

Title: *The Effect of Povidone-iodine Ophthalmic Surgical Prep Solution on Respiration in Children Undergoing Strabismus Surgery with General Anesthesia*

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Statistical Analysis: An *a priori* size calculation was conducted prior to the study. Assuming no change in the peak to peak end-tidal CO₂ interval time after drop instillation in the saline group, and a peak to peak interval time variability of ± 4 seconds, a sample size of 50 patients per group (100 patients total) provided $> 80\%$ power to detect an increase in change in peak to peak interval of 2.5 seconds in the povidone-iodine group compared to the saline group assuming equal variance between the two groups using a 2-sided test with significance level at $\alpha=0.05$.

Descriptive statistics by treatment group were estimated for patient and procedural characteristics. Differences in peak to peak interval time between the saline and povidone-iodine exposure groups were examined using a linear mixed model approach. Based on the *a priori* analysis plan, the model included fixed effects for treatment, breath number, a treatment by breath number interaction and a random subject effect to account for correlation between measures collected on the same subject. The model also controlled for factors thought to be associated with respiratory rate including age, pre-term birth, history of apnea, and breath duration prior to drop installation. Comparisons in breath duration between treatment groups at each of 15 breaths post-drop instillation were estimated from the model using Bonferroni corrected significance.

A secondary outcome of interest was occurrence of a significant change in respiration. Although apnea has been defined in the literature as a breath duration of 10 to 20 seconds, this definition is arbitrary and fails to account for within and between subject variability of breath duration. To account for within and between subject variability, we defined changes in respiration as having a breath duration greater than twice the inner-quartile range above the

75th percentile for breaths within patient for the 10 breaths prior to and 15 breaths after instillation of drops. Associations between occurrence of change in respiration with patient and procedural characteristics were evaluated using univariate logistic regression models. Notably, no participants in the saline group experienced a change in respiration; therefore, all additional univariate tests were conducted on the subset of patients that received povidone-iodine drops. All analyses were conducted in SAS v.9.4 (SAS Institute, Cary NC, USA).