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301.634.7000 www.faseb.org 9650 Rockville Pike Bethesda, MD 20814

April 7, 2020

Office of Laboratory Animal Welfare (OLAW) National Institutes of Health (NIH) RKL 1, Suite 360, MSC 7982 6705 Rockledge Drive Bethesda, MD 20892-7982

RE: NIH Request for Information: Implementation of the Updated AVMA Guidelines for the Euthanasia of Animals: 2020 Edition [FR Doc. 2020-03607 and NOT-OD-20-069]

Submitted electronically via portal and via e-mail: olaw@od.nih.gov

Dear Dr. Brown,

The Federation of American Societies for Experimental Biology (FASEB) appreciates the opportunity to provide comments on the Request for Information (RFI) (NOT-OD-20-069) seeking input on the implementation of the updated American Veterinary Medical Association (AVMA) <u>Guidelines</u> for the Euthanasia of Animals: 2020 Edition ("Guidelines"). As one of the primary issues leading to the establishment of FASEB, humane care and use of animals in biological and biomedical research remains a fundamental priority of the Federation and its 28 member societies.

FASEB commends AVMA's efforts to engage with the research community in drafting the updates to the Guidelines. As implementation proceeds, we encourage both OLAW and AVMA to preserve strong stakeholder participation to ensure the process is both transparent and inclusive of multiple research perspectives. Sustained engagement with the community is vital for the promotion and protection of laboratory animal care and welfare.

Comments on specific sections of the Guidelines are noted below.

Part I – Introduction and General Comments

In reviewing the Introduction and General Comments section, we particularly appreciated the discussion on the human-animal relationship (Section 15.5 – Human Behavior). While the Guidelines recognize that owners, veterinarians, and animal care staff can be psychologically affected when performing or observing euthanasia, the topic of compassion fatigue was only mentioned once, with minimal guidance for ways institutions and veterinary clinics can strengthen support for those working with laboratory animals. Given AVMA's exceptional leadership on this issue, FASEB encourages OLAW to coordinate with AVMA and other laboratory animal organizations to include language in the Guidelines that will facilitate institutions' ability to identify and mitigate the risks of compassion fatigue and euthanasia stress for personnel. For example, among the numerous resources AVMA offers for personal and professional

wellbeing are lists of <u>individual</u> and <u>organizational symptoms</u> of compassion fatigue. Broader distribution of such educational resources will increase awareness and encourage institutions to be proactive within their respective animal programs.

Part II – Methods of Euthanasia: M1. Inhaled Agents

FASEB applauds the change in displacement rate for carbon dioxide (CO₂) euthanasia for rodents from [10% - 30%] to [30% to 70%], consistent with recent research findings that have shown higher flow rates to reduce potential pain and distress for rodents ^{1,2,3}. The purpose of euthanasia is to minimize potential pain and discomfort for laboratory animals, and we appreciate the Panel's commitment to this aim by integrating evidence-based guidelines.

<u>Part II – Methods of Euthanasia M3. Physical Methods</u>

Thoracic (cardiopulmonary, cardiac) compression is extensively used in field research as well as university laboratories that study wild small mammals and birds. Frequently, this method is the most humane alternative available in certain research scenarios. While we recognize the Guidelines seek to maintain a precautionary approach towards euthanasia methods, we disagree with the language that states, "...data supporting this method are limited, including degree of distress induced and time to unconsciousness or death" (Section M3.12, pg. 47) as this is inconsistent with recent literature. For example, a study published in 2017 suggested that thoracic compression is an efficient euthanasia method for small birds, as it effectively obstructs venous return, subsequently causing rapid circulatory arrest⁴.

The Guidelines are also in direct conflict with previous AVMA policy statements on this issue. A 2011 factsheet referenced on OLAW's website, "Welfare Implications of Thoracic Compression," concludes that while not an acceptable method of euthanasia, thoracic compression "...should not be prohibited where its use is necessary to minimize animal suffering or is scientifically justified (such as under the oversight of an Institutional Animal Care and Use Committee (IACUC))." Contradictory language between the Guidelines and previous AVMA statements obscures the role of IACUC in seeking compliance with both the Guide and AVMA Guidelines.

Therefore, FASEB recommends revising this language in the Guidelines to reflect recent publications currently informing wildlife protocols at numerous institutions, as well as AVMA and OLAW policy. Additionally, OLAW may want to reach out to stakeholders with specific expertise in wildlife and avian research, such as the Ornithological Society and American Society of Mammologists, to provide input on this language.

¹ Hickman, D (2019). Wellbeing of Alcohol-preferring Rats Euthanized with Carbon Dioxide at Very Low and Low Volume Displacement Rates. *J Am Assoc Lab Anim Sci.* 2019; 58(1): 78-82.

² Moody CM, Chua B, and Weary DM (2014). The effect of carbon dioxide flow rate on the euthanasia of laboratory mice. *Laboratory Animals*. 2014; 48(4): 298 – 304.

³ Boivin GP et al. (2017). Review of CO₂ as a Euthanasia Agent for Laboratory Rats and Mice. *J Am Assoc Lab Anim Sci*. 2017;56(5):491–499.

⁴ Paul-Murphy JR et al. (2017). Comparison of intraosseous pentobarbital administration and thoracic compression for euthanasia of anesthetized sparrows (Passer domesticus) and starlings (Sturnus vulgaris). *Am J Vet Res.* 2017; 78(8): 887-899.

Part III – Methods of Euthanasia by Species and Environment: S2. Laboratory animals

FASEB appreciates the clarification in euthanasia procedures for laboratory rodent with altricial young (e.g., mice and rats) versus rodents bearing precocial young (e.g., guinea pigs) in Section 2.2.4.1, Fetuses and Neonates – Acceptable Methods (pg. 62). While we acknowledge AVMA's utilization of scientific literature to inform these updates, in many instances, the evidence cited does not align with the laboratory animal being discussed. For example, the conclusion that rodent fetuses are "...unconscious in utero and hypoxia does not evoke a response" is based on recordings from fetal sheep (Mellor et al., 2005). To ensure researchers and animal care personnel employ guidelines established on comprehensive evidence, we recommend incorporating citations beyond farm animal studies. In particular, we urge the integration of NIH's Guidelines for the Euthanasia for Rodent Fetuses and Neonates, a resource that provides detailed, evidence-based guidance for euthanasia procedures with this commonly used species.

Finally, we wish to express concern regarding the contradictory language located in section S3.3.3 Suckling Pigs – Manually applied blunt force trauma (pg. 76). The beginning of this section asserts that this method fulfills the definition of euthanasia when performed correctly, yet the paragraph concludes by encouraging researchers and staff to actively seek alternatives "...to ensure that criteria for euthanasia can be consistently met." While we recognize and support the search for alternatives as a key component of the 3Rs, inconsistent messaging within the Guidelines may prove counterintuitive to this objective and risks confusion for researchers utilizing this species. Therefore, FASEB recommends clarifying the meaning of "active search for alternatives" or striking this language altogether.

FASEB values the synergistic relationship between animal welfare and biomedical research progress and appreciates the opportunity to provide feedback on this RFI. We thank OLAW and the AVMA Panel on Euthanasia for their engagement with the scientific community on this important issue and encourage timely communication with stakeholders once the policy is finalized to clarify agency expectations and ensure seamless implementation.

Sincerely,

Hannah V. Carey, PhD

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FASEB President