AMERICAN ACADEMY OF OPHTHALMOLOGY®

Editorial

Waste No More

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As a teenager, I fondly remember volunteering on days specifically designated for recycling at the town dump, formally called the landfill. I sorted glass bottles by color and had the privilege of being one of the individuals pulverizing the glass into little bits so that it could be recycled. It was great fun for an energetic teenager.

The original town had been built on a piece of land that had 3 main ridges. The center ridge was Main Street. The town, as a colonial town, was a couple of hundred years old and had survived 3 lost battles to the British during the Revolutionary War; thus, old ways did not change easily. The town's landfill sat at the edge of town, below the lowest ridge. To a teenager, it was a huge piece of land that seemed unlikely ever to be filled completely.

From my view at the edge of this large landfill and tons of waste, it was hard for me to imagine how this little amount of glass would make a dent in the large amount of waste placed in the landfill each day. The landfill seemed to go as far as the eye could see. There was plenty of room for more, and it definitely never occurred to me that maybe we should be using less glass.

As the son of an ophthalmologist, eventually following my father's path to medical school and into ophthalmology, I learned the preoperative and operative routines associated with surgery. Some of the accepted routines or rules were based on scientific data for achieving better outcomes. Some were performed a particular way because that is what had been done before and why should anyone change them? One of these rules was that drug products used in the preoperative setting or the operating room were used only once. These products would never be used again at a later time, and were never used on a different patient. One use, and they were tossed into the medical waste. The amount of used product did not matter, even if the product had never been used on the patient. If it had been opened, it was thrown out at the end of the surgical case.

I have now been involved in ophthalmic drug development for more than 33 years. I learned to follow the science and the law. The way it had been done before may have been worth following if it were based on the science or the law, but it was always worth questioning. As a clinician, I count on having safe and effective products available to patients. Therefore, it is frustrating to see products in shortage or otherwise not available to patients, in part because the product has been thrown out unnecessarily. Currently, some institutions have instituted policies and rules that require discarding ophthalmic drug products after a single use, despite the packaging being a multiple-dose container. These policies often lack a scientific basis and contribute to drug shortages that make it difficult for some physicians to obtain these products. I would like to suggest that it is past time to question these internal rules or policies.

It is important to examine the justification of policies that require an ophthalmic medication to be discarded before the expiration date listed on the bottle. Most commonly, the justification is not a scientifically based study, but rather a misinterpreted citation of some other group. These other groups can be the Food and Drug Administration (FDA), the United States Pharmacopeia (USP), or The Joint Commission (TJC). As it turns out, none of these groups require a medication to be discarded before the expiration date listed on the bottle. To be sure, it is possible to contaminate an ophthalmic bottle during use. No one suggests that a contaminated bottle be used to dispense a medication to a patient, particularly before surgery, but this is not a new issue and it has been reviewed scientifically.

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In 1953, the FDA first published in the Federal Register a notice to manufacturers and re-packers of ophthalmic solutions stating that liquid preparations for ophthalmic use contaminated with viable micro-organisms had been responsible for serious eye injuries (18 FR 351 [1953], Friday, January 16, 1953). The FDA concluded that liquid ophthalmic preparations packed in multiple-dose containers (1) should contain 1 or more suitable and harmless substances that will prevent the growth of micro-organisms or (2) should be so packaged as to volume, type of container, and duration of use and with warnings as would afford adequate protection and would minimize the hazard of injury resulting from contamination during use.

In 1964, the FDA finalized a regulation (29 FR 12458 [1964]) requiring liquid preparations intended for ophthalmic use to be sterile and, if packaged in multiple-dose containers: (1) should contain 1 or more suitable and harmless substances that will inhibit the growth of micro-organisms or (2) should be so packaged as to volume, type of container, duration of use, and with warnings to afford adequate protection and minimize the hazard of injury resulting from contamination during use. The implementation of this regulation has been incorporated into the approval process that permits multiple-dose ophthalmic drug products to be approved and used safely in the United States.

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Before approval, manufacturers of multiple-dose ophthalmic products are required to establish the minimum concentration of an antimicrobial preservative to inhibit the growth of potential microbiological contaminants. The criteria are specified in the USP and include bacteria, yeasts, and molds. The concentration of the antimicrobial preservative is monitored throughout the entire shelf life of the product to ensure that the product is capable of continually affording adequate protection from injury should contamination occur during use. Monitoring of the concentration of the antimicrobial preservative as well as periodic contamination testing as specified in the USP is conducted routinely during stability studies. The established shelf life is reviewed and included in the FDA's approval of each specific drug product application. The lot number and expiration date of the product are required to be included on the bottle of every approved new drug product.

The inclusion of an antimicrobial preservative might seem unnecessary in a setting such as the operating room or professional office, where trained paraprofessionals and professionals will be administering the drug product, but this added protection is designed to minimize further any chances of injury should a contamination event occur. This additional level of protection also enables the drug product to be administered to multiple different patients over the course of time until the bottle's stated expiration date. Although the number of different individuals is not limited, the duration of use is limited by the expiration date included on the bottle.

The FDA uses established testing methodology to set appropriate expiration dating periods. To assure that a drug product meets applicable standards of identity, strength, quality, and purity at the time of use, the United States Code of Federal Regulations (21 CFR 211.137) states that the drug product shall bear an expiration date determined by appropriate stability testing described in 21 CFR 211.166. Artificial expiration dates, such as 28 days after opening on ophthalmic drug bottles, or restricting the use of ophthalmic drug bottles to a single patient use are not set with the same rigor. To the best of my knowledge, no scientific data support these artificial expiration dates or restrictions in use for topical ophthalmic drug products.

Some ophthalmic drug products have a short shelf life. These products are marked clearly with labeling that describes the expected storage conditions and the supported shelf life. Some ophthalmic drug products are appropriate for administration only to a single patient. These products are marked clearly with labeling that describes that the product is to be used only for a single patient. Products not labeled as single-dose or single-use ophthalmic products are not intended to be limited in use to a single patient. When stored as labeled, products can be expected to be used safely after opening until the expiration date included on the bottle. Many, although not all, of these bottles are labeled specifically with statements clarifying that after the bottle is opened, they can be used until their identified expiration date.

The location of the use of an ophthalmic drug product does not influence the expiration date except where the location may alter the storage temperature of the bottle. The strength and quality of an ophthalmic drug may be affected by the storage conditions, most notably the temperature. For that reason, the storage conditions on which the expiration date is based are included in the drug product's labeling. Storage of the ophthalmic bottle under conditions that differ from the drug product's labeling may alter the period that the product can be expected to maintain its strength and quality. If an alternative temperature condition can be used for a limited time without affecting the ophthalmic product, such alternative temperature conditions will be included in the labeling. Other factors, such as use in the operating room, use in a hospital room, use in an examination room, or use in a patient's home, should not be expected to alter the strength or quality of the ophthalmic drug product.

Neither TJC nor the USP has requirements to use ophthalmic drug products within 28 days. Each historically has discussed 28-day limitations for systemically injected products, but neither has ever included, nor has meant to include, ophthalmic products in those discussions. Direct communication with TJC has confirmed that no 28-day limitation for ophthalmic products by TJC exists.

I have returned to visit that colonial town where I grew up. The town hall in the center of Main Street is still the same building. However, the town landfill has been replaced by larger areas for recycling and a transfer station, a recognition that sometimes it is important to change from the past. I suggest that old customs without rationales in the preoperative and operating room also should change. If the vast landfill that I knew as a teenager can be filled, it is past time to look for ways to reduce waste. Maybe the next time you throw away an uncontaminated bottle before the expiration date stamped on that bottle, you should consider what you will do if another bottle is not available.

Footnotes and Disclosures

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