Use of Controlled Substances and Dangerous Drugs in Research

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Project Administrator, IACUC/IBC/IRE
Overview

Expectation

• Investigators are expected to become knowledgeable of and adhere to the requirements of federal and state laws/regulations regarding the use of controlled substances and dangerous drugs in research.

• Investigators are expected to keep appropriate records regarding the use of controlled substances and dangerous drugs.

• Investigators should understand what to expect and what to do in the case of a Drug Enforcement Agency (DEA) inspection.
Overview

Defined Terms

• The following terms and acronyms are used throughout this tutorial:
  ▪ DEA = Drug Enforcement Administration
  ▪ Registrant = an investigator who registers with the DEA and Ohio Board of Pharmacy to use Controlled Substances and Dangerous Drugs.
  ▪ Authorized Agent = an investigator, staff member, or student whom the Registrant authorizes to use Controlled Substances/Dangerous Drugs under their license.
Overview

Defined Terms

• Controlled Substances vs Dangerous Drugs:
  ▪ Dangerous Drugs = any drug requiring a prescription or labeled as “prescription only”
    ▪ Examples: prescription antibiotics, non-narcotic analgesics, isoflurane
  ▪ Controlled Substances = drugs regulated by the DEA
    ▪ Examples: ketamine, cocaine, narcotic analgesics
# Controlled Drug Schedules

<table>
<thead>
<tr>
<th>Schedules</th>
<th>Definition</th>
<th>Examples</th>
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<tbody>
<tr>
<td>I</td>
<td>No currently accepted medical use, lack of accepted safety for use, severe potential for abuse</td>
<td>Heroin, LSD, peyote, ecstasy</td>
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<tr>
<td>II</td>
<td>Have currently accepted medical use in the U.S.; have severe restrictions due to high potential for abuse which may lead to dependence</td>
<td>Morphine, cocaine, methadone, pentobarbital, fentanyl, methamphetamine</td>
</tr>
<tr>
<td>III</td>
<td>Have currently accepted medical use in the U.S and less potential for abuse relative to those in I/II</td>
<td>Ketamine, buprenorphine, codeine, some barbiturates</td>
</tr>
<tr>
<td>IV</td>
<td>Have currently accepted medical use in the U.S and less potential for abuse relative to those in III</td>
<td>Xanax, Klonopin, Valium, Ativan</td>
</tr>
<tr>
<td>V</td>
<td>Have currently accepted medical use in the U.S and low potential for abuse</td>
<td>Cough medicine with &lt;200 mg codeine</td>
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</table>
What must you do to use controlled substances/dangerous drugs in research at UToldeo?
The United States Drug Enforcement Administration (DEA) and the State of Ohio Board of Pharmacy regulate the use of controlled substances and dangerous drugs. The University of Toledo (UT) and its employees will comply with the federal and state laws and regulations that pertain but are not limited to ordering, storing, dispensing, recording and destruction of controlled substances and dangerous drugs used in animal and in-vitro research.

To obtain, synthesize, and use controlled substances in UToledo Institutional Animal Care and Use Committee (IACUC)-approved animal or in-vitro research, an Investigator must be either a Regrant or Authorized Agent.

The purpose of this policy is to facilitate a general understanding of the steps necessary to comply with federal and state laws and regulations governing controlled substances and dangerous drugs in UToledo animal or in-vitro research and to ensure safe handling and security of controlled substances and dangerous drugs.
Steps to Use Controlled Substances and/or Dangerous Drugs

• Register or become an Authorized Agent for a Registrant.
• Implement Security Measures.
• Follow Proper Ordering and Procurement Processes.
• Follow Proper Disposal Processes.
• Adhere to Record Keeping Requirements.
Register

• Notify the IACUC Office ([Elaine.Joseph@utoledo.edu](mailto:Elaine.Joseph@utoledo.edu)).

• Request a TDDD license from the Ohio Board of Pharmacy from their online system.
  - [https://elicense.ohio.gov/OH_HomePage](https://elicense.ohio.gov/OH_HomePage)
  - Select Pharmacy Board, then Terminal Facility Category 3 License, General Application
  - Select “Add New Business” to add University of Toledo
  - Fee is $440
Register

• Request a Research registration with the DEA via their online system.
  - [https://apps.deadiversion.usdoj.gov/webforms2/spring/main?execution=e1s1](https://apps.deadiversion.usdoj.gov/webforms2/spring/main?execution=e1s1)
  - No fee
  - Certifying Official is Mr. John Elliott
  - For schedule I research, an additional registration will be required.
Registration Address Example (HSC)

3000 Arlington Avenue
[Exact Building Name – i.e., Health Science Building]
[Exact Room Number where drugs will be stored]
Toledo, OH 43614
Register

• A separate license and registration is required for each address where controlled substances are stored.

• Name, address, or Drug Schedule changes should first be made with the Ohio Board of Pharmacy then with the DEA.
Authorized Agent

- Identify a UToldeo Investigator with a DEA registration.
- Ask their permission to become an Authorized Agent on their DEA registration.
- Sign Authorized Agent Form (on file with Registrant)
- Notify the IACUC Office.
**Authorized Agent**

- Cannot store controlled substances in their own space.
- Must obtain all controlled substances from the Registrant each business day.
- Must return all controlled substances to the Registrant at the end of business day.
- Registrant remains legally responsible for all activities of Authorized Agents use of controlled substances.
Physical Security Measures
Physical Security Measures
Physical Security Measures

Reminder

• Expired substances must be clearly labeled as expired and stored separately.

• Expired drugs cannot be used for any animal procedures.
Physical Security Measures
Compromise of Security

Reporting Theft or Loss

• Registrant must immediately report to the UToldeo police department and IACUC Office any loss, theft, or compromise of keys, combinations, locks, access codes.

• The Registrant must train all persons whose work involves controlled substances to immediately report to Registrant any compromise in access codes or keys.

• The Registrant must immediately replace any compromised access device or keys.
Ordering and Procurement

• Controlled substances may be purchased from veterinary or human pharmaceutical suppliers and must follow the UToldeo purchasing procedures.
  ▪ Example companies include Covetrus and Henry Schein Medical

• As a rule, only the minimum amount (i.e., 6 months max) needed should be ordered at any given time.

• Orders will only be delivered to the physical address that is specified on the Registrant’s registration form.
Disposal

• Registrants must properly dispose of all controlled substances when:
  ▪ The substance’s use-by date expires
  ▪ The Registrant’s DEA registration expires and is not renewed
  ▪ The substance is not needed or is in excess (i.e., waste)
  ▪ The Registrant no longer conducts research using controlled substances
  ▪ The Registrant leaves UToldeo
Disposal

• Proper disposal of controlled substances can be achieved through one of the following methods:
  ▪ The Registrant arranges for a DEA-registered reverse distributor to accept and dispose of the substances
  ▪ The uses Drug Buster or RX Destroyer to dispose of the substances
# REGISTRANT RECORD OF CONTROLLED SUBSTANCES DESTROYED
## FORM DEA-41

### A. REGISTRANT INFORMATION

<table>
<thead>
<tr>
<th>Registered Name:</th>
<th>DEA Registration Number:</th>
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<tbody>
<tr>
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</table>

<table>
<thead>
<tr>
<th>Registered Address:</th>
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<table>
<thead>
<tr>
<th>City:</th>
<th>State:</th>
<th>Zip Code:</th>
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<table>
<thead>
<tr>
<th>Telephone Number:</th>
<th>Contact Name:</th>
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### B. ITEM DESTROYED

1. **Inventory**

<table>
<thead>
<tr>
<th>National Drug Code of DEA Controlled Substances Code Number</th>
<th>Batch Number</th>
<th>Name of Substance</th>
<th>Strength</th>
<th>Form</th>
<th>Pkg Qty</th>
<th>Number of Full Pkgs</th>
<th>Partial Pkg Count</th>
<th>Total Destroyed</th>
</tr>
</thead>
<tbody>
<tr>
<td>16590-590-60</td>
<td>N/A</td>
<td>Kadian</td>
<td>60mg</td>
<td>Capsules</td>
<td>60</td>
<td>2</td>
<td>0</td>
<td>120 Capsules</td>
</tr>
<tr>
<td>0555-0767-02</td>
<td>N/A</td>
<td>Adderall</td>
<td>5mg</td>
<td>Tablets</td>
<td>100</td>
<td>0</td>
<td>83</td>
<td>83 Tablets</td>
</tr>
<tr>
<td>9050</td>
<td>B02120312</td>
<td>Codeine</td>
<td>N/A</td>
<td>Bulk</td>
<td>1.25 Kg</td>
<td>N/A</td>
<td>N/A</td>
<td>1.25 Kg</td>
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7. 
Record-Keeping

- Registrant’s must keep the following records, each of which is discussed in more detail in the following slides:
  - Initial Inventory
  - Annual Inventory
  - Usage Log (Dilution and Usage Log)
  - Purchase and Receipt Log
  - Theft or Loss Form

- Records pertaining to Schedule I and II controlled substances must be kept separate from records of Schedule III-V.
Record-Keeping – Inventory

- Registrants are responsible for performing and documenting an initial inventory of all controlled substances and dangerous drugs on hand.
- Initial inventory for Schedule I and II substances must be done separate from that of the inventory of Schedule III-V.
- The Registrant must perform an annual inventory of all controlled substances and dangerous drugs on hand following the date of the initial inventory.
- A separate inventory should be used for all expired substances.
University of Toledo
Controlled Substance Research Records
Annual Controlled Substance Inventory Form

Date: __________________________
DEA Registrant (Print Name): __________________________
DEA Registrant Address (as appears on DEA Form 223):
________________________________________________________________________
________________________________________________________________________
________________________________________________________________________
DEA Registration #: __________________________________________
State of OH Controlled Substance permanent ID # (site specific):
________________________________________________________________________

Inventory Performed by:

<table>
<thead>
<tr>
<th>Print Name</th>
<th>Signature</th>
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</table>

Inventory Witness:

<table>
<thead>
<tr>
<th>Print Name</th>
<th>Signature</th>
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<tbody>
<tr>
<td>Start of day</td>
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<td>End of day</td>
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<thead>
<tr>
<th>DEA Schedule</th>
<th>Name of Controlled Substance</th>
<th>Container or Unit Type (i.e., bottle)</th>
<th>Quantity of Containers</th>
<th>Container Volume (i.e., ml, number pills)</th>
<th>Concentration (mg/ml)</th>
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Record-Keeping – Usage Log

- The Registrant must keep a running log of the use and disposition of controlled substances and dangerous drugs. The log must be kept in a secured place.

- A separate log must be kept for each container of a controlled substance.
A separate form must be utilized for each uniquely assigned controlled substance container.

DEA Registrant Name: ________________________________

Controlled Substance: ______________________________ Container ID/Lot # __________________________

Expiration Date ________________

<table>
<thead>
<tr>
<th>Date</th>
<th>Protocol #</th>
<th>Date Protocol Approved</th>
<th># of Animals</th>
<th>Quantity Used Per Animal (ml)</th>
<th>Total Amount Used (ml)</th>
<th>Waste* Balance</th>
<th>Witness Initials*</th>
<th>Administrator Initials</th>
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Record-Keeping – Purchase/Receipt Log

• The Registrant must keep all documents relating to the order, purchase and receipt of all controlled substances and dangerous drugs.

• The Registrant’s copy of the DEA Form 222 used for orders of Schedule I and II controlled substances must be maintained as a part of this documentation.
University of Toledo
Purchasing/Receipt Log

PI/License Holder: ________________________________

Ohio TDDD License/DEA Registration Number: _______ / _______

Drug: ___________________ Concentration: ___________________ Size of container: ______________

Form: Liquid / Tablet / Powder / Patch   Schedule: I II III IV V

<table>
<thead>
<tr>
<th>Date received</th>
<th>Container ID #</th>
<th>Expiration date</th>
<th>Lot #</th>
<th>Vendor</th>
<th>Invoice #</th>
<th>Amount received</th>
<th>Initials of person receiving</th>
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Record-Keeping – Theft / Loss Form

- The Registrant must report any discrepancies that are noted in the amount of controlled substances during an inventory or audit.

- Discrepancies (thefts or losses) should be reported immediately to UToldeo police, IACUC, DEA, and the Ohio Board of Pharmacy.
UNIVERSITY OF TOLEDO
CONTROLLED SUBSTANCES DISCREPANCY FORM

Instructions: This form should be completed if a discrepancy in the amount of Controlled Substances is discovered. See page 2 for CHECKLIST OF STEPS TO BE TAKEN IN CASES OF SUSPECTED LOSS OF THEFT CONTROLLED SUBSTANCES.

Name of registrant:

Type of Discrepancy: Include discrepancies noted that are potentially indicative of a significant loss or theft of Controlled Substances.

_____ Significant Loss of Controlled Substances
_____ Theft of Controlled Substances

Date and Time of Discovery:

Location where Discrepancy was Discovered:

Name/Phone Number/Email of Person who Made Discovery:

Name(s), Schedule(s), and form(s) of Controlled Substances involved:

Description of circumstances of discrepancy, e.g., evidence of attempted break-in; broken safety tab on container; evidence of missing containers or substances; discrepancy in inventory/audit:
Record-Keeping – Retention

• The Registrant must keep all records relating to the ordering, procurement, inventory, use, and destruction (disposal) of controlled substances in research for at least six (6) years.

• Records should be kept close to or locked with the controlled substances.
DEA Inspections

• It is likely that the DEA may do a pre-registration inspection, this is normal.

• If the DEA contacts you, please contact Research and Sponsored Programs (Elaine.Joseph@utoledo.edu) as soon as possible.

• Research and Sponsored Programs will assist you with answering pre-inspection questions and be present during the inspection.
DEA Inspection Guide

• Upon notice/arrival of inspectors
• Contact Elaine Joseph immediately (if not already present)
  • Elaine.Joseph@utoledo.edu
  • 419-383-4251 / 734-945-9999
• Review their credentials (ID, etc.)
• Ask if you need to sign a Notice of Inspection (DEA Form 82)
• Upon request, provide access to the controlled substance storage space
DEA Inspection Guide

- Be prepared to provide inspector access to:
  - Ohio Board of Pharmacy TDDD license
  - Authorized Agents form (signed by those who access the controlled storage space)
  - Most recent inventory form (within one year)
  - Current usage logs
  - Disposal logs (DEA 41 forms), if applicable
  - Purchasing/receipt forms (including invoices if possible)
  - Theft/loss form (if applicable)
  - UToldeo Policy on Controlled Substances
Summary

• This module has covered the overview, applicable laws, regulations and policies relating to what Investigators must do to use controlled substances and dangerous drugs.

• Also, this module has provided you with information on registration, implementing security measures;

• It has introduced the proper ways of ordering & procuring substances and how to properly dispose of them. In addition, this module has explained how to adhere to the proper record keeping requirements.

• It has also explained what to do during a DEA Inspection
For More Information

• Research & Sponsored Programs Controlled Substances webpage utoledo.edu/research/rsp/RC/controlled-substances-and-dangerous-drugs/

• For more information on the use of controlled substances in research, as well as standardized forms, contact:
  Elaine Joseph  419-383-4251
  Elaine.Joseph@utoledo.edu