

## ASHP Guidelines on Pharmacy-Prepared Ophthalmic Products

Pharmacists are frequently called on to prepare sterile products intended for ophthalmic administration when a suitable sterile ophthalmic product is not available from a licensed manufacturer. These products may be administered topically or by subconjunctival or intraocular (e.g., intravitreal and intracameral) injection and may be in the form of solutions, suspensions, or ointments.

The sterility of these products, as well as accuracy in the calculation and preparation of doses, is of great importance. Ocular infections and loss of vision caused by contamination of extemporaneously prepared ophthalmic products have been reported.<sup>1,2</sup> Drugs administered by subconjunctival or intraocular injection often have narrow therapeutic indices. In practice, serious errors in technique have occurred in the preparation of intravitreal solutions, which resulted in concentrations up to double the intended amounts.<sup>3</sup> To ensure adequate stability, uniformity, and sterility, ophthalmic products from licensed manufacturers should be used whenever possible.

The following guidelines are intended to assist pharmacists when extemporaneous preparation of ophthalmic products is necessary. These guidelines do not apply to the manufacturing of sterile pharmaceuticals as defined in state and federal laws and regulations. Other guidelines on extemporaneous compounding of ophthalmic products also have been published.<sup>4,5</sup>

1. Before compounding any product for ophthalmic use, the pharmacist should review documentation that substantiates the safety and benefit of the product when administered into the eye. If no such documentation is available, the pharmacist must employ professional judgment in determining suitability of the product for ophthalmic administration.
2. Important factors to be considered in preparing an ophthalmic medication include the following:<sup>6</sup>
  - a. Sterility.
  - b. Tonicity.
  - c. pH, buffering.
  - d. Inherent toxicity of the drug.
  - e. Need for a preservative.
  - f. Solubility.
  - g. Stability in an appropriate vehicle.
  - h. Viscosity.
  - i. Packaging and storage of the finished product.
3. A written procedure for each ophthalmic product compounded should be established and kept on file and should be easily retrievable. The procedure should specify appropriate steps in compounding, including aseptic methods, and whether microbiologic filtration or terminal sterilization (e.g., autoclaving) of the finished product is appropriate.
4. Before preparation of the product is begun, mathematical calculations should be reviewed by another person or by an alternative method of calculation in order to minimize error. This approach is especially important for products, such as intraocular injections, for which extremely small doses are frequently ordered, necessitating multiple dilutions. Decimal errors in the preparation of these products may have serious consequences.
5. Accuracy in compounding ophthalmic products is further enhanced by the use of larger volumes, which tends to diminish the effect of errors in measurement caused by the inherent inaccuracy of measuring devices. Larger volumes, however, also necessitate special attention to adequate mixing procedures, especially for ointments.
6. Strict adherence to aseptic technique and proper sterilization procedures are crucial in the preparation of ophthalmic products. All extemporaneous compounding of ophthalmic products should be performed in a certified laminar airflow hood (or, for preparing cytotoxic or hazardous agents, a biological safety cabinet).<sup>5</sup> Only personnel trained and proficient in the techniques and procedures should prepare ophthalmic products. Quality-assurance principles for compounding sterile products should be followed, and methods should be established to validate all procedures and processes related to sterile product preparation. In addition, the following should be considered:
  - a. Ingredients should be mixed in sterile empty containers. Individual ingredients often can first be drawn into separate syringes and then injected into a larger syringe by insertion of the needles into the needle-free tip of the larger syringe. The larger syringe should be of sufficient size to allow for proper mixing of ingredients.
  - b. To maximize measurement accuracy, the smallest syringe appropriate for measuring the required volume should be used. When the use of a single syringe would require estimation of the volume (e.g., measuring 4.5 ml in a 5-ml syringe with no mark at the 4.5-ml level), the use of two syringes of appropriate capacities (or two separate syringe “loads”) should be considered in order to provide a more accurate measurement.
  - c. A fresh disposable needle and syringe should be used at each step to avoid contamination and prevent error due to residual contents.
  - d. When multiple dilutions are required, the containers of interim concentrations should be labeled to avoid confusion.
  - e. In the preparation of an ophthalmic product from either (1) a sterile powder that has been reconstituted or (2) a liquid from a glass ampul, the ingredients should be filtered through a 5- $\mu$ m filter to remove any particulate matter.
7. For ophthalmic preparations that must be sterilized, an appropriate and validated method of sterilization should be determined on the basis of the characteristics of the particular product and container. Filtration of the preparation through a 0.22- $\mu$ m filter into a sterile final container is a commonly used method; however, this method is not suitable for sterilizing ophthalmic

suspensions and ointments.<sup>7</sup> When an ophthalmic preparation is compounded from a nonsterile ingredient, the final product must be sterilized before it is dispensed. Sterilization by autoclaving in the final container may be possible, provided that product stability is not adversely affected and appropriate quality control procedures are followed.<sup>6</sup>

8. Preservative-free ingredients should be used in the preparation of intraocular injections, since some preservatives are known to be toxic to many of the internal structures of the eye.<sup>6</sup>
9. In the preparation of ophthalmic products from cytotoxic or other hazardous agents, the pharmacist should adhere to established safety guidelines for handling such agents.<sup>8,9</sup>
10. The final container should be appropriate for the ophthalmic product and its intended use and should not interfere with the stability and efficacy of the preparation.<sup>10</sup> Many ophthalmic liquids can be packaged in sterile plastic bottles with self-contained dropper tips or in glass bottles with separate droppers. Ophthalmic ointments should be packaged in sterilized ophthalmic tubes. Injectables that are not for immediate use should be packaged in sterile vials rather than in syringes, and appropriate overfill should be included. All containers should be adequately sealed to prevent contamination.
11. The pharmacist should assign appropriate expiration dates to extemporaneously prepared ophthalmic products; these dates should be based on documented stability data as well as the potential for microbial contamination of the product.<sup>11</sup> The chemical stability of the active ingredient, the preservative, and packaging material should be considered in determining the overall stability of the final ophthalmic product.<sup>12</sup>
12. Ophthalmic products should be clearly and accurately labeled. In some cases, it may be appropriate to label the products with both the weight and concentration of active ingredients and preservatives. Labels should also specify storage and handling requirements and expiration dates. Extemporaneously prepared ophthalmic products dispensed for outpatient use should be labeled in accordance with applicable state regulations for prescription labeling.

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*These guidelines were reviewed in 2003 by the Council on Professional Affairs and by the Board of Directors and were found to still be appropriate.*

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