

GUIDELINES FOR THE USE OF CONTROLLED SUBSTANCES IN RESEARCH

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REVISIONS

January 2020

RECORDS AND INVENTORIES: This section was changed to reflect changes to the State of Michigan requirements for annual inventories. The State of Michigan no longer requires that the annual inventory be mailed in. A copy of the annual inventory must be kept at the registered site. Changes were made to pages 9 and 10.

May 2022

INTRODUCTION: This section was modified to reflect a procedural change: EHS must be notified prior to beginning research with fentanyl and/or fentanyl derivatives

RECORDS AND INVENTORIES: This section was changed to reflect changes to DEA FORM 222. It is no longer issued in triplicate. Registrants/licensees must make a copy of the executed DEA Form 222 prior to sending the original to the supplier. Upon receipt of the order, registrants must complete the number of commercial or bulk containers furnished for each item and the dates the containers are received on their copy of DEA Form 222.

INTRODUCTION

In conducting research with controlled substances, University employees and any other individuals using University resources or facilities, or receiving funds administered by the University, and volunteers and representatives who may speak or act as agents for the University must comply with this guideline and federal and state regulations relating to controlled substances.

Exclusions

These guidelines do not apply to controlled substances dispensed by a practitioner to a patient in the course of professional practice as authorized by his or her license. Nor does it cover teaching activities performed within a clinical environment. However, these activities must still comply with Drug Enforcement Agency (DEA), and State of Michigan regulations applicable to practitioners and pharmacies.

Reason for Guideline

The state and federal governments have numerous regulations pertaining to the legal purchase and use of controlled substances. University employees and other individuals covered by this guide must comply with it in order to ensure they follow all applicable regulations and safely handle and prevent diversion of controlled substances.

The intent of this guide is to assist campus personnel in obtaining, storing with proper record keeping, and disposing of controlled substances by providing forms and advice on these issues.

As a general rule, this guideline is designed to ensure compliance with federal and state regulations and does not impose additional requirements. The exception to this is for research use of fentanyl and fentanyl derivatives. Please contact EHS prior to using these materials for research purposes.

RESPONSIBILITIES

Registered Controlled Substance User

- Ensure compliance with federal and state Laws
- Have employees with access to controlled substances fill out an employee questionnaire
- Ensure controlled substances are stored in a way that will not lead to theft or misuse
- Maintain proper record keeping for controlled substances
- Report any theft or loss of controlled substances
- Properly dispose of controlled substances
- Complete controlled substance awareness training
- Contact EHS prior to use of fentanyl and/or fentanyl derivatives
- Notify EHS of inspections and notifications of inspections by the DEA or State of Michigan
- Make arrangements for the transfer or disposal of any remaining inventory before leaving the University or canceling a license/registration

Authorized Agent

- Complete an employee questionnaire

- Ensure controlled substances are stored in a way that will not lead to theft or misuse
- Maintain proper record keeping for controlled substances
- Report any theft or loss of controlled substances
- Properly dispose of controlled substances
- Complete controlled substance awareness training

Environmental Health and Safety

- Provide guidance to campus units for registering with state and federal agencies
- Provide advice on storage of controlled substances
- Assist with disposal of controlled substances

CONTROLLED SUBSTANCE DEFINITIONS

Controlled substances are drugs or other chemicals with the potential to be addictive or habit-forming. The Drug Enforcement Administration, or DEA, has divided the controlled substances into five schedules based on their potential to be habit forming, and usefulness in medicine as a drug. For a more comprehensive listing, refer to the DEA's Office of Diversion Control website (deadiversion.usdoj.gov).

Schedule I

These drugs, or other substances, have a high potential for abuse, no currently accepted medical use in the United States, and have an accepted lack of safety under medical supervision.

Schedule II

These drugs or other substances have a high potential for abuse, currently have an accepted medical use in treatment in the United States, or a currently accepted medical use with severe restrictions.

Schedule III

These drugs or other substances have a potential for abuse less than schedule I or II, with currently accepted medical use in treatment in the United States. Schedule III drugs might lead to moderate or low physical and high psychological dependence.

Schedule IV

These drugs or other substances have a low potential for abuse relative to those listed in schedule III. These drugs have currently accepted medical use in the United States, and abuse of them may lead to limited physical or psychological dependence relative to those in schedule III.

Schedule V

These drugs or other substances have a low potential for abuse relative to schedule IV. These drugs have currently accepted medical use in the United States, and abuse of them may lead to limited physical or psychological dependence relative to those in schedule IV.

CONTROLLED SUBSTANCE REGISTRATION AND LICENSING

Every person who engages in research with controlled substances must acquire a State of Michigan controlled substance research license and a DEA researcher registration to receive, distribute, store, and administer controlled substances for research purposes at the University. The State of Michigan license and DEA registration must be active for the location (building and room number) where controlled substances are delivered, stored, and administered.

- Practitioners can use their license/registration (non-research) for ordering, storing and administering controlled substances at their laboratory for research purposes provided the following conditions are met:
 - The address on both the license (State of Michigan) and the registration (DEA) are the same as the laboratory address where controlled substances are stored and administered.
 - The research is within the scope of the State of Michigan license and the DEA registration in regards to coincidental activities.
- After initial approval the State of Michigan license is valid for one year. Subsequent renewals are valid for two years. The DEA registration must be renewed annually.
- Each principal investigator who stores, receives, or administers controlled substances at his or her laboratory location must be licensed with the State of Michigan and registered with the DEA at that location. A separate license is required for each principal place of business.
- The registrant/licensee may grant his or her employees' access to controlled substances by making them authorized agents. If authorized agents are to administer controlled substances, it must be done in the presence of the registrant/licensee.
- Inspections or notification of inspections by DEA Diversion Investigators, State of Michigan Bureau of Health Professions Investigators, or law enforcement agencies must be reported to Environmental Health and Safety (355-0153).
- The State of Michigan license should be submitted first as approval by the state is a requirement for federal approval.

Federal Drug Enforcement Administration Registration

Every person that engages in research with controlled substances must be registered with the Drug Enforcement Administration, or DEA. There are different activities that require different registration types. Further, one registration type might not cover two different activities, such as research with controlled substances and dispensing of controlled substances.

The DEA application for registration can be found online at deadiversion.usdoj.gov. DEA form #225 should be completed to obtain a researcher registration.

The State of Michigan License

In addition to the federal Drug Enforcement Agency paperwork, applicants in the State of Michigan must submit an online application for a State of Michigan Controlled Substance Research License. The online application system can be found at www.michigan.gov/miplus. A license is required for every person who manufactures, distributes, prescribes, dispenses or conducts research with controlled substances.

AUTHORIZED USE

The registrant/licensee is responsible for managing the controlled substances in accordance with the requirements of the regulations including inventory, record keeping and security provisions. Authorized agents of the registrant/licensee may engage in approved activities under the direction of the registrant/licensee. The activities must be delegated by the licensee/registrant to the authorized agent in writing. Lab employees can be considered authorized agents of the person with an active State of Michigan license and DEA registration if they are acting in the usual course of their business or employment and with proper screening and authorization by the registrant. The registrant/licensee must screen all authorized agents. Each authorized agent must complete a copy of the [Employee Questionnaire for Employees Who Will Have Access to Substances Regulated by the US Drug Enforcement Agency](#).

- Authorized agents must follow all state and federal regulation governing controlled substances.
- Authorized agent access to controlled substances should be kept to a minimum.
- A current list of authorized agents with access to controlled substances should be maintained. An [Authorized Agent Log](#) can be used for this purpose.
- Only the registrant/licensee and authorized agents are allowed access to the storage cabinet where controlled substances are stored.
- Only the registrant/licensee or an authorized agent is allowed to reconcile controlled substance shipments from outside vendors into the general inventory.
- If authorized agents are to administer controlled substances, that responsibility must be delegated to them in writing.
- All responsibilities delegated to authorized agents must be documented. This includes conducting inventories, receiving packages, having access to the storage location, administering drugs, etc. This documentation must be kept up to date.

State law and federal regulations provide limitations on who can be an authorized agent

State of Michigan

MI R 338.3145

Rule 45. (1) The following individuals shall not be employed or otherwise utilized, with or without compensation, by a person who is licensed by the administrator pursuant to section 7303, 17711, or 17748 of the act in any manner or capacity that allows the individuals access to controlled substances:

- (a) An individual who the licensee knows, or should reasonably know, to be a substance abuser as defined in section 6107 of the act. This subdivision does not apply to a licensee enrolled in the health professional recovery program under a current monitoring agreement.
- (b) An individual whose controlled substance license is suspended, revoked, or denied.
- (c) An individual whose license issued by this state or another state is under suspension or revoked in this state or another state for a violation that involves controlled substances.
- (d) An individual who has been convicted of a crime that involves controlled substances and who is currently under sentence for that conviction.

Drug Enforcement Agency

21 CFR 1301.90

It is the position of DEA that the obtaining of certain information by non-practitioners is vital to fairly assess the likelihood of an employee committing a drug security breach. The need to know this information is a matter of business necessity, essential to overall controlled substance security. In this regard, it is believed that conviction of crimes and unauthorized use of controlled substances are activities that are proper subjects for inquiry. It is, therefore, assumed that the following questions will become part of an employer's comprehensive employee screening program:

Question. Within the past five years, have you been convicted of a felony, or within the past two years, of any misdemeanor or are you presently formally charged with committing a criminal offense? (Do not include any traffic violations, juvenile offenses or military convictions, except by general court martial.) If the answer is yes, furnish details of conviction, offense, location, date and sentence.

Question. In the past three years, have you ever knowingly used any narcotics, amphetamines or barbiturates, other than those prescribed to you by a physician? If the answer is yes, furnish details.

RECORDS AND INVENTORIES

Controlled substance records and inventories must be maintained in conformance with State of Michigan and federal regulations. All documents related to controlled substances must be readily retrievable and available for immediate inspection. Readily retrievable means certain records are kept in such a manner that they can be separated from all other records in a reasonable time. Registrants must maintain all records at the address listed on one's state license and DEA registration.

Records must be maintained for a period of two years from the last transaction date recorded. A separate logbook should be kept containing 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 schedules I and II controlled substances must be kept separately from those of schedule III-V substances.

All records of substances in schedules III-V must be kept separately from all other records of the registrant or in such a form that the records are readily retrievable.

The following records must be maintained and readily available:

- State of Michigan controlled substance license
- DEA Certificate of Registration
- Authorized agent screening statement(s)
- Authorized agent 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
 - Annual inventory – State of Michigan
 - Biennial inventory – DEA
 - General inventory

- Usage and administration records
 - [Multiple dose usage log](#)
 - [Diluted drug solution log](#)
- Transfer records of controlled substances transferred between registrants/licensees
- Disposal records- [DEA Form 41](#)
- [DEA Form 106](#)- Report of Loss or Theft

Inventories

The following inventories must be maintained and be readily retrievable:

- [Initial inventory](#)
- [Annual inventory](#)
- [Biennial inventory](#)
- [General inventory](#)

A copy of all inventories must be kept at the registered site. Inventories must be maintained in a written, typewritten, or printed form at the registered location for two years from the date that the inventory was completed.

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

- Name, address and DEA registration number of the registrant/licensee
- Date and time the inventory was performed (should be at the beginning or the end of the day)
- Signatures of the registrant/licensee or authorized agents responsible for taking the inventory
- For each controlled substance in finished form the inventory must include:
 - Name of the substance
 - Each finished form of the substance (e.g., 5-mg tablet or 5-mg concentration per fluid ounce)
 - Number of units or volume of each finished form in each commercial container (e.g., 100-tablet bottle or 5-mL vial)
 - Number of commercial containers of each finished form (e.g., 5 100-tablet bottles or 6 5-mL vials)
- For damaged, defective or impure substances, substances awaiting disposal, substances held for quality control purposes, or substances maintained for extemporaneous compounding, the inventories must include:
 - Name of the 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/licensee 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 schedules III-V, make an estimated count or measure of the contents, unless the container holds more than 1,000 tablets or capsules in which case an exact count of the contents 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/licensee first engages in any activity covered by his or her state license and DEA registration. Initial inventories are usually zero. 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 normal annual/biennial inventories. A specific form is not required for the inventory. The [Initial Inventory Form](#) can be used or modified for this purpose.

Annual Inventory – Required by the State of Michigan

The State of Michigan requires a physical inventory of all controlled substances to be conducted on an annual basis. The annual inventory must be performed between April 1 and June 30 of each year per Michigan Public Health Code, Section 333.7321. A specific form is not required for the inventory. The [Annual Inventory Form](#) can be used or modified for this purpose. A copy of the annual inventory must be kept at the registered site.

Biennial Inventory – Required by the DEA

The DEA requires a physical inventory of all controlled substance to be conducted every two years. The inventory may be taken on any date within two years of the previous inventory date. This inventory must be kept at the registered site for two years after it is taken. It is not sent to the DEA. A copy of the State of Michigan annual inventory will satisfy this requirement.

Ongoing Records

General Inventory

A continuous general inventory is required to track acquisitions, current on-hand stocks, administration, transfers to usage logs, transfers to other registrants/licensees, and transfers of substances for disposal.

- 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.
- 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
- Registrants/licensees may use their own form provided a substance can be tracked from acquisition to research subject, experimental endpoint, transfer, or disposal.

Acquisition Records

The registrant/licensee 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 must 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/licensee or an authorized agent)
- Date received
- For schedules I and II controlled substances,
 - A copy (physical or electronic) of the executed DEA Form 222 must be made and kept on file prior to sending the original to the supplier when making an order.
 - When receiving an order: registrants must complete on their copy of the DEA Form 222 the number of commercial or bulk containers furnished for each item and the dates the containers are received.
- Invoice and acquisition records of controlled substances listed in schedules I and II must be maintained separately from all other records. Invoice and acquisition records of controlled substances listed in schedule III-V must be maintained either separately from all other records or in a form such that the information is readily retrievable.
- All invoice and acquisition records must be kept for two years from the date of the record.

Usage Logs

Controlled substances must be tracked from acquisition to administration. A separate usage form should be used for each unique vial or container. Registrants/licensees may develop their own forms to document usage or use the following forms:

- [Multiple Dose Usage Form](#)
- [Diluted Drug Solution Usage Form](#)

Compounded solutions containing a controlled substance prepared within the laboratory must also be tracked. The solutions should be labeled with the following:

- Name of the controlled substance
- Lot number
- Date vial prepared
- Final concentration and amount per container
- Expiration date

PURCHASING

Only researchers with a current State of Michigan license and DEA registration can purchase controlled substances for use in research. The licensee/registrant must contact EHS to be placed on the list of approved purchasers before an order can be placed.

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.

Schedule I or II

Any person licensed and registered to conduct research with controlled substances in schedule I or II must send a prepared and executed DEA order form # 222. EHS 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](#). Schedule I and II controlled substances can only be ordered by the licensee/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 licensee/registrant or an authorized agent of the licensee/registrant.

SECURITY

All registrants/licensees must provide effective physical security controls and operating procedures to guard against theft and diversion of controlled substances. An overall evaluation of the security measures in place will be made by the DEA and the Michigan Bureau of Health Professions during the application review to ensure the controlled substances are stored securely.

Minimum Standard

- At a minimum, controlled substances in Schedule II-V must be stored in a securely locked, substantially constructed cabinet when not actively in use.
- Schedule I controlled substances must be stored in a securely locked, substantially constructed cabinet that is anchored to a wall or the floor.
- Only authorized agents may have access to controlled substances. Access should be restricted to the minimum number of employees needed.
- Carfentanil, etorphine hydrochloride, and diprenorphine must be stored in a safe or steel cabinet equivalent to a U.S. Government Class V security container.
- Controlled substances requiring refrigeration may be stored in a locked container securely fastened within a refrigeration unit.

Physical Security

The following factors, among others, are considered when evaluating the overall security system for a researcher:

- Type and form of controlled substances handled
- Quantity of controlled substances handled. Only the minimum amount of controlled substances needed for current research projects should be stored.
- Location of the premises and the relationship such location bears on security needs (high or low crime area)
- Extent of unsupervised public access to the area
- Number of employees and adequacy of supervision over employees who have access to the storage area

Other security measures

In order to minimize the opportunities for theft or diversion of controlled substances, the DEA feels researchers have an obligation not only to provide effective physical security, but also to initiate additional procedures to reduce access by unauthorized persons as well as to provide an alarm system where necessary.

Employee or Agent – A registrant must not employ an agent or individual who has had his or her application for registration with DEA denied or revoked at any time, and who, as a result of employment, will have access to controlled substances.

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](#).

TRANSFERS

Controlled substance registrants may only transfer controlled substances to other registrants. Each registrant must be approved to possess the schedule that is transferred.

The following information must be included and maintained in the records of both the supplier and the recipient of transferred controlled substances. A Controlled Substance Transfer Form can be used for this purpose.

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

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

Sign and date the transfer form upon delivery. The form should be filed with inventory records and kept for at least two years.

Secure and log the newly received substances 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.

IMPORTANT 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 distributor registration.

DISPOSAL

The preferred method of disposal of controlled substances is complete use of the substance such that there is none left to dispose of. However, when a registrant/licensee or the authorized agent of a registrant/licensee has controlled substances that are expired or unwanted EHS should be contacted.

Disposal through EHS

If there is excess material at the completion of research, the registrant/licensee or an authorized agent must contact Environmental Health and Safety (355-0153) to arrange for disposal via a DEA approved method.

All controlled substances must be kept secure until an appropriate disposal method can be arranged.

LOSS OR THEFT

Loss or theft must be reported to the State of Michigan and to the Drug Enforcement Agency immediately upon discovery. Theft, loss or unauthorized use should also be reported to Environmental Health and Safety and the MSU Police.