

mildly alkaline wash will only delay the start of treatment. Washing should begin as close in time and place to the site of the accident as possible.” *Conn’s Current Therapy 1990* (Ref. 10) states:

The severity of the chemical burn is related directly to length of time that a given agent is exposed to the skin * * *. Exact identification of the burning chemical may suggest appropriate specific measures; but an acid should not be neutralized with a base or vice versa.

The agency is concerned that attempts to adjust the pH of the affected area, such as by testing with litmus paper and then adding drops of neutralizing solution, would delay or, at a minimum, reduce the vigorous flushing needed to prevent further eye damage. Therefore, the agency tentatively concludes that initial treatment is best accomplished by copious and continuous amounts of water or saline solution. Any attempt to provide a corrective solution, if necessary, should be left to health care professionals following transport of the accident victim to the facility’s first aid station or a hospital. Accordingly, the agency considers the term neutralization as inappropriate to describe the pharmacological action of these products.

B. Water Lavage

Four comments emphasized the importance of immediate and continuous water lavage for emergency care of the eye following chemical burns. The Tulane University Research Report (Ref. 7) compared administration of 50 milliliters (mL) of distilled water and a test product, called “Neutralize” (exact formulation not provided), to each eye 10 seconds after acid was dropped on the eye. The studies showed no significant difference in the rate of healing or in the final condition of both eyes.

The agency agrees that the medical literature and the American Academy of Ophthalmology support the use of copious amounts of fluid as the best approach for emergency eyewash care. The agency also recognizes the value of providing a sterile and stable product in large quantities in an industrial setting where flowing water may not be available.

C. Container Size and Ease of Opening

One comment referred to a 32-ounce (oz) container, intended for only one use, as having a closure that requires 1¼ turns. The comment explained that a 38-millimeter unrestricted opening is approximately the diameter needed to cover an average adult eye. The comment added that this product is easily opened by a small stature adult under stress. The comment noted that a

tamper evident plastic heat shrink seal that breaks away easily is used.

All eyewash products must comply with the monograph standards in part 349. The products must also meet current good manufacturing practices (CGMPs) as stated in 21 CFR parts 210 and 211.

The agency believes that emergency eyewash products must contain enough fluid to permit adequate flushing of the eye. While a maximum volume may depend on the configuration of the container or the plumbing system, the minimum volume should be no less than 16 oz (473 mL (500 mL or 1/2 liter is acceptable)). Because of concerns about sterility, the product should be for a single individual’s use unless it is part of a plumbing system with a one-way valve.

D. pH Adjustment

Several comments supported the pH range of 6.6 to 7.4 as appropriate for these products. One comment mentioned a lack of adverse event reports in the many years of use of these products as an indicator that the present pH is appropriate. Another comment stated it was unlikely that the pH of a product would have a clinically significant impact on the outcome of a chemical burn. One comment, however, felt that the agency should not require a specific range but define the requirement as “needing to be at or near neutral pH, 6.6 to 7.4.”

The agency agrees that 6.6 to 7.4 is an appropriate pH range for emergency eyewash solutions. The agency believes this pH range provides sufficient flexibility for manufacturers to adjust agents to maintain stability, yet provides a solution that does not cause further harm or additional irritation to the accident victim. The agency, however, agrees that the pH within this range is not likely to impact on the outcome of a chemical burn. The agency believes that the inclusion of an antimicrobial preservative would aid the stability of the product.

Accordingly, the agency is proposing the following in new § 349.22

Emergency first aid eyewashes: “These products contain water, agents to achieve the pH within a range of 6.6 to 7.4, and a suitable antimicrobial preservative agent.”

E. Buffering

One comment noted that buffering is an added feature to help neutralize the chemical burn but that both buffered and unbuffered solutions can be extremely beneficial to achieve dilution and neutralization because the main treatment is by dilution. Another

comment added that buffers help ensure product integrity during storage in an industrial setting, while another comment was unaware of any superiority of either buffering or not buffering.

The product that led to the request for data was described as a sterile phosphate buffered solution (Ref. 1) for use immediately following a chemical burn to thoroughly flush the eyes and skin for the express purpose of removing the chemical irritant, and to relieve the discomfort and burning caused by the irritating chemical prior to seeking medical treatment. The comment provided excerpts from studies presented in a Tulane University Research Report (Ref. 7) to demonstrate the superiority of its product when compared to water as an emergency first aid eyewash to treat a caustic acid splash.

The agency notes that a medical dictionary (Ref. 16) defines “buffering” as “a chemical system that prevents change in concentration of another chemical substance, e.g., proton donor and acceptor systems serve as buffers preventing marked changes in hydrogen ion concentration (pH).” The agency acknowledges the buffer system contributes to the tonicity of the ophthalmic product but adds that the tonicity of the entire formulation should approximate lacrimal fluids.

The agency agrees with the comment that stated it was unaware of any superiority of either buffering or not buffering these products. Accordingly, the agency is proposing in § 349.22 that emergency first aid eyewash products may contain agents for buffering the pH.

F. Phosphate Treatment of Chemical Burns

One comment provided references to support “phosphate therapy” to treat burns caused by acidic or basic substances (Ref. 1). The references reported a phosphate buffer is prepared by dissolving 70 grams (g) of monobasic potassium phosphate (KH_2PO_4) and 180g of dibasic sodium phosphate ($\text{Na}_2\text{HPO}_4 \cdot 12 \text{H}_2\text{O}$) in 850 mL of water. The concentration of the solution is molar with respect to phosphate, but as the phosphates are physiologically occurring substances they can be safely employed in such high concentrations and provide prompt neutralization. The comment contended that some antidotes are too acidic or alkaline; that burns caused by acids or bases require different treatment; and that the phosphate buffer is neutral in its reaction, and thus is well suited for the treatment of injuries caused by acidic or basic chemicals.