

Procedures for the Use of Controlled Substances in Laboratory and Animal Research

Effective March 2016

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I) Requirements for Acquisition

The appropriate acquisition method varies depending upon how and where the controlled substances will be used.

Acquisition Options of Controlled Substances by PIs or their designees:

1. PIs may obtain Controlled Substances for use in Institutional Animal Care and Use Committee (IACUC)-approved research, in animals (exclusively), from the Division of Comparative Medicine (DCM) stockroom at the School of Medicine campus or Danforth Animal Facilities (DAF) stockroom at the Danforth campus for research conducted on each of those campuses. Such acquisitions by the PI occur under the auspices of the WUSTL Controlled Substances Researcher Registrations, and do not require the use of a DEA Form. The PI (or designee) must complete a **Controlled Substance Request Form** for the appropriate campus (Danforth Campus or Medical School) prior to

obtaining any Controlled Substances from the applicable DCM or DAF stockroom. PIs shall keep such Controlled Substances on the campus where they were obtained. PIs (and their designees) shall not transport such Controlled Substances to different campuses or locations beyond the campus where they were obtained.

2. Controlled Substances for use in IACUC-approved research in animals may also be obtained by the PI directly from an outside commercial vendor or governmental agency. Such acquisition occurs under the auspices of the PI's Controlled Substances Researcher Registration, and requires the use of a DEA Form. Refer to DEA and BNDD links below.
3. Controlled Substances for use in research that does not require IACUC approval (i.e. *in vitro* or other) MUST be obtained by the PI directly from an outside commercial vendor or governmental agency. Such acquisition occurs under the auspices of the PI's Controlled Substances Researcher Registration, and requires the use of a DEA Form.
4. Controlled Substances for use in any research that occurs at a location other than the Danforth Campus or Medical School Campus MUST be obtained by the PI from an outside commercial vendor or governmental agency. Such acquisition occurs under the auspices of the PI's Controlled Substances Researcher Registration, and requires the use of a DEA Form.

Detailed instructions on obtaining DEA and BNDD Researcher Registrations are available on the agencies' websites:

DEA: <http://www.deadiversion.usdoj.gov/drugreg/process.htm>

BNDD: <http://health.mo.gov/safety/bnnd/faqs.php>

Controlled Substances for any use in research must NOT be obtained using a Controlled Substances Practitioner Registration.

II) Institutional Animal Care and Use Committee (IACUC) Protocols

For animal research that will utilize controlled substances, the PI must:

1. Provide information regarding the use of controlled substances in their IACUC protocol; i.e., which drugs, doses, and approximate volumes required to complete the objectives of the protocol;
2. Specify those lab personnel who will have access to controlled substances; and
3. Ensure education is completed for authorized users.

III) Background Checks

Before authorizing access to Controlled Substances, it must be verified that personnel have not been convicted of a felony offense relating to Controlled Substances or had a DEA registration

denied or revoked (21 CFR §1301.76 (a)). Therefore, all personnel who will have access to controlled substances must undergo required background checks conducted by Human Resources (HR), as described in the **Background Check Procedures**. Background checks can be initiated by either completing the campus appropriate **Controlled Substance Access Background Check Form** and submitting to HR or with an IACUC protocol or amendment submission involving controlled substances.

IV) DAF and DCM Stockroom Procedures

1. IACUC- Approved Animal Research Determination of the Controlled Substance Source:
For Investigators using controlled substances in IACUC-approved animal research on Danforth AND Medical School Campuses, two separate controlled substance use and storage locations must be maintained – one for each campus. For controlled substance use on the Danforth Campus, obtain controlled substances from the Danforth Animal Facility (DAF) stockroom, and store and maintain records for these controlled substances only on the Danforth Campus. For controlled substance use on the Medical School Campus, obtain controlled substances from the Division of Comparative Medicine (DCM) stockroom, and store and maintain records for these controlled substances only on the Medical School Campus. **CONTROLLED SUBSTANCES OBTAINED ON ONE CAMPUS MAY NOT BE MOVED TO OR USED ON THE OTHER CAMPUS OR TRANSPORTED OFF CAMPUS.**
2. When PIs need to obtain controlled substances from the stockroom, they are to present a Controlled Substance Request Form to the DAF Director or to the DCM stockroom in person, or email (DAF-Keadle@wustl.edu DCM-andrewsl@wustl.edu). The form details drug name, concentration, quantity requested, and DEA schedule. A separate request form must be completed to obtain any DEA Schedule II controlled substance. Requests may require a minimum of 2 business days for paperwork processing and longer for receipt of drugs not in stock.
3. Once the controlled substance request form is received, the DAF Director or DCM stockroom will verify that the PI's IACUC protocol number contains corresponding references to the drugs requested and that laboratory personnel with controlled substance approval are listed on the protocol. If those conditions are found not to be in order, the veterinary staff will be contacted and the PI will be informed of the discrepancy. If necessary, the IACUC protocol may need to be amended and the request form re-submitted.
4. After the request form is valid, the order will be filled. If it is an initial request, the QA/QI staff will be sent an email to initiate the need for on-site education and document when the education is completed.

5. Each bottle or package of controlled substances received by a PI will be marked with a DAF- or DCM-issued bottle identification number. This number will be important (and required) to associate with the Controlled Substance Aliquot Log. All records associated with controlled drug transactions from the DAF or DCM stockroom must be maintained by each lab for two years after the last entry on the log except as otherwise indicated.
6. For each controlled substance bottle or package obtained by the PI, the DAF or DCM stockroom will provide a corresponding Controlled Substance Aliquot Log with the DAF or DCM drug number specific for that bottle or package.
7. When an investigator receives drugs from the DAF or DCM stockroom, the Controlled Substance Request Form will be signed by authorized lab personnel. Additionally, there will be a corresponding signature for lab personnel recorded in the DAF or DCM stockroom Perpetual Drug Log.
8. Investigators will be charged for controlled drugs that they receive.
9. Authorized investigator lab staff will take controlled substances from the DAF or DCM stockroom directly to a secure location in their labs.

Danforth Animal Facility	Division of Comparative Medicine
<p>All controlled substances obtained under the Danforth registrations will be supplied through the DAF stockroom. Contact: Tammie Keadle, 314.935.6875, Keadle@wustl.edu</p>	<p>All controlled substances obtained under the MS registrations will be supplied via the DCM stockroom. Contact: Lisa Andrews-Kaminsky, 314.362.8003, andrewsl@wustl.edu</p>

V) Controlled Substance Inventories (Initial and Annual)

1. In accordance with Missouri 19 CSR 30-1.042 (Inventory Requirements), upon first receipt of any controlled substances, the investigator must fill out and have on file an Initial Inventory of the controlled substances and from that point forward, maintain an Annual Inventory of all controlled substances on hand. It is recommended the inventory records be maintained close to the secured storage location for ease of access and review during audits.

2. **Controlled Substances Initial Inventory Form** — to be completed only once, at time of original request and must be kept on file permanently and retrievable in the lab. Information on the Initial Inventory will include: date of initial stocking of controlled substance; investigator name; lab location where controlled substances are stored; name of authorized personnel performing the inventory; whether inventory was recorded at the beginning or end of the business day; drug name; drug strength (mg/ml, mg/tablet, %, etc.), drug dosage form (bottle, tablets) and quantity in stock (number of full bottles, amount in a partial bottle, number tablets, etc.). Note that Schedule II drugs must be maintained on a separate form.
3. **Controlled Substances Annual Inventory** — is entered into the EH&S database and must be performed in a single workday and the time of the inventory must be recorded (i.e. the amounts must be accurate as of the beginning of the workday or the end of the workday). Information on the Annual Inventory will include: date of annual inventory of controlled substance; investigator name; lab location where controlled substances are stored; name of authorized personnel performing the inventory; whether inventory was recorded at the beginning or end of the business day; the DEA schedule of the drug; drug name; drug strength (mg/ml, mg/tablet, % etc.), drug dosage form (bottle, tablets) and quantity in stock (number of full bottles, amount in a partial bottle, number tablets, etc.). Note that Schedule II drugs must be maintained separately in the database. The annual inventory is retrievable for two years after the last entry on the log.
 - For those who obtain materials from the **DAF stockroom**, the Annual Controlled Substance Inventory will be performed on a date to be determined by DAF. All PIs will be required to submit an electronic version of their Annual Inventory to the Environmental Health and Safety Office on a specified date. Investigators will be notified in advance, by email, when this information is required.
 - For those who obtain materials from the **DCM stockroom**, the Annual Controlled Substance Inventory will be performed on a date to be determined by DCM. All PIs will be required to submit an electronic version of their Annual Inventory to the Environmental Health and Safety Office on a specified date. Investigators will be notified in advance, by email, when this information is required.
 - For those who obtain materials under an **individual registration**, the annual inventory can be completed on any day within a year of the previous inventory. It is the responsibility of the PI to assure timely and accurate completion.

VI) Drug Storage, Records of Use & Security

1. Investigators are to maintain drugs in a secure location as described in the **Storage & Security Guidelines**. Controlled Substances shall be stored in a locked, substantially

constructed cabinet (in accordance with 21 CFR §1301.75 (http://www.deadiversion.usdoj.gov/21cfr/cfr/1301/1301_75.htm) except when they are in use. All physical security measures should be commensurate with the quantity and schedule of the Missouri Controlled Substances Regulations (in accordance with **19 CSR 30-1.031— Physical Security Requirements**). Controlled Substances must be returned to storage immediately after use. Confirmation of appropriate security measures will be conducted during lab inspections. The WUSTL Resource Management Department has a list of **recommended storage cabinets**.

2. Keys to storage areas must be accessible only to authorized individuals. The key that locks the cabinet where Controlled Substances are stored must be locked up or may be kept on a person, who is an authorized user, or in some other secure manner to ensure non-authorized users do not have access to the controlled substances.
3. Controlled Substances must be kept in their original containers (e.g. the same substance with different lot or expiration dates must not be combined.)
4. Any inventory discrepancies or other evidence of theft, loss (reviewed on a case by case basis), or diversion must immediately be reported:
 - Purchased from DAF Stockroom:
Tammie Keadle, 314.935.6875, Keadle@wustl.edu, or
Susan Cook, 314.747.0309, shcook@wustl.edu, or
WUSTL Police (Danforth Campus, 314.935.5555)
 - Purchased from DCM Stockroom:
Ken Boschert, 314.362.3773, boschertk@wustl.edu, or
Susan Cook, 314.747.0309, shcook@wustl.edu, or
Protective Services (Medical School Campus, 314.362.4357)
 - Individual Registration:
(Danforth Campus) Tammie Keadle, 314.935.6875, Keadle@wustl.edu, or
(Medical School) Ken Boschert, 314.362.3773, boschertk@wustl.edu, or
Susan Cook, 314.747.0309, shcook@wustl.edu

Once reported and reviewed, the PI will be advised when to complete the **DEA Form 106— Theft or Loss of Controlled Substances** and the **BNDD Report of Loss or Theft of Controlled Substances** form.

5. Investigators are to maintain the Controlled Substance Aliquot Log with DAF- or DCM- assigned bottle or package number for each controlled substance for two years from the last entry on the log.
6. As controlled substances are dispensed in the course of performing animal research, the date, species, animal ID (USDA covered species only), amounts used, drug balance

remaining in bottle, and purpose of use are to be recorded on the Controlled Substance Aliquot Log and initialed by the authorized lab personnel. For non-covered species, the animal ID is the number of animals that were administered controlled substances on that day.

7. If investigators combine stock bottles of controlled substances (e.g. ketamine) with other non-controlled drugs (e.g. xylazine or medetomidine) to make up “rodent cocktail” solutions, an appropriate entry must be recorded on the original stock bottle’s Controlled Substance Aliquot Log and a new, separate Controlled Substance Aliquot Log must be generated and maintained by the investigator to record activity associated with the compounded product. By law, the DAF or DCM stockrooms cannot issue compounded drugs.
8. When the bottle is empty, it should be disposed properly.
9. If any amount of controlled substance drawn from the bottle is not used in the animal, this excess amount is considered “contaminated by animal contact” and should be disposed (disposal procedures below) by the PI and the wastage noted in the Controlled Substance Aliquot Log.
10. In USDA-covered animal species with individual medical records, amounts of controlled substances administered must also be recorded in the medical record.
11. Under no circumstances may controlled substances obtained from the DAF or DCM stockroom be transferred between different investigators or to unauthorized IACUC protocols of the same investigator. All controlled substances obtained from the DAF or DCM stockroom must either be used as described in approved IACUC protocols or returned to the DAF or DCM stockroom for proper disposal.
12. If an investigator obtains controlled substances from the DAF or DCM stockroom or from individual vendors/governmental agencies, **the controlled substances must be stored in separate, secure storage units** to reflect the difference in the registrations used to obtain the controlled substances.

VII) Disposal

The appropriate disposal method varies depending upon how the controlled substances were originally acquired.

For Controlled Substances Obtained from DAF or DCM Stockroom for IACUC-approved Animal Research Projects

- DAF will only dispose of drugs originally obtained from the DAF Stockroom under the DAF registration for IACUC-approved animal research projects.

- DCM will only dispose of drugs originally obtained from the DCM Stockroom under the DCM registration for IACUC-approved animal research projects.
1. Expired drugs— By law, controlled substances administered to animals may only be used before the expiration date, normally found printed on each bottle. Any volume remaining in an expired bottle/package of drug obtained from the DAF or DCM stockroom must be returned to the DAF or DCM stockroom along with the corresponding Controlled Substance Aliquot Log form. The final entry of the aliquot log form should note that the remaining expired drug was returned to the DAF or DCM stockroom. The DAF Director or DCM stockroom will record the amounts received onto a DEA Disposal Form 41.
 2. Unwanted controlled substances must be returned to the DAF or DCM stockroom along with the assigned controlled substance aliquot log.
 3. Under certain limited circumstances, the PI may destroy the Controlled Substances on-site if the destruction is witnessed by another authorized person and the destruction is documented on the use record. These circumstances, as set forth in 19 CSR 30-1.078, are:
 - Controlled Substances which are contaminated by patient (i.e. animal) body fluids, or
 - An excess volume of a Controlled Substance which must be discarded from a dosage unit just prior to use, or
 - The remaining contents of opened glass ampoules which are not patient (i.e. animal) contaminated.

When destroying materials under these circumstances, the material must be destroyed beyond reclamation and the date, amount destroyed, and reason for destruction must be recorded. The person performing the destruction and the witness must both sign the destruction record.

4. Any fees associated with disposal of controlled substances (reverse distributors, etc.) will be charged to the corresponding PI.

For Controlled Substances Obtained With Individual Research Registrations

1. Contact the Environmental Manager for your campus for assistance in determining proper disposal procedures, which will include working with an authorized reverse distributor. **DO NOT** submit a chemical request for pick-up to request disposal— **EH&S is not authorized** to remove these materials. Controlled Substances **obtained from outside vendors** must be returned to a registered reverse

distributor for proper disposal. **DO NOT** return to the DAF or DCM stockroom. EH&S can provide a list of registered reverse distributors and assist with coordinating disposal of these materials. Individuals who need to destroy controlled substances are responsible for submitting the Form 41 to DEA to request destruction in the EH&S hazardous waste facility. Once approval is received, EH&S will escort them to the hazardous waste facility and have them witness the destruction and take care of the final paperwork. Reverse distributor disposal costs are the responsibility of the PI and may be charged to grants under which the controlled substance work is being performed.

Environmental Manager for the Danforth Campus: 314.935.4650

Environmental Manager for the Medical School: 314.362.6735

VIII) Audits

Both the WUSTL Institutional Animal Care and Use Committee and Environmental Health and Safety will audit the investigator labs at least annually. IACUC staff will visit each lab to review all aspects of animal care and use identified on the IACUC protocol. Among the items checked on these visits will include, but may not be limited to: the list of authorized controlled substances users and completion of background checks, proper security of controlled substances, controlled substance use (aliquot) logs, controlled substance inventories, verification of lab personnel who have access to controlled substances and expiration status of controlled substances. EH&S's review will include, but may not be limited to, verifying proper security of controlled substances and use logs and inventories are complete.

The Vice Chancellor for Research and the relevant department chair or dean of the appropriate school will be notified of any serious or continued non-compliance.

Individual registrations may be subject to external reviews.

IX) Sanctions

Any lab found to be deficient in any aspect will receive formal communications from either of the WUSTL Institutional Animal Care and Use Committee and/or Environmental Health and Safety office regarding the deficiency and the method for correction. Any lab with deficiencies will be re-inspected to determine compliance. Violations of the policy, procedures, or regulations that are deemed serious or continuing may subject the covered individual to corrective actions or other sanctions as deemed appropriate by the Vice Chancellor for Research in consultation with the relevant department chair or dean as appropriate.

X) Recordkeeping Requirements

All Investigators are responsible for maintaining the following records documenting acquisition, use, and disposal of controlled substances and adhere to the corresponding **record retention timeframes**.