Guidelines for the Use of Preservative-Free Pharmaceuticals and Parenteral Fluids in Laboratory Animals

This Guideline is intended to reiterate the NIH "best Practices" used to ensure the sterility and the integrity of preservative-free pharmaceuticals and parenteral fluids administered to laboratory animals. Consideration of shorter storage times after opening a preservative-free pharmaceutical or parenteral fluid is warranted, because of the variety of conditions under which these products are stored and the potential for use of inappropriate aseptic technique[1]. The US Pharmacopeia—National Formulary (USP-NF) states that opened containers of preservative-free saline for injection or IV fluids should be used within six (6) hours in an area with few particulates in the air[2]. The "best practices" listed below have been used at the NIH to safeguard the stability and efficacy of preservative-free products used in laboratory animals.

1. **Procurement of smaller volume containers of preservative-free pharmaceuticals or parenteral fluids (e.g., saline, Lactated Ringers Solution, water for injection, etc.), that can be handled as a single-use container or discarded within a 24-hour period is recommended.**
2. A preservative-free pharmaceutical or parenteral fluid container that has not been opened or accessed (e.g., needle-punctured), must be discarded in accordance with the manufacturer's expiration date.
3. When-instructions are provided by the manufacturer related to the use of reconstituted preservative-free pharmaceuticals; the reconstituted product must be handled and discarded in accordance with the manufacturer's instructions to ensure the stability, and efficacy of the product.
4. A preservative-free pharmaceutical or parenteral fluid container that has been opened or accessed (e.g., needle-punctured) and not immediately discarded **must be labeled with a maximum "Use-By Date" of not more than 30 days[2] beyond the date of the opening or first access of the container**. Ideally, the container should also be labeled with the date of opening.
5. Preservative-free pharmaceutical or parenteral fluid containers containing dextrose should be discarded 24 hours after the container has been opened or accessed (e.g., needle-punctured).
6. Preservative-free pharmaceutical or fluid containers should be stored in accordance with the manufacturer's recommendations.
7. Prior to use, always examine containers and their contents for evidence of physical damage, contamination, abnormal particulate(s), discoloration, or abnormal turbidity.
8. Never use pharmaceutical or fluid containers found to have any of the following characteristics:
   a. Mislabeled
   b. Noticeable coring, damage or deterioration of the stopper or access diaphragm
   c. Outdated
9. Pharmaceutical or parenteral fluid containers must be discarded whenever sterility is compromised or questionable.

10. Special attention must be paid to avoid contaminating the pharmaceutical or fluid container while penetrating the stopper or access diaphragm. When and where appropriate, the stopper or access diaphragm of a fluid container must be cleaned with 70% alcohol prior to each use. Use care to avoid contaminating the cleaned area before penetrating the stopper.
11. Only sterile needles, syringes, pipettes, and pipette tips, shall be used to withdraw fluids from a container for parenteral administration.
12. At no time shall a fluid container be reentered with a needle that has been previously used to inject an animal.
13. Using one sterile needle to quickly fill multiple sterile syringes, without removing the needle from the container, can help to protect the integrity of the stopper or access diaphragm. Care must be used when changing the syringe not to contaminate the needle hub or syringe tip. A needle, which is not attached to a sterile syringe, should not be left in the stopper or access diaphragm of a fluid container.
14. The introduction of air into a container to facilitate withdrawal of the fluids should be kept to a minimum.

Reference

1. Matthews, K. and Taylor, D., Assessment of Sterility in Fluid Bags Maintained For Chronic Use; J. American Association for Laboratory Animal Science, Vol. 50, No. 5, Pages 708-712, September 2001.
2. United States Pharmacopeia-National Formulary (USP34-NF 29). United States Pharmacopeial Convention. 2011.

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