(Billing Code: 4150-31)

DEPARTMENT OF HEALTH AND HUMAN SERVICES

Office of the Secretary

Findings of Research Misconduct

AGENCY: Office of the Secretary, HHS.

ACTION: Notice.

SUMMARY: Findings of research misconduct have been made against William M. Armstead, Ph.D. (Respondent), who was a Research Associate Professor of Anesthesiology and Critical Care, Department of Anesthesiology and Critical Care, Perelman School of Medicine, University of Pennsylvania (UPENN). Respondent engaged in research misconduct in research supported by U.S. Public Health Service (PHS) funds, specifically National Institute of Neurological Diseases and Stroke (NINDS), National Institutes of Health (NIH), grants R01 NS090998-01A1, R21 NS095321, and T32 NS043126 and National Institute of Child Health and Human Development (NICHD), NIH, grant R01 HD057355. The research was included in grant applications for PHS funds, specifically R35 NS116805-01, R01 NS121149-01, and R01 NS090998-02, -03, -04, and -05 submitted to NINDS, NIH, and R01 HL139506-01 submitted to the National Heart, Lung, and Blood Institute (NHLBI), NIH. The administrative actions, including debarment for a period of seven (7) years, were implemented beginning on June 19, 2023, and are detailed below.

FOR FURTHER INFORMATION CONTACT:

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SUPPLEMENTARY INFORMATION: Notice is hereby given that the Office of Research Integrity (ORI) has taken final action in the following case:

William M. Armstead, Ph.D., University of Pennsylvania: Based on the report of an investigation conducted by UPENN and additional analysis conducted by ORI in its oversight review, ORI found that William M. Armstead, Ph.D., former Research Associate Professor of Anesthesiology and Critical Care, Department of Anesthesiology and Critical Care, Perelman School of Medicine, UPENN, engaged in research misconduct in research supported by PHS funds, specifically NINDS, NIH, grants R01 NS090998-01A1, R21 NS095321, and T32 NS043126 and NICHD, NIH, grant R01 HD057355. The research was included in grant applications for PHS funds, specifically R35 NS116805-01, R01 NS121149-01, and R01 NS090998-02, -03, -04, and -05 submitted to NINDS, NIH, and R01 HL139506-01 submitted to NHLBI, NIH.

ORI found that Respondent engaged in research misconduct by knowingly and intentionally falsifying and/or fabricating fifty-one (51) figures and the methods, data, results, and conclusions reporting on the effects of various vasoactive agents on the neurologic response to traumatic brain injury in piglets of different ages and genders in the following five (5) published papers, one (1) unpublished manuscript, one (1) review article, three (3) posters, three (3) grant applications submitted for PHS funds, and four (4) NIH grant progress reports:

- Dopamine protects cerebral autoregulation and prevents hippocampal necrosis after traumatic brain injury via block of ERK MAP in juvenile pigs. *Brain Res*. 2017 Sep 1;1670:118-24. Epub 2017 Jun 15. doi: 10.1016/j.brainres.2017.06.010 (hereafter referred to as "*Brain Res.* 2017").
- Sex and Age Differences in Epinephrine Mechanisms and Outcomes after Brain Injury. *J Neurotrauma* 2017 Apr 15;34(8):1666-75. Epub 2017 Jan 13. doi: 10.1089/neu.2016/4770 (hereafter referred to as "*J Neurotrauma* 2017"). Retraction in: *J Neurotrauma* 2022 Jun;39(11-12):894. doi: 10.1089/neu.2016.4770.retract.

- Sex and age differences in phenylephrine mechanisms and outcomes after piglet brain injury. *Pediatr Res*. 2017 Jul;82(1):108-13. Epub 2017 Apr 26. doi:10.1038/pr.2017.83 (hereafter referred to as "*Pediatr Res.* 2017"). Retraction in *Pediatr Res.* 2022 Oct:92 (4):1200. doi:10.1038/s41390-022-02248-9.
- Norepinephrine Protects Cerebral Autoregulation and Reduces Hippocampal Necrosis after Traumatic Brain Injury via Blockade of ERK MAPK and IL-6 in Juvenile Pigs. *J Neurotrauma.* 2016 Oct 1;33(19):1761-67. Epub 2016 Mar 22. doi: 10.1089/neu.2015.4290 (hereafter referred to as "*J Neurotrauma* 2016"). Retraction in: *J Neurotrauma.* 2022 Jun;39(11-12):893. doi:neu.2015.4290.retract.
- Preferential Protection of Cerebral Autoregulation and Reduction of Hippocampal Necrosis with Norepinephrine After Traumatic Brain Injury in Female Piglets. *Ped Crit Care Med*. 2016 Mar;17(3):e 130-7. doi: 10.1097/PCC.0000000000000603 (hereafter referred to as "*Ped Crit Care Med.* 2016"). Retraction in: *Ped Crit Care Med*. 2022 Jul 1; 23(7):e371. doi: 10.1097/PCC.0000000000003014.
- Manuscript: Phenylephrine modulates CSF IL-6 in a sex-dependent manner to protect cerebral autoregulation and reduce neuronal death after traumatic brain injury in newborn pigs. Submitted to *Pediatric Critical Care Medicine* in 2019. Withdrawn (hereafter referred to as the "*Ped Crit Care Med* 2019 manuscript").
- Review article: Translational approach towards determining the role of cerebral autoregulation in outcome after traumatic brain injury. *Exp Neurol.* 2019 Jul;317:291-7. doi: 10.1016/j.expneurol.2019.03.015 (hereafter referred to as "*Exp Neurol*. 2019").
- Poster: Normalization of CPP after TBI protects autoregulation and hippocampal neuronal cell necrosis in female but not male piglets via block of ERK MAPK and IL-6 upregulation. 43rd Society for Neuroscience in Anesthesiology and Critical Care (SNACC) Annual Meeting, San Diego, CA, October 22-23, 2015 (hereafter referred to as the "SNACC 2015 poster").

- Poster: Norepinephrine protects cerebral autoregulation and reduces hippocampal necrosis after traumatic brain injury via block of ERK MAPK and IL-6 in juvenile pigs. Experimental Biology Annual Meeting, San Diego, CA, April 2-6, 2016 (hereafter referred to as the "Experimental Biology 2016 poster).
- Poster: Epinephrine blocks JNK MAPK, protects autoregulation and reduces histopathology after brain injury by age and sex. Neurotrauma 2016 -- The 34th Annual Symposium of the National Neurotrauma Society, Lexington, KY, June 26-29, 2016 (hereafter referred to as the "Neurotrauma Society 2016 poster").
- R35 NS116805-01, "Brain-heart relationships in outcomes after traumatic brain injury," submitted to NINDS, NIH, on July 26, 2019, administratively withdrawn on March 3, 2020
- R01 NS121149-01, "Brain Heart Interactions and Vascular Contribution to Cognitive Outcome After TBI," submitted to NINDS, NIH, on June 5, 2020, administratively withdrawn on November 1, 2022
- R01 HL139506-01, "tPA, NMDA receptor excitotoxicity, and outcome after stroke," submitted to NHLBI, NIH, on February 6, 2017, administratively withdrawn on July 2, 2019
- NINDS, NIH, R01 NS090998-02, -03, -04, and -05 grant progress reports, "Pressor Choice Influences Protection of Autoregulation in Brain Injury," Funding Period: September 1, 2015-August 31, 2020

Specifically, ORI found that Respondent intentionally and knowingly:

- Reused histopathology slides to falsely represent the controls for hippocampal neurons exposed to fluid percussion injury (FPI) and treated with norepinephrine (NE), phenylephrine (PHE), epinephrine (EPI), or dopamine (DA) in distinct experiments performed at different times in Figures 7A, 7B, 7C, 7E, 7G, and 7H of *Ped Crit Care Med.* 2016, Figures 5A, 5B, 5C, 5D, 5G, and 5H of the *Ped Crit Cre Med.* 2019 manuscript, Figures 5A, 5B, 5C, 5E, 5G, and 5H of *Pediatr Res.* 2017, Figures 6A, 6B, 6C, 6G, and 6H of *J Neurotrauma* 2017,

Figures 7A, 7B, 7C, and 7E of *J Neurotrauma* 2016, and Figures 5A, 5B, 5C, 5D, and 5E of *Brain Res.* 2017

- Reused the histopathology slides representing necrotic neurons after FPI treatment with NE in Figure 7E of *Ped Crit Care Med.* 2016 and relabeled the panel to falsely represent necrotic neurons after FPI treatment with PHE in Figure 5D of the *Ped Crit Care Med.* 2019 manuscript
- Reused and relabeled the histograms to falsely represent traumatic brain injury responses, as represented by necrotic hippocampal neurons, in piglets of different ages and/or genders exposed to different therapeutic agents in Figure 5I of the *Ped Crit Care Med.* 2019 manuscript, Figure 7I of *Ped Crit care Med.*2016, Figure 7G of *J Neurotrauma* 2016, Figure 7G of *J Neurotrauma* 2017, and Figure 5I of *Brain Res.* 2017
- Reused and relabeled histograms to falsely represent the pial artery response to different therapeutic agents for traumatic brain injury in piglets of different ages and genders in Figure 3 of *Pediatr Res.* 2017, Figures 3A and 3B of *Ped Crit Care Med.* 2016, and Figures 3 and 5I of *Brain Res.* 2017
- Falsified and/or fabricated the sham condition, experimental methods, neuronal count methodology, piglet number, data, and statistics reported in *Ped Crit Care Med.* 2016, *J Neurotrauma* 2016, *J Neurotrauma* 2017, *Pediatr Res.* 2017, *Brain Res.* 2017, and the *Ped Crit Care Med.* 2019 manuscript
- Reported falsified data, results, and conclusions highlighting the roles that age and gender have in the treatment of traumatic brain injury from *Ped Crit Care Med* 2016, *J Neurotrauma* 2016, *J Neurotrauma* 2017, *Brain Res.* 2017, and *Pediatr Res.* 2017 in *Exp. Neuro* 2019
- Reported falsified results from *Ped Crit Care Med.* 2016, *J Neurotrauma* 2016, *J Neurotrauma* 2017, and *Brain Res.* 2017 and in the SNACC 2016 poster, Experimental Biology 2016 poster, Neurotrauma 2016 poster in progress reports R01 NS090998-02, -03, -04, and -05

- Reported falsified results of the vasoactive agents NE, EPI, PHE, and DA on autoregulation and hippocampal neuronal necrosis in piglets of different ages and genders after a stroke or traumatic brain injury in Figures 4A, 4B, 5A, 5B, 6A, and 6B of R35 NS116805-01 and R01 NS121149-01, Figures 3A, 3B, 3G, and 3H of R01 HL139506-01, and the Research Strategy section of R35 NS116805-01

Respondent entered into a Voluntary Exclusion Agreement (Agreement) and voluntarily agreed to the following:

(1) Respondent will exclude himself voluntarily for a period of seven (7) years beginning on June 19, 2023 (the "Exclusion Period"), from any contracting or subcontracting with any agency of the United States Government and from eligibility for or involvement in nonprocurement or procurement transactions referred to as "covered transactions" in 2 CFR Parts 180 and 376 (collectively the "Debarment Regulations").

(2) During the Exclusion Period, Respondent will exclude himself voluntarily from serving in any advisory or consultant capacity to PHS including, but not limited to, service on any PHS advisory committee, board, and/or peer review committee.

(3) Respondent will request that the following paper be corrected or retracted:

- *Exp Neurol.* 2019 Jul;317:291-7. doi: 10.1016/j.expneurol.2019.03.015.

Respondent will copy ORI and the Research Integrity Officer at UPENN on the correspondence with the journal.

Dated: July 3, 2023.

Sheila Garrity,

Director, Office of Research Integrity,

Office of the Assistant Secretary for Health.

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