

**File No. 16632 Appendix C: Hawaiian monk seal Drugs for Use in Field**

Drug Name	Dosage/Route of Administration	Use in Hawaiian monk seals	Possible Adverse Effects	Pharmacokinetics
Atropine Sulfate	0.02 -0.2 mg/kg IM, IV, SC (CRC Handbook)	To treat bradycardia (slowed heart rate) or cardiac arrest; may be used as a pre-anesthetic to reduce respiratory secretions and block vagal mediated dive reflex.	<p>Generally dose related; mild effects in healthy patients; severe effects with high or toxic doses include gastrointestinal (constipation, vomiting), central nervous system (CNS).</p> <p>Benzodiazepines may potentiate adverse effects (Veterinary Drug Handbook, 4<sup>th</sup> Ed., Plumb)</p> <p>Used on numerous occasions in Hawaiian monk seals with no adverse reactions reported (NMFS unpubl. data). Used extensively in other pinnipeds during anesthesia with no observed side effects (Haulena and Heath 2001)</p>	Well absorbed with peak effects on heart rate within 3-4 minutes; metabolized in liver and 30-50% of dose excreted unchanged in urine. Half-life (the time required for the concentration of the drug to reach half of its original value) in humans is 2-3 hours.
Ceftiofur crystalline free acid	6.6 mg/kg IM (Meegan et al. 2010)	Long-acting cephalosporin antibiotic for prophylactic treatment of injuries and treatment of infections.	<p>Usually not serious and low occurrence; mild transient pain and possibility of abscess at injection site; diarrhea; hypersensitivity reactions include rash, fever, or anaphylaxis.</p> <p>Used in Hawaiian monk seals with no adverse effects (Permit No. 10137-07, NMFS, unpubl. data). No adverse reactions reported after use in humpback whales, California sea lions, northern elephant seals, and harbor seals (Gulland pers. comm.).</p>	<p>Half-life in cattle is 8-12 hours with peak levels after 30-45 minutes of intramuscular (IM) injection.</p> <p>A study at The Marine Mammal Center (Sausalito, CA) on 10 California sea lions resulted in maximum plasma concentrations at 24 hours post-IM injection; plasma drug levels at lower levels would likely be maintained for 5-8 days post-injection (Meegan et al. 2010).</p>

<b>Drug Name</b>	<b>Dosage/Route of Administration</b>	<b>Use in Hawaiian monk seals</b>	<b>Possible Adverse Effects</b>	<b>Pharmacokinetics</b>
Dexamethasone	0.2 - 1 mg/kg (CRC Handbook)	A glucocorticoid used for treatment of shock; may be used to treat adrenal insufficiency, inflammation, and other maladies.	Usually associated with long-term administration and manifested as clinical signs of hyperadrenocorticism; can retard growth in young animals; when given short-term, unlikely to cause significant harmful effects, even in massive doses.  Few instances of use in Hawaiian monk seals with no adverse reactions reported (NMFS unpubl. data).	Half-life in dogs is 2-5 hours; biologic activity can persist for $\geq$ 48 hours.
Diazepam	0.1-0.25 mg/kg IV	A benzodiazepine used as a sedative (anxiolytic, muscle relaxant, hypnotic) for capture events; may be used as an appetite stimulant or anti-convulsant.	Dogs may exhibit CNS excitement; in horses may cause muscle weakness and ataxia; in cats may cause irritability, depression, aberrant demeanor.  Routinely used sedative in Hawaiian monk seals with no adverse reactions reported (NMFS unpubl. data).	Highly lipid soluble and widely distributed throughout the body; readily crosses blood-brain barrier and is highly bound to plasma proteins; metabolized in liver to active metabolites nordiazepam, temazepam, and oxazepam, which are eliminated primarily in urine.
Doxapram HCL	2-5 mg/kg IV (CRC Handbook)  Administered at dosage of 5 ml (pups/juveniles) and 10 ml (subadults/adults)	A CNS/respiratory stimulant used to treat respiratory arrest; may also be administered during/after anesthesia.	Hypertension, arrhythmias, seizures, and hyperventilation, which are most probable with repeated or high doses. Increases myocardial oxygen demand and reduces cerebral blood flow.  Few instances of use in Hawaiian monk seals with no adverse reactions recorded (NMFS unpubl. data).	After intravenous (IV) injection, onset of effect in humans and animals within 2 minutes; in dogs, rapidly metabolized and excreted as metabolites in urine within 24-48 hours after administration. Serum half-life in dogs is 2.5-3.2 hours and in humans is 20-50 hours.
Emodepside + Praziquantel	0.113ml/kg topical	Topical antiparasitic (nematocide + cetocide) used to treat intestinal roundworms and tapeworms.	Most common side effects in cats include skin and gastrointestinal reactions.  Two instances of use in captive Hawaiian monk seals with no adverse effects noted; used in in wild seals under Permit No.	In cats: rapidly absorbed through skin and into systemic circulation after dermal administration; serum concentrations detectable for praziquantel after 1 hour (peak

<b>Drug Name</b>	<b>Dosage/Route of Administration</b>	<b>Use in Hawaiian monk seals</b>	<b>Possible Adverse Effects</b>	<b>Pharmacokinetics</b>
			10137-07 with no adverse reactions noted.	at 6 hours) and for emodepside after 2 hours (peak at 2 days); detectable for up to 28 days following administration.
Epinephrine	0.05-0.2 mg/kg IV, IM, SC, pericardial, intratracheal	Treatment for cardiac arrest with resuscitation; may also be used to treat anaphylaxis.	Anxiety, tremors, excitability, vomiting, hypertension (with overdose), arrhythmias, high levels of uric acid in blood, and lactic acidosis (with prolonged use or overdosage).  Few instances of use in Hawaiian monk seals with no adverse reactions reported (NMFS unpubl. data).	Well absorbed following IM or subcutaneous (SC) injection; onset of action following SC injection is 5-10 minutes; immediate action following IV injection; does not cross blood-brain barrier; actions end by uptake into sympathetic nerve endings; metabolism in liver and other tissues to inactive metabolites.
Fenbendazole	11mg/kg twice (CRC Handbook)	An antiparasitic agent for treating intestinal roundworms.	Generally no adverse effects at normal doses; hypersensitivity secondary to antigen release by dying parasites may occur, especially with high doses; vomiting reported infrequently in dogs and cats ; well tolerated at doses up to 100x recommended.  Used in research field trial in Hawaiian monk seals and in captive care; no adverse effects reported from use but difficult to administer orally in field setting (NMFS Permit No. 10137 Hawaiian Monk Seal Deworming Project: Year One Summary).	Marginally absorbed after oral administration; metabolized to active compound oxfendazole and sulfone; in sheep, cattle, and pigs, 44-50% of a dose is excreted unchanged in feces, and <1% in urine.
Flumazenil	0.05-0.1 mg/kg Flumazenil would be administered IV at a dosage of 2.5 ml (pups/juveniles)	A benzodiazepine antagonist used to reverse effects of sedative overdose (diazepam or	In humans, injection site reactions, vomiting, cutaneous vasodilatation, vertigo, ataxia, and blurred vision; deaths have been associated with its use in humans having serious underlying diseases; large IV overdoses have	Administered with rapid IV injection with therapeutic effects within 1-2 minutes; rapidly distributed and metabolized in liver; half-life in

<b>Drug Name</b>	<b>Dosage/Route of Administration</b>	<b>Use in Hawaiian monk seals</b>	<b>Possible Adverse Effects</b>	<b>Pharmacokinetics</b>
	and 5.0 ml (subadults/adults), repeated if necessary	midazolam).	rarely caused symptoms in otherwise healthy humans.  Used in Hawaiian monk seals with no adverse reactions reported; trials with captive monk seals proved effective in reversing effects of midazolam (NMFS unpubl. data).	humans is approximately 1 hour.
Furosemide	2-5 mg/kg (CRC Handbook)	A diuretic used to treat congestive heart failure or pulmonary edema.	May induce fluid and electrolyte imbalances; reported to cause hearing loss in cats and dogs given high IV doses; other effects include gastrointestinal problems, anemia, weakness, restlessness.  Few instances of use in Hawaiian monk seals with no adverse reactions reported (NMFS unpubl. data).	In dogs, the elimination half-life is approximately 1-1.5 hours; in humans, the diuretic effect takes place within 5 minutes and peak effects 30 minutes after IV injection.
Ivermectin	200 microgram/kg	An antiparasitic agent for treating intestinal roundworms; used as a heartworm preventative in captive monk seals.	Species-specific adverse effects generally from dying microfilaria or other larva, for example, swelling and itching in horses, shock-like reactions in dogs, and paralysis and staggering in cattle; may cause neurologic toxicity in mice and rats with doses slightly more than prescribed; may cause death, lethargy, or anorexia in birds.  Used in captive care of Hawaiian monk seals to treat intestinal worms and used routinely on permanently captive monk seals with no adverse reactions reported (NMFS unpubl. data; Annual Report for Permit No. 455-1760).	Oral doses absorbed up to 95%; greater bioavailability after SC administration but more rapidly absorbed after oral administration; well distributed to most tissues except in cerebrospinal fluid thus reducing its toxicity; metabolized in liver and primarily excreted in feces; less than 5% is excreted in urine; elimination half-life for dogs is 2 days.
Lidocaine HCL	1-3 ml 2 % topically	A local anesthetic used to reduce pain from skin incisions	At usual doses, serious adverse reactions are rare; most common are dose-related and rare, including CNS reactions, transient nausea	Lidocaine has a high affinity for fat and adipose tissue and is bound to plasma proteins;

<b>Drug Name</b>	<b>Dosage/Route of Administration</b>	<b>Use in Hawaiian monk seals</b>	<b>Possible Adverse Effects</b>	<b>Pharmacokinetics</b>
		such as blubber biopsies.	and vomiting, and cardiac effects.  Routinely used in Hawaiian monk seals during biopsy sampling with no adverse reactions reported (NMFS unpubl. data).	rapidly metabolized in liver to active metabolites; less than 10% of an injected dose is excreted unchanged in urine.
Midazolam	0.1-0.15 mg/kg IV, IM	An injectable benzodiazepine used as a sedative for capture events or as a preanesthetic.	Few adverse effects have been reported in humans including effects on respiratory and cardiac rates and blood pressure; other effects reported in humans include pain on injection, local irritation, headache, nausea, vomiting, and hiccups. Possibility of respiratory depression is principal concern in veterinary patients.  Used in captive Hawaiian monk seals with no adverse reactions reported; trials with captive monk seals indicated midazolam safe and effective (NMFS unpubl. data; Annual report for Permit No. 455-1760).	Rapidly and nearly completely absorbed after IM injection; highly protein-bound and rapidly crosses the blood-brain barrier; metabolized in liver; elimination half-life in dogs averages 77 minutes and in humans is approximately 2 hours.
Praziquantel	10 mg/kg (CRC Handbook)	An anticestodal antiparasitic used to treat intestinal tape worms.	In dogs, oral dosing can cause anorexia, vomiting, lethargy, or diarrhea but incidence is less than 5%; greater incidences from injectable in dogs including pain at injection site, vomiting, drowsiness, and staggering gate.  Used in research field trial (oral and IM) and in captive care (oral) of Hawaiian monk seals; no adverse effects reported from oral use in captive care; difficult to administer orally in field setting; swellings resulted from IM injections in field use (NMFS unpubl. data; Gobush et al. 2011).	Rapidly and nearly completely absorbed after oral administration; peak serum levels in dogs between 30-120 minutes; distributed throughout the body, crossing intestinal wall and blood-brain barrier into CNS; metabolized in liver and excreted primarily in urine; elimination half-life in dogs is 3 hours.

<b>Drug Name</b>	<b>Dosage/Route of Administration</b>	<b>Use in Hawaiian monk seals</b>	<b>Possible Adverse Effects</b>	<b>Pharmacokinetics</b>
Prednisolone sodium succinate	1 mg/kg	A glucocorticoid used for treatment of shock; may be used to treat adrenal insufficiency and other maladies.	Usually associated with long-term administration and manifested as clinical signs of hyperadrenocorticism; can retard growth in young animals; when given short-term, unlikely to cause significant harmful effects, even in massive doses.  Few instances of use in Hawaiian monk seals with no adverse reactions reported (NMFS unpubl. data).	Biologic half-life is 12-36 hours.

Gobush, K.S., J.D. Baker and F.M.D. Gulland. 2011. Effectiveness of an anti-helminthic treatment in improving the body condition and survival of Hawaiian monk seals. *Endangered Species Research* 15: 29-37.

Haulena, M. and R.B. Heath. 2001. Marine mammal anesthesia. In: *CRC Handbook of Marine Mammal Medicine*, Second Edition, L.A. Dierauf and F.M.D. Gulland (eds.), CRC Press LLC, Boca Raton. Pp. 655-688.

Meegan, J., W. Collard, G. S. Grover, N. Pussini, B. Van Bonn, F. Gulland. 2010. Ceftiofur pharmacokinetics. Abstract in the *International Association for Aquatic Animal Medicine 2010 Proceedings*.

Plumb, D.C. 2008. *Veterinary Drug Handbook*, Sixth Edition. Blackwell Publishing, Minnesota. 1120p.