



Prepared for:
 National Oceanic and Atmospheric Administration
 National Marine Fisheries Service

**Programmatic Environmental
 Impact Statement**

**Appendix D: Drugs Currently
 Used & Proposed**

**Final PEIS for Hawaiian Monk Seal
 Recovery Actions**

March 2014



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***DRUGS CURRENTLY USED OR PROPOSED TO BE USED DURING
HAWAIIAN MONK SEAL RESEARCH AND ENHANCEMENT ACTIVITIES***

The following table lists the drugs currently used or proposed to be used in Hawaiian monk seals, possible adverse effects including any observed in Hawaiian monk seals, and the pharmacokinetics of each drug (i.e., known information on how the body affects the drug, including how the drug is absorbed, distributed, the rate of action and duration of effect, chemical changes in the body, and effects and routes of excretion of metabolites). Information in the table is from Plumb (2008) or other references if noted. More detailed information on each drug can be found in Plumb (2008).

In addition to the drugs in the table below, supportive fluids such as electrolytes, dextrose, and sodium bicarbonate may be administered at the discretion of the attending veterinarian in response to adverse reactions to capture, handling, and drug administrations. Over the next 10 years, new drugs may become available or other drugs may be prescribed for use in Hawaiian monk seals by the attending veterinarian. Information on such new drugs would be provided by PIFSC to the OPR Permits Division and may be incorporated into the protocols if indicated by the attending veterinarian. Possible adverse effects of any new drugs would be weighed against the benefits of using the drugs for each case. Also, if any of the drugs listed in Table C-1 or any new drugs are used and severe adverse effects are reported in Hawaiian monk seals, the drugs would be discontinued or dosages modified per recommendation by the attending veterinarian.

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Table C-1 Information On Drugs Proposed For Use in Hawaiian Monk Seals During Research and Enhancement Activities

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, 4th 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, unpub. data). No adverse reactions reported after use in</p>	Half-life in cattle is 8-12 hours with peak levels after 30-45 minutes of intramuscular (IM) injection. 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

Drug Name	Dosage/Route of Administration	Use in Hawaiian monk seals	Possible Adverse Effects	Pharmacokinetics
			humpback whales, California sea lions, northern elephant seals, and harbor seals (Gulland pers. comm.).	at lower levels would likely be maintained for 5-8 days post-injection (Meegan et al. 2010).
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 5 ml (pups/juveniles) and 10 ml	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	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

Drug Name	Dosage/Route of Administration	Use in Hawaiian monk seals	Possible Adverse Effects	Pharmacokinetics
	(subadults/adults)		monk seals with no adverse reactions recorded (NMFS unpubl. data).	in dogs is 2.5-3.2 hours and in humans is 20-50 hours.
Emodepside + Praziquantel	0.11 to 0.19 ml/kg	Topical antiparasitic (nematocide + cetocide) used to treat intestinal roundworms and tapeworms.	Most common side effects in cats include skin and gastrointestinal reactions. Used in captive and wild Hawaiian monk seals with no adverse reactions recorded (NMFS unpublished data).	In cats: rapidly absorbed through skin and into systemic circulation after dermal administration; serum concentrations detectable for praziquantel after 1 hour (peak 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.	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.

Drug Name	Dosage/Route of Administration	Use in Hawaiian monk seals	Possible Adverse Effects	Pharmacokinetics
			<p>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).</p>	
Flumazenil	<p>0.05-0.1 mg/kg Flumazenil would be administered IV at a dosage of 2.5 ml (pups/juveniles) and 5.0 ml (subadults/adults), repeated if necessary</p>	<p>A benzodiazepine antagonist used to reverse effects of sedative overdose (diazepam or midazolam).</p>	<p>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 rarely caused symptoms in otherwise healthy humans.</p> <p>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).</p>	<p>Administered with rapid IV injection with therapeutic effects within 1-2 minutes; rapidly distributed and metabolized in liver; half-life in humans is approximately 1 hour.</p>
Furosemide	<p>2-5 mg/kg (CRC Handbook)</p>	<p>A diuretic used to treat congestive heart failure or pulmonary edema.</p>	<p>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.</p> <p>Few instances of use in Hawaiian</p>	<p>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.</p>

Drug Name	Dosage/Route of Administration	Use in Hawaiian monk seals	Possible Adverse Effects	Pharmacokinetics
			monk seals with no adverse reactions reported (NMFS unpubl. data).	
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 such as blubber biopsies.	At usual doses, serious adverse reactions are rare; most common are dose-related and rare, including CNS reactions, transient nausea and vomiting, and cardiac effects. Routinely used in Hawaiian monk seals during biopsy sampling with no adverse reactions reported (NMFS unpubl. data).	Lidocaine has a high affinity for fat and adipose tissue and is bound to plasma proteins; 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	Few adverse effects have been reported in humans including effects	Rapidly and nearly completely absorbed after IM injection;

Drug Name	Dosage/Route of Administration	Use in Hawaiian monk seals	Possible Adverse Effects	Pharmacokinetics
		used as a sedative for capture events or as a preanesthetic.	<p>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.</p> <p>Used in wild and 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).</p>	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.	<p>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 gait.</p> <p>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).</p>	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.

Drug Name	Dosage/Route of Administration	Use in Hawaiian monk seals	Possible Adverse Effects	Pharmacokinetics
Prednisolone sodium succinate	1 mg/kg	A glucocorticoid used for treatment of shock; may be used to treat adrenal insufficiency and other maladies.	<p>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.</p> <p>Few instances of use in Hawaiian monk seals with no adverse reactions reported (NMFS unpubl. data).</p>	Biologic half-life is 12-36 hours.
Sodium pentobarbital	1 ml/10 lbs. into extradural vein	Humane euthanasia by attending veterinarian of moribund seals, or as a last resort to remove aggressive male seals.	<p>Barbiturates depress the CNS in descending order starting with the cerebral cortex and loss of consciousness progressing to anesthesia; with overdose, deep anesthesia progresses to apnea due to depression of the respiratory center, followed by cardiac arrest (AVMA 2013).</p> <p>Used to effectively euthanize one aggressive adult male in 1991.</p>	Onset of action within 1 minute after IV administration. Distributes rapidly to all body tissues with highest concentrations in brain and liver.

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