Re: Docket No. FDA-2015-N-0045 for International Drug Scheduling; Convention on Psychotropic Substances; Single Convention on Narcotic Drugs; Ketamine; Phenazepam; Etizolam; 1-cyclohexyl-4-(1,2-diphenylethyl)-piperazine (MT-45); N-(1-Phenethylpiperidin-4-yl)-N-phenylacetamide (Acetylfentanyl); α-Pyrrolidinovalerophenone (α-PVP); 4-Fluoroamphetamine (4-FA); para-Methyl-4-methylaminorex (4,4’-DMAR); para-Methoxymethylamphetatmine (PMMA); 2-(ethylamino)-2-(3-methoxyphenyl)cyclohexanone (Methoxetamine or MXE); Request for Comments

The American Physiological Society (APS) wishes to register our strong objection to the proposal to change the international regulation of ketamine. The APS is a professional society of more than 11,000 members involved in research to understand basic biological systems and processes in humans and animals. We appreciate the opportunity to submit these comments to help shape the FDA’s position at the upcoming November 16-20 meeting of the World Health Organization’s 36th Expert Committee on Drug Dependence (ECDD).

Ketamine is currently classified in the U.S. as a Schedule III drug under the Controlled Substances Act. Consequently, it is strictly regulated, and safeguards are in place to prevent its illegal or unauthorized use. A change to this status would have deleterious impacts in clinical and research settings, where ketamine is approved as an anesthetic both for humans and animals.

Ketamine is used for sedation and analgesia in clinical veterinary practice as well as in animal research. Because ketamine acts rapidly and its effects are short-lived, it is very useful for short surgical procedures in species ranging from rodents to non-human primates. Ketamine promotes animal welfare because the risk of overdose is low so there are fewer complications.

For these same reasons—quick onset of effect, rapid recovery, and low risk of complications—ketamine is also used in human surgeries for pediatric patients.

In longer surgeries in human and animal patients, ketamine is used in combination with other drugs to produce stable anesthesia with fewer side effects.

In research settings, ketamine is often the anesthetic of choice for short surgical procedures in rats and mice, such as to implant medical devices such as catheters, pressure transducers, and osmotic mini-pumps. These implants enable researchers to measure physiological processes with less handling of the animals. Since ketamine provides rapid recovery with a minimal risk of complications, it further promotes the animal welfare objectives of implants, namely to collect data as a minimal impact on the animals.

Ketamine has attributes that are essential for certain kinds of research. It is preferable to other anesthetic agents when cortical neuron activity must be measured because it does not silence the spontaneous activity of those neurons. Without ketamine, it would be impossible to conduct many electrophysiological studies and optogenetic studies. Ketamine is also one of the few
anesthetics that does not disturb glucose metabolism, making its use critical to studies of diabetes and glucose tolerance.

Ketamine is incorporated into the research protocols for a large percentage of pre-clinical research studies. Changing the international regulation of ketamine would have a deleterious impact on this research by severely limiting access to an important anesthetic agent.

We urge the FDA to safeguard the welfare of humans and animals by strongly opposing any changes to the international regulation of ketamine that would make this drug less accessible to physicians, veterinarians, and research scientists.