Supplemental Material
Appendix 1

Apnoea Testing on veno-arterial extracorporeal membrane oxygenation (ECMO) Protocol (See Figure 2)

Preconditions
- Ensure pre-conditions are satisfied for clinical brain death testing
  - Consider neuromuscular stimulation
  - Consider opiate and benzodiazepine reversal agents
  - Consider high spinal injury

Other brain stem reflexes
- Complete other brain stem reflexes according to Australian and New Zealand Intensive Care Society (ANZICS) guideline

Baseline oxygenation and circuit setting titration
- Check baseline arterial blood gas (from right radial artery if peripheral VA-ECMO) to ensure patient oxygen saturations ($\text{SaO}_2 \geq 88\%$) and document baseline pH and partial pressure of carbon dioxide ($\text{PaCO}_2$). If $\text{PaCO}_2$ is chronically elevated, then calculate maximum target by adding on 20mmHg.

Patient oxygenation and ventilator monitoring for apnoea test
- Administer continuous flow of oxygen via a bag valve mask (BVM). Attach an end tidal carbon dioxide (ETCO$_2$) monitor and positive end expiratory valve (PEEP valve), set at 10 cmH$_2$O
- Include a capnometer in the circuit to detect ventilatory waveform
- Dedicate a staff member to observe and report ventilator effort with patient torso exposed

Commence apnoea test (reduce clearance of $\text{PaCO}_2$)
- Set inspired oxygen on fresh gas flow (FGF) to 1.0
- Reduce FGF by 50% (caution if FGF: ECMO flow < 0.5)
- Continuously observe for patient desaturation
- Monitor for signs of patient ventilatory effort

**Ensure safe circuit oxygenation and adequate hypercapnia**

- Measure arterial blood gas from post-oxygenator blood returning to the patient to ensure \( \text{SaO}_2 \geq 88\% \); if not, titrate FGF upwards until this target is met. *(ensure adequate circuit oxygenation)*
  - If \( \text{SaO}_2 < 88\% \), increase FGF to the lowest value that achieves the desired patient oxygen saturation
- Measure patient’s arterial blood gas via the right arm to ensure \( \text{SaO}_2 \geq 88\% \) *(adequate upper body perfusion)*
  - If \( \text{SaO}_2 < 88\% \) despite up titration in FGF,
    - Consider in increase in PEEP
    - Consider increasing ECMO blood flow to improve oxygen delivery (beware of access insufficiency)
    - Consider 1-2 rescue (lung) breaths

**Ensure adequate \( \text{PaCO}_2 \) for test completion**

- Continue to observe for signs of patient ventilatory effort
- Check post-oxygenator gas to ensure \( \text{PaCO}_2 > 60\text{mmHg} \)
- Recheck patient’s arterial blood gas after **five (5) minutes** or earlier if haemodynamic instability or desaturation <88% occur.
  - If \( \text{PaCO}_2 \) has not risen adequately, either wait longer if \( \text{PaCO}_2 \) beginning to rise or reduce FGF further (small decrements if FGF:ECMO blood flow < 0.5)
    - Repeat post-oxygenator (VA-ECMO) immediately then patient arterial blood gases after two minutes on new settings
    - Consider reducing FGF settings in increments of 10%. For each FGF changes, check post-oxygenator gas immediately to ensure adequate oxygenation and then check arterial blood gases at 2 minutes.

**Note:** FGF should NOT be reduced below 10% of ECMO blood flow – this may result in low saturations in post-oxygenator blood

**Endpoints for apnoea testing**
1. Patient’s blood gas and post-oxygenator gas show a rise in $\text{PaCO}_2 > 60\text{mmHg}$ (or 20% increase from baseline) with fall in $\text{pH} < 7.30$ : 

   **Consistent with brain death**

2. Development of hypoxia (arterial) and inadequate rise in $\text{PaCO}_2$ with FGF at minimum flow tolerated by patient: **apnoea testing is not possible**

3. Haemodynamic instability (mean arterial pressure [MAP] < 60 mmHg) that is unsupportable with inotropes: **apnoea testing is not possible**

4. Respiratory effort noted: **not brain dead**