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A Model Protocol for Purchase, Distribution and Use of Pharmaceuticals in Wildlife

Western Association of Fish and Wildlife Agencies, Wildlife Health Committee

The use of various pharmaceutical agents is well accepted and frequently applied in legitimate wildlife management. As such, it is critical that state wildlife management agencies be aware of changing regulations governing this activity and evolving social attitudes. Many individuals within federal and state wildlife agencies and individuals working with wildlife use a wide variety of drugs on a wide variety of species. These drugs can include antibiotics, vaccines, anthelminthics and anesthetic agents. However, the use of these agents is a revocable privilege if federal regulations or the public trust is violated.

Animal capture is a basic part of wildlife management and the use of several anesthetic agents for capture of a variety of species is common. Wildlife are also held in captivity for use in research programs and drugs of many kinds are used routinely to maintain animal health. The treatment of wildlife for various disease conditions is becoming more common and may be necessary under certain conditions.

One of the most prominent problems facing wildlife heath professionals is the continued availability and accessibility of pharmacological agents to accomplish our jobs. Many wildlife species cannot be properly or safely restrained and handled without the use of various prescription drugs. The legal use of pharmacological agents in wildlife is complex, especially under the provisions of various state pharmacy acts and the federal regulations.

This paper presents a model protocol developed by the WAFWA Wildlife Health Committee for the purchase, storage, distribution and use of prescription drugs used by wildlife agency personnel to capture, handle and treat various wildlife species. This model protocol does not supersede any state policies or laws but provides guidelines and defines appropriate actions that will enable wildlife agencies to comply with the provisions of the Animal Medicinal Drug Use Clarification Act. State agencies are encouraged to review current policy and guidelines to be sure that they are in compliance with AMDUCA as well as other state and federal regulations. It is hoped that member states will use this model to adopt appropriate policies or modify existing state policies. This protocol may be useful to wildlife management agencies in countries where AMDUCA and other U. S. law/regulations are not applicable as these guidelines provide a framework to minimize the risk to humans and wildlife that are inherent when these pharmaceuticals are used.

THE USE OF PHARMACEUTICAL AGENTS IN WILDLIFE

FOOD, DRUG AND COSMETIC ACT

The use and administration of pharmaceutical agents in animals is under the jurisdiction of the Food and Drug Administration (FDA) through the Federal Food, Drug, and Cosmetic Act (CFR 21 USC 360). The purchase, administration, dispensing and prescribing of prescription pharmaceutical agents must be done within the context of a valid veterinarian-client-patient relationship.

ANIMAL MEDICINAL DRUG USE CLARIFICATION ACT

The extra-label use and administration of pharmaceutical agents to animals is regulated by the FDA through the Animal Medicinal Drug Use Clarification Act (AMDUCA) (CFR 21, Chapter 1, Part 530). Within AMDUCA, the FDA has defined two groups of animals – food-producing and non-food producing. Under AMDUCA, wildlife species for which there is a defined take season (i.e. game species) are defined as food animals. The classification of wildlife game species as food animals directly affects the development and implementation of state wildlife management and research programs/projects. Since the majority of pharmaceutical agents used in wildlife are prescription drugs that are used in an extra-label manner (i.e. in a species, dose, or frequency that is not specified on the drug label), the provisions of AMDUCA become the predominant regulatory authority for wildlife agency personnel. Some of the critical elements defined in AMDUCA include: 1) requirement of a valid veterinarian-client-patient relationship, 2) well defined record keeping, 3) establishment of meat withdrawal times for food-producing animals receiving pharmaceuticals, 4) identification of animals receiving pharmaceuticals.

CONTROLLED SUBSTANCES ACT

The Controlled Substances Act (CFR 21 Chapter 13) is administered by the US Department of Justice Drug Enforcement Administration (DEA). The DEA is concerned with the inventory of controlled substances, not their appropriate use in animals. The DEA requires an individual to register in order to obtain, dispense or prescribe controlled substances. Typically a consulting or staff veterinarian will be the designated official responsible for controlled substances. State wildlife agencies can obtain a DEA permit but must designate an official responsible for the purchase, storage, and accounting of controlled substances. However, this does **not** allow the non-veterinarian to **use** these drugs on animals without first establishing a valid veterinarian-client-patient relationship. Persons possessing and using controlled substances within a valid veterinarian-client-patient relationship must appropriately store controlled substances and are accountable to the consulting or staff veterinarian for drugs received and used. Drugs that are not controlled substances can be procured through a local, consulting or staff veterinarian as long as **valid** veterinarian-client-patient relationship has been established.

STATE AGENCY REQUIREMENTS

In most states, regulatory agencies may also require registration by state wildlife agencies or veterinarians to obtain, dispense or prescribe controlled substances. Most states require holders of federal controlled substance permits to register with the respective State Pharmacy Board. State Pharmacy Boards may conduct their own inspections or have specific requirements that must be followed in addition to those of the DEA.

APPROPRIATE VETERINARY OVERSIGHT (VALID VETERINARY-CLIENT-PATIENT RELATIONSHIP)

One of the basic requirements of AMDUCA is the establishment of a valid veterinary-client-patient relationship prior to the dispensing or prescribing of pharmaceuticals in animals. In order to use pharmaceuticals in wildlife management activities, especially those that involve food animals and/or extra-label use, a valid veterinary-client-patient relationship must be established. It is recommended that veterinary oversight for wildlife agencies should include either staff veterinarians (state wildlife veterinarians paid by the agency) or consulting veterinarians not employed by the agency. The client is defined most frequently as a biologist or warden handling wildlife in the normal course of his/her job duties. However, other personnel that may be viewed as clients could include university or private

consultants contracted by state agencies for specific research or management services. It is recommended that any contractors or consultants clearly establish through contracts or written agreements appropriate veterinary oversight for individual projects. Veterinary oversight for contracted services must include consulting veterinarians (paid by the agency or by contractor) or, by agreement, agency staff veterinarians.

It is incumbent upon each state agency to be sure that all staff or consulting veterinarians providing oversight are adequately experienced and possess specialized training in wildlife veterinary medicine. It should not be assumed that any or all veterinarians possess the knowledge to properly, safely and appropriately administer pharmaceuticals to wildlife in either restraint or treatment situations.

DRUG WITHDRAWAL TIMES

By federal regulations, a withdrawal time for meat and/or milk must be established by a licensed veterinarian for any food producing animal that has been administered a prescription drug(s). A withdrawal time is defined as the period from when an animal was given a drug to the time that it can be safely consumed *by a human*. Withdrawal time periods apply only to those species that could be consumed by humans via harvest including hunting, trapping or fishing. For many drugs, the withdrawal times for domestic species are known. However, there is essentially no data on meat withdrawal times for most wildlife species. One of the provisions of AMDUCA is that in the absence of species specific data, an animal that has received drugs in an extra-label manner can never be used for human consumption. However, licensed veterinarians can use or extrapolate data from any reputable source to justify a specific withdrawal time for a specific drug in a specific species of wildlife. The establishment of withdrawal times in wildlife is important, especially when the use of drugs in these species occurs near or during the legal harvest season for the species.

Recommended meat withdrawal times for specific drugs are as follows, but are subject to change as new data becomes avaiable:

Acepromazine	14 days
Atipamezole	14 days
Carfentanil/Naltrexone	30 days (FARAD)
Diazepam	14 days
Etorphine	30 days
Ketamine	3 days (FARAD)
Medetomidine	14 days
Telazol (tiletamine/zolazepam)	14 days (7 days in black bears?)
Xylazine/Tolazoline/Yohimbine	30 days
Penicillin	21 days (FARAD)
Other Antibiotics	Label Defined Withdrawals
Ivermectin	49 days (FARAD)

AMDUCA requires that animals which have been given drugs in an extra-label manner, especially food-producing animals, **must** be identified. Animal identification is discretionary but highly recommended for all animals receiving drugs at any time even when there is no possibility that it could be legally harvested during the withdrawal period. Identification could be done with ear tags, neck collars or other external means. It is recommended that such animals be fitted with an appropriate

durable ear tag containing a unique number and an appropriate notification warning (e.g. NOTICE: Call XXX-XXX-XXXX prior to consumption). Ear tags will be affixed when the animal has been captured and the appropriate information will be recorded on a field form. The notification information on the ear tag will refer the collector (hunters, etc) to the individual responsible for the drug administration (wildlife veterinarian, biologist, warden). Complete records of any drug administration **must** be maintained at several source levels (i.e. the biologist, the agency regional offices, and/or state offices). If the tagged animal is harvested and the hunter contacts the responsible agency/individual, drug records on the animal can be inspected to determine if it was harvested within the withdrawal period. Animals harvested within the withdrawal periods should be condemned as unfit for human consumption. The carcass should be confiscated by the agency and appropriately discarded to avoid entrance into the human food chain. Depending on state rules, it may be suitable for the hunter to retain various parts of the animal (e.g., hide, skull, horns, antlers, claws) that are not normally consumed. If an animal is harvested beyond the withdrawal period, it should *not* be necessary to inform the collector that the animal had been given drugs.

HUMAN SAFETY AND AGENCY LIABILITY

The drugs that are used for wildlife immobilization can be potentially lethal to humans if accidental exposure occurs. Accidental exposure can occur through skin contact, ingestion, inhalation, or injection. Therefore, drug safety procedures must be developed and carefully followed at all times. State wildlife agencies should designate training and safety education responsibilities to appropriate individuals/programs to periodically provide training for personnel in all aspects of drug use. These instructions shall include knowledge of symptoms following accidental injection and emergency treatment procedures. Before using a particular drug, it is the responsibility of each program/project supervisor to see that all personnel are familiar with the human safety aspects of the drug(s) to be used. Personnel accidentally exposed to drugs should seek medical assistance immediately. Incidents of accidental human exposure to drugs should be reported in full to the appropriate supervisors.

Personnel should not use Schedule II controlled substances unless they have obtained training in the safe use of these drugs. Training is also required for users of Schedule III-V controlled substances or non-controlled substances, **unless** the individual can demonstrate **substantial experience** in the use of these drugs. Such experience may substitute for formal training at the discretion of the wildlife veterinarians. State agencies should routinely and formally survey their personnel and record training/experience levels of individuals using prescription drugs. Periodic reviews by the appropriate program supervisor should be made to note deficiencies or gaps in training that might indicate a need for further training before using prescription drugs on wildlife. The potential exposure of untrained or volunteer personnel to potentially dangerous drugs is of great concern. Project leaders must avoid permitting such personnel from participating in work that might expose them to such drugs.

ANIMAL WELFARE

Before capturing and handling wildlife, agency personnel should consult with a veterinarian to determine the best method to minimize injury and death to animals with consideration for cost effectiveness. Alternative methods to chemical immobilization, time of year, status of animals (stage of pregnancy, body condition, sex, and age), ambient temperature, environmental conditions, etc. should be considered in formulating capture and handling plans.

If chemical immobilization is to be used, it is important to ensure the proper drug(s) and dosage(s) are used to provide the necessary analgesia and anesthesia to accomplish the immobilization and handling in a humane way. Animals should be handled humanely to prevent injury during immobilization, processing and recovery.

Animals should be treated appropriately if injury occurs in the capture or handling process. If injured beyond likely recovery, animals should be humanely euthanized following American Veterinary Medical Association (AVMA) Guidelines for Euthanasia (2003) or the American Association of Zoo Veterinarians Guidelines for Euthanasia of Non-domestic Animals (2006). Agency personnel and individuals working under contracts or consultant agreements should comply with requirements (as applicable) for reporting losses of animals during capture and handling.

All animals chemically immobilized should be marked (ear tagged, tattooed, collared, leg banded, freeze branded or other appropriate method) for future identification, unless requirements dictate otherwise.

PERSONNEL QUALIFICATIONS AND TRAINING

Each agency should/must provide regular comprehensive training for personnel in all aspects of drug use. Training opportunities need to be provided to consulting and staff veterinarians to upgrade their knowledge of new drugs, regulatory changes and new techniques. Untrained personnel or personnel without substantial experience who need to capture wildlife as part of their regular duties **must** receive training on handling techniques and chemical immobilization before implementation. Training should primarily emphasize safety considerations for the animal and the handler. Standard training programs should include instruction on the animal welfare; regulatory and policy considerations for administration of pharmaceutical agents; basic drug pharmacology; species specific handling techniques; drug dose calculation and drug selection; animal monitoring including temperature, pulse and respiration (TPR); first aid procedures for immobilized animals; techniques for euthanasia; and human safety. Proper training should promote skill development as well as impart knowledge. Agencies should establish minimum training requirements or implement a certification program to limit drug use to only qualified individuals.

The establishment of a mentor program to team experienced and inexperienced employees for undertrained or new employees is strongly encouraged. Any new or supplemental information on the characteristics and safety issues unique to various drugs should be routinely provided by the staff or consulting veterinarians to keep all qualified individuals current in the appropriate administration of pharmaceuticals.

All field personnel directly involved or assisting in wildlife capture using chemical immobilization drugs **should** be trained in first aid and cardiopulmonary resuscitation (CPR). Because the individual directly handling the capture drug is most likely to suffer accidental exposure, first aid and CPR training to assistants present during capture is highly desirable. Firearms training may be necessary and should be required when target animals are dangerous and protection to handlers may be provided through firearms.

INVESTIGATIONAL NEW ANIMAL DRUGS

Occasionally drug companies or distributors will make available a drug for experimental or investigational use (Investigational New Animal Drug; INAD) that has potential applicability in wildlife species for immobilization, tranquilization, or treatment of specific conditions. The federal Food and Drug Administration issues INAD permits to allow pharmaceutical companies to gather data on the use of these drugs that will assist registration of the drug for a given species. Records of the use of INAD need to be submitted to the manufacturer and retained for examination by FDA. Use of INAD will be coordinated by the wildlife veterinarians to ensure all FDA reporting requirements are met.

State agencies should dispense INAD and handle them in the same way as controlled substance drugs. If an INAD permit is granted, the researcher must assure proper dosage, administration, and data collection. All animals given an INAD must be properly identified as discussed previously to permit future identification. Accurate individual animal records must be maintained and contain all information previously listed for individual animal forms with emphasis on: identifying markings, dosages of drug, route of administration, responses, and any adverse side effects.

SPECIFIC GUIDANCE FOR REGULATION, RECORD KEEPING, AND HANDLING

Regulations: Use of controlled substances, experimental, and prescription drugs must comply with all applicable federal and state regulations. The use of pharmaceutical agents by agency personnel must take place under the direction of a licensed veterinarian. Primary among these regulations is the licensing and registration requirement to purchase, store, and dispense controlled substance drugs. Federal Food and Drug Administration regulations affect animals used for human consumption including wildlife routinely consumed following legal regulated harvests.

Records: Accurate records of purchases, distribution, and use of controlled substances and experimental drugs must be maintained and retained for at least 2 years. A controlled substances inventory (forms or electronic database) for each controlled substance and experimental drug must be kept by the appropriate authority (in most cases staff or consulting veterinarians). Records of all prescription drugs used in animal capture and handling must be kept by the appropriate authority (in most cases a staff or consulting veterinarians).

Biologists and wardens must provide the appropriate agency authority with complete records of drug use. The record must include the following: date, location, animal identification number, species, sex, actual or estimated age and weight, health status/condition, drug(s) used, dosage(s), route of administration, and responses. Copies of the original capture sheets and all recording forms should be provided to the appropriate state authority routinely following capture events.

All records pertaining to controlled substances must be available for inspection and copying by duly authorized officials of DEA and/or FDA. Failure to comply with established record keeping procedures may result in withdrawal of the privilege of using controlled substances or prescription drugs.

Borrowing and loaning of controlled substances: There is only very limited provision in the law for borrowing or loaning of controlled substances, even between licensed users. Transfers of Class II controlled substances are especially regulated and require special paperwork. Loaning or exchanging controlled substances make it impossible to maintain accurate records and cannot be substituted for

adequate planning for drug needs and usage. For these reasons, no controlled substances purchased should be transferred to any person not directly affiliated with that agency *without previous written permission from the appropriate authority* who will assume responsibility for the transfer.

Inventory: By law, an inventory of all controlled substances must be done every two years. The appropriate agency authority should conduct the inventory. It is recommended that complete inventories of controlled substances by done on an annual to semi-annual basis. Any unexplained losses, thefts, or unaccountable shortages must be reported to the DEA. The legal requirement is that all records must be maintained for a minimum of two years.

Authority to Purchase and Dispense: As allowed by state or federal law, veterinarians may delegate via written and witnessed power of attorney, the authority to purchase and dispense controlled substances.

Storage: Controlled substances listed in Schedules III, IV and V shall be stored in a securely locked, substantially constructed cabinet or safe. Schedule II drugs (Etorphine, Diprenorphine, and Carfentanil) shall be stored in a bank safety deposit box or a safe that is equivalent to a U.S. Government Class V security container. Safes rated with Underwriter's Laboratories as TL-15 or stronger will meet this requirement. Schedule II controlled substance storage sites must be registered with DEA.

A safe for short-term storage of dispensed controlled substances should be provided, allowing personnel to store drugs while waiting to depart for the field or immediately upon return from the field, until access to the repository safe can be arranged.

Storage in the field: Biologists receiving controlled substance dispensed for a specific project are not required to meet the above storage requirements while in the field. However, it is the project leader's responsibility to see that all drugs are protected and secured by the best means available to prevent damage, accidental exposure, or theft. Portable suitcase type fire safes can be utilized while in the field to keep drugs under lock. Drugs in the field should never be left unattended.

Shipping and transportation: All drugs will be hand carried or sent by certified mail or other secure method.

Destruction: All outdated or contaminated controlled substance drugs and unused darts still containing drugs will be returned to the wildlife veterinarian for inventory purposes and proper disposal. Destruction of outdated or contaminated controlled substance drugs must be done by DEA according to procedures outlined in Title 21 of the Code of Federal Regulations.

SPECIFIC RECOMMENDED PROTOCOL FOR OBTAINING DRUGS:

1. Consult with the wildlife veterinarian to assure proper drug selection, dose, dosage, and route of administration. Discuss alternatives to chemical immobilization.
2. If the use of a new INAD is desired, apply to the FDA for an INAD permit. This process may take 6-12 months to complete.
3. Notify the veterinarian or other delegated person for preparation of the drug order. Specify the drug, concentration, and amount. Allow sufficient time to permit placement and receipt of the

order.

4. The holder of an appropriate DEA license will place the order, receive the drugs, add them to the inventory, and store them.
5. Personnel receiving drugs under a veterinary prescription should notify the veterinarian upon receipt. Controlled substances should be placed in appropriate safes or in a short-term storage safe until the researcher leaves for the field.
6. While in the field, the user is responsible for safe storage and usage on drugs, bearing in mind that loss or theft of controlled substances requires a formal report to the DEA.
7. Storage of non-controlled prescription drugs should be done in a secure manner to prevent casual access.
8. Maintain records on the use of all controlled substances while in the field. Account for all usage by maintaining a record of drug use on each animal, noting the time, date, location, species, gender, animal number, actual or estimated age and weight, health status/condition, drug(s) used, dosage(s), and responsible individual. To simplify accounting, an individual animal capture and immobilization sheet should be maintained when any controlled substance is used. This can be part of the record sheets, and a copy submitted to the appropriate authority. Note that controlled substances are accounted for by weight (usually mg), not by the number of vials or containers. The user must account for all losses (missed darts, spills, etc.) and uses of the drugs. Copies of original records of controlled substance use need to be submitted to the veterinarian on a periodic basis. Ideally, records of use of *all* drugs, controlled or not, should be maintained and copies periodically provided to staff or consulting veterinarians.

DEFINITIONS:

Controlled Substances: Controlled substances are narcotics and other drugs with human abuse potential that fall under the jurisdiction of the Controlled Substances Act. These drugs are classified into one of five groups based on their potential for human abuse and ability to cause psychic or physical dependence. Schedule I drugs have the highest abuse potential and have no accepted medical use. Schedule V have the least abuse potential. Descriptions of the drug schedules and examples are given in Table 1.

Controlled Substance Act: The Controlled Substance Act of 1970 (CFR 21) was enacted by Congress and became effective on 1 May 1971. It was designed to improve the administration and regulation of manufacturing, distribution, and dispensing of controlled substances by providing for a “closed” system of legitimate handlers of the drugs.

Drug Enforcement Administration (DEA): The federal agency under the Department of Justice charged with the responsibility to control narcotic and dangerous drug abuse through enforcement and prevention. Any licensed practitioner who distributes, prescribes, or dispenses any controlled substances must be registered with the DEA.

Experimental Drugs: See Investigational New Animal Drugs.

Food and Drug Administration (FDA): The federal agency responsible for the determination of the safety and efficacy as well as the quality of manufacture of drugs used in humans and animals.

Investigational New Animal Drugs (INAD): Unlicensed drugs not yet approved for manufacture and sale in interstate commerce. Investigational New Animal Drugs are only available on a limited basis to clinical investigators through an application administered by the FDA Center of Veterinary Medicine. Their use requires the collection and reporting of data back to the manufacturer for its use in approval of the drug.

Prescription Drugs: Those pharmaceuticals regulated by the FDA and, because of toxicity or other potential for harmful effects, restricted to use by or on the order of a licensed practitioner (veterinarian, physician, dentist). All veterinary prescription drugs are labeled: *Caution - Federal law restricts this drug to use by or on order of a licensed veterinarian.* The law requires that a valid veterinarian-client-patient relationship exists before administration, dispensing or prescribing prescription drugs.

Extra-Label (Off-Label) Use of Drugs: Extra-label (or Off-Label) use refers to the administration or application of an approved drug in a manner not according to the directions on its label. Most drugs used on wildlife species are used in an extra label manner. In 1994, Congress extended the legality of extra-label use of drugs by licensed veterinarians through passage of the Animal Medicinal Drug Use Clarification Act (AMDUCA) which took effect in December, 1996.

Veterinarian-Client-Patient Relationship: A valid veterinarian-client-patient relation is one in which: 1) the veterinarian has assumed the responsibility for making medical judgments regarding the need for medical treatment and the client has agreed to follow the instructions of the veterinarian; 2) there is sufficient knowledge of the animal(s) by the veterinarian to initiate at least a general or preliminary diagnosis of the medical condition of the animal; and 3) the practicing veterinarian is readily available for follow-up in case of adverse reactions or failure of the regimen of therapy; and 4) the client or agent agrees to abide by the veterinarians orders.

Withdrawal Time: The time from the administration of drug to an animal to the time at which the animal can be safely consumed by a human.

Table 1. Categories of controlled substances as regulated by Drug Enforcement Agency.

Schedule I Drugs: Potent and dangerous drugs with extremely high abuse potential and no accepted medical uses. Examples: heroin, LSD, marijuana, peyote.

Schedule II Drugs[1]: Potent narcotics, short acting barbiturates, amphetamines, and PCP (phencyclidine). Examples: carfentanil, etorphine, diprenorphine, fentanyl-droperidol, fetanyl.

Schedule III Drugs: Less dangerous narcotics, sedatives, tranquilizers, and ultra-short acting barbiturates with substantial potential for abuse. Examples: tiletamine/zolazepam (Telazol™), ketamine.

Schedule IV Drugs: Less dangerous drugs, with some danger for potential abuse. Examples: diazepam (Valium™), phenobarbital.

Schedule V Drugs: Drugs with less abuse potential and which consist of preparations containing limited quantities of certain narcotic drugs, generally used for antitussive and antidiarrheal purposes. Examples: lomotil, codeine, Robitussin AC.

Prescription Drugs[2]: Drugs that are to be used by or under the order of a licensed veterinarian or physician via a prescription.

[1] Possession of Carfentanil also requires a "Schedule II Special Permit" indicating a special need (Zoo and Exotic Animal Veterinary Practice, Wildlife Management Programs, and Research) and compliance with increased security and record keeping obligations. Records of the use of Schedule II drugs must be kept separately in a form that is "instantly" retrievable in the case of a DEA inspection.

[2] Distribution of prescription drugs by a physician or veterinarian requires a valid "client-patient-doctor" relationship to be legal