Injectable Agents

366.1 Introduction

These guidelines have been formulated to address concerns regarding the reconstitution, storage and use of pharmaceutical and non-pharmaceutical drugs in research using animals by the research community at Emory University. Adherence to these guidelines is required to ensure compliance with both government and manufacturer recommendations while addressing the realities of drug use in the animal research environment. Deviations from, or modifications to, these guidelines must be requested of, and approved by, the IACUC.

366.2 General

366.2.1 Multiple-dose injectable drugs vials and injectable fluids bags should be examined prior to use for evidence of physical or chemical contamination.

366.2.2 Vials or fluids bags that have the following characteristics are considered contaminated and are not to be used:

- Contain particulate matter, precipitates, turbidity, or discoloration
- Mislabeled
- Noticeable coring (damage to the rubber stopper)

366.2.3 Drugs must be stored according to manufacturer's recommendations.

366.2.4 For refrigerated drugs, after the dose to be used is removed from the vial/bag, it should be allowed to reach room temperature prior to injection.

366.3 Withdrawal of drug from vials and fluids bags

366.3.1 The top of the vial or the injection port for fluids bags should be swabbed with an alcohol prep pad prior to each use.

366.3.2 The desired quantity should be withdrawn using a sterile needle and syringe.

366.3.3 At no time will the vial be reentered with a needle/syringe which has been previously used.

366.4 Transferring a drug to another container

366.4.1 If a drug is to be transferred from the original vial and stored in another vial (e.g. diluting or mixing with another drug):

366.4.2 All needles/syringes, vials/containers and fluids used for dilution must be sterile.

366.4.3 If the drug is to be diluted and stored for more than 24 hours, it must be diluted with a sterile fluid containing a preservative (e.g.. bacteriostatic water).

366.4.4 The vial must be labeled with:

- Name of the drug
- Concentration of the drug
- Date of expiration (copied from the original vial)
- Initials of the person who transferred the drug

366.4.5 In the case where two or more drugs are combined with different expiration dates, the earliest expiration date will be used.

366.4.6 All containers, that the drug will be transferred to, must have sealed rubber stoppers

366.4.7 If the original container does not have a rubber stopper, the transfer must be done in a laminar flow hood or biosafety cabinet to ensure sterility

366.5 Expiration

366.5.1 Uncontaminated multi-dose vials must be stored according to manufacturer's recommendations and can be used up to the manufacturer's expiration date provided that they show no signs of contamination.

366.5.2 For reconstituted pharmaceutical grade drugs, the drug must be discarded at the time recommended by the manufacturer.

366.5.3 The vial must be labeled with:

- Date of reconstitution
- Initials of the person who reconstituted the drug
- Date of expiration after reconstitution

366.5.4 For reconstituted non-pharmaceutical grade drugs, the following guidelines should be followed:

- Must be prepared to USP standards for sterility (contact your respective Division of Animal Resources if you need details)
- Initials of the person who reconstituted the drug
- Date of reconstitution
- Solutions derived from non sterile components must be filtered with a sterile 0.22 µm or smaller porosity filter. A very viscous product may require a 0.45 µm filter, but this increases the chance of improper sterilization and may require verification of sterility.
- Date of expiration: Unless indisputable efficacy and quality assurance data can be provided that substantiates a more generous expiration date, the following requirements apply:
    - The drug may be given for up to 24 hours after reconstitution for any of the approved routes of administration of the drug- i.e. intravenously (IV), intraperitoneally (IP), subcutaneously (SC), intramuscularly (IM) or intracranially (IC)
    - The drug may be stored in a refrigerator or freezer for up to 30 days if the vial is sterile and has a sealed rubber stopper. Stored drug may only be used for SC injection. It cannot be use for IP, IV, IM or IC injection. It may not be used for immunocompromised animals after 24 hours.

366.5.6 For single-dose drug vials (without preservatives), the following guidelines for expiration should be followed:

- The drug may be given for up to 24 hours after opening for any of the approved routes of administration of the drug - i.e. IV, IP, SC, IC or IM
- Providing it has been labeled with the date the container was first used, the drug may be stored in a refrigerator for up to 30 days if the vial has a sealed rubber stopper or is sterilely transferred to a vial with a sealed rubber stopper. This drug may only be used for SC injection. It cannot be used for IP, IV, IM or IC injection. It may not be used for immunocompromised animals after 24 hours.

366.5.7 For injectable fluid bags (Lactated Ringers, Sodium Chloride, etc.), the following guidelines for expiration should be followed:

- The fluids may be given for up to 24 hours, after first use, for any approved route of administration.
- Providing it has been labeled with the date the bag was first used, the fluid bag may be stored in a refrigerator for up to 30 days if it has a sealed rubber stopper. This drug may only be used for SC injection. It cannot be used for IP, IV, IM or IC injection. It may not be used for immunocompromised animals after 24 hours.

However, the IACUC recommends strongly to not keep fluid bags more than seven days.

366.5.8 Note: Terminal procedures under anesthesia may be considered for exception to these guidelines with approval from IACUC. Any deviation from those guidelines must be justified and approved by the IACUC.

366.6 Suggestions

- Please note that control drugs must be disposed according to DEA requirements.
- Please, consult the Emory University IACUC policy for the non-pharmaceutical grade drugs at: http://www.emory/edu/IACU/
- Please, consult the Emory University IACUC guidelines for the use of expired materials at: http://www.emory/edu/IACU/
- The use of smaller injectable fluids bags appropriate to the immediate need is recommended to facilitate the implementation of this policy.
- Consider using the "MicroClave Vial Adapter" from Abbott (http://www.abbottanimalhealth.com/) which allows needle free aspiration or mixing of drug solutions in drug vials. Some benefits of that system are:
    - Reduces risk of contamination to vial and drug due to repeat needle sticks to the seal.
    - Prevents leaking due to repeat needle sticks to the seal, reducing loss of medications.
    - Reduces risk of accidental needle stick exposure to staff.

366.7 References

1. Buckley T, Dudley SM, Donowitz LG. 1994. Defining unnecessary disinfection procedures for single-dose and multiple-dose vials. Am J Crit Care. 3(6): 448-51.

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3. United States Pharmcopeia (USP) Chapter 797: Pharmaceutical compounding-Sterile preparations. 2008.
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4. CDC MMWR. 1997. Epidemiological notes and reports of nosocomial bacteremias associated with intravenous fluid therapy—USA. 46 (51): 1227-33.

5. ASHP guidelines on quality assurance for pharmacy-prepared sterile products. 2000. Am J Health Syst Pharm. 57(12): 1150-69.

6. Weil DC, Arnow PM. 1988. Safety of refrigerated storage of admixed parenteral fluids. J Clin Micro. 26(9): 1787-90.

366.8 Document Properties

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