



Animal Welfare Institute

900 PENNSYLVANIA AVENUE, SE, WASHINGTON, DC 20003

December 22, 2023

Re: Request for Information (RFI) on Proposed Guidance to Assured Institutions on Cephalopod Care and Use - NOT-OD-23-176

Dear OLAW Staff:

The Animal Welfare Institute strongly supports NIH's plan to release guidance on the use of cephalopods in research. The United States has lagged behind many other countries in providing protection for these animals, and it is time our country started to catch up. Their sentience, intelligence and experience of pain and emotion warrants treating cephalopods comparably to vertebrate species. Recent media coverage of new genetically altered "see-through" squid who receive dye injections into their brains (Hamilton, 2023) highlights the timeliness of regulations on the use of these species.

I. Sentience & Intelligence

Cephalopods have the most centralized and largest nervous system of all invertebrates, and are "broadly considered to be the most cognitively advanced group of invertebrates," with cognitive abilities "comparable to those found in some vertebrates, including highly developed perception, learning and memory abilities," along with "sophisticated feats of flexible behavior." (Schnell A. K., 2021a)

A recent review paper by an expert in complex learning and memory using cephalopods and corvids as "model species" has described how intelligent cephalopods really are. (Schnell A. K., 2021a) For example, octopuses are known to carry coconut shells as a protective casing—a form of tool use—which suggests future planning. Cuttlefish have demonstrated "number sense" and "lower forms of object permanence" and octopuses have shown "transfer learning" and the ability to categorize. Some cephalopods are able to adjust foraging behavior based on past experiences, and some species have been observed disguising themselves as other species. Some researchers have even suggested that some cephalopods choose their camouflage patterns based on approaching species' predatory strategies or to mimic the opposite sex during mating season. Cephalopods possess a "high capacity for learning through association" and learning from conspecifics, as well as an ability to retain learning over time. (Schnell A. K., 2021a) Indeed, octopuses seem to place a "positive value" on "gaining information" that may suggest a desire to reduce uncertainty in their environment and an interest in play. (Mather, 2022) Remarkably, one study (Schnell A. K., 2021b) has shown that cuttlefish can exert self-control and delay gratification for a better reward—sometimes called the "marshmallow test" (Tabin, 2021)—showing an ability to "overcome immediate gratification to fulfill future needs."

These examples demonstrate "behavioral flexibility," which is "widely considered to be the gold standard for evidence of complex cognition" as it is believed to show abilities such as "causal reasoning, imagination, mental time travel and mental attribution." (Schnell A. K., 2021a) As one university

veterinarian and aquatic animal researcher noted “these qualities of behavioral complexity, sensory discrimination and learning in cephalopods [...] provide ample cause for considering their welfare in the laboratory for humane and scientific reasons.” (Harvey-Clark, 2011)

II. Pain and Emotion in Cephalopods

An ongoing topic of debate in scientific literature is whether invertebrates can feel pain subjectively or whether they may only experience a nociceptive, reflexive response to aversive stimuli. There is now considerable evidence that cephalopods have emotional experiences of pain like humans and other vertebrates. Sentience and intelligence notwithstanding, cephalopods can experience pain, fear, and anxiety (as well as positive emotions), and on this basis alone they deserve regulatory protection and consideration for their welfare.

For example, causing injury to unanesthetized squid or octopuses causes immediate “escape jetting and ink release.” (Walters, 2018) Injured octopuses have shown wound-grooming behavior and holding of the injured arm, (Crook, 2021) but these and other pain-related behaviors are abolished following the administration of local anesthesia in both species. (Crook, 2021) (Walters, 2018)

Octopuses also exhibit behaviors that indicate they *remember* painful experiences, such as “avoiding contexts in which pain was experienced” or preferring a “location in which they experienced relief from pain.” These indicate an emotional response and not mere reflexive response to noxious stimuli. Similarly, injured squid also became “more likely to join schools of other squid when exposed to predator cues” consistent with an “anxiety-like state.” (Walters, 2018)

Overall, the evidence indicates that cephalopods experience the emotional component of pain, and as such, their pain must be managed appropriately, equivalent to that of vertebrates, in a research setting.

III. International Practices & Community Input

Cephalopods in research already receive protections in other countries. In Canada, protections have been extended to all cephalopods since 1991, (Staaf, 2018) in New Zealand since 1999, in Australia since 2004, and in Switzerland and Norway since 2011. (Fiorito, 2014) In the United Kingdom, crabs, octopuses and lobsters were enshrined in the law as “sentient beings” in 2021. (United Kingdom, 2021)

The 2010 EU Directive 2010/63/EU—which provides regulations on the protection of animals used for scientific research for 28 countries—represented a landmark for cephalopod protection under the law. It was the “first time that an entire class of invertebrates, covering approximately 700 known species,” was “included in laboratory animal legislation throughout the EU.” (Fiorito, 2015) Such restrictions do not seem to have impeded scientific progress; indeed, the research director of the Biology and Evolution of Marine Organisms Department at the Zoological Station Anton Dohrn, which specializes in the evolution of complex cognitive abilities using *Octopus vulgaris*, has noted that “we can do whatever research is scientifically, logically justifiable.” (Staaf, 2018)

In the United States, Harvard Law School’s Animal Law & Policy Program filed a petition for rulemaking on behalf of several NIH experts and animal protection groups requesting the inclusion of cephalopods

in the PHS Policy on Humane Care and Use of Laboratory Animals. (Harvard Law School Animal Law & Policy Program, 2020) This petition, which was followed by a call for cephalopod protections from more than a dozen lawmakers, indicates significant support within the United States for expanded cephalopod protection. (Harvard Animal Law & Policy Clinic, 2022)

“How animals are used in research depends not only on the regulatory and ethical environment but also on attitudes about which species are considered worthy of moral concern.” (Harvey-Clark, 2011) As shown above, the case for cephalopod intelligence and sensitivity to pain has only grown. It is time the United States caught up with the other countries that recognize cephalopods’ need for protection.

IV. Guidance language

AWI strongly supports the proposed requirement that “cephalopod activities are subject to review and approval by IACUCs or other oversight bodies, and subsequent post-approval oversight, in accordance with U.S. Government Principles” as a basic step needed to ensure proper protections.

However, cephalopods **must receive the same care as any other animals monitored by the IACUCs.** As indicated above, cephalopods are intelligent, sentient and able to experience pain and other emotions, and therefore should be treated similarly to vertebrates by IACUCs and animal researchers. Accordingly, the proposed language should be amended from “may choose” and “are encouraged” to “must.”

Namely:

“Institutions **must** include cephalopod programs in other methods of post-approval monitoring used by the institution and **must** self-report any deficiencies to OLAW.”

“IACUCs and oversight bodies **must** develop institutional policies and Standard Operating Procedures (SOPs) that summarize expectations and promote consistency and quality of cephalopod care and use.”

Including cephalopods in IACUC oversight would be largely futile without required reporting of deficiencies to OLAW. Unlike the USDA, OLAW does not conduct inspections and relies heavily on institutions to engage in self-monitoring. Required reporting is a necessary level of protection in such a system.

AWI also strongly supports a requirement that institutions follow the American Veterinary Medical Association’s Guidelines for the Euthanasia of Animals, which includes guidance on the humane euthanasia of invertebrates. AWI also endorses the RFI language that states institutions “are expected to provide appropriate husbandry and veterinary care by employing research, husbandry, veterinary care, and physical plant staff with qualifications and training relevant to the species being used” (OLAW, 2023) as this will encourage incorporation of “good scholarship, best practices, and use of the most current information.” (Harvey-Clark, 2011) As indicated below, it is our hope that significant research will be devoted to better determining appropriate care guidelines for these species, and experts in their care will be needed to keep up with changing scientific knowledge.

AWI also feels it is important to encourage more research into pain alleviation and proper care in cephalopods. While significant advances have been made in advancing the 3Rs for cephalopods,

including effective pain alleviation (see Fiorito et al. 2015; Crook, 2021), more research is needed to make knowledge in these species comparable to that regarding vertebrates. “Because these are a fundamentally different evolutionary branch of animals, it’s really hard to know whether a drug that you would give to enhance welfare in a vertebrate animal is at all effective in a cephalopod.” (Mullin, 2023) To properly protect these animals, more research into their specific needs is necessary.

V. Conclusion

Evidence strongly indicates that cephalopods experience the “emotional state” of pain rather than just a simple reflex response based on nociception. (Crook, 2021) Furthermore, the precautionary principle suggests that “neural and cognitive complexity is sufficient to suggest that an animal can experience pain” even if conclusive evidence is currently lacking. (Crook, 2021) As noted by renowned marine biologist Chris Harvey-Clark “in the absence of a definitive understanding of welfare implications in these species, scientists and IACUC members should strive to respect life, follow 3Rs principles (reduce, refine, replace), and minimize the trauma and severity of procedures when possible.” (2011) The evidence above clearly shows we have reached a point where we need to treat cephalopods as we do vertebrates.

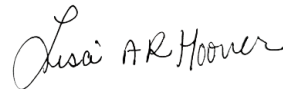
Harvey-Clark has also noted that “the value of a conscientious IACUC in oversight of the use of invertebrates in research cannot be overstated, reflecting the leadership and overall institutional conscience concerning the use of all animals.” (2011) Ultimately, cephalopods should not be regarded as “second class citizens” (Harvey-Clark, 2011) and must be accorded the same protections as vertebrate research animals.

Thank you for your consideration.

Sincerely,



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