Supplementary Online Content

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Supplement 15. A Checklist for Determination of Brain Death/Death by Neurologic Criteria

This supplementary material has been provided by the authors to give readers additional information about their work.

APPENDIX 15: DETERMINATION OF BRAIN DEATH/DEATH BY NEUROLOGIC CRITERIA CHECKLIST FOR USE IN ADULTS AND CHILDREN ≥ 36 WEEKS OF AGE

I. PATIENT INFORMATION

First Name		Affix patient label
Last Name		
Date of Birth *(YYYY-MM-DD)*		
ID number		

II. PREREQUISITES FOR CLINICAL EXAMINATION

*Pathological conditions, confounders and/or reversible conditions that may mimic brain death/death by neurologic criteria (BD/DNC) must be excluded before commencing the clinical exam. If any cannot be excluded (i.e. prerequisites are marked "no" or "not performed" below), ancillary testing is required. Refer to **Appendix A** and **Appendix F** (TTM) for further details.*

1. Established neurological diagnosis capable of causing BD/DNC	☐ Yes ☐ No Specify condition:
2. Neuroimaging demonstrating evidence of intracranial hypertension (severe cerebral edema and herniation) or intracranial pressure measurements ≥ MAP	☐ Yes ☐ No ☐ Not performed
3. Core body temperature ≥ 36°C	☐ Yes ☐ No Value:
4. Systolic BP ≥ 100 mmHg or MAP ≥ 60 mmHg for adults; age appropriate targets for pediatric patients	☐ Yes ☐ No Value:
5. Absence of pharmacologic paralysis	☐ Yes ☐ No
6. CNS depressing medications excluded	☐ Yes ☐ No
7. Alcohol intoxication excluded (If tested, alcohol blood levels are ≤ 80 mg/dL)	☐ Yes ☐ No
8. Absence of severe metabolic, acid-base and/or endocrine derangements that could impact the exam	☐ Yes ☐ No
9. Adequate observation period has taken place to establish irreversibility of coma (min 24 hours following birth asphyxia, resuscitated cardiac arrest and rewarming from therapeutic hypothermia)	☐ Yes ☐ No Observation period (hours):
Evaluation completed by	
Date (*YYYY-MM-DD*)	

III. CLINICAL EXAM

*Must be completed to fullest extent possible. Refer to **Appendix B** for testing details.*	FIRST EXAM			SECOND EXAM*		
	Yes	No	Not tested	Yes	No	Not tested
10. Coma	☐	☐		☐	☐	
11. Absent pupillary reflexes	☐	☐	☐	☐	☐	☐
12. Absent oculocephalic reflexes	☐	☐	☐	☐	☐	☐
13. Absent oculovestibular reflexes	☐	☐	☐	☐	☐	☐
14. Absent corneal reflexes	☐	☐	☐	☐	☐	☐
15. Absence of grimacing, facial muscle movement or motor response of the limbs other than spinally-mediated peripheral motor reflexes	☐	☐	☐	☐	☐	☐
16. Absent gag reflexes	☐	☐	☐	☐	☐	☐
17. Absent cough reflexes	☐	☐	☐	☐	☐	☐
18. Absence of sucking and rooting reflexes (newborns)	☐	☐	☐	☐	☐	☐

Final clinical examination results (check one):

☐ All elements of the clinical exam were completed and findings were consistent with BD/DNC.

☐ A portion of the clinical exam could not be performed; however, the remainder of the test was performed to the fullest extent possible and responses were consistent with BD/DNC. (Ancillary testing required.)
Reason(s) for incomplete testing (check all that apply):

- ☐ Anophthalmia
- ☐ Corneal trauma
- ☐ Fracture of the base of the skull or petrous temporal bone
- ☐ High cervical cord injury
- ☐ Ophthalmic surgery that influences pupillary reactivity
- ☐ Severe facial trauma
- ☐ Severe pre-existing neuromuscular disorder
- ☐ Severe orbital or scleral edema or chemosis
- ☐ Other (specify):

☐ One or more elements of the clinical exam were inconsistent with BD/DNC.

Examination performed by		
Date performed (*YYYY-MM-DD*)		
Time performed (*HR:MM AM/PM)*		

** Second exam required for pediatric patients*

IV. APNEA TEST

*Must be conducted only after clinical testing has been performed to the fullest extent possible and responses found to be consistent with BD/DNC. Refer to **Appendix C** for testing details.*	FIRST EXAM		SECOND EXAM* (if required)	
	Yes	**No**	**Yes**	**No**
APNEA TESTING PREREQUISITES				
19. No spontaneous respirations are being taken when the ventilator is set on a spontaneous breathing mode in a normocarbic state	☐	☐	☐	☐
20. Based on the ventilator requirements and pulmonary status, apnea testing is likely to be tolerated	☐	☐	☐	☐
21. Core body temperature ≥ 36°C	☐	☐	☐	☐
	Value:		Value:	
22. Systolic BP ≥ 100 mmHg or MAP ≥ 60 mmHg for adults; age appropriate targets for pediatric patients	☐	☐	☐	☐
	Value:		Value:	
APNEA TESTING PERFORMED	☐	☐	☐	☐
23. Pre-$PaCO_2$ value (mmHg)				
24. Pre-PaO_2 value (mmHg)				
25. Pre-testing pH value				
26. Apnea duration (minutes)				
27. Post-$PaCO_2$ value (mmHg)				
28. Post- PaO_2 value (mmHg)				
29. Post-testing pH value				
30. Time of post-testing lab results (*HR:MM AM/PM)*				

Final apnea testing results (check one):

☐ Apnea confirmed – no spontaneous respiratory efforts observed and targets reached (pH < 7.30 and final $PaCO_2$ ≥ 60 mmHg (8.0 kPa) or ≥ 20 mmHg (2.7 kPa) above any known chronic baseline $PaCO_2$ in patients with pre-existing hypercapnia).

☐ Apnea testing is inconclusive (could not be completed) due to:

- ☐ Systolic BP became < 100 mmHg or MAP < 60 mmHg
- ☐ Sustained oxygen desaturation < 85%
- ☐ Other (specify):

☐ Apnea testing is negative – spontaneous respirations were seen; findings are not consistent with BD/DNC.

Examination performed by		
Date performed (*YYYY-MM-DD*)		
Time performed (*HR:MM AM/PM)*		

**Second exam required for pediatric patients*

V. ANCILLARY TESTING

*Must be conducted only after clinical testing has been performed to the fullest extent possible and responses found to be consistent with BD/DNC. Refer to **Appendix D** for testing requirements.*	
31. Reason(s) for ancillary testing:	☐ Confounding conditions that could not be resolved ☐ Inability to complete all clinical tests ☐ Inability to complete apnea test ☐ Uncertainty regarding interpretation of spinally vs. cerebrally mediated motor responses ☐ Isolated brainstem pathology (if whole brain death is required) ☐ Required by law/regional guidelines ☐ Assist in family understanding/acceptance of BD/DNC ☐ Other (specify):
32. Type of ancillary testing performed	☐ Conventional 4 vessel cerebral angiography (DSA) ☐ Radionuclide study (SPECT) ☐ Transcranial Doppler (Do not use for pediatric patients): ☐ 2 exams performed ≥ 30 minutes apart ☐ Acoustic window confirmed ☐ Electroencephalography (EEG) and: ☐ SSEP ☐ BAER ☐ Other (specify):

Final ancillary testing results (check one):			
☐ Ancillary testing results are consistent with BD/DNC			
☐ Ancillary testing results are <u>not</u> consistent with BD/DNC			
☐ Ancillary testing results are inconclusive			
Date of testing *(YYYY-MM-DD)*		Time (*HR:MM AM/PM)*)	
Date of interpretation of results *(YYYY-MM-DD)*		Time (*HR:MM AM/PM)*	
Results interpreted by		Specialty	

VI. SUMMARY OF FINDINGS

Check one

☐	**BRAIN DEATH/DEATH BY NEUROLOGICAL CRITERIA CONFIRMED CLINICALLY** • Prerequisites for clinical testing have been fulfilled, (Section II), and • Results of clinical exams, including apnea testing, have been fully completed and are consistent with BD/DNC (Section III, IV) Date *(YYYY-MM-DD)* and time of death (*HR:MM AM/PM):* *(Record time of death in accordance with regional legislation, or if not dictated, as time the arterial $PaCO_2$ reaches the target during the apnea test as reported by the laboratory, for the most recent test if more than one test is performed)*
☐	**BRAIN DEATH/DEATH BY NEUROLOGICAL CRITERIA CONFIRMED WITH CLINICAL ASSESSMENT AND ANCILLARY TESTING** • Results of clinical exams, including apnea testing, where tested are consistent with BD/DNC (Section III, IV), and • Ancillary testing has been performed and results are consistent with BD/DNC (Section V) Date *(YYYY-MM-DD)* and time of death (*HR:MM AM/PM):* *(Record time of death in accordance with regional legislation, or if not dictated, as time the ancillary test results are formally interpreted and documented by the attending physician)*
☐	**BRAIN DEATH/DEATH BY NEUROLOGICAL CRITERIA NOT CONFIRMED** Provide reasons:

VII. SIGNATURE(S)

*Refer to **Appendix E** for details on required qualifications for determination of BD/DNC.*

FIRST EXAMINER		**SECOND EXAMINER (if required)**	
Name		Name	
Signature		Signature	
Specialty		Specialty	
Date (*YYYY-MM-DD*)		Date *(YYYY-MM-DD)*	
Time (*HR:MM AM/PM)*		Time (*HR:MM AM/PM)*	

APPENDIX 15: DETERMINATION OF BRAIN DEATH/DEATH BY NEUROLOGIC CRITERIA CHECKLIST FOR USE IN ADULTS AND CHILDREN ≥ 36 WEEKS OF AGE

APPENDIX A: PREREQUISITES FOR CLINICAL EXAMINATION

Brain death/death by neurologic criteria (BD/DNC) is defined as the complete and permanent loss of brain function as defined by an unresponsive coma with loss of capacity for consciousness, brainstem reflexes and the ability to breathe independently. This may result from permanent cessation of oxygenated circulation to the brain and/or after devastating brain injury. Persistence of cellular level neuronal and neuroendocrine activity does not preclude the determination. In the context of death determination, 'permanent' refers to loss of function that cannot resume spontaneously and will not be restored through intervention.

It is recommended that an assessment for determination of BD/DNC be made in all persons with devastating brain injuries who are believed to potentially meet criteria for BD/DNC, regardless of whether or not they are potential organ donors.

Established neurological diagnosis capable of causing BD/DNC	Prior to commencing a determination of BD/DNC, it must be demonstrated that the person has an established neurological diagnosis, the nature and severity of which is capable of resulting in the irreversible loss of the capacity for consciousness, the irreversible loss of all brainstem reflexes, and the irreversible loss of the ability to spontaneously breathe in the face of a carbon dioxide and acidosis challenge. Ensuring irreversibility of a person's clinical state in BD/DNC does not require performance of interventions to decrease intracranial pressure that are not judged to be clinically indicated. It is recognized that interventions to decrease intracranial pressure, such as hyperosmolar therapy, ventricular drainage and decompressive craniectomy, should be applied when clinically indicated during therapeutic phases of care. It is recommended that if these types of interventions are not indicated for the treatment of devastating brain injury, they should not be performed simply for the purpose of demonstrating irreversibility of the clinical state. If an assessment for BD/DNC is being made in a region that equates "whole brain death" with BD/DNC, in the setting of an isolated brainstem lesion or posterior circulation vascular lesion, ancillary testing should be performed. In these circumstances, it is suggested that BD/DNC should not be diagnosed until supratentorial and infratentorial blood flow is lost, even if the clinical examination and apnea test are suggestive of BD/DNC.
Neuroimaging	There should be neuroimaging demonstrating evidence of intracranial hypertension (severe cerebral edema and herniation) or intracranial pressure measurements ≥ MAP. In the absence of herniation on neuroimaging, caution should be taken when considering an evaluation for BD/DNC. For patients treated with TTM: If, after rewarming, their exam appears consistent with BD/DNC, it is recommended that neuroimaging be obtained to assess for both severe cerebral edema and brainstem herniation consistent with severe intracranial hypertension. If the imaging study does not show evidence of severe cerebral edema and brainstem herniation consistent with intracranial hypertension, a determination for BD/DNC should not be performed, as the injury may be reversible. *Refer to **Appendix F** for flow diagram for determination of BD/DNC in persons treated with TTM.*

Core body temperature	Minimum core body temperature of 36°C is required, as defined by esophageal, bladder, rectal or central venous or arterial catheter temperature measurements, with use of a warming blanket, automated temperature regulation device, thermal mattress, warmed fluids and/or warmed oxygen as needed.
Systolic BP or MAP	Adults should have a systolic blood pressure of ≥ 100 mmHg, or a mean arterial pressure ≥ 60 mmHg; Age appropriate targets should be used in pediatrics; with use of vascular volume, vasopressors and/or inotropes as needed.
Pharmacologic paralysis	Pharmacologic paralysis must be excluded through use of a train-of-four stimulator if available, or assessment of the presence of deep tendon reflexes if a train-of-four-stimulator is not available.
CNS depressing medications	The influence of central nervous system (CNS) depressing medications including toxins, taking into consideration the elimination half-life that may be prolonged by organ dysfunction and/or hypothermia, must be excluded by: • Use of a toxicology screen if there is concern for a toxic exposure, and • Serially measuring drug levels to ensure they do not exceed the therapeutic range, and, even if within the therapeutic range, are not felt to confound the clinical examination, or • Allowing 5 elimination half-lives to pass before an evaluation for BD/DNC be made (assuming normal hepatic and renal function), or • Performing ancillary testing in addition to the complete clinical examination and apnea test if there is concern about prolonged or unknown drug elimination. *Refer to **Appendix F** for flow diagram for determination of BD/DNC in persons treated with TTM.*
Alcohol	If alcohol intoxication is suspected or confirmed, the alcohol blood levels must be ≤ 80 mg/dL)
Severe metabolic, acid-base and/or endocrine derangements	Severe metabolic, acid-base and endocrine derangements that could impact the examination must be corrected. If these cannot be corrected and are judged to be potentially contributing to the loss of brain function while the complete clinical exam and apnea attest are consistent with BD/DNC, ancillary testing should be performed to confirm this determination.
Adequate observation period to establish irreversibility of coma	A minimum of 24 hours is recommended following birth asphyxia, anoxic brain injury after resuscitation from cardiac arrest and after rewarming from therapeutic hypothermia. The time period for other brain injuries has not been established and should be determined on a case-by-case basis. As a general rule, clinicians should err toward caution, and if there is uncertainty about the potential reversibility of the clinical state, for any reason, the observation time should be the time felt necessary to exclude reversibility without any doubt.

APPENDIX B: CLINICAL TESTING GUIDELINES

BD/DNC is first and foremost a clinical determination. The same fundamentals – etiology, prerequisites, minimum clinical criteria, apnea testing targets and indications for ancillary testing – apply to adults and children (≥ 36 weeks gestation), with and without ECMO. (Age appropriate hemodynamic targets apply for pediatric patients.)

BD/DNC testing should not be performed in newborns < 36 weeks old.

A single exam, including apnea testing, is the minimum standard for determination of BD/DNC in adults. Two exams are required for pediatric patients. If 2 evaluations are performed:

- No intervening time period is required between tests,
- The examinations should be performed by two separate examiners,
- Only 1 positive apnea test is required for adults,
- The time of death is the time that the second examination is completed.

All tests must be completed to the fullest extent possible. If any aspect of the clinical examination cannot be completed (except as stipulated below), but the exam, to the extent completed, is consistent with BD/DNC, ancillary testing is recommended.

Coma

There is no evidence of arousal or awareness to maximal external stimulation (including noxious visual, auditory and tactile stimulation).

Pupillary reflexes

Test	Shine a bright light into each of the person's eyes, looking for pupillary constriction and measuring the diameter of the pupils. Use of a magnifying glass and/or pupillometer is suggested.
Response consistent with BD/DNC	There should be absence of ipsilateral and contralateral pupillary response, with pupils fixed in a midsize or dilated position (~4-6 mm), in both eyes.
Considerations	• Constricted pupils are not consistent with BD/DNC and suggest the possibility of drug intoxication or locked-in syndrome. • Pupils can be any shape (round/oval/irregular). • Corneal trauma or prior ophthalmic surgery may influence pupillary reactivity and preclude adequate evaluation, necessitating ancillary testing. • Ocular instillation of drugs may artificially produce transiently nonreactive pupils. • In the setting of anophthalmia or inability to see the pupils, ancillary testing is recommended.

Oculocephalic (OCR) and oculovestibular (OVR) reflexes

Test	OCR: Rotate the head briskly horizontally to both sides. There should be no movement of the eyes relative to head movement. Testing vertically is optional. OVR: Examine the auditory canal for patency and an intact tympanic membrane. Elevate the head to 30° to place the horizontal semicircular canals in the correct vertical position. Irrigate with ≥ 30 mL of ice water for at least 60 seconds using a syringe or a syringe attached to a catheter placed inside the canal. Test both sides separately and with a 5-minute interval between to allow the endolymph temperature to equilibrate.
Response consistent with BD/DNC	There should be absence of extraocular movements. Detection of any extraocular movements is not compatible with BD/DNC.

Considerations	• Confirm the integrity of the cervical spine before proceeding with the OCR test. If the OCR cannot be performed, but the OVR is performed and there are no extraocular movements, ancillary testing is not required. • Ensure the integrity of the tympanic membrane. Presence of a ruptured tympanic membrane does not negate the clinical testing but may risk introducing infections in the ear. • A fracture of the base of the skull or petrous temporal bone may obliterate the response on the side of the fracture, and ancillary testing is recommended in this instance. • Severe orbital or scleral edema or chemosis may affect the free motion of the globes, and ancillary testing is recommended in this instance. • In the setting of anophthalmia, ancillary testing is recommended.

Corneal reflex

Test	Touch the cornea of both eyes with a cotton swab on a stick at the external border of the iris, applying light pressure and observing for any eyelid movement.
Response consistent with BD/DNC	No eyelid movement should be seen.
Considerations	• Care should be taken to avoid damaging the cornea. • In the setting of anophthalmia, severe orbital edema, prior corneal transplantation or scleral edema or chemosis, ancillary testing is recommended.

Motor responses of the face and limbs

Test	Apply deep pressure to all of the following: i. the condyles at the level of the temporomandibular joints ii. the supraorbital notch bilaterally iii. the sternal notch iv. all four extremities, both proximally and distally. Insert a cotton swab on a stick in each nostril to perform nasal tickle testing.
Response consistent with BD/DNC	Noxious stimuli should not produce grimacing, facial muscle movement or a motor response of the limbs other than spinally-mediated reflexes. Noxious stimuli above the foramen magnum should not produce any movement in the face or body. Noxious stimuli below the foramen magnum should not produce any movement in the face but may elicit spinally-mediated peripheral motor reflexes.
Considerations	• The clinical differentiation of spinal responses from brain-mediated motor responses requires expertise. Consultation with an experienced practitioner is recommended if the origin of a response is unclear. Alternatively, if interpretation is unclear, ancillary testing is recommended. • Ancillary testing is recommended if a person has a pre-existing severe neuromuscular disorder, such as amyotrophic lateral sclerosis or a pre-existing severe sensory neuropathy. • Ancillary testing is not required if a person does not have all four limbs; absence of a limb does not preclude motor testing to pain on that side of the body. • Severe facial trauma and swelling may preclude evaluation of facial motor response, so ancillary testing is recommended in this setting.

Gag and cough reflexes

Test	Stimulate the posterior pharyngeal wall bilaterally with a tongue depressor or suction catheter. Stimulate the tracheo-bronchial wall to the level of the carina with deep endotracheal placement of a suction catheter.
Response consistent with BD/DNC	Absence of cough and gag reflexes.
Considerations	• The efferent limb for the cough reflex includes the phrenic nerve, which may be injured in persons with high cervical cord injuries, so ancillary testing is recommended in this setting.

APPENDIX C: APNEA TESTING PROCEDURE

Do not proceed with apnea testing:

- In the setting of a high cervical cord injury
- In pediatric patients with chronic hypoxemia due to cyanotic heart disease
- In V-V and V-A ECMO patients with cardiopulmonary instability
- In any patient where, based on the ventilator requirements and pulmonary status, apnea testing is unlikely to be tolerated

I. Procedure

1. Pre-oxygenate patient with 100% O_2 for at least 10 minutes.
2. Adjust minute ventilation to establish normocarbia ($PaCO_2$ of 35-45 mmHg/ 4.7-6.0 kPa), confirmed by arterial blood gas testing prior to apnea testing.
3. Use a functioning arterial line to provide continuous blood pressure monitoring and to quickly draw blood gases during apnea testing.
4. Bare the chest and abdomen to allow for observation of respiratory effort.
5. Perform apnea testing:
    a. The application of positive airway pressure with the use of CPAP/PEEP may prevent derecruitment and decrease the risk of cardiopulmonary instability, so 100% oxygen can be delivered to the lungs (i) via CPAP on the mechanical ventilator or (ii) via a resuscitation bag with a functioning PEEP valve,
    b. Oxygen can also be delivered via the oxygen insufflation method via placement of a tracheal cannula.
    Note: Do not use tracheal insufflation for apnea testing in newborns, infants and young children.
6. Test arterial blood gas 10 minutes after commencing apnea testing.
    - If point-of-care testing is available and the patient is stable, they can be kept off the ventilator with repeated arterial blood gas sampling every 2-3 minutes until it is determined that the $PaCO_2$ is ≥ 60 mmHg (≥ 20 mmHg above any known chronic baseline $PaCO_2$ in persons with pre-existing hypercapnia).
    - If point-of-care testing is not available, the patient should be reconnected to the ventilator when the arterial blood gas is sent at 10 minutes.
    - While non-invasive capnography may guide the duration of apneic observation, the arterial $PaCO_2$ should be used to confirm adequate elevation of CO_2 during apnea testing.
7. Abort the test if:
    - Spontaneous respirations are witnessed during apnea testing,
    - Systolic blood pressure < 100 mm Hg or mean arterial pressure <60 mm Hg despite titration of fluids/inotropes/vasopressors,
    - There is sustained oxygenation desaturation below 85%,
    - An unstable arrhythmia occurs.

Note: While aborting the apnea test because of cardiorespiratory instability, an arterial blood gas should be sent for testing. If the $PaCO_2$ target is met, the apnea test can be considered positive (consistent with BD/DNC).

II. Decision Table

Condition	Action
Test aborted due to spontaneous respirations during testing	Patient is not dead. Continue clinical management and repeat apnea testing after 24 hours if the clinical evaluation otherwise remains consistent with BD/DNC.
Test aborted due to patient instability	If patient can be stabilized, re-attempt apnea testing after pre-apnea recruitment maneuvers, induction of hypercarbia with CO_2 or carbogen before disconnecting from the ventilator, or utilizing CPAP to maintain oxygenation, **OR** Perform ancillary testing.
Test inconclusive – after 10 minutes monitoring, pH and/or $PaCO_2$ targets have not been reached	If patient is stable, repeat the test after re-establishing pre-oxygenation, normocapnea and a normal pH, and extend the test by several minutes, **OR** Perform ancillary testing.
Apnea confirmed - pH and $PaCO_2$ targets reached	Perform ancillary testing if required. If ancillary testing not required, declare BD/DNC.

III. Considerations for patients receiving ECMO:

1. In persons receiving V-A ECMO for circulatory and respiratory support, maintain extracorporeal blood flow during the clinical evaluation and apnea test in order to prevent hemodynamic instability and maintain a MAP ≥ 60 mmHg in adults and age-appropriate targets in pediatrics. Increase V-A ECMO flow rates to support the MAP if required before or during testing.
2. Prior to apnea testing, provide a period of pre-oxygenation for all persons on ECMO by administering 100% inspired oxygen via the mechanical ventilator and increasing the O_2 in the membrane lung from the ECMO machine to 100% for at least 10 minutes.
3. Conduct apnea testing in patients on ECMO:
    a. Deliver 100% oxygen to the lungs via CPAP on the mechanical ventilator, a resuscitation bag with a functioning PEEP valve, or oxygen flow via a tracheal cannula,
        - Similar to apnea testing in general, the application of positive airway pressure with the use of CPAP/PEEP may prevent derecruitment.
        - It is recognized that some patients may not be mechanically ventilated during ECMO and suspected BD/DNC. Under these conditions, while an apnea test can still be conducted, maintaining oxygenation during the apnea test may be challenging due to the inability to deliver oxygen to the lower airway. Oxygenation will depend on providing 100% oxygen in the sweep gas. If oxygenation cannot be maintained appropriately, the test will need to be aborted and ancillary testing will be required.
        - In cases of VA-ECMO with intrinsic cardiac output, blood gases should be measured simultaneously from the distal arterial line and post oxygenator ECMO circuit. The apnea tests

targets for *both* sampling sites should be pH < 7.30 and $PaCO_2$ of at least 60 mmHg (20 mmHg above the patient's baseline $PaCO_2$ for persons with pre-existing hypercapnia).

b. Maintain oxygen in the membrane lung at 100% throughout the duration of the testing,

c. Titrate the sweep gas flow rate to 0.5-1 L/min while maintaining oxygenation,

d. Assess for spontaneous breathing while targeting traditional apnea test targets via serial blood gases, keeping in mind that achieving a pH < 7.30 and $PaCO_2$ of at least 60 mmHg (20 mmHg above the patient's baseline $PaCO_2$ for persons with pre-existing hypercapnia) may take longer than in a person without ECMO support,

- Terminating the test immediately if the person exhibits any kind of spontaneous respiratory movements or becomes unstable.
- Restart mechanical ventilation and return to the prior ECMO sweep gas flow rate when the pH reaches < 7.30 and $PaCO_2$ reaches 60 mmHg (20 mmHg above his/her baseline $PaCO_2$ if there is premorbid hypercapnia).

APPENDIX D: ACCEPTABLE ANCILLARY TESTING MODALITIES

If ancillary testing is performed and demonstrates the presence of brain blood flow, BD/DNC cannot be declared at that time. Repeat testing at another point in time if the clinical examination and apnea test continue to be consistent with BD/DNC or consider alternative end-of-life care.

Acceptable Modalities	Results consistent with BD/DNC
Digital subtraction angiography *(Conventional 4 vessel cerebral angiography)*	Absent filling at the points where the internal carotid and vertebral arteries enter the skull base, with a patent external carotid circulation.
Radionuclide studies: • Diffusible radiopharmaceuticals be used preferentially, • SPECT be chosen over planar imaging, • Perfusion scintigraphy with anterior and lateral planar imaging be used, with appropriate time intervals to demonstrate static filling of the posterior fossa, if SPECT is not available.	Absence of intracranial isotope.
Transcranial Doppler • Perform two exams ≥ 30 minutes apart. (Note that 10% of patients have no acoustic windows. Circulatory arrest can only be established in the presence of some preceding signal on earlier examination that indicated flow, establishing the presence of an adequate window.) • Perform the exams bilaterally, anteriorly and posteriorly to include both internal carotid arteries as well as the vertebrobasilar circulation. • TCD should not be used for pediatrics in the absence of validation studies in this population.	Exams illustrate biphasic oscillating flow and systolic spikes with reversal of flow in diastole.
EEG • It is suggested that EEG no longer be utilized routinely as an ancillary test in adults, but it may be required by regional laws or policy, or if craniovascular impedance has been affected by an open skull fracture, decompressive craniectomy, or an open fontanelle/sutures in infants. • If performed as an ancillary test, EEG should be used in conjunction with somatosensory and brainstem auditory evoked potentials given the limitations of EEG for evaluating brainstem function.	Interpret according to regional criteria. In the absence of regional criteria, consider guidance from: American Clinical Neurophysiology Society[1], Bleck[2], The Korean Society of Clinical Neurophysiology[3], Société de Neurophysiologie Clinique de Langue Française[4]

APPENDIX E: QUALIFICATIONS FOR DETERMINATION OF BD/DNC

[1] American Clinical Neurophysiology Society. Guideline 3: Minimum technical standards for EEG recording in suspected cerebral death. *J Clin Neurophysiol.* 2006;23(2):97-104.

[2] Bleck TP. Electrophysiologic evaluation of brain death: a critical appraisal. In Aminoff M (ed), Electrodiagnosis in clinical neurology (ed 6). Philadelphia: Elsevier 2012:789-811.

[3] Lee SY, Kim WJ, Kim JM, Kim J, Park S. The Korean Society of Clinical Neurophysiology Education Committee. Electroencephalography for the diagnosis of brain death. *Ann Clin Neurophysiol.* 2017;19(2):118-124.

[4] Szurhaj W, Lamblin MD, Kaminska A, Sediri H, Societe de Neurophysiologie Clinique de Langue F. EEG guidelines in the diagnosis of brain death. *Neurophysiol Clin.* 2015;45(1):97-104.

APPENDIX 15: DETERMINATION OF BRAIN DEATH/DEATH BY NEUROLOGIC CRITERIA CHECKLIST FOR USE IN ADULTS AND CHILDREN ≥ 36 WEEKS OF AGE

BD/DNC determinations must be performed by practitioners who have completed training and are licensed to independently practice medicine.

- These practitioners must be trained in determination of BD/DNC, including the effects of hypothermia on elimination of medications and in counselling families at the end of life.
- Practitioners must have experience in the management of devastating brain injury.
- It is suggested that practitioners be periodically certified in determination of BD/DNC.
- The apnea test must be performed by personnel with experience in resuscitation should the patient decompensate during testing.
- Experienced pediatric clinicians with training and qualifications in pediatric critical care, neonatology, pediatric neurology, pediatric neurointensive care, neurosurgery or traumatology must perform testing to determine BD/DNC in pediatrics.

APPENDIX F: FLOW DIAGRAM FOR DETERMINATION OF BD/DNC IN PERSONS TREATED WITH TH