AN INTERNATIONAL ORGANIZATION DEDICATED TO PROTECTING THE RIGHTS OF ALL ANIMALS

PETA

PEOPLE FOR THE ETHICAL TREATMENT OF ANIMALS

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March 19, 2024

Lisa Buchanan
Director
Division of Compliance Oversight
Office for Human Research Protections

Via e-mail: Lisa.Buchanan@hhs.gov

Dear Ms. Buchanan:

I'm writing on behalf of People for the Ethical Treatment of Animals (PETA) to share concerns about the preclinical research associated with clinical trial NCT04870125, "Safety Study of Inhaled Carbon Monoxide to Treat Pneumonia and Sepsis-Induced Acute Respiratory Distress Syndrome (ARDS)," and funded by the National Institutes of Health under Project R33HL153011. The study proposes to test carbon monoxide (CO) as a novel therapeutic modality in sepsis-induced ARDS, based on data obtained in preclinical experiments of sepsis and ARDS. However, many of these preclinical experiments have recently been called into question for data manipulation, raising concerns about the use of human patients in this clinical trial.

Several of the studies supporting this Phase 1B trial appear to have been retracted, corrected, and/or flagged for duplicative or manipulated images. More specifically, Project R33HL153011's co-Principal Investigator (PI) Augustine Choi of Weill Cornell Medicine, has had at least ten publications retracted in the past several months for image duplication and/or manipulation.[1,2,3,4,5,6,7,8,9,10] Several of these publications describe the use of CO as a treatment in nonhuman animals.[6,7,9,10] Each of these retracted publications was determined to have had either duplicated image panels, spliced images, and/or included images from previous publications.[11,12,13,14,15,16,17,18,19,20] An additional four of PI Choi's relevant publications have required corrections[21,22,23,24] and there are several other publications for which Choi is a co-author and/or corresponding author that have concerns about duplicated or manipulated images[25,26,27,28,29,30] as noted on the online forum PubPeer.

Additionally, Mark. A Parella of Brigham and Women's Hospital and Harvard Medical School, who is a co-author on several of Choi's publications as well as co-investigator for clinical trial NCT04870125, has had two papers retracted [31,32] and multiple other images noted on PubPeer as duplicative in several of his relevant publications.[33] Two other publications specifically listed as references for NCT04870125 also appear to have potentially problematic images. For example, Figures 3A, 5A and 9A in the referenced article, "The HO-1/CO system regulates mitochondrial-capillary density relationships in human

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skeletal muscle,"[34] have been flagged for review on PubPeer. Another cited publication, "Carbon monoxide, skeletal muscle oxidative stress, and mitochondrial biogenesis in humans,"[35] has been flagged on PubPeer for similarities in Figure 5A.

The number of retractions, corrections, and peer comments associated with the preclinical experiments used to support clinical trial NCT04870125 raise concerns about whether the necessary criteria as required in Federal Regulation 45 CFR 46 "Protection of Human Subjects" or the "Common Rule" were met. More specifically, it is unclear whether the risks to humans are being minimized, whether the risks to subjects are reasonable in relation to anticipated benefits, and whether the human volunteers are being properly informed about the risks and benefits before giving consent.

As it is the OHRP's mission to protect the rights, welfare, and well-being of subjects involved in research conducted or supported by the US Department of Health and Human Services, we wanted to make you aware of our concerns, and are hoping that someone from your office can investigate whether any of problematic images identified in the myriad publications listed above were used to determine whether this treatment should be tested in human volunteers.

Thank you for your time and consideration.

Sincerely,

Katherine V. Roe Ph.D.

Chief Scientist
Laborotory Investigations Department

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