AN INTERNATIONAL ORGANIZATION DEDICATED TO PROTECTING THE RIGHTS OF ALL ANIMALS

PETA

PEOPLE FOR THE ETHICAL TREATMENT OF ANIMALS

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Chancellor
University of California–San Diego
c/o Rosie Goldberg, Executive Assistant to the Chancellor

Via e-mail: pkhosla@ucsd.edu; chancellor@ucsd.edu; m1goldberg@ucsd.edu

Dear Dr. Khosla:

Thank you in advance for your time. I'm writing as a graduate of the University of California–San Diego (UCSD) and on behalf of People for the Ethical Treatment of Animals—PETA entities have more than 9 million members and supporters globally, more than 660,000 of whom live in California. **Based on the disturbing information presented below, we urge you to immediately terminate all active decompression sickness/illness (DCS/DCI) experiments on animals at UCSD in favor of more effective, ethical, and economical animal-free research methods.**

Records Confirm Cruel DCS/DCI Experiments on Animals at UCSD
According to public records obtained by PETA from the U.S. Navy, UCSD experimenter Peter Lindholm conducted painful and/or deadly procedures using rats in his protocol titled "Nitrogen Gas Uptake and Excretion During Compression/Decompression to Simulate Diving," which was approved by the UCSD Institutional Animal Care and Use Committee (IACUC) through November 26, 2022.[1] His experiments on rats for his project titled "Where Is the Gas? A New Method to Study Nitrogen During Diving and Decompression: FY2019-000313-AS" is reportedly receiving $1,009,127 in taxpayer money from the Office of Naval Research from August 1, 2020, to July 31, 2023.[2]

Per Lindholm's aforementioned IACUC protocol, his experiments entail forcing rats to run on a treadmill for 1.5 hours, and if they fail, they're electrically shocked. They're enclosed in a decompression chamber set to high pressures of up to 700 kilopascals for up to 45 minutes. A breathing device is attached to the rat's face, forcing them to inhale various gases,

[1]U.S. Navy. Responsive Records. UCSD. Accessed June 21, 2023. https://www.peta.org/wp-content/uploads/2023/06/peter-lindholm-bumed.pdf
[2]Defense Technical Information Center. Award Number: N000142012763. Where is the gas? A new method to study nitrogen during diving and decompression: FY2019-000313-AS. Accessed June 21, 2023. https://publicaccess.dtic.mil/search/#/grants/simpleSearch

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including pure oxygen and radioactive nitrogen, while they're used for imaging.[3] Lindholm's "Where Is the Gas?" study was assigned the broad agency announcement number N00014-20-S-B001.[4] A set of these proposed experiments included procedures on sheep, for which he reportedly didn't have approval.[5] The Office of Naval Research ultimately approved the affiliated protocol on April 24, 2020.[6]

Poor Data Translation From DCS/DCI Animal Testing to Humans

The detrimental effects from DCS/DCI or oxygen toxicity in humans (and other diving and nondiving animals)—ranging from slight or severe pain to paralysis or even death—are well established.[7,8,9] While the mechanistic triggers of these symptoms are still active areas of research, using animals in experiments as models for DCS/DCI or oxygen toxicity in humans is inhumane and ineffective. Meaningful evaluation of gas diffusion dynamics in live animals—and subsequent translation of this data to humans—is inaccurate due to the inherent complexity of the system under study, in which even the most subtle movements, such as breathing, can and too often do produce spurious results.[10]

In his May 12, 2010, reply to PETA's March 30, 2010, complaint regarding using animals in DSC/DCI testing to then Secretary of the Navy Ray Mabus, then Director of the Navy Medical Research and Development Center W.W. Cheatham, M.D., admitted, "The impact of physiological differences between species with regard to disease processes, to include diving related issues, is well recognized throughout the medical research community."[11] Numerous experts have noted the inherent limitations of using animals to predict the effects of DCS/DCI in humans. For instance, diving expert John Lippmann stated, "The problem with these animal experiments is that no animal model can replicate what happens in a human."[12]

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[3]U.S. Navy. Responsive Records. UCSD. Accessed June 21, 2023. https://www.peta.org/wp-content/uploads/2023/06/peter-lindholm-iacuc-protocol.pdf

[4]U.S. Navy. Responsive Records. UCSD. Accessed June 21, 2023. https://www.peta.org/wp-content/uploads/2023/06/peter-lindholm-abstract.pdf

[5]U.S. Navy. Responsive Records. UCSD. Accessed June 21, 2023. https://www.peta.org/wp-content/uploads/2023/06/navy-email-re-peter-lindholm.pdf

[6]U.S. Navy. Responsive Records. UCSD. Accessed June 21, 2023. https://www.peta.org/wp-content/uploads/2023/06/peter-lindholm-navy-approval.pdf

[7]Pollock NW, Buteau D. Updates in Decompression Illness. *Emerg. Med. Clin. North Am*. 2017;35(2):301-319. doi:10.1016/j.emc.2016.12.002

[8]Tal D, Shachar-Bener H, Hershkovitz D, Arieli Y, Shupak A. Evidence for the initiation of decompression sickness by exposure to intense underwater sound. *J. Neurophysiol*. 2015;114(3):1521-1529. doi:10.1152/jn.00466.2015

[9]Cronin WA, Khan K, Hall AA, Bodo M, Mahon RT. The effect of the perfluorocarbon emulsion Oxycyte™ in an ovine model of severe decompression illness. *Undersea Hyperb. Med.* 2021;48(1):25-31. doi:10.22462/01.03.2021.3

[10]Walsh C, Stride E, Cheema U, Ovenden N. A combined three-dimensional *in vitro–in silico* approach to modelling bubble dynamics in decompression sickness. *J. R. Soc. Interface.* 2017;14(137):20170653. doi:10.1098/rsif.2017.0653

[11]Cheatham, WW. Letter to Shalin G. Gala. PETA.org. Published May 3, 2022. Accessed May 3, 2022. https://www.peta.org/wp- content/uploads/2022/05/letter-to-navy-reply.pdf

[12]Lippmann J. *The Essentials of Deeper Sport Diving: An Overview of the Theory and Requirements of Deeper Diving*. Locust Valley, NY: Aqua Quest Publications; 1992.

The Naval Medical Research Command itself has stated the following:

> [A]nimal DCS in many cases is more severe than that in humans and, therefore, appears "different" from the average human case. … Among species, there certainly are differences in tolerance to decompression, with relative susceptibility to DCS tending to increase with species size. … These observations suggest that response differences among species to the insult of decompression may reflect a combination of factors, including differences in gas exchange and tolerance to excess gas in the body.[13]

Superior Non-Animal DCS/DCI Research Methods Are Widely Available
Thankfully, modern non-animal technology is available for studying DCS/DCI based on human tissue and data obtained from human divers.[14,15,16,17,18,19]

Some options include the following:

- *In vitro* studies of human endothelial cells—later confirmed by human trials—provide researchers with evidence in simulated diving conditions of nitric oxide dynamics, a chemical compound that can protect against bubble formation.[20,21,22]

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[13]Lillo RS, Himm JF, Weathersby PK, Temple DJ, Gault KA, Dromsky DM. Using animal data to improve prediction of human decompression risk following air-saturation dives. *J. Appl. Physiol.* 2002;93(1):216-226. doi:10.1152/japplphysiol.00670.2001
[14]Palkovic M, Novomeský F, Zaviacic M, Danihel L, Kovác P, Danisovic L. The use of cell cultures for in vitro decompression sickness simulation, *Soud. Lek.* 2007;52(1): 9-16.
[15]Jang DH, Owiredu S, Ranganathan A, Eckmann DM. Acute decompression following simulated dive conditions alters mitochondrial respiration and motility. *Am. J. Physiol. Cell. Physiol.* 2018;315(5):C699-C705. doi:10.1152/ajpcell.00243.2018
[16]Wienke BR. Computer validation and statistical correlations of a modern decompression diving algorithm. *Comput. Biol. Med.* 2010;40(3):252-260. doi:10.1016/j.compbiomed.2009.11.021
[17]Germonpré P, Lafère P, Portier W, Germonpré FL, Marroni A, Balestra C. Increased risk of decompression sickness when diving with a right-to-left shunt: Results of a prospective single-blinded observational study (the "Carotid Doppler" study). *Front. Physiol.* 2021;12:763408. Published October 29, 2021. doi:10.3389/fphys.2021.763408
[18]Honěk J, Šrámek M, Honěk T, et al. Screening and risk stratification strategy reduced decompression sickness occurrence in divers with patent foramen ovale. *JACC Cardiovasc. Imaging.* 2022;15(2):181-189. doi:10.1016/j.jcmg.2021.06.019
[19]Han KH, Hyun GS, Jee YS, Park JM. Effect of water amount intake before scuba diving on the risk of decompression sickness. *Int. J. Environ. Res. Public Health*. 2021;18(14):7601. Published July 16, 2021. doi:10.3390/ijerph18147601
[20]Hesthammer R, Eide T, Thorsen E, Svardal AM, Djurhuus R. Decrease of tetrahydrobiopterin and NO generation in endothelial cells exposed to simulated diving. *Undersea Hyperb. Med.* 2019;46(2):159-169.
[21]Hesthammer R, Eide T, Thorsen E, Svardal AM, Djurhuus R. Hyperoxia and lack of ascorbic acid deplete tetrahydrobiopterin without affecting NO generation in endothelial cells. *Undersea Hyperb. Med.* 2019;46(4):509- 519.
[22]Hesthammer R, Dahle S, Storesund JP, Eide T, Djurhuus R, Svardal AM, Thorsen E. Nitric oxide in exhaled gas and tetrahydrobiopterin in plasma after exposure to hyperoxia. *Undersea Hyperb. Med.* 2020;47(2):197-202. doi: 10.22462/04.06.2020.4

- Reanalysis of existing human diver data has led to improved models that may be better able to predict DCS/DCI symptoms and risk factors.[23,24]
- Machine-learning techniques may aid in the prediction of symptoms such as seizures during hyperbaric oxygen therapy.[25]
- Computational modeling can also improve the performance of dive computers to better equip divers in avoiding DCS/DCI,[26] and laboratory studies using human subjects are yielding novel data.[27,28]
- The technological advances of our time have also facilitated the development of a combined "biomimetic *in vitro* tissue phantom and a three-dimensional computational model, comprising a hyperplastic strain-energy density function to model tissue elasticity," as well as investigating key areas of gas diffusion dynamics and developing more accurate dive algorithms.[29]

Precedents for Ending DCS/DCI and Oxygen Toxicity Testing on Animals

Per public records obtained by PETA, in one Navy-funded decompression experiment at the University of Wisconsin–Madison, initially approved from August 11, 2020, through August 10, 2023,[30] two healthy sheep were placed in a hyperbaric chamber for behavioral and equipment monitoring. A UW-Madison internal investigation found that on October 11, 2021, "the compressor for the chamber was not working" and that the animals inside the chamber had shown signs of discomfort and were then euthanized.[31] This experiment—and a separate Navy-funded decompression experiment at UW-Madison initially approved from June 2, 2021, through June 1, 2024, examining survival rates and cardiopulmonary function in sheep subjected to long-term exposure of hyperbaric air[32]—were *both* terminated on July 19, 2022, well ahead of schedule. This action follows

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[23]King AE, Andriano NR, Howle LE. Trinomial decompression sickness model using full, marginal, and non-event outcomes. *Comput. Biol. Med.* 2020;118:103640. doi:10.1016/j.compbiomed.2020.103640

[24]Cialoni D, Pieri M, Balestra C, Marroni A. Dive risk factors, gas bubble formation, and decompression illness in recreational SCUBA diving: Analysis of DAN Europe DSL data base. *Front. Psychol.* 2017;8. doi:10.3389/fpsyg.2017.01587.

[25]D'Angelo G, Pilla R, Dean JB, Rampone S. Toward a soft computing-based correlation between oxygen toxicity seizures and hyperoxic hyperpnea. *Soft. Computing.* 2018;22(7):2421-2427. doi:10.1007/s00500-017-2512-z

[26]Wienke BR, O'Leary TR. On bubble regeneration and broadening with implications for decompression protocols. *Significances Bioeng. Biosci.* 2018;2(4). doi:10.31031/sbb.2018.02.000543

[27]Hess HW, Hostler D, Clemency BM, St. James E, Johnson BD. Carotid body chemosensitivity is not attenuated during cold water diving. *Am. J. Physiol. Regul. Integr. Comp. Physiol.* 2021;321(2):R197-R207. doi:10.1152/ajpregu.00202.2020

[28]Hess HW, Hostler D, Clemency BM, Johnson BD. Carotid body chemosensitivity at 1.6 ATA breathing air versus 100% oxygen. *J. Appl. Physiol.* 2020;129(2):247-256. doi:10.1152/japplphysiol.00275.2020

[29]Walsh C, Stride E, Cheema U, Ovenden N. A combined three-dimensional *in vitro–in silico* approach to modelling bubble dynamics in decompression sickness. *J. R. Soc. Interface*. 2017;14(137):20170653. doi:10.1098/rsif.2017.0653

[30]UW-Madison Institutional Animal Care and Use Committee Protocol Number V00: V006375. Accessed January 13, 2023. https://www.peta.org/wp-content/uploads/2023/01/uw-madison-iacuc-V006375.pdf

[31]UW-Madison School of Veterinary Medicine Animal Care and Use Committee Closed Session [Minutes]—October 12, 2021. Accessed January 13, 2023. https://www.peta.org/wp-content/uploads/2023/01/uw-madison-iacuc-closed-session.pdf

[32]UW-Madison Institutional Animal Care and Use Committee Protocol Number V006315. Accessed January 13, 2023. https://www.peta.org/wp-content/uploads/2023/01/uw-madison-iacuc-V006315.pdf

PETA's June 8, 2023, letter to Secretary of the Navy Carlos Del Toro urging an end to these tests.[33]

Furthermore, the Navy also pulled its funding for similar decompression experiments on sheep at UW-Madison in 2010 following a criminal investigation launched in response to a petition filed by PETA and Alliance for Animals,[34] for which a court-appointed special prosecutor reported that "[t]he Department of the Navy has pulled its grant and the [decompression] research using sheep has stopped. In reviewing the more recent literature, it appears that the efficacy of these types of studies is now in question."[35]

Internationally, the British and French navies have already ended their respective DCS animal-testing programs.[36] In 2008, Derek Twigg, then U.K. parliamentary under-secretary of state at the Ministry of Defence, wrote to the British Parliament, stating, "The Ministry of Defence (MoD) has today announced the end of its immediate requirement for testing on live goats as part of its hyperbaric research in support of the MoD's submarine escape rescue and abandonment system."[37] He described the findings motivating this decision as follows:

> The testing programme was aimed at improving the accuracy of the information relating to the likely probability and consequence of decompression illness following escape from a submerged submarine in varying depths and internal submarine pressures. This requirement has now been achieved, and the review has concluded that the remaining associated areas of uncertainty in submarine escape and rescue relate to events that are considered highly unlikely, and do not therefore need to be addressed by means of animal testing. The MoD has endorsed these recommendations and as a result, it has no immediate need to continue animal testing of this type.[38]

UCSD's DCS/DCI Testing on Animals Appears to Contravene Federal Standards

The use of animals in DCS/DCI and oxygen toxicity testing flies in the face of existing regulations to minimize animal use in experiments. The U.S. Government Principles for the Utilization and Care of Vertebrate Animals Used in Testing, Research, and Training (1985) states, "The animals selected for a procedure should be of an appropriate species

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[33]Pon S. Letter to U.S. Secretary of the Navy. PETA.org. June 8, 2022. Accessed June 20, 2023. https://www.peta.org/wp-content/uploads/2022/08/2022-06-08-letter-to-usn-re-dcs-tests.pdf

[34]State of Wisconsin Circuit Court. Dane County. Brief in Support of Petition to Circuit Court Judge for Relief Pursuant to Wis. Stat. § 968.02(3). Injunction Relief 30704. March 16, 2010. Accessed January 13, 2023. https://www.peta.org/wp-content/uploads/2022/10/UW-sheep-decompression-brief-031610.pdf

[35]State of Wisconsin Circuit Court. Dane County. Report and Determination by Special Prosecutor. Case Number 10CV1398. May 19, 2011. Accessed January 13, 2023. https://www.peta.org/wp-content/uploads/2022/05/final-report-of-special-prosecutor.pdf

[36]Norton-Taylor R. Navy used goats in submarine experiments, MoD reveals. *The Guardian*. February 6, 2008. Accessed May 9, 2022. https://www.theguardian.com/uk/2008/feb/07/animalwelfare.military

[37]Hansard House of Commons. Written Ministerial Statements. February 6, 2008. Accessed May 9, 2022. https://publications.parliament.uk/pa/cm200708/cmhansrd/cm080206/wmstext/80206m0002.htm

[38]Hansard House of Commons.

and quality and *the minimum number required to obtain valid results*" [*emphasis added*].[39] Given the widespread availability of non-animal, human-focused testing methods, the number of animals used for DCS/DCI and oxygen toxicity testing should be zero.

Furthermore, given that Lindholm's experiment received Navy funding, approval of such testing appears to contravene Defense Health Agency-Multi-Service Regulation (DHA-MSR) 6025.02, which states, "Alternatives to animal use will be considered *and used* whenever possible and appropriate to attain the objectives of [Research, Development, Test, and Evaluation] or training if such methods produce scientifically or educationally valid or equivalent results" [*emphasis added*].[40] It's clear from the aforementioned precedents set at UW-Madison and by the British and French navies that there are valid alternatives to using animals for DCS/DCI and oxygen toxicity testing, and per this military regulation, such animal-free experimental methods should be used in place of experiments on animals.

Request for Action

There is no scientific, ethical, or legal justification for subjecting animals to DCS/DCI or oxygen toxicity experiments. Therefore, we urge you to terminate all DCS/DCI and oxygen toxicity experiments—including the ones conducted by Lindholm—on animals at UCSD immediately.

Thank you for your time and consideration of this important matter. I look forward to your response.

Sincerely yours,

Shriya Swaminathan
Science Policy Advisor
International Laboratory Methods
Laboratory Investigations Department

[39]National Institutes of Health. National Center for Biotechnology Information. National Research Council Committee for the Update of the Guide for the Care and Use of Laboratory Animals. Appendix B: U.S. government principles for the utilization and care of vertebrate animals used in testing, research, and training. Accessed March 10, 2022. https://www.ncbi.nlm.nih.gov/books/NBK54048/

[40]Cheatham, WW. Letter to Shalin G. Gala. PETA.org. Published May 3, 2022. Accessed May 3, 2022. https://www.health.mil/-/media/Files/MHS/Policy-Files/DHAMSR-602502-The-Care-and-Use-of-Animals-in-DoD-Research.ashx