Non-pharmaceutical and Pharmaceutical Grade Compounds in Research Animals

Policy Statement

Pharmaceutical-grade compounds are to be used in research and teaching animals when available through human or veterinary suppliers. Non-pharmaceutical grade medications can be used only in research/teaching activities if reviewed and approved by the IACUC. The following elements must be provided to the IACUC for consideration:

- The research activity requires the use of non-pharmaceutical grade medications for reasons of scientific necessity.
- Acceptable veterinary or human pharmaceutical grade medications are not available.

Reason for Policy

To remain compliant with the guidance provided by the Office of Laboratory Animal Welfare (OLAW), the United States Department of Agriculture – Animal Plant Health Inspection Service
(USDA-APHIS), and the 8th edition of the *Guide for the Care and Use of Laboratory Animals*, this document details what is required for the use of non-pharmaceutical grade chemicals or compounds in laboratory animals at IUB.

Animal welfare must be considered when using all non-pharmaceutical grade drugs. Drugs used for anesthesia and analgesia must be properly prepared, reconstituted, labeled, and stored.

**WHAT DO THE REGULATIONS SAY?**

*8th edition of the Guide for the Care and Use of Laboratory Animals* (p. 31)

The use of pharmaceutical grade chemicals and other substances ensures that toxic or unwanted side effects are not introduced into studies conducted with experimental animals. Pharmaceutical grade chemicals should be used, when available, for all animal-related procedures (NIH 2008; USDA 1997b). There may be circumstances when the use of a non-pharmaceutical grade chemical or substance is necessary to meet the scientific goals of a project or when a veterinary or human pharmaceutical grade product is unavailable. The use of non-pharmaceutical grade chemicals or substances should be described and justified in the animal use protocol and be approved by the IACUC (Wolff et al. 2003). Consideration should be given to the grade, purity, sterility, pH, pyrogenicity, osmolality, stability, site and route of administration, formulation, compatibility, and pharmacokinetics of the chemical or substance to be administered, as well as animal welfare and scientific issues relating to its use (NIH 2008).

**OLAW**

OLAW and USDA consider that the use of non-pharmaceutical grade compounds should be based on:

- scientific necessity;
- no availability of an acceptable veterinary or human pharmaceutical-grade compound; and
- specific review and approval by the IACUC.

Investigators and IACUCs should consider relevant animal welfare and scientific issues including safety, efficacy, and the inadvertent introduction of new variables. Cost savings alone do not adequately justify the use of non-pharmaceutical-grade compounds in animals. Although the potential animal welfare consequences of complications are less evident in non-survival studies, the scientific issues remain the same and the principles and need for professional judgment outlined above still apply.

USDA

Investigators are expected to use pharmaceutical-grade medications whenever they are available, even in acute procedures. Non-pharmaceutical-grade chemical compounds should only be used in regulated animals after specific review and approval by the IACUC for reasons such as scientific necessity or non-availability of an acceptable veterinary or human pharmaceutical-grade product. Cost savings is not a justification for using non-pharmaceutical-grade compounds in regulated animals.

The IUB-IACUC acknowledges non-pharmaceutical-grade compounds often are necessary for scientific research. Where the use of non-pharmaceutical-grade substances may be essential for the conduct of science, the goal of the IUB-IACUC is to consider the health and well-being of the animals while aiding the researcher in minimizing potentially confounding experimental variables and maximizing reproducibility of the research.


DEFINITIONS

Pharmaceutical grade compound:

OLAW: Is a drug, biologic, or reagent that is approved by the Food and Drug Administration (FDA) or for which a chemical purity standard has been established by the United States Pharmacopeia-National Formulary (USP-NF), or British Pharmacopeia (BP).

USDA: Pharmaceutical-grade compound is any active or inactive drug, biologic, reagent, etc., which is approved by the FDA for which a chemical purity standard has been written or established by any recognized pharmacopeia, which is a book or a compendia, such as the US Pharmacopeia [USP], the National Formulary [NF], the British Pharmacopoeia [BP], the Pharmacopoeia of the Council of Europe [EP]. Note the USP and the NF have combined their standards into one compendia... [http://www.usp.org/usp-nf].

Analytical Standards: “Certificate of Analysis” is a document that accompanies each product run. This certificate lists the formula for the ingredients as well as the amount of each raw material/ingredient. The product name and lot number are listed to avoid confusion with other batches. The Certificate of Analysis also may contain results of tests for contaminants.

Analytical Grade: ~99% purity; Certificate of Analysis usually available; appropriate preparation is imperative.

Reagent ACS: This designates the highest quality commercial chemical. The “ACS” is the American Chemical Society. A Certificate of Analysis is available upon request.

Reagent Grade: The highest quality commercial chemical; however, ACS has not set specifications for materials. A Certificate of Analysis is usually not available.
GUIDANCE FOR COMPOUNDS FOR WHICH PHARMACEUTICAL GRADE ALTERNATIVES EXIST

Although pharmaceutical grade chemicals/compounds should be used in experimental animals whenever possible, the use of non-pharmaceutical-grade chemicals/compounds in experimental animals is an acceptable practice under certain circumstances.

PIs should use appropriate knowledge of the compounds available to ensure that the preparation, evaluation, storage, use, and disposal standards are maintained.

When selecting anesthesia and analgesic compounds, the following options are potentially available:

- FDA approved veterinary or human pharmaceutical compounds;
- FDA approved veterinary or human pharmaceutical compounds used to compound a needed dosage form;
- Drug obtained via one of the compounding pharmacies in the Resources section of this document;
- Use one of the recipes included in this document. Note that these recipes have been approved by a IU SOM pharmacist;
- Justify the use of non-pharmaceutical grade drugs (see discussion below).

Procedures

HOW DO I FIND OUT IF A COMPOUND EXISTS IN PHARMACEUTICAL GRADE?

A Google search with the terms “pharmaceutical grade” and an agent of interest may yield the best results with the least amount of effort. Alternatively, OLAW and the USDA suggest consulting the FDA database. The Orange Book is the reference for FDA-approved human drugs. The Green Book is the reference for FDA-approved veterinary drugs.

FDA database: http://www.fda.gov/Drugs/InformationOnDrugs/default.htm
Orange Book: http://www.accessdata.fda.gov/scripts/cder/ob/default.cfm
Green Book: http://www.fda.gov/AnimalVeterinary/Products/ApprovedAnimalDrugProducts/ucm042847.htm

HOW DO I KNOW WHEN I NEED TO JUSTIFY THE USE OF A NON-PHARMACEUTICAL GRADE COMPOUND, AND THEN, HOW DO I JUSTIFY IT?

The goal is for the BIACUC and Investigators to work together in determining an optimal way to conduct experiments within the context of humane animal care while minimizing the level of pain and distress. If a pharmaceutical grade compound is available and an Investigator seeks to provide scientific justification for using a non-pharmaceutical grade, the deliberation of the IUB-IACUC regarding scientific justification will rely on the following two factors: Will purity differences result in toxic and adverse effects? Will there be an increase in pain and distress?
When considering the use of non-pharmaceutical grade compounds, IUB faculty can use the following decision criteria when preparing a protocol/amendment:

- Justification that is always acceptable when supported by appropriate rationale.
- Known impact on measured experimental outcomes, which is substantiated by data or published reports.
- Not available from a veterinary or medical supplier.
- Not available from a veterinary or medical supplier in the desired concentration (e.g., high concentration of penicillin to produce seizures; supersaturated solution of potassium chloride to euthanize pigs) or cannot be achieved by simple dilution of an existing product.
- More pure in a reagent grade version than a pharmaceutical grade version.
- Use is required in order to produce data that is comparable to previous data, if there is a scientific rationale for *direct comparison* with previous data. Acceptable use of chemical-grade reagent includes:
  - The ongoing collection of data for experiments that are not yet completed;
  - The need to replicate methods from previous studies; or
  - The pharmaceutical grade contains unwanted fillers or non-toxic vehicles.
- To avoid the inadvertent introduction of new variables, a non-pharmaceutical grade compound is scientifically necessary if a vehicle control is not available using USP materials.
- An available USP compound does not meet the non-toxic vehicle requirements for the specified route of administration.
- Pharmaceutical grade only is available in a form not suitable for the route of administration.
- Exorbitant costs make the compound logistically unavailable.
- When dilution or a change in formulation of an USP compound occurs, there may be no additional advantage gained by using the USP formulation. In this situation, use of the highest grade reagent may have the advantage of single-stage formulation and also may result in purity that is equal to or higher than the human or veterinary drug.
- No pharmaceutical grade is available.

Justification that is generally acceptable:

- Detailed concerns about potential detrimental effects on established models or experimental paradigms.
Possible adequate justification, requiring particular attention to details:

- Unpublished, anecdotal experience on benefits of the model or detrimental effects of alternatives.

- Experimental logistics or personnel safety, which include:
  - Access to specialized equipment (e.g., fume hoods, vaporizers/scavengers);
  - Interference with measurements or procedures;
  - Based upon performance standards affording outcomes that are non-injurious to animal subjects; or
  - Security of regulated drugs (in rare circumstances).

- Inadequate justification, when no additional justification is present:
  - Cost savings;
  - Administrative burden of acquiring and maintaining a DEA license; or
  - Consideration/elimination of only one pharmaceutical-grade alternative.

When possible, the description justifying the use of non-pharmaceutical grade drugs should include the chemical grade of the agent(s) being used (see definitions below), source of the reagents, as well as a description of the appropriateness of the agent, its formulation and vehicle. Formulations and vehicles may need to be adjusted depending on the route and site of administration, as well as the species under consideration. The recipe for formulating the compound mixture should be detailed in the protocol.

**WHAT DOES A GOOD JUSTIFICATION LOOK LIKE?**

- “The XXX protein used will be synthesized and purified in several variations in our lab. This will be carried out using automated chromatography equipment to ensure the tightest, most reproducible column-based purification possible. However, given the nature of the process, it is not practically possible to generate pharmaceutical-quality protein reagent in a basic research lab, as the equipment, training, and facilities required are specialized.”

- “The compound I injection, YYY, will be used in a 10 microliters/dose. The commercially available concentration is too low to dose the animal with the appropriate volume.”

Consideration will be given to the grade, purity, sterility, pH, pyrogenicity, osmolality, stability, site and route of administration, formulation, compatibility, and pharmacokinetics of the chemical or substance to be administered. This is a very comprehensive list. Not all of these factors may be applicable in all circumstances. The IUB IACUC may not need all parameters in every situation.
WHAT ABOUT USE IN NON-survival PROCEDURES?

A euthanasia solution (e.g., Euthasol, Fatal Plus) may not be used as an anesthetic (alone) for survival or non-survival procedures. OLAW in concert with USDA agree that a procedure may be performed as a part of euthanasia. This would be limited to terminal perfusion or exsanguination. In both cases, death is an immediate outcome of the procedure.

However, it is acceptable to use non-sterile euthanasia solution (e.g., Euthasol or Fatal Plus) for euthanasia as well as non-pharmaceutical grade pentobarbital as long as it is administered appropriately.

WHAT IF I CAN OBTAIN A COMPOUND THAT IS NO LONGER AVAILABLE IN THE U.S. FROM A SUPPLIER IN ANOTHER COUNTRY?

The compound will be considered non-pharmaceutical grade. You will be required to scientifically justify its use in the animal protocol and to follow the documentation and other practices in this document.

GUIDANCE FOR NOVEL TEST COMPOUNDS & COMPOUNDS WITH NO ACCEPTABLE PHARMACEUTICAL GRADE ALTERNATIVE

The IUB IACUC acknowledges that many test compounds and experimental agents are used in research and generally classifies these agents as non-pharmaceutical grade compounds without an acceptable pharmaceutical grade alternative. As such, their use is an acceptable practice. However, PI’s should use appropriate information ensuring that chemical properties of the compound are appropriate for the study and the route of administration (e.g., the purity, grade, stability in and out of solution, solution vehicle properties, pH, osmolality) The compatibility of the solvent and other components of final preparation should be known to ensure that the non-pharmaceutical grade agents are prepared under sterile conditions and stored properly.

When Preparing Test Compounds:

- When drugs or chemicals are formulated for injection, they must be prepared in a sterile manner. This requires sterile constituents (e.g. sterile powder, sterile diluents), a sterile container, and a means of keeping the preparation sterile. Injection vials (samples and ordering information are available from LAR) are preferred as they make it easier to load a syringe and allow removal of solution without exposing the contents to outside contaminants.

- Diluents or vehicles must be specified in the animal use protocol. Use of solvents will be evaluated on a case-by-case basis. Use of such solvents may limit amounts, concentration and routes of administration. See list of acceptable solvents below.

- Containers must be labeled with the drug, concentration, and date of preparation. Note that sterile injection vials can be obtained from LAR.
• When possible, prepared solutions must be passed through a syringe **filter** (typically 0.22 to 0.45 um but could be finer) at the time of preparation. This can be done in the process of transfer to an injection vial. If there is any question about the sterility of a stored solution, it must also be filtered at the time of use. If filtering is not possible (e.g., nanoparticles), sterile components should be mixed using sterile technique.

• Prepare only as much as can be used in a reasonable period of time. Drug solutions prepared and stored properly in a suitable injection vial can be stored for up to six months. Drugs must be stored properly (e.g., freezer, refrigerator). Solutions must not be used if they are cloudy, discolored, precipitated, etc.

• **Expired drugs** must be disposed of properly. If not discarded, expired drug containers must be labeled “expired” and stored separate from drugs in use. **Controlled substances** cannot be discarded without appropriate paperwork. All controlled substances must continue to be stored in an approved secure cabinet or safe until discarded appropriately.

• **pH** of solutions must be between pH 4.5 and 8.0. Use of a solution with a pH outside this range must be addressed in the animal use protocol.

• **Pyrogens**, such as **endotoxins**, may cause **fever** when injected into an animal. All pharmaceutical drugs are tested for pyrogens. Sterility does not ensure that pyrogens are not present. Filtering does not remove pyrogens. Pyrogen testing is not practical for small lots of prepared drug. Pyrogenicity is a potential experimental variable that researchers should be aware of when using non-pharmaceutical grade drugs.

**Acceptable solvents**

• Distilled water

• PSS (0.9% NaCl), PBS, balanced salt solution (e.g., Hanks)

• 60% (v/v) propane-1:2-diol (propylene glycol)

• 0.5% (w/v) carboxymethyl cellulose

• 10% (v/v) Tween 80 (polyoxyethylene (20) sorbitan mono-oleate)

• 10% (v/v) ethyl alcohol*

• 50% (v/v) dimethylformamide

• 50% (v/v) dimethylsulphoxide (DMSO)

• Cyclodextrins\(^5\) (e.g. 2-hydroxypropyl-beta-cyclodextrin, Trappsol \(^\circledast\))

• USP oil for injection

*Exceptions can be approved on a protocol-by-protocol basis.
Resources

The following companies may provide veterinary grade agents to researchers who are able to supply a DEA Researcher License in lieu of a veterinary license. The IACUC cannot endorse these pharmaceutical firms, nor can it guarantee that these firms will continue to supply these pharmaceuticals in forms suitable for animal studies.

- **Butler Schein Animal Health**, Vet Institute Extension, 1-800-552-8387, Ext.# 5406, Ask for Clay. Researchers with state and DEA Researcher License can obtain any drugs, including controlled substances, and any veterinary medical supplies.

- **Indiana University Pharmacy**, Bloomington, contact Dr. Randalyn Shepherd by email or phone to verify availability of drugs and to arrange an order. IU Pharmacy will need a letter requesting the drug from the PI. The letter should include the PI’s name, IACUC protocol number, the drug requested, and a brief statement describing how the drug will be used.

- **Wedgewood Pharmacy**, Veterinary Compounding Pharmacy, 1-877-357-6613, ask for Barry Yager. Controlled substances not available, but they may be able to compound some drugs not readily available. A veterinary prescription is needed.

  MedVet has an in-house veterinarian who reviews all veterinary product orders. The veterinarian may permit the purchase of these veterinary products (controlled or non-controlled) with a DEA Researcher License, particularly if the recipient is with a research institution.

- **Southern Anesthesia** ([http://sasvet.com/](http://sasvet.com/)), ask for Cooper (800-456-0757 ext 265)
  Currently, researchers holding a DEA Researcher License may purchase veterinary drugs.

- **TW Medical** (888-787-4483) [http://www.twmedical.com/](http://www.twmedical.com/)


- Currently, pharmaceutical grade powdered Sodium Pentobarbital can be ordered from PCCA (Professional Compounding Centers of America). Contact at www.pccarx.com or 1-800-331-2498. A copy of the DEA-222 license will need to be mailed to PCCA for regulatory purposes.

- Pharmaceutical Grade Tricaine Methanesulfonate (MS222)
  - **Finquel**: [http://www.argent-labs.com/argentwebsite/ms-222.htm](http://www.argent-labs.com/argentwebsite/ms-222.htm)

Identifying sources of pharmaceutical grade compounds can be challenging. If the investigator is having difficulty identifying a vendor that provides a specific compound available in a
pharmaceutical grade, the University veterinarians can provide assistance. Please contact the university veterinarians at iubdvm@indiana.edu or phone# 855-6397.

IU IACUC APPROVED RECIPE FOR SODIUM PENTOBARBITAL

INGREDIENTS

- 6 Gm sodium pentobarbital
- 10 ml ethanol (95%)
- 40 ml propylene glycol USP
- qs to 100 ml with 0.9% saline

- Dissolve the pentobarbital powder in the ethanol.
- Add 25 ml of saline - **but only after the pentobarbital is completely dissolved**, then mix thoroughly.
- Add 40 ml propylene glycol, mix.
- Bring to final volume (100 ml) with 0.9% saline.

The pentobarbital concentration in the final solution is 60 mg/ml. A dose of 50 mg/kg IP in rats is suitable.

NOTES:

- Stock solutions must be protected from light and maintained at 4°C no longer than 6 months.
- Stock solutions must be passed through a sterile 0.2 micron filter prior to being stored.
- Stock solutions must be prepared and stored in sterile tubes.
- Please see the section on Guidance for Novel Test Compounds & Compounds with No Acceptable Pharmaceutical Grade Alternative for guidance on filtration and preparation.
- Working solutions can be prepared and maintained similar to stock solutions, but can be stored at room temperature for up to 30 days.
- Transfer of solutions must utilize sterile supplies and techniques (e.g. sterile needles and syringes).
- All containers must be labeled with material name, concentration, date prepared, storage requirements, expiration date, and the initials of the person making the solution.
- Use must be recorded similar to other controlled substances.
- Standard procedures for monitoring plane of anesthesia apply and supplemental dosing is to be given as needed.
**IUB IACUC Approved Recipe for MS-222**

MS222 can be used for axolots, aquatic salamanders, and fish. FINQUEL is the best form of this material on the market.

**INGREDIENTS**

- MS-222 powder
- Artificial pond water mixture
- Sodium Bicarbonate
- pH paper

**MIXING**

- Dissolve MS-222 in artificial pond water (20% Holtfreter's Salts).
- Adjust the pH to about 7.4 using only powdered Sodium Bicarbonate.
- Use a 5 pad pH paper (pH 2-14 from Fisher) to monitor the pH.

**NOTE**

- MS-222 should be made fresh weekly.
- For surgical purposes, fresh solution should be made for every surgery to minimize contamination and infection.
- Discard old MS-222 down the sink diluted with lots of fresh cold water.
- The concentration used for anesthesia is 0.2-0.5% depending on the animal size.
- Use 10% strength of anesthetizing solution (most frequently 0.025% (wt/vol) MS-222) as an analgesic to reduce pain and surgery stress for 20 minutes right after the surgery.
- MS222 does cause a GI response, as some fish (especially those larger in size) might vomit if feeding occurs within the last 24 hours.

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**IU IACUC Approved Recipe for Urethane**

Urethane will produce an extended period of anesthesia with minimal physiological changes in laboratory animals. The use of urethane anesthesia for non-survival studies, clinical veterinary medicine, and other applications is limited, due to adverse post-operative health effects observed in animals and suspected health risks to humans. Urethane has been classified as a mutagen (Lewis, 2004) and as a group 2B carcinogen by the International Agency for Research on Cancer (IARC). It is readily absorbed through the skin, targets multiple organs, suppresses bone marrow, readily crosses the placenta, induces fetal tumor formation (*in utero*), and initiates preneoplastic changes in the skin (Field and Lang 1988). These potentially severe side effects make urethane exposure a significant health threat to laboratory staff, animal handlers, and other personnel who may be accidentally exposed.
NOTE: When handling urethane in the crystalline or powdered form and when mixing urethane into aqueous solutions, *always* use a fume hood, wear a lab coat, protective eye-wear, and chemical resistant gloves. Urethane should only be heated if mixing takes place in a fume hood. Containers of urethane should never be opened outside of a fume hood. Once mixed into an aqueous solution, urethane should then be transferred into a sealed bottle to prevent volatilization and potential employee exposure. Due to the teratogenic potential, pregnant women should avoid working with urethane. Urethane should be limited in use to non-recovery procedures due to its long term carcinogenic effects in laboratory animals.

**PERSONAL PROTECTIVE EQUIPMENT**

- Lab coat
- Nitrile gloves
- ANSI Z-87 approved safety glasses
- ANSI Z-87 approved chemical safety goggles if a splash hazard exists
- Appropriate laboratory attire.

**Engineering Controls**

- Certified fume hood

**INGREDIENTS**

- Urethane (800 mg/kg)
- PBS
- alpha-chloralose (at least 99% pure, 80 mg/kg)

**MIXING**

- Mix the urethane (800 mg/kg) in solution with PBS.
- Add the alpha-chloralose (at least 99% pure, 80 mg/kg).
- Warm up the solution while continuously stirring, allowing the chloralose to dissolve.
- Allow solution to cool.
- Please see the section on Guidance for Novel Test Compounds & Compounds with No Acceptable Pharmaceutical Grade Alternative for guidance on filtration and preparation.

**DOsing**

- Inject 55 mg/kg IP
- You may want to give a female a smaller dose to start (~70% of male dose), then 20 minutes later, give 10% more of the dose and check the level of anesthesia. Repeat this step until there is no response to tail pinching and the blinking reflex is gone.
REDOSING

- The anesthetic should last for at least 3 hours without needing supplementation.
- Supplement with the same urethane-chloralose solution (re-warm it and stir for a short time before using it), so that the concentration is the same, with no more than 0.2 cc (~10-20% of the initial dosage) at the 4th hour after first injection and every hour afterward or as needed.

NOTES

Urethane is for non-survival procedures only.

STORAGE AND DISPOSAL

Do not administer non-sterile solutions, outdated solutions, high concentrated solutions, or higher doses than recommended above. Store the solution in a sealed container and according to the EHS Chemical Hygiene Plan. Urethane solutions are very stable and can be stored up to 6 months in sealed containers. Dispose of outdated urethane solutions using standard EHS chemical disposal guidelines.

Deviations from the IACUC policy with respect to preparation, dose, storage, and disposal must be outlined and justified in your IACUC protocol.

For more information on the preparation and storage of tribromoethanol, please refer to:


Henshaw PS and Meyer HC (1944) Minimal number of anesthetic treatments with urethane required to induce pulmonary tumors. Journal of the National Cancer Institute 4, 523-525.


Sanctions

Failure to comply with IACUC policies may result in noncompliance reports to the Institutional Official, the Office of Laboratory Animal Welfare (OLAW), the U. S. Department of Agriculture (USDA), and/or the suspension of animal use privileges. In addition, the availability of
sponsored research funds may be affected when an Investigator is found to be in violation of these policies.

## Contacts

<table>
<thead>
<tr>
<th>Subject</th>
<th>Contact</th>
<th>Phone</th>
<th>Fax/Email</th>
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</thead>
<tbody>
<tr>
<td>Availability and acquisition of pharmaceutical grade drugs</td>
<td>Laboratory Animal Resources (LAR)</td>
<td>855-2356</td>
<td><a href="mailto:lar@indiana.edu">lar@indiana.edu</a></td>
</tr>
</tbody>
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## Web Address for this Policy

http://researchcompliance.iu.edu/iacuc/iub/biacuc_policies.html

## Related Information

PHS Policy on Humane Care and Use of Laboratory Animals

http://grants.nih.gov/grants/olaw/references/phspol.html

*The Guide* for the Care and Use of Laboratory Animals, 8th Edition

http://www.nap.edu/catalog.php?record_id=12910

USDA Policy #3: Veterinary Care


## References

Arizona State University “Use of Drugs and Compounds in Animal Studies” 8/13/12

Emory University “IACUC Policy for Non-Pharmaceutical Grade Drugs” 3/4/09

http://www.iacuc.pitt.edu/druglist.pdf


University of Colorado Denver “Use of Non-Pharmaceutical-Grade chemicals/Compounds” 7/12/10
University of Illinois “Policy on Use of Expired Drugs and Materials and Non-Pharmaceutical Grade Compounds in Animals” 12/2/03


University of Houston “Use of Non-Pharmaceutical Grade Compounds in Laboratory Animals” http://www.uh.edu/research/compliance/iacuc/iacuc-pol-guide/Use%20of%20Non-Pharmaceutical%20Compounds_1.15.16.pdf

OLAW Webinar, March 1, 2012. Use of Non-Pharmaceutical-Grade Chemicals and Other Substances in Research with Animals
