*Aquatic Mammals* 2023, *49*(1), 94-103, DOI 10.1578/AM.49.1.2023.94

# Evaluating the Use of Diazepam in Stranded Dolphins and Porpoises for Husbandry and Veterinary Purposes

Ronald A. Kastelein,[1] Martin J. Bakker,[2] Nancy Jennings,[3] and Jennifer Covi-Dijkhuizen[4]

[1]*Sea Mammal Research Company (SEAMARCO), Julianalaan 46, 3843 CC Harderwijk, The Netherlands*
*E-mail: rk@seamarco.nl*
[2]*Kaatstraat 123, 3513 BV Utrecht, The Netherlands*
[3]*Dotmoth, 1 Mendip Villas, Crabtree Lane, Dundry, Bristol BS41 8LN, UK*
[4]*Trinserhof 106, 6152 Trins, Austria*

## Abstract

We evaluated the use of diazepam (Valium®) during the rehabilitation of odontocetes (dolphins and porpoises) to facilitate husbandry and for veterinary purposes, by analyzing detailed records from a period of 14 years of the treatment of 16 stranded individuals: harbor porpoises (*Phocoena phocoena*), white-beaked dolphins (*Lagenorhynchus albirostris*), a common dolphin (*Delphinus delphis*), and a striped dolphin (*Stenella coeruleoalba*). Diazepam was used occasionally (once per case or for a few days at a time) to facilitate husbandry, including for managing stressful and transitional circumstances and during transport. It was also used occasionally (once per case) for veterinary purposes, such as to reduce stress or to facilitate x-ray scanning, gastroscopy, blood sampling, or wound treatment. Diazepam was found to be effective as an anti-anxiety drug, to cause drowsiness (i.e., reduce activity levels), as a muscle relaxant, and as an appetite stimulant. The doses used were similar for husbandry and veterinary purposes (0.03 to 0.44 mg/kg body weight), and the drug was administered almost exclusively orally (via fish) or via intramuscular injection.

**Key Words:** diazepam, Valium®, rehabilitation, standings, stress, common dolphin, harbor porpoise, striped dolphin, white-beaked dolphin, odontocetes

## Introduction

Diazepam (most common trade name: Valium®) is a benzodiazepine drug that increases the effect of gamma-aminobutyric acid (GABA), an inhibitory neurotransmitter in mammals, thus reducing neuronal excitability in the nervous system. The result is anxiolysis, anticonvulsion, and sedation (Mason, 2004), so the drug can be used to reduce anxiety, to increase drowsiness (Švob Štrac et al., 2012), to treat epileptic seizures, and as a pre-anesthetic. It is also used to stimulate appetite in emaciated mammals (e.g., in cats and horses; Walsh & Gearhart, 2001).

Diazepam's impact on the cardiovascular system is minor, which makes it a favorable medication to facilitate stressful procedures. Diazepam does not have an analgesic effect (Riebold et al., 1995), but it is used as a pre-anesthetic. However, the depressive effect on the respiratory system of some anesthetics can be increased by the sedative effect of diazepam (Erhardt et al., 2004). If treatment with diazepam continues long-term, human patients can develop pharmacological tolerance (adaptation of the brain to the drug), which results in reduced effectiveness of the same dose over time (Göthert et al., 2001). Physical addiction to diazepam can also occur. Therefore, long-term use should be avoided, and if it is required, the dose should be reduced gradually when possible to minimize anxiety, withdrawal symptoms, and muscle cramps (Sloan et al., 1993; O'Brien, 2001).

Diazepam is prescribed to humans and for use in veterinary medicine; its use in marine mammals is common, but not well documented (Dierauf & Gulland, 2001). During the rehabilitation of stranded wild odontocetes (toothed whales), stressful situations can occur, and treatment and examination for veterinary purposes is required. Most stranded odontocetes are emaciated and sick or injured. Stress may lead to suppressed immunity (Dhabhar, 2009), slow wound healing (Gouin & Kiecolt-Glaser, 2011), and reduced food intake. Particularly in recently stranded odontocetes, a decrease in food intake may further slow or prevent recovery, so an anxiolytic drug is indicated. Larger stranded odontocete species may cause

injury to staff during husbandry and veterinary procedures. Diazepam can reduce the risk of bodily harm to the handlers by reducing the animals' anxiety and making them calmer and more cooperative.

We analyzed historical records to evaluate whether diazepam is a beneficial drug to facilitate husbandry and for veterinary purposes in stranded odontocetes, and to recommend effective doses. Detailed records, kept during the rehabilitation of 16 individual stranded odontocetes over a period of 14 y, formed the basis of our qualitative analysis.

## Methods

We analyzed historical records of diazepam usage during the rehabilitation of 16 individual odontocetes that had stranded on the Dutch and Belgian coasts (Kastelein et al., 1990, 1997a): 11 harbor porpoises (*Phocoena phocoena*), three white-beaked dolphins (*Lagenorhynchus albirostris*), one common dolphin (*Delphinus delphis*), and one striped dolphin (*Stenella coeruleoalba*). In most cases, diazepam was given to the subjects before a husbandry or veterinary procedure, either orally (via fish) about 1 h before or by intermuscular injection about 30 min before. Diazepam is a Schedule IV controlled drug under the United Nations' International Convention on Psychotropic Substances and a prescription drug in most countries. The use of diazepam at the doses reported here was prescribed by author Martin Bakker, DVM. Rehabilitation staff kept careful records of doses, responses, and effectiveness. Experiences and information from this database are presented here, divided into cases in which diazepam was used for husbandry purposes (including transport; Table 1) and cases of veterinary use (Table 2).

## Results

### *Use of Diazepam for Husbandry Purposes*

*Transport of Stranded Odontocetes from the Coast to a Rehabilitation Facility*—Becoming stranded must be one of the most stressful things that can happen to an odontocete. A stranded odontocete finds itself on land, unable to move, overheating due to the lower thermal conductivity of air compared to water, and with pressure points on the chest and abdomen (in water, the body is more evenly supported). Individuals are usually in poor condition before stranding and may die on the coast or during transport to a rehabilitation facility. If rescue is attempted, odontocetes with sufficiently high respiration force and frequency can be given diazepam anally or intramuscularly to reduce the stress caused by transportation. This was done with harbor porpoises, white-beaked dolphins, and a striped dolphin (Table 1).

*Swimming*—Wild odontocetes swim freely in open water with plenty of space around them. In rehabilitation facilities, space is much more confined. The senses of recently stranded odontocetes are often less acute than normal, and their motor control is often reduced. As a result, some odontocetes either swim into the pool wall or swim along the wall while in contact with it. Both can cause injuries, such as broken jaws, wounds, bruises, or abrasions of body parts (e.g., the rostrum, the tips of tail flukes, or pectoral fins). In some cases, diazepam can reduce the animals' activity levels and thus their swimming speed, therefore reducing the chance of injuries. The correct low dose is very important in this case: too much diazepam can reduce the acuity of the senses and the precision of motor control, leading to increased collisions. Diazepam was used for this purpose in harbor porpoises and a striped dolphin (at low doses: 0.06 and 0.03 mg/kg, respectively; Table 1).

Some stranded odontocetes cannot swim on arrival at a rehabilitation facility. If they are too big to be supported by staff, there are not enough staff to provide constant support, or the pool is too deep for staff to stand in, these animals need to be supported in hammocks. If their tail movements are strong, skin abrasions can be caused by the edges of the hammock. Tail movements can be reduced with diazepam; this was done for several days at a time with white-beaked dolphins and a common dolphin (Table 1; Kastelein et al., 1995). Harbor porpoises are relatively easy to handle due to their small size, so they are usually supported by staff, thus avoiding abrasions and the need for diazepam.

*Feeding*—Wild odontocetes do not eat dead fish, but most captive odontocetes are fed on thawed fish. Newly stranded individuals are reluctant to eat dead fish. To avoid further malnutrition (as odontocetes often strand in an emaciated condition), most odontocetes are assisted with feeding several times (e.g., by placing fish in their mouth until they swallow) before they begin to take thawed fish voluntarily from the hand or from the water. Assisted feeding, which involves handling the odontocete (opening its mouth) and restricting its movements (especially lateral movements of the jaws), can be stressful. Diazepam was administered to reduce stress during assisted feeding of harbor porpoises and a striped dolphin. The diazepam given via a fish in one feed can facilitate the next feed (Table 1).

**Table 1.** The diazepam doses given for husbandry purposes to 11 harbor porpoises (*Phocoena phocoena*), three white-beaked dolphins (*Lagenorhynchus albirostris*), one common dolphin (*Delphinus delphis*), and one striped dolphin (*Stenella coeruleoalba*). IM = intramuscular injection; PO = per oral (i.e., a pill or capsule put into the fish which was fed or given during assisted feeding).

| Reason for administering diazepam | Anti-anxiety | Reduce activity | Muscle relaxant | Appetite stimulant | Body weight (kg) | Dose (mg/ kg body weight) | Number of animals | Dosage, frequency, and notes | Administration method |
|---|---|---|---|---|---|---|---|---|---|
| **Harbor porpoise** | | | | | | | | | |
| Transport from the coast to the rehabilitation facility (sick; after stranding) | ✓ | | | | 15-39 | 0.25 | 8 | Once for each animal, just before transport | Anal/IM |
| Assisted feeding (newly arrived; stranded) | ✓ | | | ✓ | 28 | 0.07 | 1 | Each meal to facilitate the next meal. Continued until the porpoise was used to the assisted feeding procedure. | PO |
| Transition to hand-feeding | ✓ | | | | 21 & 24 | 0.24 | 2 | Each meal to facilitate the next meal. Continued until fish was taken from the hand. | PO |
| Taking body measurements, including weight | ✓ | ✓ | | | 30 | 0.24 | 1 | On one occasion (a newly arrived animal) | PO |
| Dangerous swimming relative to pool wall | | ✓ | | | 27 & 32 | 0.06 | 2 | One animal once, and one animal for 31 d | PO |
| Social sexual problems | | ✓ | | | 34 | 0.05 | 1 | Four days until the problems ceased | PO |
| Social aggressive problems | | ✓ | | | 29 | 0.06 | 1 | Several times a day for 7 d until the problems ceased | PO |
| Too active social interactions relative to health condition | | ✓ | | | 21-33 | 0.09 | 3 | Several times until the problems ceased (for 11, 9, and 2 d, respectively) | IM/PO |
| Changes in environment: introduction of a new large object in the pool | ✓ | | | | 24 | 0.12 | 1 | On one occasion | PO |
| Tattooing an identification code | ✓ | ✓ | | | 28-32 | 0.25 | 3 | Once per animal, a week before release at sea | PO |
| Transport to another facility to improve physical condition for release at sea (healthy) | ✓ | | | | 24-37 | 0.13 | 7 | Once per transport, which lasted a few hours | IM/PO |
| **White-beaked dolphin** | | | | | | | | | |
| Transport from the coast to the rehabilitation facility (sick; after stranding) | ✓ | | | | 54 | 0.09 | 1 | Once, just before transport | IM |
| Supported swimming in hammock | ✓ | | ✓ | | 54-70 | 0.14 | 3 | Several times until able to swim without support | PO |
| Draining pool for maintenance | ✓ | ✓ | | | 110 | 0.14 | 1 | Once per occasion (one a week for several months) | PO |
| Transport for release at sea (healthy) | ✓ | ✓ | | | 70 & 70 | 0.14 | 2 | Once per animal for transport | PO |

| Reason for administering diazepam | Anti-anxiety | Reduce activity | Muscle relaxant | Appetite stimulant | Body weight (kg) | Dose (mg/kg body weight) | Number of animals | Dosage, frequency, and notes | Administration method |
|---|---|---|---|---|---|---|---|---|---|
| **Common dolphin** | | | | | | | | | |
| Tube-feeding | ✓ | | | | 124 | 0.09 | 1 | Each meal to facilitate the next meal until the dolphin became used to the procedure (3 d) | PO |
| Supported swimming in hammock | | | ✓ | | 124 | 0.08 | 1 | Twice on 1 d until able to swim without support | PO |
| Draining pool for maintenance | ✓ | ✓ | | | 119 | 0.06 | 1 | Once per occasion (two occasions) | IM/PO |
| **Striped dolphin** | | | | | | | | | |
| Transport from the coast to the rehabilitation facility (sick; after stranding) | ✓ | | | | 61 | 0.24 | 1 | Once, just before transport | IM |
| Assisted feeding (newly arrived) | ✓ | | | ✓ | 61 | 0.20 | 1 | Each meal to facilitate the next meal until the dolphin became used to the procedure (2 d) | IM |
| Reduce dangerous swimming (relative to the pool wall) | | ✓ | | | 65 | 0.03 | 1 | Several times; each time for 1 d until the problems ceased | PO |
| Weighing | ✓ | ✓ | | | 66 | 0.12 | 1 | Once per weight measurement (10 occasions) | IM/PO |
| To facilitate gating | ✓ | | | | 68 | 0.08 | 1 | Three times until the gate was passed through voluntarily | PO |
| Transport to another facility to improve physical condition (healthy) | ✓ | ✓ | | | 63 | 0.16 | 1 | Once, just before transport; four times (back and forth from the rehabilitation facility to a bigger floating pen) | IM/PO |
| Tattooing an identification code | ✓ | ✓ | | | 67 | 0.07 | 1 | Once, a week before release at sea | PO |
| Transport for release at sea (healthy) | ✓ | ✓ | | | 67 | 0.07 | 1 | Once, just before transport | PO |

The transition from assisted feeding to hand-feeding can be stressful since just seeing a fish in a human hand or a fish thrown into the water is stressful at first. The transition can be accelerated by the use of diazepam. Diazepam was used for this purpose in harbor porpoises (Table 1).

Young odontocetes that were still being nursed by their mothers at the time of stranding often need to be given formula, either via a bottle with a nipple or by tube-feeding via a large syringe attached to a stomach tube (Kastelein et al., 1997b). In our experience, young odontocetes are more adaptable than adults and do not seem to find tube-feeding particularly stressful. Adult animals that are emaciated and dehydrated are also sometimes tube-fed, which can be stressful for them. Tube-feeding involves animals being handled and immobilized, which can be dangerous for them and their handlers. To reduce the stress of this feeding method in odontocetes, diazepam can be used; this was done in a common dolphin (Table 1). If tube-feeding is conducted properly (with or without diazepam), animals usually become accustomed to it after a few days and no longer find it stressful.

**Table 2.** The diazepam doses given for veterinary purposes to 11 harbor porpoises, three white-beaked dolphins, one common dolphin, and one striped dolphin. IM = intramuscular injection; PO = per oral (i.e., a pill or capsule put into the fish which was fed or given during assisted feeding).

| Reason for administering diazepam | Anti-anxiety | Reduce activity | Muscle relaxant | Appetite stimulant | Body weight (kg) | Dose (mg/ kg body weight) | Number of animals | Dosage, frequency, and notes | Administration method |
|---|---|---|---|---|---|---|---|---|---|
| **Harbor porpoise** | | | | | | | | | |
| Gastroscopy | ✓ | | | | 22-37 | 0.14 | 4 | Once per occasion; generally twice per animal | IM |
| Transmitter attachment with pins to dorsal fin | ✓ | | | | 33 & 34 | 0.22 | 2 | Once per procedure and per animal | PO |
| Blood sampling from tail fluke | ✓ | ✓ | | | 19 & 30 | 0.18 | 2 | Twice per animal | PO |
| Treatment of painful wound | ✓ | ✓ | | | 19-30 | 0.05 | 3 | Several times (26 times, twice, and once per porpoise) until the wound seemed less painful | PO |
| Reduce belly cramps (given with an opioid) | | | ✓ | | 20 | 0.10 | 1 | Once per occasion on two occasions | PO |
| Reduce stereotypical swimming patterns | ✓ | | | | 20 & 32 | 0.11 | 2 | Several times per day until the problem ceased (10 and 19 d, respectively) | PO |
| Reduce shaking through stress | ✓ | | ✓ | | 15 & 28 | 0.44 | 2 | Once per animal during severe stress | IM |
| To increase appetite | | | | ✓ | 21 & 30 | 0.10 | 2 | Once per animal; also to ensure that oral medication was taken | PO |
| **White-beaked dolphin** | | | | | | | | | |
| Reduce pain or stiffness in tailstocks | | | ✓ | | 70 & 70 | 0.16 | 2 | Several times in the first few days after arrival at the rehabilitation facility until tailstocks became more supple | PO |
| Capture in pool for veterinary examination and carrying out examination | ✓ | ✓ | | | 128 | 0.12 | 1 | Once on each of two occasions until the dolphin was used to the procedure | PO |
| **Common dolphin** | | | | | | | | | |
| Reduce very forceful coughing | | | ✓ | | 107 | 0.09 | 1 | In one case | IM |
| Gastroscopy next to pool | ✓ | ✓ | | | 107 | 0.09 | 1 | On one occasion | IM |
| X-ray examination at human hospital | ✓ | ✓ | | | 127 | 0.11 | 1 | On three occasions | IM |
| Computed tomography scanning next to pool | ✓ | ✓ | | | 124 | 0.16 | 1 | In one case | IM |
| Potentially painful physiotherapy | ✓ | ✓ | ✓ | | 126 | 0.32 | 1 | Several times over 3 d until the tailstock became supple | IM |

| Reason for administering diazepam | Anti-anxiety | Reduce activity | Muscle relaxant | Appetite stimulant | Body weight (kg) | Dose (mg/kg body weight) | Number of animals | Dosage, frequency, and notes | Administration method |
|---|---|---|---|---|---|---|---|---|---|
| Striped dolphin | | | | | | | | | |
| Reduce high respiration rate due to stress | ✓ | | | | 61 | 0.16 | 1 | Once shortly after first arrival at the rehabilitation facility | IM |
| Reduce belly cramps (given with an opioid) | | | ✓ | | 61 | 0.16 | 1 | On one occasion | IM |
| Capture for veterinary examination | ✓ | | | | 62 | 0.19 | 1 | On five occasions | PO |
| Gastroscopy next to pool | ✓ | | | | 62 | 0.24 | 1 | On one occasion | IM |
| Ultrasound scan | ✓ | | | | 63 | 0.19 | 1 | In one case | PO |

*Taking Body Measurements*—Taking and monitoring body measurements, such as body weight, length, girth, and blubber thickness, are important parts of animal husbandry, especially during rehabilitation. Newly arrived beached odontocetes are untrained and should remain untrained if they are to be released soon after recovery. Taking body measurements often requires lifting them from the water and handling them, which is stressful. Diazepam can reduce stress during handling, so the procedure will not get more difficult over time but, instead, will become easier to perform. In larger odontocetes, diazepam also reduces the risk of bodily harm to the handlers by reducing the animals' anxiety, making them calmer and more cooperative. Diazepam was used while taking body measurements from some harbor porpoises and a striped dolphin (Table 1).

*Gating*—Gates within rehabilitation pools are used to separate animals; to move them around; and to confine them to areas suitable for treatment, feeding, or body measurements. Stranded odontocetes should not be trained, but they must become accustomed to gating procedures, despite their natural reluctance to be confined and to go through narrow passages. Diazepam can be used to facilitate habituation to gating and the luring process required for gating. Diazepam was used to help facilitate the gating process for a striped dolphin (Table 1).

*Social Situations*—If a newly arrived stranded odontocete needs to be treated in a pool that already houses another more active and perhaps healthier animal (a conspecific or another species), this can cause problems to the recuperating animal if the social interactions are too vigorous for its health status. The more active animal may approach the recuperating animal sexually, aggressively, or playfully, causing stress or injury to the recuperating animal (for instance, water may enter the blowhole of the recuperating animal). The recuperating animal may be unable to avoid, rebut, or accept these advances, and the social interactions may prevent or hinder the rehabilitation of the recuperating animal. Diazepam can be used to reduce the activity level of the more active animal for a while until the recuperating animal recovers sufficiently to respond appropriately, or until the animals can be separated (e.g., when another pool becomes available). Diazepam was used in harbor porpoises for this purpose (Table 1).

*Changes in the Environment*—Changes to the rehabilitation environment, made for maintenance, improvement, or by the introduction of new equipment, can cause stress. Diazepam can be used in the short term to reduce this stress, as was done for some harbor porpoises (Table 1).

Draining the pool completely for maintenance or cleaning can evoke stress in some odontocetes, especially if the pool is emptied and the animals are temporarily "beached." In such cases, the administration of diazepam can reduce stress and thus prevent overheating and injury to the odontocetes or, in the case of larger animals, injury to staff. This was done for white-beaked dolphins and a common dolphin (Table 1).

*Transport to Other Facilities or for Release at Sea, and Preparation for Release*—Diazepam was used in preparation for release at sea: to facilitate tattooing identification numbers on the tailstocks of harbor porpoises and a striped dolphin by reducing anxiety and activity (Table 1).

After successful veterinary treatment, odontocetes may need to be transported to a bigger rehabilitation

facility or to a soft-release pen to improve their physical condition and to allow them to swim fast and dive deep. Eventually, they can be transported for release at sea. In contrast to during transport after stranding, they are healthy and strong at this time, and their senses are acute. Transport (which usually occurs in a hammock or on a foam mattress) can still be stressful for them due to their immobility and the noise in transport vehicles (e.g., vans, helicopters, or ships), and odontocetes can become overheated or injure themselves in the transport equipment. Larger species may also pose a risk to staff. We administered diazepam to healthy harbor porpoises, white-beaked dolphins, and a striped dolphin for transport (Table 1).

*Use of Diazepam for Veterinary Procedures*

*Capturing an Animal for Veterinary Investigations and Procedures*—Odontocetes, especially those that stranded recently, must be handled for most veterinary investigations and procedures, sometimes several times per day (e.g., for gastroscopy, blood sampling, injection of medication, wound treatment, etc.). Catching odontocetes in a pool is difficult and can be stressful. Administration of diazepam to the subject orally sometime before the capture event can help to make capture less stressful. In very rare cases, pool-mates of the subject that have a more anxious personality may need to be given diazepam as well, as they may also find the capture procedure stressful, especially if they are herded simultaneously with the subject. We administered diazepam to a white-beaked dolphin and a striped dolphin for capture for veterinary examination (Table 2).

*Facilitating Veterinary Procedures and Preparation for Release at Sea*—Odontocetes may find veterinary procedures stressful, which may result in injury to them or to staff. A relatively high dose of diazepam can be given before the procedure to ensure that the animal becomes drowsy and lies calmly. After the procedure, the animal should be returned to the pool with extra staff to prevent accidental collision with the pool wall or rolling over (which may result in drowning). Once the animal's behavior has returned to normal (generally in less than 1 h), the staff can leave the pool. Diazepam was used to facilitate one or more of the following veterinary procedures in all four species: gastroscopy, ultrasound scanning, x-ray examination, general veterinary examination, computed tomography scanning, blood sampling, tailstock physiotherapy, and wound treatment (Table 2). In preparation for release at sea, diazepam and lidocaine (a local analgesic) were used to facilitate attaching a transmitter to the dorsal fin of a harbor porpoise with pins going through the fin (carried out in collaborative research, but included here as "veterinary" as it is an invasive procedure; Table 2).

*Reducing Stress and Reactions to Pain*—Some stranded odontocetes are so stressed that they shake, breathe very frequently, swim in stereotypical patterns, or swim much faster than usual, which increases their energy requirement; this can cause problems, especially in animals that are emaciated. Diazepam can be given to reduce their physical exertion, thus saving energy that can be used to gain weight. Stranded odontocetes that cannot swim may experience painful cramps in the abdomen (shown by the tailstock bending towards the abdomen); weak animals may die if cramps are severe. Diazepam can be given as a muscle relaxant in combination with an opioid to make an animal with abdominal pain feel more comfortable. Diazepam can also be used to reduce very forceful and prolonged coughing, which can be accompanied by apparent pain. Diazepam was given for these reasons to harbor porpoises, a common dolphin, and a striped dolphin (Table 2).

*Intake of Food and Medicine*—The appetite of a stranded odontocete may be reduced due to psychological and physiological factors brought about by the environment or due to pathological factors. Increasing the appetite is important to facilitate recovery, weight gain (which enhances thermal insulation), or growth, but also to allow oral administration of drugs and vitamins inside fish. Some medication can only be given orally, which is the least stressful and invasive method of administering drugs. Puncture wounds caused by injection of drugs heal slowly in odontocetes and can be pathways for infection. In addition, intramuscular injection can result in pain and reduced appetite. Diazepam can increase the appetite to expedite recovery (Walsh & Gearhart, 2001), or sufficiently enough to keep an animal eating at least a few fish per meal (allowing medication to be given orally without assisted feeding, which may involve stressful herding) for as long as, for instance, treatment with antibiotics is required. Diazepam was used to increase the appetite of some harbor porpoises (Table 2).

## Discussion

*Dosage of Diazepam*

Knight (2013) describes the effects of various doses of diazepam on bottlenose dolphins (*Tursiops truncatus*): at low doses it reduces excitability; at moderate doses it reduces anxiety and may increase interactive behavior; and at high doses it produces sedation, incoordination, disorientation, and, in some animals, sleepiness and vomiting. Knight suggests doses of diazepam for captive bottlenose

dolphins of 0.1 to 0.2 mg/kg intramuscularly and 0.25 to 1.0 mg/kg orally. Diazepam was given to bottlenose dolphins to reduce anxiety intramuscularly at doses of 0.14 to 0.152 mg/kg, and oral diazepam was given to increase appetite in two long-term captive belugas (*Delphinapterus leucas*) for 2-wk periods and in four bottlenose dolphins for 1-wk periods at 0.09 mg/kg (Brian Joseph, pers. comm.). In the present study, doses ranged from 0.03 to 0.44 mg/kg, and dose ranges for intramuscular and oral administration overlapped (Tables 1 & 2). In all cases, the desired effect was achieved. Each dose reported here was given only to one or a few individuals, sometimes only once, so our data on optimizing dose and dosage remain limited. The doses given should therefore be used only as general indications (Tables 1 & 2). The dose of diazepam required to elicit a certain effect can vary greatly between individual animals of the same species (Dean, 2012). In each individual, treatment should start with a low dose, and careful records should be kept of responses and behavior so that, if the drug is needed again, the veterinarian will have a better knowledge of the appropriate dose.

*Frequency of Diazepam Administration and Effective Duration*

In many cases (Tables 1 & 2), a dose of diazepam was only given once to an individual (e.g., for a specific procedure such as transport or a veterinary examination). A dose was given several times per day (every ~4 to 8 h, if necessary, through the night) to individuals that required effects over several days (e.g., for assisted feeding, supported swimming in a hammock, or appetite stimulation). Effects lasted for several hours after each dose of diazepam was administered.

*Methods of Administering Diazepam*

Oral administration of diazepam is the least stressful and least invasive method, and it is preferred unless there is a reason to avoid it. Diazepam pills or capsules can be administered orally inside fish given to odontocetes that are eating voluntarily, or they can be given during assisted feeding; this does not cause additional stress.

Diazepam is given via intramuscular injection (generally in the dorsal muscles) to odontocetes that are not eating or when it is undesirable to have food in the stomach (for instance, before or during transport, or before gastroscopy and bronchoscopy). In emergencies, when quick effects are desired, intramuscular injection is the best way to administer diazepam. However, injections require handling and immobilization of the animal, cause stress, and require more staff than oral administration. Injections also cause puncture wounds in the skin which heal more slowly than in most terrestrial mammals, can be entry points for bacteria or viruses causing infections, and may cause pain.

Diazepam is sometimes given with another drug for sedation (intramuscularly or intravenously). If a large dose of diazepam is given intravenously, respiratory arrest can occur due to the muscle relaxation induced (Löscher, 2003). In fur seals (*Arctocephalus philippii*), internal body temperature and heart rate were higher after intravenous application of ketamine together with diazepam than when the same drugs were given intramuscularly (Sepúlveda et al., 1994). We avoided the intravenous injection of diazepam because all the stranded odontocetes in the present study were too active for the precision required.

*Disadvantages of Diazepam and Interaction with Other Drugs*

We encountered only one disadvantage of diazepam. After a relatively large dose had been administered for a procedure on land, some individuals required support while swimming once they had been returned to the pool. Without support, they would list, submerge, or bump against the pool wall, potentially injuring their rostrum. However, these effects may have been exacerbated by the illness of the animals. In preparation for any problems, staff would be ready in their wetsuits to support and guide the animal in the water, if required, for about 1 h after the procedure.

Possible side effects of diazepam in bottlenose dolphins are confusion, reduced coordination, aggression, excitation, reduced liver and kidney function, built-up tolerance, and addiction (Knight, 2013). These side effects seem unlikely if high doses and long-term use are avoided.

Diazepam may interact with antacids used as a treatment for gastric ulceration. Antacids may inhibit the elimination of diazepam and increase the risk of toxicity (Knight, 2013).

*Uses of Diazepam*

We used diazepam mainly as an anti-anxiety drug, to reduce activity levels, as a muscle relaxant, and as an appetite stimulant.

*Anti-Anxiety Drug*—Diazepam was used successfully as an anti-anxiety drug in procedures such as transport, assisted feeding, tube-feeding, transition to hand-feeding, taking body measurements, changes in the environment or housing, drainage of the pool for maintenance, gating, blood sampling, and wound treatment, and also to reduce stereotypical swimming, to reduce shaking of the body, and to reduce respiration rate. Diazepam (doses from 0.14 to 0.15 mg/kg in about 40 instances) was given to long-term captive bottlenose dolphins to slow respiration and ease anxiety during transport (Brian Joseph, pers. comm.).

*Reduce Activity Levels*—Diazepam was used to cause drowsiness and reduce activity levels when swimming speed was too fast for safety; when animals were too active or rough while interacting socially, sexually, or aggressively; when swimming forcefully while supported in a hammock; to reduce forceful coughing; and to facilitate tattooing identification numbers, transmitter attachments, x-ray examination, ultrasound scanning, computed tomography scanning, gastroscopy, and capture for veterinary examination.

*Muscle Relaxant*—Diazepam was used as a muscle relaxant when newly stranded animals appeared to have pain or stiffness in their tailstocks, probably because they had suffered muscle damage due to moving their tails and overheating while out of the water (beached). It was also used successfully when abdominal cramps were observed and during potentially painful physiotherapy (of the tailstock).

*Appetite Stimulant*—Diazepam was used to stimulate the appetite for recovery, weight gain, and growth, and so that other drugs could be given orally instead of via intramuscular injection. Oral diazepam was given as an appetite stimulant to two belugas for 2-wk periods and to four bottlenose dolphins for 1-wk periods at 0.09 mg/kg. Treatment was successful and did not interfere with orientation or social behavior (Brian Joseph, pers. comm.).

*Conclusions and Recommendations*

Our qualitative analysis demonstrates that diazepam is a highly beneficial and safe drug that can be used to facilitate husbandry and for veterinary purposes in the short term in stranded odontocetes. We recommend similar doses for husbandry and veterinary purposes (0.03 to 0.44 mg/kg body weight), with administration orally (via fish) or via intramuscular injection.

Use of diazepam in veterinary practice with odontocetes is common, but dosage and administration vary depending on the procedure, the species, the age of the subject, and the veterinary practitioner (Jay Sweeney, pers. comm.), and are not well documented. We only have experience with stranded odontocetes of the species described herein and, therefore, cannot confidently advocate prescribing diazepam to other species. However, it seems likely that the drug would be effective in other odontocetes. Whether diazepam is needed or useful for the animal's well-being or recovery depends on the species, the individual animal's personality and health condition, and the context.

We emphasize that diazepam should only be used to tackle short-term problems (lasting a few days at most), such as those described in this paper. If diazepam is required long term or repeatedly, an underlying major health, social, or housing problem needs to be solved. However, diazepam can be useful for the occasional facilitation of husbandry or veterinary procedures in stranded harbor porpoises, white-beaked dolphins, common dolphins, and striped dolphins, thus improving the health and well-being of those animals.

## Acknowledgments

We thank Brian Joseph, DVM, Jay Sweeney, DVM, and Jesse Dijkhuizen for their constructive comments on this manuscript. This study was funded by SEAMARCO, the Netherlands.

## Literature Cited

Dean, L. (2012). Diazepam therapy and CYP2C19 genotype. In V. M. Pratt, S. A. Scott, & M. Pirmohamed (Eds.), *Medical genetics summaries* [Internet]. National Center for Biotechnology Information (USA). https://www.ncbi.nlm.nih.gov/books

Dhabhar, F. S. (2009). Enhancing versus suppressive effects of stress on immune function: Implications for immunoprotection and immunopathology. *Neuroimmunomodulation*, *16*, 300-317. https://doi.org/10.1159/000216188

Dierauf, L. A., & Gulland, F. M. D. (Eds.). (2001). *CRC handbook of marine mammal medicine* (2nd ed.). CRC Press.

Erhardt, W., Henke, J., & Kroker, R. (2004). Allgemeinanästhesie [General anesthesia]. In W. Erhardt, J. Henke, & J. Haberstroh (Eds.), *Anästhesie und Analgesie beim Klein- und Heimtier* [Anesthesia and analgesia in small animals and pets] (pp. 16-87). Schattauer.

Göthert, M., Bönisch, H., Schlicker, E., & Helmchen, H. (2001). Psychopharmaka: Pharmakotherapie psychischer Erkrankungen [Psychotropic drugs: Pharmacotherapy of mental illnesses]. In W. Forth, D. Henschler, W. Rummel, U. Förstermann, & K. Starke (Eds.), *Allgemeine und Spezielle Pharmakologie und Toxikologie* [General and special pharmacology and toxicology] (8th ed., pp. 335-374). Urban & Fischer.

Gouin, J-P., & Kiecolt-Glaser, J. K. (2011). The impact of psychological stress on wound healing: Methods and mechanisms. *Immunology Allergy Clinics of North America*, *31*(1), 81-93. https://doi.org/10.1016/j.iac.2010.09.010

Kastelein, R. A., Bakker, M., & Dokter, T. (1990). The medical treatment of 3 stranded harbor porpoises (*Phocoena phocoena*). *Aquatic Mammals*, *15*(4), 181-202.

Kastelein, R. A., Bakker, M. J., & Staal, C. (1997a). The rehabilitation and release of stranded harbour porpoises (*Phocoena phocoena*). In A. J. Read, P. R. Wiepkema, & P. E. Nachtigall (Eds.), *The biology of the harbour porpoise* (pp. 9-61). De Spil Publishers.

Kastelein, R. A., Dokter, T., & Hilgenkamp, J. (1995). A swimming support for dolphins undergoing veterinary care. *Aquatic Mammals*, *21*(2), 155-159.

Kastelein, R. A., Schooneman, N. M., Staal, C., & Boer, H. (1997b). A method for tube-feeding juvenile harbour porpoises (*Phocoena phocoena*). In A. J. Read, P. R. Wiepkema, & P. E. Nachtigall (Eds.), *The biology of the harbour porpoise* (pp. 63-83). De Spil Publishers.

Knight, J. A. (2013). *Diazepam – Its use in captive bottlenose dolphin (*Tursiops truncatus*)*. https://endcap.eu/wp-content/uploads/2015/06/Diazepam-its-use-in-captive-bottlenose-dolphin.pdf

Löscher, W. (2003). Pharmaka mit Wirkung auf das Zentralnervensystem [Drugs that affect the central nervous system]. In W. Löscher, F. R. Ungemach, & R. Kroker (Eds.), *Pharmakotherapie bei Haus- und Nutztieren* [Pharmacotherapy in domestic and farm animals] (pp. 55-108). Parey Buchverlag/Blackwell Verlag GmBH.

Mason, D. E. (2004). Anesthetics, tranquillizers and opioid analgesics. In J. J. Bertone & L. J. I. Horspool (Eds.), *Equine clinical pharmacology* (pp. 267-310). W. B. Saunders.

O'Brien, C. P. (2001). Drug addiction and drug abuse. In J. G. Hardman, L. E. Limbrid, & A. G. Gilman (Eds.), *Goodman and Gilman's: The pharmacological basis of therapeutics* (10th ed., pp. 621-642). McGraw-Hill, Medical Publishing Division.

Riebold, T. W., Geiser, D. R., & Goble, D. O. (1995). *Large animal anesthesia* (2nd ed.). Iowa State University Press.

Sepúlveda, M. S., Ochoa-Acuña, H., & McLaughlin, G. S. (1994). Immobilization of Juan Fernandez fur seals, *Arctocephalus philippii*, with ketamine hydrochloride and diazepam. *Journal of Wildlife Diseases*, *30*, 536-540. https://doi.org/10.7589/0090-3558-30.4.536

Sloan, J. W., Martin, W. R., & Wala, E. (1993). Effect of the chronic dose of diazepam on the intensity and characteristics of the precipitated abstinence syndrome in the dog. *Journal of Pharmacological Experimental Therapy*, *265*(3), 1152-1162.

Švob Štrac, D., Muck-Šeler, D., & Pivac, N. (2012). The involvement of noradrenergic mechanisms in the suppressive effects of diazepam on the hypothalamic-pituitary-adrenal axis activity in female rats. *Croatian Medical Journal*, *53*(3), 214-223. https://doi.org/10.3325/cmj.2012.53.214

Walsh, M. T., & Gearhart, S. (2001). Intensive care. In L. A. Dierauf & F. M. D. Gulland (Eds.), *CRC handbook of marine mammal medicine* (2nd ed., Chapter 30). CRC Press.