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## A Triphasic Physiologically Based Pharmacokinetic Model of Vitamin D3 and Metabolites in Vitamin D Insufficient Patients

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**Presenter Information**

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**Title:** A Triphasic Physiologically Based Pharmacokinetic Model of Vitamin D<sub>3</sub> and Metabolites in Vitamin D Insufficient Patients

**Presenter:** Dr. Colton W Sawyer, Southern New Hampshire University

**Abstract:** A physiologically based pharmacokinetic (PBPK) model of vitamin D<sub>3</sub> and metabolites was developed to model patients with vitamin D insufficiency status (25(OH)D<sub>3</sub> concentrations below 30 ng/ml) in a triphasic study design where patients moved between three vitamin D sufficiency states (insufficient, replenishing, sufficient). In this study, vitamin D insufficient patients were provided with a single dose of 125 ug cholecalciferol, followed for 14 days, and then provided with daily supplementation of 125 ug cholecalciferol for up to 16 weeks until vitamin D replete (plasma concentrations of 25(OH)D<sub>3</sub> above 30 ng/ml). Stimulatory and inhibitory effects of 1,25(OH)<sub>2</sub>D<sub>3</sub> were incorporated using fold-changes in the primary metabolic enzymes CYP27B1 and CYP24A1. The induction rate of each enzyme was allowed to vary based on total 1,25(OH)<sub>2</sub>D<sub>3</sub> concentration in target tissues, namely the liver, kidney, brain, or intestine. Measures of model predictions agree well with data from metabolites, with 85%-97% of data falling within 2-fold of unity for metabolites. This PBPK model could be a useful tool for understanding connections between vitamin D and its metabolites under a variety of clinical situations.