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, due to 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 in an ISO Class 5 environment [2]. While the use of parenteral fluids past the 6-hour standard recommended by the USP can be viewed as low risk, the consequences of contaminated fluid administration can be animal morbidity or mortality as well as altered research data. 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 at the end of the work day is recommended.**
2. However, a preservative-free parenteral fluid container that has been opened or accessed (e.g., needle-punctured) and which is not immediately discarded **must be labeled with a maximum "beyond use date" of not more than 28 days[1,3] beyond the date of the opening or first access of the container, unless otherwise specified by the manufacturer**. Ideally, the container should also be labeled with the date of opening.
3. When provided, manufacturer instructions as to handling and discarding of reconstituted preservative-free pharmaceuticals must be followed to ensure the stability, and efficacy of the product.
4. 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.
5. Preservative-free pharmaceutical or parenteral fluid containers containing dextrose should be discarded by the end of the day the container was 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. Containers and their contents should be examined prior to use for evidence of physical damage, contamination, abnormal particulate(s), discoloration, or abnormal turbidity.
8. Pharmaceutical or fluid containers found to have any of the following characteristics should never be used
    a. mislabeled
    b. noticeable coring, damage or deterioration of the stopper or access diaphragm

c. outdated,
d. improperly stored.

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. The user should perform proper hand hygiene: by washing hands with soap and water, using hand sanitizers, and/or donning clean gloves. The stopper or access diaphragm of a fluid container must be cleaned with 70% alcohol and allowed to dry prior to each use, using 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 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.

References

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 2011.
2. United States Pharmacopeia-National Formulary (USP38-NF33). United States Pharmacopeial Convention. 2016.
3. Unpublished data (2016) of cultures of preservative-free fluids in use in two separate animal facilities. One facility's samples remained sterile for bacteria (anaerobes, aerobes and Mycoplasma) and fungi for a total of 56 days. From 8 bottles, the average number of taps/bottle was 11.8 (range 5-33). The other facility tested several random use bags of preservative free fluids (5% Dextrose, Saline, water) after 30 days of use and were found negative for colony forming units.

Approved – 01/11/2012, 04/27/16