Laboratory demin/remineralization models have been used successfully to evaluate the likely efficacy of fluoride (F) toothpastes with 1100 ppm F or less, but these have not been able to differentiate among higher F concentrations. **Objective:** To design and test a new pH-cycling model that would demonstrate a fluoride dose response and discriminate between 1100 and 2800 ppm F. **Methods:** A series of experiments led to the following model. The mineralizing solution composition was formulated based upon analyses of natural saliva with the same Ca/P ratio but with a lower degree of supersaturation. Crowns of human molars (15 teeth/group, based on power analyses) were subjected to 14 days of alternating demineralization (6hr, pH 4.3, acetate, 2.0 mM Ca and P) and remineralization (17 hr, pH 7.0, 0.8 mM Ca, 2.4 mM P) with dentifrice treatment (1:3 slurry in DDW) 2x daily for 1 minute each (before and after the demin period). F dose response dentifrice formulations (NaF in hydrated silica abrasive) were: a) 250 ppm F, b) 1100 F, c) 2800 F, d) 5000 F. Results were assessed by cross-sectional microhardness, and mineral loss was calculated (\( \Delta Z \), vol. % mineral x \( \mu m \)). **Results:** Mean ± SD \( \Delta Z \) values were: a) 2846 ± 967; b) 1689 ± 801; c) 712 ± 604; d) 485 ± 168, with a > b > c = d (p < 0.05 ANOVA/Tukey). The dose response for log F versus \( \Delta Z \) was linear (r squared = 0.990). **Conclusions:** This new pH cycling model readily discriminates between 1100 and 2800 ppm F in dentifrice formulations and has an excellent fluoride dose response.