

Calvin College Environmental Health and Safety	Use of Controlled Substances in Research	Guidance Document
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The information contained in this document is provided to support faculty and staff if they are using or intend to use controlled substances in research activities. The principal investigator (the registered user) retains full responsibility for compliance with state and federal regulations as conveyed by the U.S. Drug Enforcement Administration (DEA) and the State of Michigan Department of Licensing and Regulatory Affairs.

Biomedical research, testing, and teaching programs often require that controlled substances be administered to produce anesthesia, analgesia, tranquilization, sedation or hypnosis or to study the actions of particular drug regimens. Controlled substances can also be illegally diverted and misused.

Accordingly, state and federal drug enforcement entities require individuals using controlled substances to hold a state registration and federal registration, and abide by the regulations and policies which pertain to the licensing, storage, distribution, and use of these chemical agents. Registration for use of controlled substances is an individual action; there are no federal or state regulatory provisions requiring institutional management.

Principal Guidance

[U.S. Drug Enforcement Administration - Title 21](#)

[Michigan Public Health Act 368 - Controlled Substances](#)

Prior to obtaining or using controlled substances, researchers at Calvin College must register with the US DEA and the State of Michigan. Researchers must also notify the Environmental Health and Safety office in writing of their intention to purchase and use controlled substances in research. The notification must include the substance, the vendor, the date the order is or will be placed, where the substance will be stored, the quantity (how many bottles), the volume (how much material in each container) and who will be authorized to have access to the controlled substance.

Each registrant must:

- Follow pertinent regulations
- Maintain continuous registration
- Abide by the conditions of the registration: activities and use of the permitted controlled substances.
- Maintain all required records in a consistent and clear manner.
- Control and safeguard the controlled substance inventory

Purpose of this Guidance Document

If you intend to use controlled substances in your research, this manual will provide clear and concise guidance. The main requirements are listed below:

A. Notify Environmental Health and Safety if you intend to use [Controlled Substances](#).

B. Register with the State of Michigan and the US Drug Enforcement Agency

These registrations establish an accountable relationship between the individual (principal investigator) and the regulatory agencies.

C. Provide a secure location for controlled substances

D. Allow only trusted individuals access and use of controlled substances

E. Be able to track the life cycle of all controlled substances; from ordering to receipt to use to disposal. You must be able to establish (in writing) how each drug was used and by whom and for what purpose.

F. Report any and all suspicious activity to Campus Safety: loss, theft or misuse of controlled substances

Licensing with the State of Michigan:

[Application for Controlled Substance Research License](#)

The State of Michigan Controlled Substance Research License application packet consists of the following:

- Fingerprinting Information
 - Fingerprinting is performed outside of Calvin College. The link below provides a list of vendors qualified to collect your fingerprints: [Private Live Scan Vendors](#)
 - Fingerprinting can be performed **prior to or after** the Application For Controlled Substance Research License is mailed.
- Fingerprinting Request Form (page 3)
- Two page - Application For Controlled Substance Research License
 - The following must be mailed to the State of Michigan
 - Application For Controlled Substance Research License (Two pages)
 - Document with Information to be Included With Application (see pg 3)
 - Brief NIH Biosketch or CV if research not funded by NIH
 - Check for \$85.00 payable to the "State of Michigan"
 - Mail completed packet to: Michigan Department of Licensing and Regulatory Affairs, Board of Pharmacy, P.O. Box 30670, Lansing, MI 48909

Instructions for Application For Controlled Substance Research License

1. Check box - Schedule 2-5 Research Fee: \$85.00
2. Name, DOB, SS#, and phone#
3. Business Name: Calvin College – and indicate your department
4. Business address:
 - a. Building name

- b. Building street address
- c. Room number where controlled substances will be stored
- d. City, State, Zip code
5. Federal Employer Number = 383071514
6. Answer 7 questions
7. Signature and Date

Instructions for Information to be Included With Application (All applicants)

Credentials to Conduct the Proposed Research (Including FDA and DEA approval):

- Attach a NIH biosketch or CV if not NIH funded
- Ignore FDA or DEA approval - *Do not submit a DEA 225 researcher registration application until your state controlled substance research application is approved.*

Protocol of the Proposed Research

- Briefly describe your overall research goals in a non-scientific manner.
- Indicate that controlled substances are needed for anesthesia and analgesia of laboratory animals. Indicate that all animal use protocols were reviewed and approved by Calvin's Institutional Animal Care and Use Committee.
- If applicable, indicate controlled substances will be used for *in vitro* or analytical research.

List of Controlled Substances and Doses to be Used

- List all controlled substances that would be stored for research purposes in your laboratory. Include name(s) of controlled substance(s), concentration or powder, and estimated number of vials or containers. Include dose used for anesthesia and analgesia.
- For example:
 - Buprenorphine: 5 x 1 ml vials, 0.3mg/ml, Dose = 0.05-0.1 mg/kg (mouse)
 - Ketamine: 4 x 10 ml vials, 100mg/ml, Dose = 80-120 mg/kg (mouse)
 - Sodium pentobarbital: 1 x 50ml vial, 50mg/ml, Dose = 40 mg/kg (mouse)

Procedures for Storage and Security of Drugs

Indicate the following:

- Controlled substances will be stored in a locked safe or cabinet bolted to an immovable object.
- Controlled substances will be stored separately from other drugs and materials.
- Only limited authorized personnel will have access to the controlled substances.
- Authorized personnel will be screened per [CFR 1301.90](#)
- Authorized personnel will receive controlled substance compliance training.
- An authorized personnel list will be maintained.
- Only authorized personnel may secure new controlled substance shipments into the safe or cabinet.
- Controlled substance inventory and usage records will be reconciled on a routine basis.
- Controlled substances will be stored in an area with minimum traffic flow.

- Controlled Substance storage room will be locked when not in use.
- Calvin College Campus Safety Department is available 24/7.

List of Other Staff/Persons Involved

- List authorized personnel (including their job titles) who will have access to the storage cabinet or safe where controlled substances will be stored.
- List all administrative staff that may accept delivery shipments or perform controlled substance ordering for the lab.

Registration with the Federal Government:

[DEA Form 225](#)

Security and Storage

Principal Investigators with DEA registrations must provide effective controls and procedures to guard against theft and diversion of controlled substances.

[Title 21, CFR.1301.71\(a\)](#)

Efforts must be focused on physical security, entry procedures, limited access, and record keeping to prevent theft and diversion.

In Summary:

- Controlled substances must be stored in a securely locked, substantially constructed cabinet or safe that is bolted to the floor or wall. Double locks are not required.
- Access to the controlled substance storage unit must be restricted to authorized personnel.
- The storage area should have minimal laboratory traffic flow.
- Locks, keys, or combinations must be reset if authorized personnel are terminated or if a loss/theft is suspected or reported.
- Do not leave controlled substances unattended.
- Portable storage boxes and outside laboratory corridor storage is not allowed.
- Controlled substances requiring refrigeration must be stored in a locked container securely fastened within a refrigeration unit unless the refrigeration unit can be locked from the outside.

Security Requirements for those who have access to controlled substances

Authorized Users are individuals who are approved to use specific controlled substances under the sanction of the registrant. It is the responsibility of the registrant to screen these employees prior to granting authorization. The Employee Security Questionnaire asks each potential authorized user to answer the following questions:

1. Within the past five years, have you been convicted of a felony, or, within the past two years, any misdemeanor, or, are you presently charged with committing a criminal offense?
2. In the past three years, have you knowingly used narcotics, amphetamines, or barbiturates other than those prescribed to you by a physician?

3. Have you had an application for registration with the DEA denied, revoked, or surrendered for cause?

Registrants must maintain the completed questionnaires for authorized personnel in a secure place.

Purchasing Controlled Substances

Schedule I controlled substances may be purchased through federally approved Schedule I vendors.

A DEA Form 222 must be utilized to purchase or transfer schedule II controlled substances.

DEA Form 222 must be ordered directly from the DEA. [DEA Office of Diversion](#) (Order Forms).

- The DEA Form 222 is a triplicate form with preprinted information unique to each registrant.
- DEA Form 222s are numbered serially and are sent in batches of 7 or 14.
- Each DEA Form 222 must be completed with no errors otherwise the supplier will reject the order.
- All DEA Form 222s must be tracked including voided, used, and unused forms.
- DEA Form 222s must be stored in a locked location
- Lost DEA Form 222 serial numbers must be reported to the Detroit DEA office:
 - DEA Diversion, Room 610, 211 West Fort St., Detroit, MI 48226

Completing a DEA Form 222

- Copy 1 (brown) and Copy 2 (green) must remain attached (with carbons intact) and are mailed or delivered to the supplier.
- Copy 3 (blue) is retained and completed by the purchaser when the shipment arrives.
- Complete Copy 3 (blue) columns Date of Receipt and Number of Items Received
- Only the Principal Investigator registrant can sign a DEA Form 222. (Per Michigan law 333.7331, a Power of Attorney must possess a State of Michigan controlled substance license).

Order Processing and Lost Shipments

- A supplier may refuse or void all or any part of an order on a Form 222.
 - Supplier shall notify purchaser in writing.
 - No explanation is necessary. Order not acceptable is sufficient.
 - For order rejections, Copy 1 and Copy 2 will be returned to the purchaser
 - The purchaser shall retain rejected Copy 1 and Copy 2 along with Copy 3 in their records.
- Suppliers must ship orders within 60 days of the date on the Form 222.
- If a supplier does not receive the Form 222:
 - Purchaser must contact supplier in writing indicating the original Form 222 serial number, the date of the form, and the agents listed on the order form.
 - Attach a copy of the statement to Copy 3 of missing form.

- A new 222 form should be prepared exactly as the first missing form.
- Report missing completed forms to the Detroit DEA field office.
- If the missing form is received the supplier shall not accept it and return it to the purchaser to be stored in their records.
- Purchaser shall retain all returned forms.

Additional Information

CFR Title 21, Part 1305 - <http://www.deadiversion.usdoj.gov/21cfr/cfr/2105cfr.htm>

DEA Form 222 FAQs: <http://www.deadiversion.usdoj.gov/faq/dea222.htm>

Managing Controlled Substances

Vigilant onsite management of controlled substances is required at all laboratory levels, from ordering to receipt to use to disposal. The ability to track the life of a controlled substance must be demonstrated consistently in the laboratory setting.

The components of a management system for controlled substances include:

1. Personnel and Physical Security: Limited and reliable authorized users and control of access to controlled substances.
2. Receipt of controlled substances: Each order is verified and recorded by the registrant or an authorized user.
3. Recordkeeping: A written system which provides an accurate, continuous and current record to track the acquisition, use and disposal of controlled substances.
4. Disposal: Practice of properly disposing of waste, unneeded and expired controlled substances.
5. Audit and Assessment: An ongoing auditing program which provides corrective and beneficial review of the laboratory controlled substance process.
 - a. The registrant is required to audit every two years, although it is recommended that the registrant audit every quarter.
 - b. The EHS Department will audit at least annually (appendix F).

Receiving of Controlled Substances

Either the Registrant or an Authorized User may receive controlled substances.

The receiving individual must:

- Verify the contents of the order received. Sign and date.
- Resolve discrepancies immediately. Contact the vendor/seller to correct document errors, etc. A copy of the DEA Form 222 may be used to document initial quantities.
- Sign and date the original receiving documents. Maintain these documents for three years.

The use of purchase & receipt logs are highly recommended. Appendix A & B provides an example of a Purchase Log Form.

Recording the Use (Dispensing of Controlled Substances)

An accurate, continuous and current record of controlled substances is mandatory under state and federal regulations. While specific forms are not mandated, it is prudent to use a form which will provide a clear audit trail of controlled substance usage.

A written record should include:

- Name of the substance
- Source of the substance
- Date of expiration of the substance
- Date of receipt
- Unique identification number for the bottle
- Starting quantity of controlled substance
- Date of use
- Protocol (or project) for which it is being used
- Animal (or group of animals) for which it is being used
- Person dispensing the medication from storage
- Person administering the medication to the animal(s)
- Quantity (cc/ml/grams) of agent dispensed, administered and wasted.
- Quantity remaining in the vial/bottle/box

Appendix C provides a template usage log.

Inventory of Controlled Substances

It is recommended that controlled substances be inventoried every quarter even though the regulatory requirement stipulates every year.

In addition to balance log records, initial and ongoing inventory records are required for all schedules of controlled substances. Schedule I substances must be completed on a separate record from other schedules. The inventory should include the name of each substance, each finished form of the substance (solid, tincture, inhalant, etc.), the number of units or volume of each finished form and number of containers of each finished form. Damaged, defective, expired, or impure substances awaiting disposal must be included in the inventory (until they are official disposed). Refer to the DEA Diversion web site for further information: [DEA Inventory Requirements](#)

It is important to note that expired drugs must not be stored with active drugs. Expired drugs must also be stored in a locked cabinet.

Theft or Significant Loss

Theft or significant loss must be reported immediately to the following:

- Campus Safety and Environmental Health & Safety Departments. Ensure that an official police report is filed.
- DEA

Send a fax report to the Detroit DEA Field Office regarding theft or significant loss of any controlled substance within one business day of discovery of such loss or theft.

DEA Detroit Office - Contact Information

211 W. Fort Street
Suite 610
Detroit, MI 48226

Diversion Number: (313) 226-7537
Diversion Fax: (313) 226-7545
Diversion Program Manager Fax: (313) 226-7541

Diversion Program Manager - James Geldhof

After an initial fax is sent to the Detroit Field office, a [DEA Form 106: Theft or Loss of Controlled Substances](#) must be submitted (preferably online).

Non-significant Loss

The Controlled Substance Act does not define the term "significant loss".

Per DEA Diversion website guidelines:

When determining whether a **loss** is significant, a registrant should consider, among others, the following factors:

1. The actual quantity of controlled substances lost in relation to the type of business;
2. The specific controlled substances;
3. Whether the **loss** of the controlled substances can be associated with access to those controlled substances by specific individuals, or whether the **loss** can be attributed to unique activities that may take place involving the controlled substances;
4. A pattern of losses over a specific time period, whether the losses appear to be random, and the results of efforts taken to resolve the losses; and, if known
5. Whether the specific controlled substances are likely candidates for diversion; and
6. Local trends and other indicators of the diversion potential of the missing controlled substances.

Non-significant loss secondary to miscounts or clerical errors must be documented in the inventory or usage record and recorded on a DEA Form 106 (Theft or Loss).

When used to document non-significant loss the DEA Form 106 is not sent to the DEA office and a copy of the form is maintained with your records. Do not submit online.

A review of security and record keeping policies must be performed if multiple or chronic record discrepancies occur.

Refer to Appendix E for a discrepancy report.

State of Michigan Annual Inventory

This inventory does not apply since Calvin does not dispense controlled substances.

DEA Biennial Inventory

This inventory must be performed every two years after initial inventory and records kept for two years. Do not mail to the State of Michigan or DEA.

Inventory must include:

- Name, address and DEA registration number of the registrant
- Date and time (opening or closing of the day) inventory was performed
- Signatures of the registrant or authorized users responsible for taking the inventory
- The name of the substance
- Each finished form of the substance
- The number of units or volume of each finished form in each commercial container
- The number of commercial containers of each such finished form
- Report zero inventory if no controlled substances on hand at laboratory location.

Schedule II controlled substances must be listed on a separate form or separately from Schedule III-V controlled substances

Refer to Appendix D for an inventory template.

Appendix A

Use of Controlled Substances in Research: DEA Form 222 Purchase Log

222 Form Serial #	Date Received	Date Blank 222 Form Used	Order Sent To: (Supplier)	Authorized Agent Initials	Date Order Received and 222 Form Copy 3 Completed	Authorized Agent Initials

Appendix B
Controlled Substance Receipt Log

Registrant Name	
DEA Number	
Location where drug will be stored	

Date of Receipt	Drug Name	Concentration (mg/ml)	Bottle Volume (total mg)	Quantity (# of bottles)	Assigned Unique ID #	Liquid (L) or Powder (P)	Vendor	Purchase Order #	Initials of Person Receiving

Appendix D

DEA Biennial Controlled Substance Inventory

Date	
DEA Registrant	
Registrant Lab Address <small>(as on DEA Form 223)</small>	
DEA Registration #	
MI Controlled Substance Permanent ID #	
Inventory performed by	
Inventory Witness	

Start of day
 End of day

DEA Schedule *	Controlled Substance	Container Unit Type (vial, powder, liquid, syringe, or patch)	Container Quantity	Container Volume	Concentration

**Schedule I and II drugs must be listed together, but separate from Schedule III – V drugs*

Keep the biennial inventory record at the licensed-registered lab location. Do not submit a copy of the biennial inventory to the DEA or State of Michigan unless requested.

Appendix E

Controlled Substance Discrepancy Report

Name of person completing report:	
Check the type of discrepancy:	
<input type="checkbox"/>	Loss or other discrepancy of controlled drugs
<input type="checkbox"/>	Discrepancy discovered during semi-annual inventory
<input type="checkbox"/>	Broken safety tab
<input type="checkbox"/>	Apparent break-in

Description of discrepancy (include date discovered, location, individual involved, etc)

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Date	
Signature of person completing report	
Witness Name and Signature	
Registrant Name	

Send this report to Campus Safety and Environmental Health and Safety.

Appendix F

Controlled Substance (CS) Audit Checklist

Date	
Auditor	
Principal Investigator	

CATEGORY	S/NS/NA*	COMMENTS
Administration		
Copy of Guidelines available		
SOP available		
MI & USDEA registrations current		
Copy of registration available		
Physical Security		
All CS kept under a minimum of 2 locks		
Locked keyed differently		
Keys not kept together		
Locks in good condition		
Substantially constructed cabinet or safe in use		
Accessible only to authorized personnel		
Personnel Security		
Background checks completed on authorized personnel		
Registrants completed questionnaires for authorized personnel maintained in secure location		
Personnel trained in CS protocols		
Access limited to PI and designated personnel		
Means of access to CS limited to authorized personnel		
Ordering		
Ordering protocol follows Guideline, Section VIII		
Receipt records maintained and recorded		
Inventory Control		
Written record in place		
Record up-to-date		
Form matches data required in Guidelines		
Inventory inspected annually		
Labeling		
Container labeled		
Unique ID # on each container		
Expiration date present		
Use Area		
Area security established (alarm, key, etc)		
Contamination Control		
No uncontained substances observed		
General housekeeping maintained		
Personnel Exposure Control		
Fume hood functioning		
PPE available		
Discrepancies		
Any discrepancies (Yes/No)		
Discrepancy protocol followed		
Disposal		
Disposal accounted for in writing		
Disposal document DEA Form 41 used		
Non-notification disposal follows protocol		

S= satisfactory; NS = not satisfactory; NA = not applicable