively high solubility ( $>1$  mg/mL) at pH 1-2 and very low solubility ( $1-50$   $\mu$ g/mL) at intestinal pH (5-7). Such compounds achieve high solubility in the stomach and maintain a certain level of supersaturation in the intestine before crashing out to a much lower equilibrium solubility state. If the compound's absorption is not permeability limited and supersaturation is maintained for a reasonable length of time in the intestine, a high fraction of the drug will likely be absorbed. However, in reality, many oncology patients are taking proton pump inhibitors (PPI) that cause a significant increase in stomach pH to  $\sim 5$  and thus reducing the benefit of the drug's supersaturation in the intestine leading to a lower percentage of its fraction absorbed and resulting in inter and intra patients variability especially in Phase I clinical trials. To reduce exposure variability, scientists are often reformulating the drug and performing relative bioavailability studies to move forward with the new formulation. In this presentation, an in-vitro model was proposed to test for the "PPI" effect and test potential formulations options to mitigate this effect. Besides, absorption modeling examples are presented to outline the significant effect of higher stomach pH on the absorption of weakly basic drugs.

### **Biography**

Faraj Atassi is a registered pharmacist and received his Master's degree in Medicinal Chemistry from Philadelphia College of Pharmacy and PhD in Industrial and Physical Pharmacy from Purdue University. He is currently a Principal Scientist supporting Chemical and Pharmaceutical Profiling at Novartis. His areas of expertise include biopharmaceutics modeling, crystal engineering, solid-state characterization, and solid form selection. Previous to his current position he worked at Eli Lilly and Company in Indianapolis. He authored several peer-reviewed articles in the areas of solid state characterization and biopharmaceutics.

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