

Questions for the manufacturer. Responses should be an amendment to the current PMA supplement (S14). Responses are likely to become part of the material sent to the panel.

1) The operator's manual page 587 and subsequent appears to be based on infant and child trials, and pilot studies of adults. The tables and some other material is based on the "Multi-center controlled trials" which are not defined but in context appear to be infant or child trials. I think that the discussion page 587, and page 594, and other pages should be oriented toward the adult randomized study currently under review, and the source of the information should be clearly designated (Prospective Randomized Multicenter Oscillator ARDS Trial (MOAT2)). Similarly, the data page 593 should be derived from the adult randomized study currently under review. Patient weights should be included in the table page 593.

2) Minimal information was provided on the physiologic variables observed during the course of the study. Data on these variables would aid in understanding aspects of the study results that are not apparent from the statistical outcomes alone. Please provide tabulated or graphical information for the HFOV and the Conventional group values (Mean, standard deviation and number of patients for that point) at intervals during the study (see for example table 3, page 1305 in: The Acute Respiratory Distress Syndrome Network: Ventilation with lower tidal volumes as compared with traditional tidal volumes for acute lung injury at the acute respiratory distress syndrome, N Engl J Med 2000;342:1301-1308. A column for the values prior to entry into the controlled treatment should also be provided. Subsequent data points should be included only when the patients were on their initially assigned ventilator. Variables can include mean airway pressure, PEEP, ventilator rate, Conventional tidal volume, HFOV delta P, arterial pH, PCO₂, PaO₂, FIO₂ PaO₂/FIO₂, Cardiac Output, PA wedge, Mean PA pressure, and CVP. The times to be displayed might be selected as one pre-treatment, two of the first day times, and one time on day 2, day 4, and day 6.

3) The outcome error page 164 table 8 last entry for CMV should be corrected.

4) In your submission (on page 46), you summarize testing of your device to determine its mean time to failure. Three units were tested, and each was shown to operate for at least 2000 hours. The mean time to failure was 2680 hours. In each case, the failure was due to a torn driver diaphragm. However, in the course of the clinical study, at least six driver diaphragm ruptures occurred over the less than 457 total days of ventilation with the Model 3100B. The associated estimate of the mean time to failure is 1828 hours. Please explain why failure of the driver diaphragms does not affect the safety and effectiveness of this device, and describe how the risk to the patient from an intra-procedure failure of your device is mitigated. It is possible that more frequent replacement of the oscillator assembly (which is now replaced every 2000 hours) would more effectively mitigate this risk.

5) The operator's manual for your device includes graphs which summarize its performance (see pages 516-520 of the submission). We note that the maximum driver power for the Model 3100B is greater than the maximum driver power for the approved Model 3100A. Please confirm that these performance graphs are for the Model 3100B.

6) Please provide an analysis of the poolability among sites and analysis of the effects on the statistical analysis of the protocol deviations "other" and "withdrawal of consent" table 6 PMA page 22.