



Prepared for:



# DRAFT Programmatic Environmental Impact Statement Appendices A-L

Hawaiian Monk Seal Recovery Actions

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*Appendix C*  
*Drugs Currently Used or*  
*Proposed to be Used During*  
*Hawaiian Monk Seal Research*  
*and Enhancement Activities*

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***APPENDIX C - 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	Use in Hawaiian Monk Seals	Possible Adverse Effects	Pharmacokinetics
Atropine Sulfate	To reduce bradycardia (slowed heart rate) or treat 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, central nervous system (CNS).</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	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>Not used in Hawaiian monk seals. 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>
Dexamethasone	A glucocorticoid used for treatment of shock; may be used to treat adrenal insufficiency, inflammation, 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>	Half-life in dogs is 2-5 hours; biologic activity can persist for $\geq 48$ hours.

Drug Name	Use in Hawaiian Monk Seals	Possible Adverse Effects	Pharmacokinetics
Diazepam	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	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	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 reactions recorded (Permit No. 10137-06 modification request).	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	Treatment for cardiac arrest with resuscitation; may also be used to treat anaphylaxis.	Can induce feelings of fear or anxiety, tremor, 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	An antiparasitic agent for treating intestinal	Generally no adverse effects at normal doses; hypersensitivity secondary to antigen release by dying parasites may occur, especially with high doses; vomiting	Marginally absorbed after oral administration; metabolized to active compound oxfendazole and sulfone; in sheep, cattle, and pigs, 44-50%

Drug Name	Use in Hawaiian Monk Seals	Possible Adverse Effects	Pharmacokinetics
	roundworms.	<p>reported infrequently in dogs and cats ; well tolerated at doses up to 100x recommended.</p> <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>	of a dose is excreted unchanged in feces, and <1% in urine.
Flumazenil	A benzodiazepine antagonist used to reverse effects of sedative overdose (diazepam or midazolam).	<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>	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.
Furosemide	A diuretic used to treat congestive heart failure or pulmonary edema.	<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 monk seals with no adverse reactions reported (NMFS unpubl. data).</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.
Ivermectin	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.	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.



Drug Name	Use in Hawaiian Monk Seals	Possible Adverse Effects	Pharmacokinetics
		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).	
Lidocaine HCL	A local anesthetic used to reduce pain from skin incisions such as blubber biopsies.	<p>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.</p> <p>Routinely used in Hawaiian monk seals during biopsy sampling with no adverse reactions reported (NMFS unpubl. data).</p>	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	An injectable benzodiazepine used as a sedative for capture events or as a preanesthetic.	<p>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.</p> <p>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).</p>	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	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 gate.</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</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	Use in Hawaiian Monk Seals	Possible Adverse Effects	Pharmacokinetics
		administer orally in field setting; swellings resulted from IM injections in field use (NMFS unpubl. data; Gobush et al. <i>in prep</i> ).	
Prednisolone sodium succinate	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.

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