Controlled Substances Used in Research Guide

Department of
Environmental Health Safety and Risk Management
Laboratory Safety Program

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Contents

Introduction

All research activities involving the use of controlled substances must be performed in compliance with all applicable laws and regulations as well as with The University of Texas Rio Grande Valley (UTRGV) policies and procedures. This guide is designed to assist researchers who work with controlled substances to maintain compliance with Drug Enforcement Agency (DEA) mandates. The DEA is a division of the Department of Justice. It is the responsibility of each Principal Investigator (PI) to fully understand and comply with the most current DEA mandates. This guide is specific to researchers and does not apply to DEA registrations of licensed physicians or pharmacists.

Other references:

DEA's Office of Diversion Control (website for information):
http://www.deadiversion.usdoj.gov/

Title 21 CFR, Part 1300-1399 (regulations):
http://www.deadiversion.usdoj.gov/21cfr/cfr/

Title 21 United States Code (USA) Controlled Substance Act (Statute):
http://www.deadiversion.usdoj.gov/21cfr/21usc/

Controlled Substance Definitions

Controlled substances are drugs or other chemicals with the potential to be addictive or habit forming. The DEA has divided controlled substances into five schedules based on their potential to be habit forming, and their usefulness in medicine. The definition of a controlled substance is "…a drug or other substance, or immediate precursor, included in schedule I, II, III, IV or V..." (USC Title 21, Section 802).

The five established federal schedules of controlled substances (I-V) are updated and republished annually by the DEA (USC Title 21, Section 812). These lists describe the basic or parent chemicals and do not describe the salts, isomers and salts of isomer, esters, ethers and derivatives which may be controlled substances. These DEA lists are intended as general references and are not comprehensive. A link to the federal list is at http://www.deadiversion.usdoj.gov/schedules/

Exempt Amounts

The Drug Enforcement Agency allows certain analytical standard, preparations and products to be purchased and used without the need for the user to have a DEA registration. Please refer to http://www.deadiversion.usdoj.gov/schedules/#exempt for information on the Exempted Lists.

List I and II Chemicals (Precursors)

In addition to the scheduled controlled substances, there are also chemicals that are regulated under the Chemical Diversion and Trafficking Act (CDTA) because they are precursors to, or reagents used in, the manufacture of illicit drugs. Many of these chemicals are common laboratory reagents; many have a threshold below reporting requirements and ordering does not require DEA registration. The DEA Chemical Handler's Manual can be consulted for additional information.

A table of these chemicals can be found at http://www.deadiversion.usdoj.gov/chem_prog/34chems.htm

Controlled Substance Registration

The PI or person who engages in research with controlled substances must be registered with the DEA. There are different activities that require different registration types. Further, one registration type may not cover two different kinds of activities, such as research with a controlled substance and dispensing of controlled substances.

The PI (registrant) is ultimately responsible for the use, storage and security of the products and the authorization of their staff that will have access to and use of the products. The registrant is responsible for ensuring compliance with all applicable laws and regulations as well as adherence to The University of Texas Rio Grande Valley policies and procedures.

Each registrant who receives, stores, or administers controlled substances must be registered with the Drug Enforcement Agency for that specific laboratory location. A separate registration is required for each principal place of business. Information on applying for a license (DEA Form 225) is available at www.deadiversion.usdoj.gov/drugreg/reg_apps/225/225_instruct.htm#6

In addition to the application form, faculty and staff may need to provide the following information to the DEA:

- The applicant's social security number.
- The applicant's curriculum vitae.
- A copy of the research protocol summarizing the procedures to be performed using controlled substances, including specific information on monitoring drug usage, inventory control, destruction, security, storage and access to the material.
- Names of all persons who will have access to, or records of, the controlled substances.

A separate registration is required for researchers who wish to work with Schedule I controlled substances. Researchers requesting Schedule I drug registration must submit a DEA application and follow the protocol found in 21 CFR 1301.18.

The DEA registration must be maintained at the registered location in a “readily retrievable” manner (21 CFR 1301.35).

Note: The State of Texas does not issue registrations for research use of controlled substances.

DEA links for registration:

Registration program website:
http://www.deadiversion.usdoj.gov/drugreg/

For information on categories and fees:
http://www.deadiversion.usdoj.gov/drugreg/categories.htm

Renewal of DEA Registration

The DEA registration for research is valid for one year and must be renewed annually. The registrant will be contacted by the DEA at the time of renewal. Do not allow your registration to expire. You will have to start over again and this will ultimately put you in a state of non-compliance with the federal regulations if you possess any controlled substances.

The University of Texas Rio Grande Valley Department of Environmental Health Safety and Risk Management (EHSRM) registration

Because EHSRM audits compliance activities involving controlled substances, the registrant must notify the EHSRM using the Controlled Substance Registration Form.

Security Requirements

Effective physical security and operating procedures must be in place to guard against theft and diversion of controlled substances. Overall evaluations of the security measures may be made by the DEA during the application review process to ensure that controlled substances are stored securely.

Minimum Requirements (21 CFR 1301.71(a))

- **Schedule I** controlled substances must be stored in a securely locked, substantially constructed safe (vault or GSA class 5 rated safe, cabinet, or a secure containment apparatus that has been approved by DEA). Vault or GSA Class 5 Rated Safe/Cabinet must be of substantial masonry and have a multiple position combination lock, relocating device (or equivalent) and a door having a thickness of steel plate of at least ½ inch. If the vault is newly constructed, it must have walls, floors and ceilings constructed of at least 8" reinforced concrete. Vaults must be six-sided or have floor constructed as described above. For a GSA Class 5 safe/cabinet, the door must contain a multiple-position combination lock, a relocking device (or equivalent) and a steel plate having a thickness of at least ½ inch. Safes or cabinets weighing less than 750 lbs. must be bolted or cemented to the floor. The acronym GSA stands for General Services Administration (an independent agency of the United States government).
- **Schedule II-V** controlled substances must be stored in a stationary, securely locked and substantially constructed cabinet (metal) or a secure containment apparatus that has been approved by the DEA when not actively in use.
- Minimum requirements for working stocks of schedules I, II, III and IV is a stationary, locked, double cabinet. Both cabinets must be key-locked doors with separate keys. Spring locks or combination dial locks are not acceptable. Cabinets must be made of steel or other approved metal.
- Carfentanil etorphine hydrochloride and diprenorphine shall be stored in a safe or steel cabinet equivalent to a U.S. Government Class V container.
- Only registrants or authorized users may have access to controlled substances.

Physical Security

The following factors, among others, are considered when evaluating the overall security system for a researcher: (21 CFR 1301.71(a))

- Type, form and quantity of controlled substance
- Limit the amount of stored controlled substances to the minimum that is needed for the research projects
- Location of the premises and the relationship such location bears on security needs
- Extent of unsupervised public access to the area
- Number of employees and adequacy of supervisors over employees who have access to the storage areas

Other security measures

In order to minimize the opportunities for theft or diversion of controlled substances, registrants have the obligation to provide effective physical security measures and procedures to reduce access by unauthorized persons. It is highly recommended that registrants request Campus Safety Services to evaluate work practices, security measures and integrity of cabinets to assure requirements for security and safety are met, and to evaluate other security measures that might be considered such as alarm systems as appropriate.

DEA order Forms

Unused DEA Order Forms should be kept in a secure location to prevent theft.

For additional information regarding security requirements, refer to the DEA Controlled Substances Security Manual located at http://www.deadiversion.usdoj.gov/pubs/manuals/sec/

Authorized Users

The registrant is responsible for managing controlled substances in accordance with federal regulations including inventory, record keeping and security provisions. Authorized users may engage in approved activities under the direction of the registrant. The activities must be delegated by the registrant to authorized users in writing. The registrant can authorize any individual who has been successfully screened and directly reports to him/her, works under his/her direction and is directly involved with a research project related to the specific DEA registration.

The registrant must performed security and background checks for all individual(s) prior to granting authorization as an authorized user (21 CFR 1301.90). These individuals must complete the University Employee Questionnaire. The University of Texas Rio Grande Valley Office of Human Resources can assist the registrant in performing these background checks.

A registrant may not allow any individual to have access to controlled substances if an application for registration was submitted by the individual and denied or revoked by the DEA.

Responsibility of Registrant

The registrant is responsible to:

- Comply with all applicable regulations
- Assure that back ground checks are performed for all authorized users
- Maintain an accurate and up to date Authorized User(s) Controlled Substance User Log.
- Assure that unauthorized user(s) do not have access to the storage cabinet and/or controlled substances
- Assure that only the registrant or authorized users are allowed to reconcile controlled substance shipments from outside vendors into the inventory logs
- Provide written documentation to each authorized user related to his/her specific responsibilities and authorization. This includes conducting inventories, receiving packages, having access to storage locations, administering drugs, etc.
- Assure that all authorized users are properly trained and are aware of all applicable regulations
- Assure current familiarity with DEA regulations and change in category of controlled substances
- Readily make available all required documentation upon request by EHSRM or DEA

Inspections

The DEA may make unannounced inspections at any time to any registration holder. This could be for any registrant, no matter what scheduled product they use. The DEA may also do an inspection of any potential registrant prior to granting actually registration.

You are required to notify University Counsel and EHSRM immediately for any scheduled and/or unannounced inspection by any outside agency.

The EHSRM Department may also conduct audits.

Reporting Theft or Missing Controlled Substances

The registrant must have complete accountability of all controlled substances received, stored or used at all times to assure that any shortages or misuse of controlled substances will not go unnoticed. Theft or misuse of a controlled substance is a criminal act that must be immediately reported to the following:

By phone, nearest DEA office within one (1) day of discovery

DEA McAllen Field Office
1200 N McColl Rd
McAllen, TX 78501
(713) 693-3000
Central DEA Call Center: 800-882-9539

The University of Texas Rio Grande Valley Environmental Health & Radiation Safety (EHSRM)
(956) 665-3690

In addition to phone reporting, a Report of Theft or Loss of Controlled Substances (DEA Form 106) must be completed and submitted to the DEA McAllen Field Office. The DEA recommends that the form be submitted electronically by completing the online version of Form DEA-106.

A copy of all reports and/or investigations must be kept by the registrant.

Additional information on the DEA requirements for the reporting of theft or loss of controlled substances can be found at http://www.deadiversion.usdoj.gov/21cfr_reports/theft/

Records and Inventories

Controlled substance records and inventories must be maintained in conformity with federal regulations (21 CFR-Part 1304). All documents related to controlled substances must be readily retrievable and available for any audit. “Readily retrievable” means that specific records are kept in such a manner that they can be separated from all other records and retrieved in a reasonable time frame. Registrants must maintain all records at the address listed on one’s DEA registration. The registrant must maintain complete and accurate accounting of all controlled substances from the time they are ordered until they are completely used or otherwise disposed in accordance with regulations.

Records and inventories must be maintained for at least two years. (CFR 1304.04(a)) A separate logbook should be kept containing the controlled substance information. All records must be stored in a secure location, preferably locked in the cabinet or safe containing the controlled substances.

All records of schedule I and II controlled substances must be kept separately from those of schedule III-V substances. (CFR 1304.04(g))

All records of controlled substances in schedule III-V must be kept separately from all other records of the registrant in such a form that the records are retrievable. (CFR 1304.04(g))

The following records must be maintained and be readily available (CFR 1304.04):

- DEA Certificate of Registration
- Authorized users background checks evaluation and authorized user log
- Acquisition and ordering invoices
    - Signed and dated supplier invoices or packing slips
- DEA Form 222s
    - Used, voided and unused Form 222s
- Inventory records
    - Initial inventory
    - Biennial inventory
    - General inventory
- Usage and administration records
    - Multiple dose usage log
    - Diluted drug solution log
- Transfer records of controlled substances between registrants
- Disposal records
- DEA Form 106-Report of Loss or Theft

Inventories (CFR 1304.11)

The following inventories must be maintained and be readily retrievable:

- Initial inventory
- Biennial inventory
- General inventory

All inventories must be kept at the registered site. Inventories must be maintained in a written, typewritten, or printed form at the registered location (or approved DEA location) for at least two years from the date the inventory was completed.

Inventories (initial, biennial and general) must include the following information:

- Name, address and DEA registration number of the registrant
- Date and time the inventory was performed (at the beginning or the end of the day)-Initial and Biennial
- Signatures of the registrant or authorized users responsible for taking the inventory. Initial and Biennial

- For each controlled substance in finished form the inventory must include:
    - Name of substance
    - Each finished form of the substance (ex. 5-mg tablet or 5-mg concentration per fluid ounce)
    - Number of units of volume of each finished form in each commercial container (ex. 100-tablet bottle or 5-mL vial)
    - Number of commercial containers of each finished form (ex. 5 100-tablet bottles or 6 5-ml vials)
- For damaged, defective or impure substances, substances awaiting disposal, substances held for quality control purposed, or substances maintained for extemporaneous compounds , the inventories must include:
    - Name of substance
    - Total quantity of the substance to the nearest metric unit weight or the total number of units of finished form.
    - 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.
- When determining the number of units of each finished form of a controlled substance in a commercial container which has been opened, do the following:
    - If the substance is listed in schedule I or II, make an exact count or measure of the contents.
    - If the substance is listed in schedule III-V, make an estimated count or measure of the contents, unless the container holds more than 1,000 tablets or capsules in which the exact count of the content must be made.
- Schedule I and II controlled substance inventories must be separated from inventory records of schedule III-V substances.

Initial Inventory

A separate inventory for each location must be performed on the date the registrant first engages in any activity covered by his or her registration (21 CFR 1304.11(b)). It is advised that this be done when the registrant receives their initial DEA registration.

An initial inventory must be taken for any newly scheduled substance that was not previously listed on any schedule. The substance should then be accounted for on the Initial Controlled Substances Inventory Form.

Biennial Inventory

The DEA requires a physical inventory of all controlled substances be conducted every two years (21 CFR 1304.11(c)). The inventory may be taken on any date within two years of the previous inventory date. The inventory must be kept at the registered site for at least two years after completion of inventory. The Biennial Controlled Substance Inventory Form can be found here.

Ongoing Records (21 CFR Part 1304-Continuing Records)

General Inventory

A continuous general inventory log is required to track acquisitions, current on-hand stocks, administration, transfer to usage logs transfers to other registrants and disposal. (21CFR 1304.21) The Controlled Substance General Inventory Log can be found here.

- A separate general inventory log should be created for each stock of drug and its associated strength or container size.
- Schedule I and II records must be separate from schedule III-V records.
- Inventories of controlled substance containers should be transferred from the general inventory log to separate usage logs for tracking doses delivered from the same container.
- Individual vials or containers should be assigned a unique number or code upon receipt to assist with tracking.

There are specific requirements for inclusion of data in the records. Refer to 21CFR 1304.22 for detailed information on what needs to be recorded and maintained.

Usage logs

Controlled substances must be tracked from acquisition to administration. A separate usage form should be used for each unique vial or container. In some applications, a stock controlled substance will be used to make a solution. In these cases, records must be kept for both the diluted as well as the stock solution.

Acquisition Records

The registrant for each registered location must maintain complete, current and accurate purchasing records if controlled substances are stored, delivered or administered at that location.

- The following information should be recorded when receiving a controlled substance shipment:
  - Name, address, and DEA registration number of the supplier
  - Name, concentration or weight, dosage form, and quantity of controlled substance received
  - Signature of the person receiving the shipment (this must be either the registrant or an authorized user)
  - Date received
- For schedule I and II controlled substances, copy 3 of the triplicate DEA Form 222 must be completed, maintained and kept separate from all other records. (21 CFR 1305.17).
- Invoice and acquisition records of controlled substances listed in schedule I and II must be maintained separately from all other records. Invoice and acquisition records of controlled substances listed in schedules III-V must be maintained either separately from other records or in a form such that the information is readily retrievable.
- All invoice and acquisition records must be kept for at least two years from the date of record.

Purchasing

Only researchers with a current DEA registration can purchase controlled substances for use in research.

NOTE: A clinical practitioner (i.e. physician, veterinarian, etc...) shall not issue a prescription to themselves to obtain controlled substances to be stored or dispensed for research purposes.

Delivery of a controlled substance can only be made at the address on the DEA registration.

Schedule I or II

Any person registered to conduct research with schedule I or II controlled substances must send, in triplicate, DEA order from #222. EHSRM does not have copies of this form. This form can only be obtained through the DEA. Researchers must contact the DEA directly at 1-800-882-9539 or submit an online request through the DEA. Schedule I and II controlled substances can only be ordered by the registrant.

Schedule I that is not commercially available

Requests to obtain schedule I controlled substances not commercially available must be made to the National Institute on Drug Abuse.

Schedule III-V

Schedule III-V controlled substances may be purchased by contacting a commercial supplier. Schedule III-V controlled substances can only be ordered by the registrant or an authorized Users of the registrant.

Transfers

Import/Export

Special procedures, authorization and reporting forms are required. This may include interstate activities. Researchers intending to engage in these activities must thoroughly research applicable procedures and requirements before proceeding. Information from the DEA on the import/export of controlled substances for scientific purposes can be found at http://www.deadiversion.usdoj.gov/imp_exp/

Transfer between Registrants/Research Groups

Registrants may only transfer controlled substances to other registrants. Each registrant must be approved to possess the scheduled drug or chemical that is transferred.

The following information must be included and maintained in the records of both the supplier and the recipient of the transferred controlled substances. The following information must be included in any document used to transfer a controlled substance:

- Name, address, and DEA registration number of the recipient
- Name, address, and DEA registration number of the supplier
- Name, concentration, and quantity of controlled substance transferred
- Transfer Date

A DEA Form 222 must be used for transfers of Schedule I and II substances. The recipient must submit attached copies one and two to the supplier. The supplier must retain one and submit copy two to the DEA.

Any documentation must be signed and dated by both the supplier and recipient upon delivery. The form/document should be filed with inventory records and kept for at least two years.

Secure and log the newly received controlled substance into the current inventory upon delivery. The recipient must complete copy three of DEA Form 222 if the substances received are in schedule I or II.

Note: Registrants can only transfer up to 5 percent of their annual total controlled substance dosage units to other registrants without having to acquire a separate distributer registration.

Decommissioning of Laboratory

The registrant must certify that all Controlled Substances have been removed or transferred to another authorized DEA registrant. The registrant must provide the EHSRM with a completed EHSRM "Certificate of Vacancy" form before outside personnel can enter the laboratory.

Disposal

The registrant is responsible for the proper disposal of any controlled substance in their possession. The preferred method of disposal of controlled substances is complete use of the substance. The registrant must properly dispose of any controlled substance in their possession prior to retiring, leaving the University or allowing their registration to expire. Failure to do so is a violation of DEA regulations and the registrant may be subject to penalty that may include fines and imprisonment.

The registrant may dispose of out-of-date, damaged, or otherwise unusable or unwanted controlled substances, including samples, through the Department of Environmental Health Safety and Risk Management-Environmental Protection Division who will in turn dispose of the substances to the registrant who is authorized to receive such materials. These registrants are referred to as "Reverse Distributors." Schedule I and II controlled substances should be transferred via the DEA Form 222, while Schedule III-V controlled substances may be transferred via an invoice. All disposal records must be kept at the registrants' location for a period of two years.

Refer to DEA Drug Disposal Information for additional information on the proper disposal of a controlled substance.

Related Information:

USA Drug Enforcement Administration
1200 N Mcoll
McAllen, Texas 78501
(956)992-8400
Central DEA Call Center: 800-882-9539