CONTROLLED SUBSTANCE
USE AND MANAGEMENT PROCEDURES

1. **PERFORMANCE STANDARD:** Duke University researchers, employees, faculty, students, or staff who use Controlled Substances in animal based research, testing, or testing; shall comply with all federal regulations, state rules, and institutional requirements.

2. **BACKGROUND / PURPOSE:** Biomedical research, testing, and teaching programs involving animals often require Controlled Substances for prevention of pain or distress. Controlled Substances are used to produce anesthesia, analgesia, tranquilization, sedation, hypnosis, euthanasia, or as a means to study the actions of specified drug regimens. Controlled Substances have the potential for misuse. Accordingly, the federal agencies (DEA) and state offices (DHHS) require individuals using Controlled Substances to obtain both state and federal registrations, and to abide by the guidance describing licensing, storage, distribution, use, and disposal of Controlled Substances.

Registration for use of Controlled Substances is an individual obligation – there is no statutory requirement for institutional management of Controlled Substance registration. Even so, Duke University has an interest in the health and well-being of its animals and regulatory compliance of its researchers, employees, faculty, students, and staff. Therefore, Duke University has appointed the Duke Office of Animal Welfare Assurance (OAWA) to assist Controlled Substance Registrants by providing guidance and oversight, which will help assure compliance with all federal regulations, state rules, and institutional requirements.

The Duke Institutional Animal Care & Use Committee (IACUC), OAWA, and the Division of Laboratory Animal Resources (DLAR) have established mutually supportive procedures for local use of Controlled Substances in animals under Duke approved research protocols. These procedures support the guidances of the state and the federal agencies.

3. **DEFINITIONS:**
   a. **Authorized User:** Duke University or Duke University Medical Center faculty, staff, students, or employees authorized by the Controlled Substance license holder (the Registrant) to order, have access to the cabinet, administer, or destroy Controlled Substances (except for schedule I and schedule II) under the authority of the Registrant. High School/Undergraduate students or temporary individuals are not authorized to order Controlled Substances, have access to the Controlled Substance cabinet, or destroy waste substances. High School/Undergraduate students or temporary individuals may administer Controlled Substances according to the approved protocol, and may serve as the witness for destruction of waste substances. More details on Authorized Users in Section III.

The Duke University Animal Care & Use Program is committed to advancing healthcare for humans and animals through compassionate care and progressive animal use.
b. **Controlled Substance:** Any substance listed in the Controlled Substances Act, Code of Federal or Substance Regulations (21 CFR, part 1300 to end), the North Carolina Controlled Substances Statute(Chapter 90, Article 5) or the North Carolina Administrative Code (10A; Sections 26E and 26F).

c. **Controlled Substance Record / Log Book:** The file (or folder) where transactions of Controlled Substances are recorded. An accurate, continuous, and current record reflecting the acquisition, dispensing, administration, transfer, or disposal of Controlled Substances is necessary to validate proper use of Controlled Substances. Controlled Substance Records must be maintained for 3 years after use or destruction of the Controlled Substance. Several recommended forms are provided as a part of this procedure plan (see web links). The Registrant may choose to use the recommended forms or any form that captures the necessary information in an accurate, logical, and structured manner.

d. **Department:** A department, division, institute, center, or other association of like investigators and/or similar areas or fields of investigation. The Department Chair (i.e., Center Director, Institute President, etc.) issues a memorandum identifying an individual who will serve as the Registrant for the department. Department registration must specify the Registrant of the department and include the name of the department. (e.g., Dr. John Smith; Department of Pediatrics). This must be included on the application form (see procedures under I.A.).

e. **Disposal/Destruction:** The approved method of discarding Controlled Substances which are outdated, redundant, contaminated, wasted, or no longer needed.

f. **Diversion:** A transfer of a Controlled Substance from a lawful to an unlawful channel of distribution or use. This includes administration of a Controlled Substance by an individual not on the approved protocol, not listed as an Authorized User, or not associated with the Registrant as a member of the ‘department’ (if departmental registration) or laboratory (if hierarchical).

g. **Division of Laboratory Animal Resources (DLAR):** The administrative unit for Duke veterinarians engaged in provision of direct veterinary care. DLAR holds a Controlled Substance distributor registration for the sale of Controlled Substances to Duke Registrants; and a researcher registration to provide necessary Controlled Substances for veterinary medical treatments, training, and technical support of protocol activities.

h. **Drug Enforcement Administration (DEA):** The unit within the United States Department of Justice that establishes and enforces the federal regulations for Controlled Substances. The DEA employs federal agents to oversee the provision of the federal regulations. Federal agents should always identify themselves using their federal badge.

i. **Department of Health and Human Services (DHHS):** The unit within the North Carolina state government that establishes and enforces the state regulations for Controlled Substances. The DHHS employs state agents to oversee the provision of the state regulations. DHHS agents should identify themselves with their state badge.

j. **Expired:** There are differing definitions of the term expired, depending upon the Controlled Substance:
– Single agents purchased from a registered vendor: The date listed on a bottle or box of Controlled Substances, after which, its use is prohibited.
– Mixtures / Compounds: The earliest date listed on any agent which is mixed or compounded. See the Policy on “Use of Pharmaceuticals and Non-Pharmaceutical Grade Substances in Laboratory Animals.”

k. **Experimental agents**: These agents may not have an expiration date, but must be assured of stability and purity prior to use in an animal. See the Policy on “Use of Pharmaceuticals and Non-Pharmaceutical Grade Substances in Laboratory Animals.”

l. **Institutional Animal Care and Use Committee (IACUC)**: The Duke activity which approves the use of animals in research, testing, teaching, or exhibition. Duke IACUC approval of an animal activity (a protocol) is the justification required for obtaining a state and federal license for Controlled Substances. The Duke University IACUC and the OAWA Compliance Liaisons provide semiannual third-person audits of Registrant’s Controlled Substance cabinets during routine semiannual laboratory inspections.

m. **Location**: The physical location of the Controlled Substance cabinet. For Department Registrations (see below), there may be a primary location and secondary location(s), as long as the secondary location(s) are within the same building. Secondary locations in the same building must be included in the same Department Registration. The Department Registrant is responsible for all Controlled Substances at all locations.

– **NOTE**: The state defines ‘building’ as inside a single-walled structure, or two-walled structures having a covered and closed walk-way or bridge. For example:

  – MSRB I and Jones buildings are a ‘single building’ for Controlled Substance Registration purposes (covered pedestrian bridge between the two buildings).
  – MSRB I and GSRB II are separate buildings (across the street from each other).

n. **Operational Terms Used in this Policy**:

– **Order**: The act of requesting Controlled Substances from a supplier.

– **Dispense**: The act of drawing from the Controlled Substance cabinet a required quantity of agent for administration into an animal.

– **Administration**: The act of dosing, injecting, or applying the Controlled Substance to the animal.

– **Dispose**: The act of destroying or denaturing a Controlled Substance so it cannot be diverted to illegal use or otherwise manipulated.

o. **Protocol**: The approved application for animal use is called a protocol. The protocol describes the methods and manners in which animals will be used and which products will be experimented, provided to animals, or administered to prevent pain and suffering. Most highly effective medications for management of pain or suffering are controlled, and consequently, the use of Controlled Substances is critical for humane animal case and humane animal use. While Controlled
Substances are generally authorized via an IACUC-approved protocol, there are circumstances when Controlled Substances could be required for research use, but there would be no IACUC-approved protocol. For example, Controlled Substances may be required for animal tissue (e.g., in-vitro) use, physiology studies of cellular responses to cells, etc. Researchers working only with animal tissues and not having an animal protocol must obtain a Controlled Substance registration prior to ordering or using Controlled Substances for in-vitro purposes. The DHHS has agreed to use the ‘OAWA Controlled Substance Memorandum’ in the place of an approved protocol to substantiate the need for a ‘registration.’ The ‘OAWA Controlled Substance Memorandum’ will be provided on a case by case basis. Contact the Director, OAWA for more information regarding department registrations. NOTE: ALL personnel on a protocol using Controlled Substances MUST take the Controlled Substances online training.

– NOTE: Use of a <live animal> Controlled Substance Registration for In-Vivo research: A researcher having a Controlled Substance registration for live animals may use the same registration for tissue culture work – assuming the work has been approved in the Duke animal protocol.

p. Registration: The formal process of obtaining approval from the DHHS and the DEA to use Controlled Substances in research animals for experimentation, management of pain/distress/anxiety, clinical veterinary care, or euthanasia. There are two styles of registration possible for Duke animal researchers:

q. Individual Registration: This is the most common style of Controlled Substance registration, and is usually, but not always, held by a protocol Principal Investigator. The Registrant must be the hierarchical leader (human resources definition of personnel relationships) or senior member responsible for the individuals using or having access to their Controlled Substances. Members of the Registrant’s research group may use the Controlled Substances of the individual Registrant, if they are listed as:

– Authorized Users,
– Approved in section A-3 (personnel) of the protocol, and
– Have completed Controlled Substance Training though the Duke Safety Site.

r. Department Registration: This is an alternate style of Controlled Substance registration where a department (see definition below) may have a single Controlled Substance registration for members of that department. This style of registration is assigned to a single individual as the ‘Registrant’ for the department by the Chair or Head of the department. The Registrant is responsible for all Controlled Substance activity under this registration. Members of the department may use the Controlled Substances of the department Registrant, with the following stipulations:

– The Controlled Substance is included on their (the user’s) Duke IACUC-approved animal protocol;

– The individual administering the Controlled Substance is on the Authorized Users list (approved by the Registrant);

– The individual administering the Controlled Substance is in Section A-3 (Role Delineation) of the approved protocol;
– The Controlled Substance Registrant is in Section A-3 (Role Delineation) of the approved protocol (Role = C.S. Registrant); and

– The Controlled Substance registration information is in Section D-3 (Controlled Substance Use) of the approved protocol.

– **NOTE:** The DHHS has agreed to use the ‘OAWA Controlled Substance Memorandum’ in the place of an approved protocol to substantiate the need for a ‘departmental registration.’ The ‘OAWA Controlled Substance Memorandum’ will be provided on a case by case basis. Contact the Director, OAWA for more information regarding department registrations.

s. **Registrant:** The Registrant is the individual who holds the DHHS and DEA registration for the use of Controlled Substances in research animals at Duke. Registrants have several obligations and responsibilities, which include:

– Registrants are legally responsible for ordering, storing, administration, and disposal of Controlled Substances.

– Registrants are obligated to ensure compliance of all activities and personnel associated with Controlled Substances use under their DHHS and DEA registrations, and this procedure plan.

– Registrants may appoint Authorized Users to assist with management of Controlled Substances, however, the Registrant retains the obligation for accurate recordkeeping, secure storage, protocol approved use, and appropriate destruction of Controlled Substances. Deficiencies or discrepancies in recordkeeping are the responsibility of the Registrant.

– Registrants, their Power of Attorney, or their Authorized Users, are the only individuals who may order, dispense, or dispose of Controlled Substances assigned to the Registrant’s Controlled Substance cabinet (see details under Authorized Users).

– Registrants must be listed as approved personnel on all Duke IACUC protocols for which their registration is being used.

– Registrants cannot transfer their registration to another individual. Controlled Substance Registrations are specific for a specific Registrant. A change of Registrant requires submission of a new application to establish a new registration (and Registrant).

t. **Research:** Any animal-related activity for which a Duke animal use protocol exists, regardless of funding source. The term research includes testing, teaching, exhibition, and animal care procedures (any activity where Controlled Substances may be used).

u. **Vendor (or supplier):** Any registered entity (including DLAR, public supply company, or pharmaceutical provider) that holds a Controlled Substance distributor registration for selling Controlled Substances.

4. **APPLICABILITY:** These procedures apply to those situations where Controlled Substances are being used for animal anesthesia, analgesia, euthanasia, restraint, or experimentation under the auspices of the Duke
University animal care & use program. All Controlled Substance use must be in accordance with the IACUC-approved protocol, OAWA Controlled Substance Memorandum, or under accepted clinical veterinary guidelines as prescribed by a Duke veterinarian. Failure to abide by federal and state Controlled Substance regulations may serve as a basis for suspension or termination of the affected animal research protocol by the Duke IACUC. Suspension or termination of a protocol based upon Controlled Substances diversion shall also result in a report to Duke compliance officials, and notification of the state and federal agencies.

5. **PROCEDURES FOR CONTROLLED SUBSTANCE REGISTRATION, RECORDKEEPING, & USE IN DUKE ANIMAL CARE OR USE ACTIVITIES:** The Controlled Substance Registrant must hold both North Carolina Department of Health & Human Services (DHHS) and federal Drug Enforcement Agency (DEA) registrations to place an order, store, or dispense Controlled Substances in animal care & use activities.

a. North Carolina:

   – Obtaining a Controlled Substance registration: (Individuals must obtain the state Controlled Substance registration prior to applying for a federal Controlled Substance registration):
     
     - Form: Complete North Carolina Department of Health and Human Services (DHHS) Form 225.

     - Submit: Submit DHHS Form 225 to the address listed on the form.

     - **NOTE:** Questions concerning the state Controlled Substance application should be directed to Cheanette Hill at Cheanette.Hill@dhhs.nc.gov

     - **NOTE:** The DHHS Form 225 is available for download from the Duke Animal Program Web Site.

     - **NOTE:** For department registrations, identify the ‘name of the department’ and the ‘name of responsible individual’ on the NAME OF APPLICANT line on Form 225.

     - **NOTE:** For department registrations, identify the ‘primary location’ and all ‘secondary locations’ on the LOCATION line for the DHHS Form 225.

   – Registration Fee Payment: The DHHS requires the registration fee at the time of submission. The state licensing fee may be paid from departmental funds, non-federal funds, or personal funds. You cannot use federal grant funds (e.g., NIH funds) to pay for the Controlled Substance registration. NIH Grants Policy prohibits the use of federal funds for the Controlled Substance registration.

     - **NOTE:** When paying by credit card, FAX a copy of the DHHS Form 225 with your credit card information (listed below) to Ms. Evelyn Johnson (FAX number 919.733.1037):

       ✓ Visa or Mastercard

       ✓ Credit card number

       ✓ Expiration date on the card

       ✓ Name on the card

       ✓ Phone number of the card holder (for clarifications)

   – Inspection: An agent of the DHHS will contact the applicant and schedule an inspection of the proposed holding location. Inspections are generally an on-site physical inspection; however, the DHHS inspector may choose an alternate form of assessment (e.g.,
photographs). But, you should anticipate a physical inspection of your Controlled Substance box and log books prior to receiving your registration.

- **NOTE:** You may call the Duke Office of Animal Welfare Assurance (919.668.6720) prior to the scheduled DHHS physical inspection by the state agent and arrange a pre-visit by Duke OAWA staff. OAWA will review the proposed location and offer suggestions to address common DHHS / DEA concerns with Controlled Substance management (See: DEA/DHHS Inspections http://vetmed.duhs.duke.edu/PDF/Policies/Controlled%20Substance/Procedure%20Plan%20for%20DHHS-DEA%20inspections.pdf.

- Validating the need for an individual registration: A copy of your Duke approved protocol indicating the need for Controlled Substances must be available for review by the DHHS inspector. The protocols should not be in the Controlled Substance box, but must be accessible to the inspector.

- Validating the need for a department registration: The DHHS will use the OAWA Controlled Substance Memorandum in the place of an approved protocol to substantiate the need for Controlled Substances.

- **NOTE:** The DHHS application, inspection, and licensure process may take several weeks to complete. Early application is advised. You may submit the animal use protocol to the Duke IACUC and the DHHS application for a Controlled Substance registration at the same time, but, the DHHS will not grant a registration until the IACUC has approved the protocol describing the use of Controlled Substances.

- **NOTE:** For other questions concerning the state process, contact the DHHS at:

  Department of Health and Human Services  
  Gerald Peacock  
  Raleigh, North Carolina 27699-2025  
  gerald.peacock@dhhs.nc.gov

b. Federal Registration (Drug Enforcement Agency - DEA):

- Complete the Federal Form 225 (New Application for Manufacturer, Distributor, Researcher, Analytical Laboratory, Importer, Exporter). The DEA preferred option is to file on-line. Click for the on-line federal DEA form 225.

- **NOTE:** If you choose the hard copy option, mail paper copies to:  
  Drug Enforcement Administration  
  Registration Section/ODR P.O. Box 2639  
  Springfield, VA 22152-2639

- **NOTE:** Wait to receive the North Carolina State registration number before filing for a federal registration. The federal office will not process an application for federal registration until DHHS has issued a state Controlled Substance registration number.
– **NOTE:** The federal agents generally require a physical inspection for all Schedule I substances. Physical inspections for Schedule II-V Controlled Substances may not be required in certain circumstances, based upon the decision of the federal agents. However, if an inspection is requested, please review the following procedure and contact the OAWA office. (Procedure: DEA/DHHS Inspections: http://vetmed.duhs.duke.edu/PDF/Policies/Controlled%20Substance/Procedure%20Plan%20for%20DHHS-DEA%20Inspections.pdf)

– A copy of the DHHS registration must be available for review. A copy of the IACUC approved protocol which requires Controlled Substances (or the OAWA Controlled Substances Memorandum) must also be available for review. Protocols should NOT be copied or otherwise provided to DEA or DHHS agents in a manner that removes the protocol from Duke property or something to this effect.

– For other questions concerning the federal registration, visit the DEA website.

c. **Fees:** The cost of maintaining state and federal Controlled Substance licensure is the responsibility of the Registrant using the Controlled Substances. Fees are currently:

  – DHHS (state):
    – Initial application: $125.00
    – Annual Renewal: $125.00 (Due date for ALL annual renewals is October)

  – DEA (federal):
    – Initial application: $244.00
    – Annual Renewal: $244.00 (Due date is the anniversary of YOUR INITIAL APPROVAL)

d. **Annual Registration Renewal:** Both the state and the federal agencies require an annual renewal. The fees for the annual renewal are listed above.

  – DHHS Registration: Individuals should receive a notice from the state in September of each year reminding them to renew the state registration. October is the renewal month for all registrations in Durham County, regardless of when in the calendar year the registration was initially granted.

  – Federal Registration: The federal registration is also annual, but is based upon the calendar of the original federal registration (anniversary year). Procedures for applying for the annual renewal are the same as the original registration (a re-inspection of the holding location is not routinely performed).

e. **Registration Troubleshooting:**

  – Addresses: Address mis-matches are the most common disconnect item. To prevent a delay in your registration (or annual renewal), assure the following:
    – The address on the state and the federal registration must be the same.
    – The address on the registration must be the geographic location (i.e., building name and room number) of the Controlled Substances.
Postal Address vs. Physical Addresses: If the specific location does not have U.S. Postal delivery (e.g., the storage location is a lab bench in a back room), then list the nearest postal delivery address, and on the next line list the geographic location by building / room number). Addresses must have the geographic location of the Controlled Substance storage cabinet.

Address differences: If you discover that the addresses are different, one or the other must be adjusted to make it consistent with the other.

Shipping Addresses: The ‘Ship To’ address is the address on the federal DEA registration. It is a violation to ship to any address other than the federal DEA address listed on the registration. This address must be the storage location (not your Office postal box).

Correcting Addresses: First decide if the state, and or the federal address require adjustment. It may be that one (e.g., the state) accurately reflects the physical location, while the other (e.g., the federal) registration reflects the postal box and not the physical location of the c.s.

To change the state registration address: Send a letter to the DHHS requesting an address change. Include an explanation why the addresses were different. The letter should be mailed to:

N.C. Department of Health and Human Services
Drug Control Unit- MH/DD/SAS
3008 Mail Service Center
Raleigh, NC 27699-3008

NOTE: You must make the change on the state registration first and receive the new registered address from the state prior to initiating any federal address change!

To change the federal registration address: You have two options for the federal registration change:

Use the federal website link to make an address change. That link is:
(https://www.deadiversion.usdoj.gov/webforms/jsp/regapps/common/updateLogin.jsp) or

Send a letter to the DEA/DOJ in Greensboro. Include an explanation why the addresses were different. The letter should be mailed to:

Diversion Control, DEA, Department of Justice
Attn: Agent Bill Stockmann
1801 Stanley Road, Suite 201
Greensboro, NC 27407

Phone: (336) 547-0506
William.P.Stockmann@usdoj.gov

NOTE: Ordering and/or receiving Controlled Substances to an address which is not your federal DEA registered address and/or is not your geographic location for the
storage location is a serious issue! For example, if the registration only has the mailing address on it, and the Controlled Substances are stored in a separate location (even if in the same building), that is an violation of the Controlled Substances regulations and has the potential for a fine (fines may be as high as $10,000). If receipt and storage are two different locations, then the registration should read (as example):

Dr. Jane Smith  
Mail Stop: South Blue Devil Hall, Room 123  
Bioelectrical Neural Lab, Room 444  
Duke University  
Durham, NC 27705

- The ‘Mail Stop’ is the delivery location. The lab room is recognized as the storage location. This Registrant can receive Controlled Substances at her Office (room 123) and store them in her lab (Room 444).

- Schedules of Agents: The schedules of agents listed on one registration (e.g., federal DEA) must be the same as the schedules listed in the other registration (e.g., state). Any schedule of agent listed on either a state or federal registration must have that agent as part of a Duke IACUC approved protocol.

- NOTE: It is a citable non-compliance to have an agent in your Controlled Substance cabinet which is not listed in an approved Duke IACUC protocol – the approved protocol serves as the validation document for holding a particular agent in your Controlled Substance cabinet.

- NOTE: Schedules II & IIN, and Schedule III and IIIN are designated for ‘narcotic’ and ‘non-narcotic’ agents. While may seem paradoxical, the ‘N’ in each schedule refers to the non- narcotic substance. Narcotics are listed under either II or III (no ‘N’).

6. **SECURITY FOR CONTROLLED SUBSTANCES:** Controlled Substances should be maintained behind a minimum of two (2) locks.

   a. **Options for storage of the Controlled Substances are:**

      - A locked container inside a locked cabinet. (The PREFERRED OPTION is for the locked container to be secured to an immovable surface such as a wall or shelf secured to a wall).

      - A locked cabinet in a locked room. NOTE: The ‘locked room’ must always be locked when it is not occupied by either the Registrant or an authorized user. Leaving lab associates not on the Authorized Users list in the lab when no Authorized used is present in the lab is a violation.

      - Locks may be cipher locks (combination locks) or key locks; key locks are preferred.

      - Combinations or Keys must not be readily accessible to individuals not on the ‘Authorized Users’ List. If key locks are used, then:
– The two locks must be keyed differently.

– The two keys must not be stored together (not on the same ring).

– Both keys must be safeguarded and not accessible to unauthorized users.
  
  – **NOTE:** In select circumstances, a securely affixed single locked device may be approved by the DHHS inspector.
  
  – **NOTE:** Drugs must be maintained at the registered location.

7. **AUTHORIZED USERS:**

a. An Authorized User is an individual who has been approved by the Registrant for access to the Controlled Substance(s).

b. All Authorized Users must be approved personnel on a Duke IACUC Protocol. Authorized Users may be added via the routine protocol amendment process.

c. A list identifying the Authorized Users must be maintained inside the Controlled Substance file. A copy of the suggested Authorized Users Form is available on the animal program web site.

d. Addition or removal of Authorized Users:
  
  – List all Authorized Users on the log (to show a current approved list of Authorized Users). The log should show both the addition and the removal of an Authorized User. **DO NOT** create a new Authorized User log every time a new person is added or removed.
  
  – Authorized Users must be included under Section A-3 of the applicable protocols. These additions may be made with a standard animal program ‘Personnel Amendment form.’

e. Registrants are responsible for all activities of the Authorized Users. Registrants should choose Authorized Users who are reliable, trustworthy, and without adverse histories regarding Controlled Substances.
  
  – **NOTE:** Authorized Users may not have a criminal conviction for a drug-related offense.
  
  – **NOTE:** The Duke animal protocol template Section A-3 lists ‘DLAR veterinary staff’ as an Authorized User for the purpose of administering Controlled Substances to prevent pain management or allow euthanasia. This authorizes DLAR veterinary staff to provide support for your research laboratory, if requested or required.

8. **ESTABLISHING A POWER OF ATTORNEY (if desirable):**

a. An individual authorized with a Power of Attorney may be used to:
– Sign the DEA 222 form on behalf of the Registrant and receive Schedule II drugs in the absence of the Registrant.

– Perform other duties as the Registrant’s representative (e.g. transfer, destruction of expired or excess Controlled Substances, etc.).

b. A Power of Attorney template is available if required.

c. A copy of the Power of Attorney should be provided to each distributor / vendor to allow Controlled Substances transactions.

9. PURCHASING OF CONTROLLED SUBSTANCES:

a. Schedule I Controlled Substances are not available through DLAR. The Schedule I Registrant will legally procure these substances through federally approved public vendors.

b. Schedule II Controlled Substances may be purchased through DLAR or a public vendor/supplier. A DEA Form 222 is required to purchase these substances. Form 222 is unique to each Registrant – you CANNOT SHARE your blank Form 222s with other Controlled Substance Registrants. Form 222 must be ordered on-line from the DEA website.

c. Schedule III – V Controlled Substances for animal studies may be purchased from the DLAR Pharmacy or registered public vendors/suppliers. DLAR pharmacy forms are available on the DLAR web site at ‘Pharmacy Request.’

10. STORING CONTROLLED SUBSTANCES: Generally, Controlled Substances should be stored in the containers in which they were shipped. In certain cases, changing the method of storage could impact the efficacy of the substance (certain Controlled Substances, e.g., diazepam <valium> and similar agents, should not be stored in a plastic container such as a syringe, as plastic degrades the agent and will render it ineffective). Always confirm the appropriate storage container prior to use.

11. RECEIVING OF CONTROLLED SUBSTANCES:

a. Schedule I: The Registrant must receive the Controlled Substance. Authorized Users may not receive Schedule I agents.

b. Schedule II: The Registrant or Power of Attorney may receive Controlled Substances.

c. Schedule III-V: The Registrant, Power of Attorney or Authorized User may receive Controlled Substances.

d. The receiving individual must:

– Count and verify the contents of the order received; sign (and date) the receiving form that the count and product are accurate; maintain forms and reports in the log book.

– Document and rectify discrepancies prior to using the substances; report discrepancies to the seller immediately. For schedule I and II, a copy of the DEA Form 222 MUST be used to
document initial quantities (or quantities added to the cabinet); maintain forms and reports in the log book.

– Sign, date, and maintain the original documents (e.g., packing slips, receipts) for three (3) years.

– All receipt, discrepancies, or other documents must be maintained in the log book.

  – NOTE: Receiving Schedule II substances: Sign the Form 222 and keep the ‘blue’ page for your Controlled Substance records. The remainder of the Form 222 is remitted to the vendor for their records. This blue sheet must be maintained in the Registrant’s Controlled Substance files to serve as the ‘source document’ for receipt of the Controlled Substances for a period of 3 years.

  – NOTE: Blank 222 forms should be securely locked where they may not be obtained. These are controlled documents.

12. TRANSFER OF CONTROLLED SUBSTANCE BETWEEN DUKE REGISTRANTS: While the general expectation is that Controlled Substances are not transferred between Duke Registrants (except DLAR and Duke researchers), in SPECIAL SITUATIONS, one Duke Registrant may transfer a Controlled Substance to another researcher at Duke. Examples of SPECIAL SITUATIONS include: the medication is not on-hand, but has been ordered and has not been received where failure to provide the medication on schedule will cause animal pain or distress, or create research variables which will affect research outcomes. The requesting Registrant (the laboratory needing the substance) must complete either a requisition form or a DEA Form 222 and provide a copy of the form to the source Registrant (the laboratory that has the substance).

  – NOTE: DEA Form 222 is required for any transfer of Schedule II substances between researchers.

  – NOTE: Requisition forms are used for transfer of Schedule III-V substances (provides documentation of legal transfer).

  – NOTE: Schedule I substances transfer between Registrants is prohibited.

13. ADDING A NEW AGENT TO A CURRENT REGISTRATION: On occasion, a researcher will identify a new agent that is required for animal care or use activities. Steps for adding a new agent include:

   a. An amendment to the Duke IACUC adding that agent must be approved.

   b. When the substance is approved by the Duke IACUC, the Registrant sends an email to the DHHS and the DEA requesting addition of the new agent to their current registration. Generally, an email is sufficient for the DHHS and the DEA response. While it is important that the Duke IACUC approve the addition of the new agent to an approved protocol first, the emailing of the request to add the agent to the state and federal registration may occur at the same time. There is no need to wait for state approval prior to requesting federal approval for an agent which is being added to an existing registration and which has been Duke IACUC approved.
c. For NC state DHHS registration modification: Send the items listed below in an email from your ‘duke.edu’ email address to the DHHS (joi.baker@dhhs.nc.gov). If the Registrant is already approved for the same schedule drug as being requested, they will receive a confirmation email from DHHS noting approval of the additional Controlled Substance(s). If the Registrant is not already approved for the schedule of drug being added, they will receive a confirmation email from DHHS noting approval of the additional substance(s) as well as a modified registration form with the updated schedule for retention by the Registrant. The information in the email to the DHHS should include:

- Registrant Name and contact information (email, phone number etc),
- Registrant DHHS number iii. Registrant DEA number
- Name of drug to be added
- Drug Code and Schedule of Drug to be added (insert hyperlink to on-line schedule and codes)
- Reason for addition of the new Controlled Substance(s)
- Approved protocol title and date of approval.

- NOTE: If a Registrant is approved for schedule II-V Controlled Substances and wishes to add a schedule I agent, a separate registration is required for the schedule I agent (refer to section I.a. above).

d. For federal DEA registration modification: The Registrant should contact the DEA office directly at 336.547.4219 and ask to be directed to a DEA agent regarding the addition of Controlled Substances to an existing research registration. The DEA agent will provide specific details regarding submission of the necessary documentation for the request. The Registrant should be ready to provide:

- Registrant Name and contact information (email, phone number etc),
- Registrant DHHS number
- Registrant DEA number
- Name of drug to be added
- Drug Code and Schedule of Drug to be added (insert hyperlink to on-line schedule and codes)
- Reason for addition of the new Controlled Substance(s)
- Approved protocol title and date of approval.

e. When ordering from DLAR: If Registrant is not already approved for the schedule of drug required, the Registrant should provide a copy of the updated registration to DLAR Pharmacy at the time of ordering the new substance.

14. RECORDKEEPING FOR DISPENSING OF CONTROLLED SUBSTANCES: Any written (paper) recording system may be used for maintaining controlled drug dispensing data. Suggested templates are available on the animal program web site. Recordkeeping must include:

a. Name of the substance (may be in page header)
b. Source of the substance (may be in page header)
c. Date of expiration of the substance (may be in page header)
d. Date of receipt (may be in page header)
e. Unique identification number for the bottle. Unique identifiers may be determined by the Registrant. Any system of unique identification may be used, as long as each container is uniquely identifiable. See ‘Labeling of Controlled Substances’ for additional information.
f. Starting quantity of Controlled Substance
g. Date of use
h. Protocol (or project) for which it is being used
i. Animal (or group of animals) for which it is being used
j. Person dispensing the medication from storage
k. Person administering the medication to the animal(s)
l. Quantity (cc/ml/grams) of agent dispensed
m. Quantity remaining in the vial/bottle/box
n. Quantity wasted

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NOTE: Schedule I substances require a bound book rather than a loose leaf or 3-ring binder. A 3-ring binder is recommended for maintaining all records for Schedules II-V Controlled Substances.

15. LABELING OF CONTROLLED SUBSTANCES: Each bottle (or box) of Controlled Substances must be individually identified by a unique (not re-used) number.

a. Original packaging showing the product information should be used when possible. Controlled Substances containers (vials, ampoules, or boxes) may be removed from the original packaging if the interior container(s) has been labeled to include: the name of the Controlled Substances, the lot number (or unique identifier), the final concentration, the amount per container, and the expiration date (either as per the manufacturers recommendations or the most recent expiration date of the combined substances, if mixed).

b. If syringes are filled and stored in the Controlled Substance cabinet; or if Controlled Substances are compounded, diluted or combined, each container must be labeled and tracked separately. The label must include the following:
   - the name of the Controlled Substances,
   - the lot number (or tracking number) of the product,
   - the date reconstituted (powders) or combined/mixed (see item the final concentration,
   - the amount per container, and
   - the expiration date (either as per the manufacturer’s recommendations or the most recent expiration date of the combined substances).

16. MIXTURES OF CONTROLLED SUBSTANCES: When mixing substances (e.g. ketamine & xylazine, buprenorphine & saline), there are three options:

a. Completely used during that day with no ‘left-overs.’

b. Almost completely used during that day and the remaining quantity disposed of as waste.

b. When the mixture is maintained for subsequent use, it must be tracked using the Record of Controlled Substance Administration/Dispensed – Combination Drug.

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   NOTE: Mixing a Controlled Substance with a non-Controlled Substance makes the new mixture controlled.

   Mixtures must be labeled with an expiration or discard-by date. Please see policy “Use of Pharmaceutical and Non-pharmaceutical-grade Substances in Animals.”

17. LOSSES OF CONTROLLED SUBSTANCES: Losses should be reported by the Registrant to the Duke OAWA & federal DEA within 24 hours of discovering the loss. Minimize the risk of losses by documenting the
Controlled Substance tracking sheet for the specific Controlled Substance. The DEA does not specify the minimal amount of loss which must be reported, therefore, consider any loss as reportable. When losses occur:

- Report to the OAWA using the email address: IACUC@duke.edu or call 919-668-6720 AND
- Report to the federal DEA via the DEA website (DEA Form 106).

  - NOTE: Reporting losses to the DHHS is not necessary.

  - NOTE: It is common for suppliers to add a small amount of ‘extra’ substance in a bottle; a 10 ml bottle may contain as much as 11 ml of substance. Therefore, it is not surprising to audit a little more than is recorded in the log book. However, in cases of discrepancies (e.g., even small discrepancies such as 1.8 ml over a 4 week period with 12 extractions from the bottle), a brief email or phone call to the DEA may provide a response that this loss is minimal and does not need to be reported. It is preferred to ask and get a response that a report is not necessary, than to not ask and be audited at a later date with missing agent that is several months old.

18. METHODS FOR DISPOSING OF ‘WASTE’ CONTROLLED SUBSTANCES: There are several methods for disposing of excess, expired, contaminated, or unneeded Controlled Substances. The options include:

a. Use of Laboratory Disposal System – SMALL QUANTITIES: In cases where the amount to be disposed is minimal (generally less than 0.5 ml leftover from an experiment or procedure, an almost empty bottle, etc.), the Registrant may dispose of the unneeded materials by one of the methods described below and in 19. The Registrant may also request the Director, OAWA assist with disposal as described below.

b. Use of the Animal Program Disposal System – SMALL & MODERATE QUANTITIES: The DHHS has authorized the Director, Office of Animal Welfare Assurance, to serve as the local Destruction Officer for moderate quantities of Controlled Substance, Schedules I - V. The Registrant (or authorized user) and the Director, OAWA will complete a DHHS Form (DISPOSAL OF CONTROLLED SUBSTANCES BY REGISTRANTS AND PRACTITIONERS) to document the disposal. The Director, OAWA and either the Registrant or an authorized user will sign the form. Copies will be maintained as:
   - White Copy: Mailed to the DHHS (monthly);
   - Canary Copy: Maintained by the Registrant;
   - Pick Copy: Scanned and stored on the animal program server.

   - NOTE: The Director has the discretion of performing a systems audit, including other records, storage processes, and Controlled Substances registrations, when disposing of Controlled Substances.

   - NOTE: Expired Controlled Substances must remain in the Controlled Substance cabinet (for security reasons), but should be marked ‘EXPIRED’ (preferably in red lettering) and placed in an inner box of inner container so that they are separated from in-date Controlled Substances.

c. Use the Reverse Distributor Disposal System – LARGE QUANTITIES <Schedules 2,2N,3,3N,4,5>: In cases where the Animal Program Disposal System is not the proper route of disposal (e.g., large quantities of Controlled Substances), Registrants may use the Reserve Distributor System. While
there is no specific definition for what must be disposed via the Reverse Distributor process, generally this applies to multiple bottles of Controlled Substances which may be excess or expired. Registrants must contact a DEA certified reverse distributor to arrange for reverse disposal. In North Carolina, the approved reverse distributors change from time to time, so while a complete list is not possible, at the time of this plan preparation, the following vendor provides reverse distribution of Controlled Substances: Pharmaceutical Dimensions877-297-4851, Email: returns@phdreturns.com, Website: www.phdreturns.com

d. Found on Campus: On occasion, while cleaning out an old supply closet or moving furniture, bottles of Controlled Substance may be found. In this case:

  – First secure the substance by locking the substance in your c.s. cabinet, or if you do not have a cabinet, place it in a safe or locked desk drawer where very few people have access.

  – Second, immediately contact the Duke Office of Animal Welfare Assurance and arrange for OAWA-assisted immediate destruction of the substance.

19. METHODS OF DISPOSAL: Controlled Substances are chemicals, at times environmentally harmful chemicals. Historically, these substances have been disposed in less than desirable manners. For the Duke animal program and all Controlled Substance registrations used under Duke-approved animal protocols, the appropriate means of Controlled Substance disposal includes:

a. Powders: Mix powders with liquid (e.g. Clorox or other disinfectant), pour onto absorbent material (e.g. soda-sorb, cat litter) and discard in a sharps container that will be incinerated; or inject into a euthanized animal carcass and discard via an incinerator (carcass).

b. Liquids: Pour onto absorbent material (e.g. soda-sorb, cat litter), or inject into a euthanized animal carcass and discard the carcass via an incinerator or digester. Discard empty bottle in a sharps container that will be incinerated.

c. Empty bottles: Remove the top of the bottle, dispose of any remaining drops of liquid by pouring onto absorbent material (e.g. soda-sorb, cat litter), or inject into a euthanized animal carcass and discard the carcass via an incinerator or digester. Discard empty bottle in a sharps container that will be incinerated.

d. Patches: Cut into small pieces and place the pieces in a sharps container.

e. Terminal amount in a syringe: Inject the substances onto absorbent material (e.g. soda-sorb, cat litter) and discard in a sharps container that will be incinerated; or inject into a euthanized animal carcass and discard via an incinerator (carcass).

  – NOTE: Do not under any circumstances pour any Controlled Substance down the sink drain. This is not an environmentally appropriate way to dispose of chemicals.

20. DOCUMENTATION OF DISPOSAL: Each disposal must be witnessed regardless of quantity. The individual disposing of the substance must sign the disposal log book. The witness (Authorized User or Director, OAWA) must sign the disposal log book. Entries in the disposal log must include:

a. Name of Controlled Substance
b. Date and time it was disposed
c. Quantity disposed
d. Method of disposal
e. Signature of individual disposing of the agent
21. AUDITING OF CONTROLLED SUBSTANCES:

a. Local (laboratory) Auditing of Controlled Substances:
   – Quarterly: The animal program recommends the Registrant (or their designee) perform an audit of their Controlled Substance cabinet and the records of dispensing on a quarterly basis. At the conclusion of the audit, the auditor will write in the next open line of the tracking log the following statement: “Audited on <date> by <print name> and found to be accurate (or define discrepancies). <sign name>”

b. Biennial: By Controlled Substance regulation, the Registrant (or their designee) must audit the Controlled Substance cabinet and the records of dispensing at least once every two years. At the conclusion of the audit, the auditor will write in the next open line of the tracking log the following statement: “Audited on <date> by <print name> and found to be accurate (or define discrepancies). <sign names>”

22. INSTITUTIONAL AUDITS: While licensure is strictly between the Registrant and the state and federal agencies, the Duke University animal program will perform audits of Controlled Substances as a routine process to assist the Registrant with compliance. These audits focus on accurate and appropriate documentation.

a. IACUC Audits: IACUC Semiannual Inspection Subcommittees shall include assessment of the Controlled Substance cabinet as a part of the routine semiannual laboratory review process.

b. Compliance Liaison Audits: Either as part of the routine compliance liaison process or as a directed audit, a review of the Controlled Substance cabinet will be performed as an unscheduled review to assist the Registrant in Controlled Substance management.

   – NOTE: The Registrant may request an out-of-cycle OAWA audit at any time. OAWA offers to perform these audits to assist with Controlled Substance management and is not considered punitive.

   – NOTE: Significant deficiencies noted during an institutional audit may affect the IACUC approved status of the animal protocol.

23. FEDERAL OR STATE AUDITS: Federal and state audits may occur at random intervals determined by the state or federal agency. Annual audits should be expected by the Registrant. Effective management of Controlled Substances by controlling access, recording use, documenting disposal, and auditing the process, decreases the likelihood of problems being found during a state or federal audit. The Office of Animal Welfare Assurance recommends that the registrant let them know when an audit is scheduled so they can assist, as necessary. (919-668-6720)

24. USE of DLAR Technical Services Protocol (for provision of Controlled Substances): In certain cases, researchers may require the use of Controlled Substances but may not have their registration (e.g. the
The protocol should note that DLAR will provide support for Controlled Substance administration for all required Controlled Substance use. In the case of subsequent receipt of a Controlled Substance registration, an amendment is necessary to add the new Registrant and remove DLAR Technical Services from provision of Controlled Substances. Contact DLAR for additional details concerning use of the DLAR Technical Services protocol for Controlled Substance administration to research animals.

25. **LIST DLAR VETERINARY STAFF AS AUTHORIZED USERS:** The Duke protocol template has listed as a default (Section A3) that DLAR veterinary staff are Authorized Users for the approved protocol. The purpose for this protocol default is to authorize DLAR veterinary staff to provide Controlled Substance support for your research laboratory in the event of an unanticipated event which could delay the provision of pain relieving medications to research animals. When engaging DLAR veterinary staff to provide Controlled Substances as part of a research activity, the DLAR veterinary staff must be provided Controlled Substances out of the Registrant’s Controlled Substance cabinet (under DHHS policy, only one Controlled Substance cabinet may be used for a given situation or set of animals). The sole exception is when DLAR veterinarians are using DLAR Controlled Substances for the purpose of clinical veterinary care.

26. **DLAR VETERINARY STAFF PROVIDING CLINICAL CARE:** DLAR veterinarians may administer Controlled Substances in the provision of necessary clinical care for Duke owned animals, at their discretion. When providing non-protocol related clinical care or euthanasia, DLAR veterinarians must use DLAR Controlled Substances. DLAR veterinarians may not use DLAR Controlled Substances as a replacement for protocol approved medications.

27. **DEA FORM 222:** Purchasing Schedule I or Schedule II Controlled Substances requires the use of a DEA Form 222. These forms are only available from the Department of Justice, Diversion Control Office. There are certain important use aspects of a form 222. Form 222s are:

   a. A federal document, much in the same way as a social security card, and must be protected from theft or mis-use (keep under lock & key);
   b. Individually numbered by the federal government (the numbered forms you receive are assigned to your name);
   c. Assigned to a specific individual (it is a violation of the Controlled Substance act to ‘share’ your 222 forms with another Registrant);
   d. Location specific (if you change your storage location you will need to request new forms (along with a new registration);
   e. Signed only by the Registrant or power of attorney;
   f. Provided to the vendor/supplier/DLAR Pharmacy upon request for purchase of a Controlled Substance.
      
      - Note: *The vendor will forward a copy of your 222 used for purchase to the federal agents.*
   
   g. Maintained for at least three years past the date of use (it is a good idea to scan a copy of the old used forms prior to destruction).
28. TRANSFERRING A CONTROLLED SUBSTANCE REGISTRATION TO A NEW INDIVIDUAL: The role of ‘Registrant’ is not transferrable. The registration is not transferrable. Do not attempt to transfer or re-assign the Registrant role. The new Registrant will require a new registration.

29. TRANSFERRING A CONTROLLED SUBSTANCE REGISTRATION TO A NEW LOCATION: While registrations are not transferrable, there is the occasion when the Registrant must move from one location to a second location on campus. Prior to moving, the Registrant must contact the state and federal agents and request a new registration at the new location. The state and/or federal agents may require a physical visit to the new location prior to issuing the new registration certificate. Once a new registration (state and federal) has been issued for the new location, all c.s. must be transferred between the old storage location(s) to the new storage location using the procedures described above.
   a. State: Requires a new registration.

30. CANCELLATION OF A CONTROLLED SUBSTANCE REGISTRATION: If a Registrant no longer requires the Controlled Substance or is no longer Duke employee, the Registrant must:
   a. Dispose of Controlled Substances as per sections 18, 19, 20 of this policy or transfer Controlled Substances, as per item –section 12 of this policy, to another approved registration. Should the PI be relocating to continue their research at another location or institution, they can transfer their drugs from their Duke registration to their new registration at the other location once approved. A separate new registration is required for a change in location, even when the Registrant will be the same and use the same drugs for the same purpose.
   b. Notify the DHHS to terminate their registration, and
   c. Notify the DEA to terminate their registration.
   d. 
   e. NOTE: Former Registrants must still maintain their documentation of purchase, administration, and storage for three years post cancellation in the same secure area.

This concludes the Duke animal program Controlled Substances Use & Management Procedures. The current version is November 2015 and shall remain in effect until rescinded by modified or updated requirements as issued by the institution, the state, or the federal agencies.