

PROCEDURE: Individual Investigator Use of Controlled Substances in Non-Therapeutic Research

Applies to: UC personnel who hold individual, or work under a college-based program using federal Drug Enforcement Administration (DEA) research or instructing registrations and State of Ohio Board of Pharmacy (OBP) Terminal Dangerous Drug Distributor Licenses (TDDDL) to specifically use controlled substances in animal or laboratory research. The policy also applies to faculty, staff, and students acting as an authorized agent under such registrations.

I. Registration

A. University

1. 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 and their unit head) prior to registering with the Ohio Board of Pharmacy and/or the DEA.
2. The investigator must complete a Controlled Substance Program Security Release (Controlled Substance Form).
3. Once OBP licenses and DEA registrations and/or renewals have been obtained (see below), registrants must provide copies to their college (e.g., associate dean for research).

B. State of Ohio Board of Pharmacy

1. Investigators who are not pharmacists independently licensed by the State of OBP must obtain a Terminal Dangerous Drug Distribution License (TDDDL) by applying to the State of Ohio Board of Pharmacy (see [Limited License Application](#)).
2. If not a licensed pharmacist, investigators should request a Category III license, which would allow the licensee to possess, have custody or control of, and distribute any controlled substances contained in Schedules II-V and/or possess and have custody or control of Schedule I controlled substances contained in certain locations (e.g., research facilities, laboratories).
 - a. In addition to the application, the following three documents must also be submitted to the Board of Pharmacy when requesting a Category III license:
 - b. List of personnel having access to and/or administering drug,
 - c. Protocol, and
 - d. Drug list.

C. Drug Enforcement Administration (DEA)

1. The DEA generally requires that an investigator first obtain a TDDDL from OBP before the DEA will issue a registration for researchers or teaching institutions.
2. Investigators need to determine which activities will be performed to determine which type of registration to request.
3. Investigators may apply for a [DEA registration online](#) (DEA's preferred method of application).
4. Investigators wishing to use Schedule I compounds must submit both an application and a protocol to conduct research with controlled substances listed in Schedule 1 must be submitted. Refer to [21 CFR §1301.18](#) for specific requirements.

NOTE: The fee waiver for UC is only available to full-time UC employees who use the DEA license for research. Clinical licenses obtained through UC Health do not qualify for the fee waiver.

D. Renewal Applications for OBP and DEA

1. Each registrant is responsible for ensuring their registrations remain valid.
2. License and registration renewal must take place through the OBP and the DEA processes, respectively.
3. Schedules for renewal vary based on the type of license/registration.

E. Registration Changes

1. Registrants with name, address, schedule, and/or drug code changes should first make those change requests with the OBP. Once approved by the state, the registrant must submit a change request to the DEA via the [DEA website](#). Changes will become effective immediately upon DEA approval.
2. Registrants seeking to terminate their DEA registration because they discontinue research requiring a registration or plan to leave the university must notify in writing their college, (e.g., Associate Dean for Research) and department chair, the [State of Ohio Board of Pharmacy](#), and the DEA at DEA.Registration.Help@usdoj.gov.
3. Registrants who seek to terminate their DEA registration by transferring such research activities to another person must submit in person or by registered or certified mail, return receipt requested, to the DEA Special Agent in Charge, at least 14 calendar days in advance of the date of the proposed transfer the following information:
 - a. The name, address, registration number, and authorized business activity of the registrant discontinuing the business (registrant-transferor);
 - b. The name, address, registration number, and authorized business activity of the person acquiring the business (registrant-transferee);
 - c. Whether the business activities will be continued at the location registered by the person discontinuing business, or moved to another location (if the latter, the address of the new location should be listed);
 - d. Whether the registrant-transferor has a quota to manufacture or procure any controlled substance listed in Schedule I or II (if so, the basic class or class of the substance should be indicated); and
 - e. The date on which the transfer of controlled substances will occur.
4. Should transfer of controlled substances inventory also need to accompany the transfer of registration, refer to [21 CFR §1301.52](#) for specific requirements.
5. Registrants are required to notify their college and/or department of any changes to the registration.

II. Agent Authorization and Training

A. Agent Authorization

1. Investigators wanting to conduct animal or laboratory research with controlled substances as an authorized agent should contact the registrant for their college and/or department (or their responsible program administrator).
2. The laboratory members of such investigators in turn become authorized agents themselves, and must be documented on the Controlled Substances Authorized Agent List. Copies of completed forms must be provided to the College Research Officer.
3. Students under the age of 18 and volunteers are not permitted to serve as authorized agents under this policy.

B. Training

1. All registrants and authorized agents must undergo appropriate training on

the use of controlled substances in research to meet the regulatory requirements.

2. The college and/or department of the registrant under whom the research is being conducted must provide the training required by this policy whenever possible. Alternatively, training can be provided by another college/department, with its permission.
3. Training is required for all registrants, authorized agents, and/or students before they may be involved in controlled substance use in research.
4. The registrant or their responsible program administrator must maintain all training records associated with their registration.
5. A required, but not exhaustive, list of training elements includes: regulatory overview, controlled substance schedules, recordkeeping requirements and form use, storage, disposal, personnel changes, and best practices.
6. Continuing education and/or re-training may take place as necessary (e.g., as new regulatory requirements are published, as part of a corrective action plan, etc.).

III. Purchasing/Ordering

- A. As a general rule, only the minimum amount of controlled substances needed for current research projects should be obtained.
- B. Controlled Substances Purchased from University-Based Pharmacies
 1. Where applicable controlled substances may be purchased and/or acquired through UCHealth research pharmacies (e.g., Investigational Drug Services).
 2. Registrants are responsible for maintaining the DEA Form 222s for Schedule I or II controlled substances (and recording the use thereof on Controlled Substance Form should they choose).
 3. Registrants and authorized agents may obtain controlled substances by providing the following to a university-based pharmacy:
 - a. An approved university requisition, which includes the following information:
 - i. Name of individual picking up (this person must be on the Controlled Substances Authorized Agent List.
 - ii. Location (must match location on the list of approved sites).
 - iii. Item number, quantity, name and estimated price of the controlled substance(s) being purchased.
 - b. A DEA Form 222 (only required by individual DEA registrants submitting a request for Schedule I/II controlled substances).
 - c. A copy of the investigator's current DEA research or instructing registration, if applicable.
 - d. A current university ID.
 - e. A copy of the Controlled Substances Authorized Agent List. Only those listed on the form or the registrant will be permitted to receive controlled substances.
 4. Registrants and authorized agents are responsible for maintaining copies of university requisitions or other purchasing records used for each controlled substance purchase.
- C. Controlled Substances Purchased from Non-University Pharmacies or Distributors
 1. Registrants and authorized agents are responsible for obtaining and maintaining the following information for all controlled substances purchased from non-university pharmacies or distributors:
 - a. A copy of the invoice, purchase order, or requisition.
 - b. A copy of the shipping document, packing slip, or receipt.
 - c. The name, address, and DEA number of the company from which the

- controlled substance was purchased.
- d. The name of the controlled substance purchased.
- e. The size and strength of the controlled substance purchased.
- f. The amount purchased (which should match the amount received).
- g. For Schedule I/II controlled substances, a copy of the invoice and individual DEA Form 222.
- h. Optional for Schedule I/II controlled substances, a Record of DEA Form 222 Use (Controlled Substance Form) to maintain accountability for all DEA Form 222s used. If used, the dates and amounts received entries on this form must match the corresponding entries on the Controlled Substances Record (Controlled Substance Form) for each controlled substance purchased.

D. DEA Ordering Forms

1. The Controlled Substance Ordering Form (DEA Form 222) is a paper-based form used to order Schedule I/II controlled substances. This form is requisitioned directly from the DEA and is required to be filled out. The DEA Form 222 also allows the exchange of Schedule I/II controlled substances from the registrant to another party registered with the DEA (typically used when a controlled substance is sent to a reverse distributor for credit or disposal). Save a copy of the completed form for your records.
2. Requests for DEA Form 222 can be made online at the [DEA Forms & Applications page](#). Alternatively, a registrant may obtain a Controlled Substance Ordering System (CSOS) digital certificate from the DEA Certification Authority to sign electronic orders for controlled substances. See [21 CFR §1311 subpart B](#).
3. Registrants will receive the maximum number of order form books allowed for their business activity.
4. Schedule III, IV, and V controlled substance orders do not require a DEA Form 222. These controlled substances can be ordered directly from the manufacturer or university-based pharmacy.
5. All unused DEA Form 222s must be submitted to the nearest DEA office if the registrants' DEA research or instructing registration or OBP TDDDL terminates because they die, discontinue their research, change the name or address as shown on their registration, or are suspended.

IV. Storage and Security

- A. Registrants and authorized agents may only receive and store the minimum amount of controlled substances needed for current research. All controlled substances must be stored in a locked steel cabinet, a locked substantially constructed cabinet, per [21 CFR §1301.72](#). Controlled substances should not be located near a glass panel where they can be visible from the outside.
- B. Registrants and authorized agents using and storing controlled substances must provide effective controls to guard against theft. This includes, but is not limited to, restricting the number of keys that access the controlled substances and limiting the number of employees who will have access to these keys. Keys for locked cabinets must be kept in secure locations when not in use. If controlled substances are locked using a combination or numerical coded lock, combinations/codes must be changed upon turnover of an employee who has knowledge of the combination/code. In addition to locked access control, only authorized personnel should be permitted to access a university laboratory where controlled substances are used or stored.
- C. Non-laboratory personnel/visitors entering areas where controlled substances are used or stored must always provide identification and a rationale for access. Controlled substances must never remain unlocked or unattended during laboratory maintenance

work or other required access by individuals who are not the registrant or authorized agent.

- D. The Colleges are responsible for ensuring that audits are conducted at least annually. Most licensees will be audited semi-annually during IACUC inspections which may satisfy the college.

V. Inventory

- A. This section delineates the responsibilities of registrants and authorized agents in maintaining an up-to-date physical inventory of all controlled substances in their laboratories. Monitoring and auditing of inventories is a college/department function.
- B. Each inventory must contain a complete and accurate record of all controlled substances on hand on the date the inventory is taken. The inventory may be taken at either the opening of business or at the close of business on the inventory date, and this must be indicated on the inventory.
- C. Inventory must be maintained on a Controlled Substance Record (Controlled Substance Form) for each controlled substance used in their laboratories. The Controlled Substance Form must meet DEA requirements for controlled substance inventory, administration, and use documentation requirements. Refer to [21 CFR §1304.11](#) for complete DEA inventory requirements.
- D. Minimum inventory requirements include:
 - 1. Initial inventory date.
 - 2. Annual inventory date (while the DEA requires bi-annual inventory, OBP requires an annual inventory).
 - 3. Inventory date for substances that are newly listed on Controlled Substance Schedules I-V.
 - 4. For each controlled substance in finished form the inventory must include:
 - a. The name of the substance;
 - b. Each finished form of the substance (e.g., 10-milligram tablet or 10-milligram concentration per fluid ounce or milliliter);
 - c. The number of units or volume of each finished form in each commercial container (e.g., 100-tablet bottle or 3-milliliter vial);
 - i. If the substance is listed in Schedules I or II, make an exact count or measure of the contents; or
 - ii. If the substance is listed in Schedule III, IV, or V, make an estimated count or measure of the contents, unless the container holds more than 1,000 tablets or capsules in which case there must be an exact count of the contents.
 - d. The number of commercial containers of each such finished form (e.g., four 100-tablet bottles or six 3-milliliter vials); and
 - e. Expiration date and lot number.
 - 5. For any other controlled substances not in current use (e.g., damaged, defective or impure substances awaiting disposal; substances held for quality control purposes; or substances maintained for extemporaneous compounding) the inventories must include:
 - a. The name of the substance,
 - b. The total quantity of the substance to the nearest metric unit weight or the total number of units of finished form, and
 - c. The reason for the substance being maintained by the registrant and whether such substance is capable of use in the manufacture of any controlled substance in finished form.
- E. Investigators who Leave the University

1. Controlled substances obtained are the responsibility of the person named on the registration. Registrants and authorized agents who plan to leave the university must contact their college and/or department prior to their departure to arrange appropriate disposition of the controlled substances and return of any DEA Form 222s to the DEA.
In the event of the unexpected or sudden departure of a registrant or authorized agent (e.g., death, suspension, etc.), the college/department must be immediately notified and all unused controlled substances and order forms for controlled substances (i.e., DEA Form 222s) must be immediately secured. The registrant is the person responsible for the controlled substance. If unsecured controlled substances are identified they must be immediately secured, notify your unit leadership and the DEA for guidance.
2. The University Office of Research will work with the college/department and University Police if necessary to arrange for and ensure the appropriate disposition of the controlled substances and/or order forms.

VI. Administration/Use

- A. Registrants and authorized agents must maintain administration/use records documenting the following information on the university-controlled substances record (Controlled Substance Forms):
 1. The animal species or cell culture or analytical system in which the controlled substance was administered/used.
 2. The date administered/dispensed.
 3. If not administered/used personally by the registrant, the initials of the person who administered/used the controlled substance.
 4. The name of the controlled substance.
 5. The strength and size of the controlled substance.
 6. The amount administered/used/wasted (number of units or volume).

VII. Spills/Loss

- A. Breakage, spills, or other witnessed, accidental controlled substance losses do not need to be reported to the DEA. However, any such loss must be documented and witnessed by the registrant or authorized agent on the university-controlled substances record (Controlled Substance Forms).
- B. Controlled substances that can be recovered after a spill, but cannot be used because of contamination (e.g., tablets, powders), must be handled pursuant to the disposal/destruction requirements in Procedure VIII below.
- C. If the spilled/lost controlled substance is not recoverable (e.g., liquids), the circumstances of the spill/loss must be documented, witnessed by the registrant or authorized agent, and co-signed on the university controlled substances record (Controlled Substance Forms).

VIII. Disposal

- A. Registrants and authorized agents should only purchase and store those quantities of controlled substances needed for current research or instructional activities. Damaged, expired, unwanted, unusable, or non- returnable controlled substances must be accounted for, stored, and disposed of in accordance with applicable state and federal regulations.
- B. Disposal of a controlled substance must render it non-retrievable. Though the DEA does not specify destruction methods, it does state, "the process utilized to render a substance 'non-retrievable' shall permanently alter the substance's physical or

chemical condition or state through irreversible means and thereby render the substance unavailable and unusable for all practical purposes. A substance is considered 'non-retrievable' when it cannot be transformed to a physical or chemical condition or state as a controlled substance or controlled substance analogue."

- C. There are three disposal options for expired or unwanted controlled substances. Authorized agents should contact the registrant or their college and/or department to help determine the correct disposal method. Two employees of the registrant must handle or observe the handling of any controlled substance until it is transferred or rendered non-retrievable.
 - 1. On-site disposal: Small quantities of controlled substances can be disposed onsite by the DEA registrant or authorized agent using the following procedure:
 - a. Complete the [Registrant Record of Controlled Substances Destroyed](#) (DEA Form 41) prior to disposal (see section D below).
 - b. The controlled substance must be rendered non-retrievable by permanently altering the substance's physical or chemical condition or state through irreversible means and thereby rendering the substance unavailable and unusable for all practical purposes.
 - 2. Reverse distribution: For large quantities or volumes of controlled substances, contact a reverse distributor. This option transfers ownership of the controlled substance to a DEA-approved pharmaceutical returns processor for re-use, re-sale, or destruction at a hazardous waste incinerator. This process may involve the completion of DEA Form 222 or invoice depending on the reverse distributor and the substances involved.
 - 3. Contact the supplier: Some suppliers will take back controlled substances for credit. This process may involve the completion of manufacturer-specific return or recall transaction records or DEA Form 222 depending on the supplier and the substances involved.
- D. [Registrant Record of Controlled Substances Destroyed](#) (DEA Form 41) must be completed prior to disposing of any controlled substance and a copy must be retained by the registrant or authorized agent for at least five years, pursuant to the statute of limitations and the data retention requirements of the university Research Data policy.
- E. Registrants and authorized agents must maintain disposal records with the following information:
 - 1. The registrant's DEA number, name, and address.
 - 2. If a reverse distribution is done, the reverse distributor's DEA number, name, and address.
 - 3. The number of units (in finished forms and/or commercial containers) disposed of in any manner, including the manner of disposal.
 - 4. The date when the products were sent for destruction and left the registrant's or authorized agent's inventory.
 - 5. Any additional documentation recording the exchange of custody.

IX. Reporting of Theft or Missing Controlled Substance

- A. Registrants and their authorized agents must maintain complete accountability at all times of all controlled substances stored or used in their laboratory. Generation and retention of all records related to the use of controlled substances is essential so that any shortages or missing controlled substances will not go unnoticed. Theft or misuse of a controlled substance is a criminal act. Anyone who has knowledge of theft or misuse must report it to the following agencies, university departments, and individuals:
 - 1. OBP ([Theft & Loss Reporting website](#));
 - 2. DEA (see sections B and C below);

3. Registrant responsible for the controlled substance;
 4. Registrant's chief research officer for the college (e.g., Associate Dean for Research);
 5. Registrant's unit head (e.g., chair); and
 6. University Office of Research (integrity@uc.edu)
- B. Federal regulations require that registrants notify the DEA Field Division Office in their area, in writing, of the theft or significant loss of any controlled substance within one business day of discovery of such loss or theft. The registrant must complete a [Report of Theft or Loss of Controlled Substances](#) (DEA Form 106) and submit this report to the Ohio DEA office. Simultaneous with notification of the DEA, copies of DEA Form 106 must also be submitted to the college and department of the registrant (to the dean for research or college research officer) as well as the Office of Research Compliance. Registrants and authorized agents must keep one copy of any DEA Form 106 submitted to the DEA for at least five years.
- C. Online reporting to the DEA is also necessary if small quantities of controlled substances become unaccounted for on a re-occurring basis. The online reporting process can be accessed by registrants at the [Theft/Loss Reporting page](#). Copies must also be submitted to the college and/or department of the registrant as well as their responsible program administrators if applicable, and the University Office of Research. Registrants should print and keep a copy of any online DEA Form 106 submitted in their controlled substance inventory records.

X. Exempt Chemical Preparations

- A. Exempt chemical preparations are controlled substance preparations that do not present any potential for abuse and are intended for laboratory, industrial, educational, or special research purposes only and not for administration to a human or animal.
- B. Investigators may order controlled substances in the forms described on the DEA exempt chemical preparation list without a DEA registration pursuant to [21 CFR § 1308.24](#). For a complete list of chemical preparations and suppliers (see [Exempt Chemical Preparations List](#)).
- C. These preparations are exempt from the controlled substances storage and security requirements outlined in Procedure IV above, as well as the maintenance of records and reporting requirements outlined in Procedure V-IX above.
- D. Labeling of Exempt Chemical Preparations
 1. The label of an exempt chemical preparation must be prominently marked with the preparation's full trade name or other description and the name of the manufacturer/supplier, in such a way that the product can be readily identified as an exempt chemical preparation.
 2. The label and labeling must also include in a prominent manner the statement "For industrial use only" or "For chemical use only" or "For *in vitro* use only—not for human or animal use" or "Diagnostic reagent—for professional use only" or a comparable statement warning the person reading it that human or animal use is not intended.

Business Activity	Controlled Substances	DEA Application Forms	Registration Period	Coincident Activities Allowed
Dispensing or Instructing Includes practitioner, hospital/clinic, retail pharmacy, central fill pharmacy, teaching institution	Schedules II through V	New – 224 Renewal – 224a	3 years	May conduct research and instructional activities with those controlled substances for which registration was granted, except that a mid-level practitioner may conduct such research only to the extent expressly authorized under state statute. A pharmacist may manufacture an aqueous or oleaginous solution or solid dosage form containing a narcotic controlled substance in Schedule II–V in a proportion not exceeding 20% of the complete solution, compound, or mixture. A retail pharmacy may perform central fill pharmacy activities.
Research	Schedule I	New – 225 Renewal – 225a	1 year	A researcher may manufacture or import the basic class of controlled substance or substances for which registration was issued, provided that such manufacture or import is set forth in the protocol required in 21 CFR § 1301.18 and to distribute such class to persons registered or authorized to conduct research with such class of substance or registered or authorized to conduct chemical analysis with controlled substances.
Research	Schedules II through V	New – 225 Renewal – 225a	1 year	May conduct chemical analysis with controlled substances in those schedules for which registration was issued; manufacture such controlled substances if and to the extent that such manufacture is set forth in a statement filed with the application for registration or reregistration and provided that the manufacture is not for the purposes of dosage form development; import such controlled substances for research purposes; distribute such controlled substances to persons registered or authorized to conduct chemical analysis, instructional activities or research with such controlled substances, and to persons exempted from registration pursuant to 21 CFR § 1301.24 ; and conduct instructional activities with controlled substances

Agency/Office	Phone	Additional Contact Information
State of Ohio Board of Pharmacy	614.446.4143	614.752.4836 (fax) pharmacy.ohio.gov/Licensing/dea106.aspx
DEA Cincinnati Resident Office 36 EAST 7TH STREET SUITE 1900 CINCINNATI, OH 45202	571.362.1757	571.362.5984 (fax)
University Police	513.556.1111	publicsafety@uc.edu
Office of Research	513.558.5034	integrity@uc.edu ; iacuc@uc.edu

Position or Office	Responsibilities
Investigators, registrants, and authorized agents	<ol style="list-style-type: none"> 1. Maintain and retain appropriate records and inventories of all controlled substances used in their research or instruction at the university on university and/or DEA-approved controlled substances forms. Provide controlled substance documentation to the state, federal and university oversight entities listed in this policy. 2. Complete training before being involved in controlled substance use in research. 3. Ensure that training records related to your registration are maintained. 4. Follow requirements to purchase/order controlled substances from university-based pharmacies and non- university pharmacies or distributors. 5. Store all controlled substances in a locked steel cabinet or a locked substantially constructed cabinet or vault. Provide effective controls against theft. 6. Maintain up-to-date physical inventories of all controlled substances in their laboratories and follow all inventory requirements. 7. Follow requirements for administration/use documentation. 8. Document spills/losses as required. 9. Account for, retain, and dispose of damaged, expired, unwanted, unusable, and non-returnable controlled substances in accordance with state and federal regulations; maintain disposal records as required. Contact the college and/or department to help determine the correct disposal method. 10. Maintain complete accountability at all times of all controlled substances stored or used in their laboratory. 11. Report theft/misuse of controlled substances to the agencies listed in this policy. 12. Follow requirements for exempt chemical preparations, if applicable. 13. <i>Investigators seeking to become registrants:</i> <ol style="list-style-type: none"> a. Follow the requirements for registering with the university, the Board of Pharmacy, the DEA, and any requirements for renewals and changes in registration. b. Notify the college and/or department prior to registering with the Board of Pharmacy and/or DEA and of any changes in registration. c. Provide copies of licenses and registrations to college and/or department. 14. <i>Registrants and investigators:</i> follow transfer/disposal requirements prior to leaving the university, license termination, or making changes to the registration. 15. <i>Authorized agents:</i> follow requirements to become an authorized agent.
College and/or department of the registrant	<ol style="list-style-type: none"> 1. Monitor and oversee of this policy as it applies to registrants and their agents. 2. Monitor the registration, recordkeeping, inventory, security, and disposal of controlled substances used in research by their investigators. 3. Audit all registrants on an annual basis. Conduct additional audits to determine if corrective action has resolved any found deficiencies. 4. Conduct off-cycle audits at college/department discretion. 5. Provide appropriate training on the use of controlled substances in research and/or ensure that all registrants and authorized agents have undergone such training (see required list of training topics). 6. Designate a responsible program administrator(s) as necessary to oversee training, auditing, etc. 7. Notify Office of Research Compliance of serious and/or recurring issues of noncompliance; review issues of noncompliance arising from those audits, and determine and enact corrective action plans in consultation with Legal Affairs and applicable university units.
University Office of Research	<ol style="list-style-type: none"> 1. Monitor and oversee this policy as it applies to registrants and their agents. 2. Review issues of noncompliance arising from annual reviews conducted by the college and/or department of registrants. 3. Provide assistance to university investigators holding individual DEA research registrations and Terminal Distributor Licenses (i.e., registrants). 4. Maintain and update website with policy and supplemental information (e.g., university-approved controlled substance forms).
UC Police/Public Safety	<ol style="list-style-type: none"> 1. Work with the Office of Research to temporarily and securely store controlled substances and order forms when needed.

Revision History

Date Approved	Description of Changes
2/21/2023	Document approved.