



Harvard University
Controlled Substance Researchers' Guide

Introduction

Due to their potential for abuse, items identified by the United States Department of Justice, Drug Enforcement Administration (DEA), and the Massachusetts Department of Public Health (DPH) as Controlled Substances are subject to extensive licensing, registration, storage, security, use, disposal, and inventorying requirements. The regulations governing Controlled Substances include the following: United States Department of Justice, Drug Enforcement Administration, Controlled Substances Act, 21 C.F.R. Sections 1300 et. seq.; and Massachusetts Department of Public Health, 105 C.M.R. 700.000 et. seq.

In general, the regulations are designed to ensure a system of security and accountability in the acquisition, use and disposal of Controlled Substances. Thus, they require license holders to document the receipt of Controlled Substances once they are ordered and to continue to document use until the time they are properly disposed of. They also call upon license holders to keep track of the individuals who are authorized to have access to the substances and the places in which the Controlled Substances are stored.

The government has indicated that substantial compliance with the regulations depends on the following factors:

1. The type of activity conducted (e.g., processing of bulk chemicals, preparing dosage forms, packaging, labeling, buying, possessing, and conducting research, etc.);
2. The type and form of controlled substances handled (e.g., bulk liquids or dosage units, usable powders, non-usable powders);
3. The quantity of controlled substances handled;
4. The location of the premises and the relationship such location bears on security needs;
5. The type of building construction comprising the facility and the general characteristics of the building or buildings;
6. The type of vault, safe, and secure enclosures or other storage system (e.g., automatic storage and retrieval system) used;
7. The type of closures on vaults, safes, and secure enclosures;
8. The adequacy of key control systems and/or combination lock control systems;
9. The adequacy of electric detection and alarm systems, if any, including use of supervised transmittal lines and standby power sources;
10. The extent of unsupervised public access to the facility, including the presence and characteristics of perimeter fencing, if any;
11. The adequacy of supervision over employees having access to manufacturing and storage areas;
12. The procedures for handling business guests, visitors, maintenance personnel, and non-employee service personnel;
13. The availability of local police protection or of the registrant's or applicant's security personnel; and
14. The adequacy of the registrant's or applicant's system for monitoring the receipt, manufacture, distribution, and disposition of controlled substances in its operations.

Violations of the Controlled Substances laws, even when unintended, can lead to substantial civil and criminal liability.

1. Responsibilities

In order to ensure compliance with Harvard's obligations under the Controlled Substance regulations and licenses, it is important that authorized faculty and research staff, laboratory administrators, and affected departments understand their responsibilities in connection with obtaining, preparing, handling, and using Controlled Substances.

License Holders shall have the primary responsibility for complying with the requirements set forth in this guide; for ensuring that security and access procedures are in place in each of the labs; for ensuring that licenses are regularly updated; for maintaining an updated list of Authorized Individuals (AIs); for purchasing and distributing Controlled Substances and, in appropriate circumstances, for maintaining purchase and use records relating to the Controlled Substances program; for ensuring faculty and research staff receive training on their obligations for handling Controlled Substances under the licenses, regulations, and any applicable Harvard policies; and for working with PIs to implement any corrective actions that may be needed. Principal Investigators, Department Administrators or Department Chairs may be License Holders.

Principal Investigators (PIs) shall have responsibility for managing the use of Controlled Substances in their labs. PIs shall have responsibility for ensuring that Controlled Substances are licensed and registered for use in their labs and maintained in the manner that is indicated on the licenses; for restricting access only to users they authorize (Authorized Individuals or AIs); for notifying the License Holder of any additions and deletions of Authorized Individuals; for ensuring that usage logs are properly maintained; and for documenting a full inventory of Controlled Substances every two years. In the event that the PIs are on leave or are otherwise absent, they may designate through a written Power of Attorney another appropriate Authorized Individual to carry out the duties under the Controlled Substance program on their behalf.

Environmental Health & Safety Department (EH&S) will provide informational materials and web-based training to License Holders, PIs and Authorized Individuals. EH&S shall also have responsibility for assisting License Holders in the disposal of Controlled Substances and providing options for proper disposal. Coordinating with license holders or their designee, EH&S may conduct periodic audits of laboratories that have licenses to use Controlled Substances. EH&S will provide an inspection summary report, including corrective action recommendations, to the License Holder & PI. Upon request, inspection findings may be shared with the Environmental Safety Compliance Officer (ESCO) for the School.

The Harvard Center for Comparative Medicine (HCCM) and the Office of Animal Resources (OAR) shall have responsibility for assisting departmental administrators in the disposal of animals injected with Controlled Substances. HCCM and OAR (along with EH&S) may also be called upon to assist departmental administrators in determining how best to store and maintain Controlled Substances.

2. Definitions

"Controlled Substance" is defined as a drug or other substance, or immediate precursor, included in schedule I, II, III, IV, or V of the Controlled Substances Act. In addition, under Massachusetts law, a Controlled Substance is also defined as a prescription drug that is not otherwise included in Schedules I-V. The DEA does not regulate Schedule VI prescription drugs.

In general, the schedules identify materials containing any quantity of a substance with a stimulant, depressant, or hallucinogenic effect on the higher functions of the central nervous system and having the tendency to promote abuse or physiological or psychological dependence, as designated in state and federal Controlled Substance schedules. Schedules I and II are the most stringently regulated, and include many widely known street drugs, including heroin, LSD, and cocaine as well as such drugs as pentobarbital. Schedule III compounds include many stimulants and depressants, pain killers, and anesthetics, including ketamine and buprenorphine. Schedule IV substances cover the balance of lower-abuse potential stimulants and depressants, while Schedule V includes therapeutic drug mixtures containing very limited quantities of Controlled Substances, but which still have potential for abuse or diversion. Each Controlled Substance has a specific drug code assigned to that particular drug. A general list of Controlled Substances can be found at www.deadiversion.usdoj.gov/schedules/.

Schedule VI Controlled Substances under Massachusetts law include all prescription drugs not already regulated by DEA. Non-prescription grade pharmaceuticals are not included in Schedule VI nor are Over-the-Counter (OTC) drugs.

“Authorized Individuals” (AIs) are those lab personnel who handle or manage Controlled Substances in approved research. Authorized Individuals must be trained by the license holder in Controlled Substance shipping, receiving, security, inventorying, and recordkeeping procedures as outlined in this Guide and how they specifically apply to the license holder’s operation. License holders should supplement the Harvard Training Portal (HTP) module, Controlled Substance Use in Research (LAB504), with site-specific protocols, security procedures, and requirements.

3. Licensing and Registration

A license from the DEA and DPH is required to acquire, make, possess or use a Controlled Substance. Licenses are (i) issued to an individual, who may authorize other individuals to operate under his/her license, (ii) specific to drug schedules identified on the license, and further limited to specific drug codes applied for, and (iii) identify a specific location where the Controlled Substances are to be stored and must be amended when the location of storage changes.

When applying for a license to use Schedule I-V substances, she or she should, as a matter of good practice, be sure to include in his/her application to the state agency a request for Schedule VI prescription drugs, as well. Examples of these include isoflurane and other prescription medication.

Departmental administrators, Departmental Chairs or individual PIs must obtain licensure from the Massachusetts Department of Public Health and from the Federal Drug Enforcement Administration. The DEA will not grant an applicant a license until he/she has already obtained a license from the DPH, although both applications may be submitted at the same time.

Because the University cannot, by law, maintain a blanket registration for Controlled Substances, individuals must obtain appropriate licenses and registration. In some cases, it may be appropriate or required to have PIs apply for licenses. Once PIs obtain licenses for their labs, they can authorize others in their labs to access the materials. In other cases, it might be more appropriate for a department or school administrator to hold the license. Again, the administrators, with the input from the PIs in their labs or departments, can authorize others to access the materials. Regardless of how the licensing is structured, copies of licenses shall be provided to an appropriate administrator (e.g., Department Administrator, School Administrator, Research Operations Manager, Lab Director). This will help to ensure that the administrator is aware of the individuals who are licensed to use Controlled Substances as well as the location of all Controlled Substances on campus. It is ultimately the individual identified

on the licenses (i.e., the license holder) or their designated authorized user that has responsibility for ensuring proper acquisition, use, maintenance, and accountability of Controlled Substances.

Synthesis of chemicals or drugs that have been deemed illegal or illicit by the DEA or state authority are prohibited unless pre-approved by an appropriate University official and are consistent with a research protocol that is submitted to the DEA or state authority with appropriate application. Registration for Schedule I substances require submission to DEA of a research protocol.

PIs who obtain a license may authorize members of their research staff or other PIs or other administrators to access Controlled Substances by maintaining a list of those individuals, with their Social Security number or HUID, with their licenses. This information is Harvard Level 4 Security data and must be secured separately and not available to anyone other than the license holder or their authorized designee. DPH generally requires a license holder upon application or renewal to provide the agency with names of all Authorized Individuals. DEA does not generally require this information.

If, during the course of the year, there are additions or deletions or changes to the Authorized User list, license holders should take steps to ensure that they have a record of any such changes. License holders are not obligated, however, to notify DPH of additional Authorized Individuals during the term of their license. Except for Schedule I substances, license holders are not obligated to notify DPH if they wish to purchase additional Controlled Substances, provided their license includes the schedule within which the new Controlled Substance falls. DEA does, however, want to be notified (a letter is acceptable) whenever a new drug code within an authorized schedule is added to the license. Drug codes may be found in [Title 21 Part 1308](#) of the Code of Federal Regulations. The local office of the DEA will also provide drug codes upon request. In any event, license holders must provide complete, updated information about AIs, drug codes, schedules, and licenses when they renew their licenses with both DPH and DEA.

The number of Authorized Individuals should be kept to the minimum personnel essential for efficient operation. By limiting the number of Authorized Individuals, labs can better ensure accountability. Persons previously convicted of a felony offense relating to Controlled Substances, had an application for registration with a state or federal agency denied, or who surrendered a registration for any cause may not be authorized to work with these materials. Only those individuals authorized by the license holder will be permitted access to Controlled Substances. In addition, the Controlled Substances must be stored only in the place indicated on the DEA and DPH applications.

Importantly, the Schedule I-V Controlled Substances must be stored only in places indicated on the license holder's application with the DPH and DEA. Controlled Substances may be used, but not stored, by Authorized Individuals in other facilities; provided, however, that the other facilities occupied by the Authorized Individuals are connected to the license holder's primary place of storage by a courtyard, walkway, hallway, adjoining buildings, or tunnel. If an Authorized Individual is storing controlled substances in a location that is not connected to the license holder's place of storage by such means, then the Authorized Individual must arrange to obtain his/her own license. If the license holder changes location and wishes to change the storage location indicated on his/her license, he/she should notify the DPH and DEA in writing and make certain that the new storage cabinet and location meets the Controlled Substance requirements. In some cases, the regulators may approve the move without further action. In other cases, the regulators may request that the license holder apply for a new license.

Researchers who occupy Harvard-owned space, but are employed at other institutions or affiliated hospitals, should contact their primary institutions or hospitals for assistance in obtaining appropriate licenses from the state and federal authorities. Their own institution's policies and procedures govern these license holders.

4. **Scope of Use**

Controlled Substances may only be used for duly authorized, legitimate medical or scientific research purposes to the extent permitted by the registrant's license and registration and in conformity with state and federal statutes and regulations.

5. **Initial Purchase**

License holders or individuals designated by them by a Power of Attorney should take responsibility for all ordering of Schedule I-V Controlled Substances. You will need to provide the following information to a vendor when ordering controlled substances.

- (a) Basic purchase information;
- (b) Proof of legitimate research use;
- (c) Storage location;
- (d) DEA and MPH registration numbers.

The stocks of Controlled Substances should be kept to the smallest quantity needed for efficient operation to conduct the indicated research.

For Schedule I & II Controlled Substances, an official DEA Order Form (Form 222) will have to be prepared. Form 222 is available on DEA's website www.deadiversion.usdoj.gov/faq/dea222.htm or by calling the DEA's Boston office at (617) 557-2468. The top and middle portions of the form will be forwarded to the supplier and the remaining portion will be kept with other Controlled Substance records, such as the licenses and [Authorized Individuals list](#). Once the shipment is received, the Order Form will be annotated to show the actual amount received and the date of receipt in the appropriate column of the Order Form.

6. **Maintaining Security in the Lab**

Schedule I-V Controlled Substances shall be stored in securely locked, substantially constructed drug cabinets in locations where access is limited. The vendor of the safes should be able to confirm the appropriateness of the storage. Generally, standard file cabinets are not sufficient for the storage of Controlled Substances. Under Massachusetts regulations, Schedule VI prescription drugs need not be stored in a safe or locked cabinet. Schedule VI substances can be stored together on a nearby shelf to the drug cabinet or in an unlocked cabinet but should not be stored with Schedule I-V substances unless the license holder obtains specific permission from the DEA to store Schedule VI prescription drugs with the substances that the DEA regulates. Schedule I-II controlled substances may be stored with Schedule III-V substances provided access to the area is not substantially increased and only if permission for such storage is obtained in advance from the local DEA Field Office.

Particular laboratories may find that they only experiment with diluted forms of Schedule III, IV, and V Controlled Substances. Thus, they may wish to segregate further in separate safes or vaults non-diluted substances from diluted substances. Please be aware that both drug safes or vaults must be in the location listed on the license. Laboratories may wish to call upon HCCM, OAR, EH&S, or their departmental administrator to assist them in determining how best to store and maintain Controlled Substances.

All Schedule I-V Controlled Substances, including their diluted forms, must be kept locked in their storage location except for the actual time required for authorized individuals to remove, legitimately work with and replace the Controlled Substances. Controlled Substances must not

be left unattended, and when they are not being used for research, they must be securely stored in their designated drug cabinet or safe. Some experiments may necessitate preparing and using many doses of diluted Schedule I-V Controlled Substances over a relatively short period of time. In those instances, Authorized Individuals should log out the smallest quantity needed for efficient operation, generally no more than a single vial at one time and must return any unused portions to the safe or vault during those times when they cannot attend to them or no longer need them.

Controlled access to the drug cabinet is critical to establishing security for Controlled Substances. For this reason, keys and combinations to the cabinets or safes should be secure and under the control of a limited number of Authorized Individuals.

7. Reporting of Loss, Destruction, Theft, or Unauthorized Use

Thefts, suspect thefts or unauthorized uses of any Controlled Substance must be reported immediately to the license holder and to the Harvard University Police Department upon discovery. Other losses, including spills or breakages must be reported immediately to the license holder. The license holder has an obligation to report promptly the loss to the state or federal authorities. For example, the Massachusetts Department of Public Safety and the Federal Drug Enforcement Agency require laboratories to report losses within one business day of discovery. DEA Form 106, available on DEA's website, is required to be used by both the DEA and the DPH when a formal report is made, after an initial investigation.

In addition, any unauthorized person who gains access to Controlled Substances for the purpose of diversion or theft must be reported to the Harvard University Police Department and be subject to the disciplinary policies of the University.

8. Recordkeeping and Inventorying

Laboratories are required to keep track of each Controlled Substance using [Harvard University's Controlled Substances Logbook](#) or equivalent. Usage Log sheets shall be numbered, bound, and secured in a drawer near the safe or in the locked safe or cabinet along with the Controlled Substances. Logbooks must be maintained for a minimum of two years after the complete use and disposal of Schedule I-V Controlled Substances and be readily available for inspection by the DEA, Massachusetts Public Safety, or Harvard University. Laboratories are not required to maintain usage logs for Schedule VI Controlled Substances.

All laboratories that work with Schedule I-V Controlled Substances are to conduct self-inspections on a quarterly basis to ensure that the laboratory's Controlled Substance Usage Logs match the physical inventory. The results of those self-inspections shall be recorded in the logbook and shall be maintained by the license holder for a minimum of two years. The quarterly self-inspection is a Harvard University requirement.

In addition, on a biennial institutional cycle, all laboratories licensed to work with Controlled Substances shall record a complete inventory of Controlled Substances in order to comply with the federal requirement to conduct biennial inventories. For such biennial requirements, laboratories may use the biennial inventory form, located in the back of the Harvard University Controlled Substances Logbook. This biennial inventory must be noted on the biennial form but also in the main log as an entry for each item inventoried with the date, biennial inventory, and the authorized individuals name completing the inventory. License holders (or their designee, with power of attorney) shall sign this form in addition to the Authorized Individual who conducted the inventory. If an Authorized Individual with power of attorney conducts the inventory, a second Authorized Individual must witness and sign the inventory.

All records generated in connection with the Controlled Substances program should be maintained by the license holder for at least two years following termination of any license. Following this two-year period documents should be disposed of in a secure manner such as shredding.

9. Controlled Substances of Unknown Origin

Registrants must maintain possession of controlled substances until the material has been used in an authorized research process or disposed of in accordance with DEA and Harvard approved procedures. Before leaving the university, researchers are required to work with EHS to properly dispose of all controlled substances that were purchased under their license. If not managed properly, laboratories or animal facilities may come across Controlled Substances of an uncertain origin. In those circumstances, the laboratory or other facility should take the following steps: (1) make sure that the Substance is secured in a license holder's locked safe or cabinet; and (2) contact the EH&S office for disposal assistance and coordination.

10. Disposal

Controlled Substances consumed in a reaction or converted into a hazardous waste mixture from which a Controlled Substance is not recoverable may be disposed of through routine waste disposal procedures from Environmental Health & Safety. Animal carcasses that were injected with Controlled Substances must be disposed of through the Harvard Center for Comparative Medicine or the Office for Animal Resources.

When controlled substances expire, Authorized Individuals should request waste assistance from EHS. Sometimes, at the conclusion of an experiment, a small amount of a Controlled Substance will remain in the vial or syringe. If the material in the vial or syringe is non-recoverable (e.g. cannot be drawn up for use), the vial or syringe may be disposed of into a biohazard sharps container. If the laboratory uses the controlled substances in animals, recoverable expired drugs must be labelled "expired: not for use in animals" and be stored in the drug safe until destruction by EH&S. In any event, no materials should be disposed of through laboratory drains or out through regular trash. The authorized individual must remain in secured possession of expired or unwanted controlled substances, including diluted forms, until they have been properly destroyed or transferred to a reverse distributor for disposition. For further details on destruction process, including required documentation, see <http://ehs.harvard.edu/node/7529>.

11. Shipping & Transfer Procedures

Federal law prohibits the export of Controlled Substances unless certain requirements are met, including, in most cases, export permits. Violators of the law risk arrest or fines both in the United States and the foreign country. Licensed brokers are available for transport of controlled substances. Contact EH&S for assistance in arranging for any necessary transport of Controlled Substances.

Transfer of controlled substances between license holders requires additional documentation and notification. Contact EH&S for assistance.

12. Resources and References

The departments identified below may be a resource for questions about the Researchers Guide for Use of Controlled Substances:

Environmental Health and Safety:

(617) 496-3797 (Cambridge)

(617) 432-1720 (Longwood/Southborough)

Harvard Center for Comparative Medicine: (617) 432-1289

Office for Animal Resources: (617) 432-1289

Director of Office for Research Compliance: (617) 432-3884

Associate Dean for Research Administration, Faculty of Arts and Sciences:

(617) 495-4083

Office of the General Counsel: (617) 495-1280

For additional information about the regulatory requirements, you may consult the following websites:

Massachusetts Department of Public Health, Drug Control Program:

www.mass.gov/eohhs/gov/departments/dph/programs/hcq/drug-control/.

United States Department of Justice, Drug Enforcement Administration, Office of

Diversion Control: www.deadiversion.usdoj.gov/index.html.

A copy of this Controlled Substance Researchers' Guide is available on the EH&S website at ehs.harvard.edu/programs/controlled-substances.