

**IACUC Annual Protocol Review Report
Walter Reed Army Institute of Research/ Naval Medical Research Center
503 Robert Grant Ave, Silver Spring, MD 20910-7500**

Category E Justification

A Category E Justification must be written so as to be understood by lay persons as well as scientists. This information may be released to the public and should NOT include PII information such as names (principle investigators and research staff), addresses, protocols, meeting notes (either in part or in full), the animals room numbers, grant information, veterinary care programs, and the like.

1. Protocol number: 18-OUMD-13L
2. Species (common name) of animals reported as Category E: Swine
3. Number of animals used in this study reported as Category E: 10
4. Explanation of the procedure (the cause of the pain) producing pain and/or distress to the animal:

The swine will be exposed to hyperbaric air at 5ATA for up to 8.5 days. The oxygen content of the hyperbaric air is equivalent to 100% oxygen on surface (1ATA). This level of oxygen exposure is expected to evoke pulmonary oxygen toxicity which can induce progressive tracheobronchitis, pulmonary edema, and death.

5. Provide scientific justification why the pain/distress could not be relieved.

The goal of this project is to evaluate the feasibility of an existing operational execution plan. This plan is designed to save the lives of trapped submariners, which if in a disabled submarine (DISSUB), historically have a high probability of death. The extremes of the operation of this plan will never be tested in humans due to the ethical considerations and, yet, physiologically, the current plan may not be feasible as described in the background section. To understand the gaps in the plan and increase the probability of success for the future rescue operations to save the lives of submariners, we need to evaluate the feasibility. These submariners will be in a life or death situation and, therefore, to stop at an end-point short of death will be a disservice to the evaluation of this current plan and more importantly the lives of the future submariners that we are working to save. Using death as an endpoint will allow us to identify the gaps in feasibility for future research and DISSUB rescue plan development.

6. State methods or means used to determine that relieving pain and/or distress would interfere with the study objectives (i.e. studies to test whether analgesics impact study outcome).

The goal of this project is to evaluate the feasibility of an existing operational execution plan. This plan is designed to save the lives of trapped submariners, which if in a DISSUB, historically have a high probability of death. The extremes of the operation of this plan will never be tested in humans due to the ethical considerations and, yet, physiologically, the current plan may not be feasible as described in the background section. To understand the gaps in the plan and increase the probability of success for the future rescue operations to save the lives of submariners, we need to evaluate the feasibility. These submariners will be in a life or death situation and, therefore, to stop at an end-point short of death will be a disservice to the evaluation of this current plan and more importantly the lives of the future submariners that we are working to save. Using death as an endpoint will allow us to identify the gaps in feasibility for future research and DISSUB rescue plan development. Nonetheless, we want to minimize confounding variables that may affect mortality. As a result, the swine will not receive any sedation or anesthesia during the dive. The swine will be anesthetized with intramuscular xylazine/ketamine for their pre-dive evaluation and preparation. The swine will not receive any sedation or anesthesia during the dive. The primary rationale for this is that any administration of drug will be potentially confounding, and the interactions of the drugs in the setting of the extreme environment are unknown. Furthermore, there are insufficient medical stores carried on a submarine to sedate/provide analgesia for the entire crew for the rescue scenario (assuming the spaces where the medical supplies are kept are accessible) meaning that providing analgesia and sedation during the dive scenario would be a deviation from what the rescuees would experience. Moreover, there are numerous technical factors that would be necessary to provide pain relief intradive. We are concerned that technical failures of this equipment would potentially lead to an inequitable delivery of pain/distress management across the study, further confounding our results. In the post-dive, we will provide sedation/pain relief as clinically indicated in the form of diazepam and/or buprenorphine. This mimics the operational scenario where the rescuees receive medical care once evacuated from the DISSUB.