Appendix 1

Description of the IntellO$_2$™ device and Closed Loop Control Algorithm

The IntellO$_2$ proportional-integral-derivative (PID) controller algorithm works in concert with the Precision Flow nasal High Flow system, using patient SpO$_2$ to control FiO$_2$ delivery based on patient need. A Masimo oximeter incorporated into the IntellO$_2$ is used to measure the patient's SpO$_2$ (normal sensitivity, averaging time window set at 8 seconds). The use of the Masimo smart averaging and hysteresis algorithms by the Masimo SET™ SpO$_2$ helps limit the effect of artefacts that could cause rapid cycling of oxygen. Further, the SpO$_2$ monitor includes information on both perfusion detection and validity of the signal on which the algorithm acts. If the SpO$_2$ signal integrity is lost for 2 minutes or is degraded significantly by more than 50% over 4 minutes during automatic control, the device will adjust FiO$_2$ delivery to the greater of the following two FiO$_2$ fail-safe values: the set backup FiO$_2$ value (set by the clinician for the patient), or the median value of the last three auto FiO$_2$ values for 15 seconds delivered prior to the SpO$_2$ signal failure.

The device allows immediate override of automated control if a user performs a manual adjustment of FiO$_2$ on the Precision Flow HF system, returning to automated control on the next controller cycle (<10 seconds). The clinician user sets the target SpO$_2$ value, but also can set high and low alarm limits for SpO$_2$ (range 60-100%), FiO$_2$ (range 21-100%), and pulse rate (50-200 bpm). For this study, the SpO$_2$ target was 93%. For this study all patients were being monitored simultaneously on the normal NICU monitors with alarm settings set and responded to by the nursing staff.

The control algorithm functions to reduce the FiO$_2$ when SpO$_2$ exceeds the target value and is increased when SpO$_2$ falls below it. Unlike control systems which employ an SpO$_2$ target range, the IntellO$_2$ controller uses a discrete target value. The magnitude of the FiO$_2$ automatic adjustments is proportional to the relationship between the SpO$_2$ value and the target value, and the current dynamics of the SpO$_2$ response to FiO$_2$ administration.