University of CINCINNATI **Category:** Administration **Policy applicable for:** Colleges/ Faculty/ Staff/Students	*Policy Title:* **Individual Investigator Use of Controlled Substances in Non-Therapeutic Research** **Effective Date: 11/10/2022**	*Policy Number:* **1.9.10** **Policy Owner:** VP for Research **Responsible Office(s):** Office of Research

Definitions

"Controlled substances" are drugs that are regulated by the Drug Enforcement Administration (DEA) and the State of Ohio Board of Pharmacy (OBP) because of potential for abuse. DEA regulations and OBP rules allow researchers to obtain and use controlled substances in animal research, in culture systems, or *in vitro* (other approvals apply as appropriate). To do so, investigators must either:

1. hold a current individual DEA research and an OBP Terminal Distributor of Dangerous Drugs License (TDDDL), or

2. conduct their research as an authorized agent of a university official or investigator who holds a current DEA registration and OBP TDDDL.

Policy

This policy does not apply to controlled substances used in research involving the use of human subjects by researchers who are licensed healthcare practitioners in the State of Ohio and hold current DEA registrations. Further, this policy does not apply to controlled substances used in veterinary care by veterinarians licensed in the State of Ohio who hold current DEA registrations for veterinary use.

Investigators who seek to obtain a research or instructing registration for use of controlled substances in animal or laboratory research must first notify their college (the chief research officer for the college, e.g., Associate Dean for Research as well as the head of their unit) prior to registering with the Ohio Board of Pharmacy and/or the DEA.

I. Permitted Users of Controlled Substances in Research
   A. Practitioners
      1. To use controlled substances in non-therapeutic animal or laboratory (non-human subjects) research, investigators who are licensed practitioners must also hold a current DEA research registration or be an authorized agent as defined above. Clinical practitioners must not issue a prescription to themselves to obtain controlled substances to be stored or dispensed for research purposes.
   B. Investigators
      1. Practitioner and non-practitioner researchers may be registered as such under DEA regulations. To obtain a DEA research registration, an investigator must first obtain a separate OBP TDDDL.
      2. With a current DEA research or instructing registration, investigators may purchase and use/administer controlled substances in research on animals or in

laboratory research.

3. Investigators with DEA research registrations may not use controlled substances in research involving the use of human subjects, or dispense, or write prescriptions.
4. When using controlled substances in research, researchers must comply with all other relevant regulations (e.g., IACUC approval for use in animals). Without a DEA registration, investigators may use research drugs provided by LAMS veterinary personnel (e.g., ER buprenorphine), and/or may lawfully purchase, use in research, and store only those controlled substances in the forms described on the DEA exempt chemical preparation list pursuant to 21 CFR §1308.24. Such distribution, possession, or use must be intended for laboratory, industrial, or educational purposes and not for immediate or subsequent administration to a human being or other animal; see Exempt Chemical Preparations List.

C. Authorized Agents
   1. Authorized agents may also use controlled substances in animal or laboratory research under a research registration if they are specifically listed on the **Controlled Substances Authorized Agent List**. Authorized agents using controlled substances are also required to comply with the terms of this policy. Before receiving approval to use controlled substances as an authorized agent under this policy, authorized agents must provide documentation of training.

II. Recordkeeping Requirements
   A. Every researcher holding a DEA research or instructing registration and an OBP TDDDL is responsible for maintaining appropriate records and inventories of all controlled substances used in their research or instruction at the university. These investigators will be referred to as “registrants.”
   B. Authorized agents are also responsible for maintaining appropriate records and inventories of controlled substances used in their research or instruction at the university.
   C. Registered/licensed researchers must retain controlled substance records for five years.
   D. Controlled substance records must otherwise conform to the record keeping and inventory requirements of federal law and the procedures. Controlled substance records include all purchasing records; all inventory, administration, use, transfer, and waste/destruction records; all controlled substance ordering forms, including DEA Form 222 for Schedule I/II controlled substances; and all authorized agent records.
      1. Separate records are recorded for each research location and for each independent activity for which an investigator is registered (e.g. dispensing or instructing, research, manufacturing, etc. (see 21 CFR § 1301.13 for a complete listing of independent activities).
      2. Separate records are required for each controlled substance product or formulation.
      3. When recording dates of receipt, distribution, or other transfers, the date on which the controlled substances are received, distributed, or otherwise transferred must be used as the date of receipt or distribution on any documents of transfer (e.g., invoices or packing slips).
   E. Federal regulations require that records pertaining to controlled substances in Schedules I/II (see schedule table at the end of this document) must be maintained separately from all other records of the registrant and authorized agent. Records for Schedule III, IV, and V controlled substances (see schedule table at the end of this document) must be maintained either separately from all other records or in such form that the information required can be separated out from other records in a reasonable time from the ordinary business records of the registrant and authorized agent.

F. Controlled substance records must be made available immediately upon request by the U.S. Department of Justice Drug Enforcement Administration, the State of Ohio Board of Pharmacy, the State Medical Board of Ohio, officials of the University of Cincinnati, and the college and/or department under which the registration was obtained.

III. Monitoring and Auditing Requirements

A. The college and/or department of the registrant is responsible for monitoring the registration, recordkeeping, inventory, security, and disposal of controlled substances used in research by their investigators.

A. All registrants and their authorized agents must be audited by the college and/or department on an annual basis to assure compliance with DEA and Board of Pharmacy regulations and this policy. Many licensees will be audited semi-annually during IACUC inspections which may satisfy the college.

B. Audits must be performed by impartial individuals who are free of conflicts of interest and who are not involved in the day-to-day maintenance of the controlled substance inventory or conduct of the research using controlled substances.

C. Requirements for annual audit include:

1. Audits must be performed at times when no controlled substances are being used in the inspected laboratory. Audits are the responsibility of the college, but where relevant, the college may choose to use documentation from IACUC semi-annual inspections.
2. Minimum requirements
    a. Inventory: per the DEA, “the registrant shall take a new inventory of all stocks of controlled substances on hand.” This includes:
        i. The name of each substance.
        ii. Each finished form of the substance (e.g., 10mg tablet or 10mg/ml concentration).
        iii. The number of units (or volume, weight, etc.) of each substance: for Schedules I and II make an exact count or measure of the contents for Schedules I and II; for Schedules III, IV, and V make an estimated count or measure of the contents unless the container holds more than 1,000 tablets or capsules in which case make an exact count of the contents.
        iv. The number of commercial containers of each finished form (e.g., four 100-tablet bottles).
        v. For any damaged, defective, or impure substance awaiting disposal, also record the total quantity of the substance to the nearest metric unit weight or total number of units of finished form, the reason for the substance being maintained, and whether the substance is capable of use in the manufacture of another controlled substance in finished form.
3. Additional information to review and record
    a. License/registration: verify licensee, expiration date, location, substances to determine if in alignment with use/storage.
    b. Storage:
        i. Controlled substances are stored in a locked and secure location with access limited to those authorized to use the controlled substances; this typically requires 2 distinct security mechanisms.
    c. Forms and recordkeeping:
        i. Ordering, inventory, destruction, and use/administration/waste records are maintained on the proper forms.

ii. All personnel involved in the use of controlled substances are on the authorized agent list (i.e., Controlled Substance Form) and training records exist for them.
iii. Any records pertaining to Schedules I/II controlled substances are maintained separately from all other records.

d. Drug accountability
i. Amounts of controlled substances purchased can be reconciled against inventory, use, administration, and waste records.
ii. Inventory is not past the expiration date. Expired drugs must be clearly labelled and segregated from unexpired/in use drugs.

D. Should deficiencies be noted on any audit or annual review, additional audits must take place to determine whether corrective action has been taken or if deficiencies still exist.
E. Should any reports of violations of this policy be received, an investigation and/or audit led by the college and/or department of the registrant must take place.

IV. Corrective Measures
A. Failure of registrants and authorized agents to follow the requirements of this policy may result in personal civil and criminal liability under state and federal law. Registrants and authorized agents who violate this policy may be denied privileges to conduct research at the university. Individuals who violate this policy may be subject to corrective or disciplinary action, up to and including termination or dismissal, in accordance with applicable policies, rules, collective bargaining agreements, or the relevant Code of Conduct.
B. When issues of non-compliance are identified, the college and/or department of the registrant, in consultation with applicable university units, will be responsible for determining the corrective action plan and/or disciplinary actions to be taken. Corrective action plans may include, but are not limited to, re-training of faculty, staff, and students; purchasing ability limitations; and laboratory shutdown.
C. The college and/or department of the registrant must notify the University Office of Research of any violations.

General Storage Rules

- All controlled substances must be stored behind at least two differently keyed locks at all times.
- For keyed lockboxes
  - Do not store the keys near the lockbox; and
  - Do not store the keys together.
- For combination lock lockboxes
  - Only the registrant and as few responsible individuals as possible should know the combination.
  - Whenever anyone who knows the combination is terminated from employment, the combination(s) must be changed.
- Schedule I and II substances (e.g., Pentobarbital is a Schedule II drug)
  - Must be stored in a safe or steel cabinet of substantial construction.
  - If the safe or steel cabinet is less than 750 lbs., it must be mounted or secured to something of substantial construction (e.g., bolted to a wall or the floor, or the base imbedded in concrete).
  - The safe/cabinet should have an inner and outer door with the locks for each door keyed differently.
  - Standard “narcotics cabinets” can be purchased through a variety of resources.
- Schedule III, IV, and V controlled substances (e.g., Ketamine and Buprenorphine, are Schedule III controlled substances)

    - Should be stored using one of the following methods:
    - Preferred method: a wall mountable controlled substance lockbox with two doors and two locks (each lock is keyed differently).
    - A single-lock lockbox that is stored in a drawer or cabinet that is secured at all times with a hasp and padlock. The drawer and cabinet should be substantially constructed such as in a drawer that is part of either a bench or cabinet that is mounted to the wall or floor.
    - If a lab is not accessible to the public, then an option is to use a single-lock lockbox, stored in a drawer or cabinet in a room that is kept locked at all times.
    - Schedule III, IV and V substances can also be stored with Schedule I and II substances. Non-controlled substances may not be stored with controlled substances.
- Recordkeeping Forms and Logs
    - Controlled Substance Notebooks must be maintained and contain all relevant documents demonstrating the chain of custody and closed system of distribution. The sections below are strongly encouraged and each contains the relevant logs and forms needed. Documentation for Schedules III – V can be maintained together in one notebook. Schedule I and II must be maintained separately.
    - Logs must include (minimum) Authorized User Signature form (specific to schedules in the registration); Initial and Biennial Inventory form; Acquisition/Purchase log; Usage and Disposal form; Reverse Distribution confirmations/instructions.

Schedules of DEA Controlled Substances
Controlled substances are designated by the DEA as Schedule I-V according to their medical use, potential for abuse, and safety or dependence liability. Each controlled substance, or basic class thereof, has been assigned an "Administration Controlled Substances Code Number" for purposes of identification of the controlled substances or class on certain certificates of registration issued by the administration pursuant to 21 CFR §1301.35 and on certain order forms issued by the administration pursuant to 21 CFR §1305.05(d). Refer to 21 CFR §1308 for the schedules of controlled substances (see also U.S. Department of Justice Controlled Substance Schedules).

Term	Definition
Authorized agent	Researchers acting directly on behalf of a registrant. The faculty, staff, and student laboratory members of such investigators in turn become authorized agents themselves. Students under the age of 18 and volunteers are not permitted to serve as authorized agents under this policy.
Controlled substances	Drugs that are regulated by the DEA and the Board of Pharmacy because of potential for abuse.
DEA research or instructing registration	A special DEA license that allows practitioner and non-practitioner investigators to obtain and use controlled substances in animal or laboratory research.
Investigator	A faculty or staff researcher; most often a principal investigator of a research study.
Practitioner	A physician, dentist, veterinarian, pharmacist, nurse practitioner, or other licensed medical professional, possessing a DEA registration to prescribe, dispense, or administer a controlled substance in the course of their professional practice.
Non-practitioner	An investigator who conducts animal or laboratory research at the university and does not have a practitioner’s license.
Registrant	A university official or investigator who holds an individual federal DEA research or instructing registration specifically for the use of controlled substances in animal or laboratory research.