Published in final edited form as:

J Am Acad Dermatol. 2016 August ; 75(2): 454–455. doi:10.1016/j.jaad.2016.03.051.

Ensuring that injectable bicarbonate-buffered lidocaine-epinephrine complies with 2015 *United States Pharmacopeia* (USP) compounding provisions

Prescilia Isedeh, MD^a, M. Laird Forrest, PhD^b, Deede Liu, MD^a, and Daniel Aires, MD, JD^a

^aDivision of Dermatology, University of Kansas Medical Center, Kansas City, Kansas

^bDepartment of Pharmaceutical Chemistry, University of Kansas, Lawrence, Kansas

Keywords

bicarbonate-buffered lidocaine-epinephrine; compounded sterile preparations; International Organization for Standardization class; microbial risk; *United States Pharmacopeia*

Lidocaine's rapid onset and relatively short duration make it a popular choice in dermatology practice.¹ Because it is pregnancy category B, lidocaine can safely be used in most patients, including children and pregnant women.^{1,2}

Epinephrine is often added at 1:100,000 or 1:200,000 to constrict blood vessels, thus prolonging the duration of anesthesia. Because epinephrine is stable only in acidic environments, pH of lidocaine-epinephrine is lowered to 3.5 to 5.5 via acidic preservatives.¹ This can cause injection site pain, and delay anesthesia onset.¹ "Buffering" by adding 1 part 8.4% sodium bicarbonate to 10 parts lidocaine-epinephrine can raise pH to address both pain and delay.^{1,2} Other less commonly used local anesthetics such as bupivacaine and mepivacaine can also be buffered.³ Combining 2 medicines, such as lidocaine-epinephrine + bicarbonate, in a single syringe, is considered to be "compounding," defined as combining, mixing, or altering ingredients of 2 or more drugs to create a medication tailored to the needs of an individual patient.⁴ Because epinephrine activity declines at 25% per week in alkaline or neutral environments, standard texts recommend that it be used within 1 to 2 weeks after initial preparation.^{1,2,5,6} Because infections from in-office compounding of lidocaine-epinephrine + bicarbonate have not been reported, textbook guidelines are based on the loss of epinephrine activity rather than the potential infection risk.

The *United States Pharmacopeia* (USP) Convention develops and publishes standards for drug substances, drug products, excipients, and dietary supplements in the USP-National Formulary. USP drug standards are enforceable in the United States by the Food and Drug Administration (FDA), and these standards are used in more than 140 countries.⁷ USP-National Formulary standards for compounded preparations may be enforced by both the

states and FDA, as compounded preparations remain subject to the adulteration and misbranding provisions of the Federal Food, Drug, and Cosmetic Act, which require conformance to *USP*–National Formulary standards.⁷ In 2015, the *USP* published revised *USP* General Chapter<797>Pharmaceutical Compounding–Sterile Preparations. These standards apply to all compounded sterile preparations. *USP*<797> covers all persons who prepare medications and all places where they are prepared, including physician’s offices. The main objective of *USP*<797> is preventing harm from microbial contamination, bacterial endotoxins, chemical and physical contaminants, and other dangers.⁸

High-risk-level compounded sterile preparations are either contaminated or at a high risk for contamination, such as preparations not compounded under International Organization for Standardization class-5 conditions by improperly garbed personnel. Virtually all dermatology offices fall into the high-risk category. The recommended compounded sterile preparation storage period for high-risk-level preparation cannot exceed 24 hours at controlled room temperature, or 3 days at cold temperature, which is defined as any temperature not exceeding 8°C (46°F).⁸

The *USP* also has an immediate use provision that allows drug products to be prepared without International Organization for Standardization class-5 containment, gowning, and other precautions immediately before patient use. This exemption is intended for those cases where containment facilities would not be available normally or patient health would be at risk by waiting. Examples might be drugs for cardiac resuscitation or ambulance drugs; most drug treatment situations in dermatology practice would not meet the requirements of immediate use.⁸ Noncompounded multidose containers such as lidocaine or lidocaine + epinephrine vials generally contain antimicrobial preservatives, and unless otherwise specified by the manufacturer, the *USP* recommends a 28-day beyond-use date after initial opening.⁸

Research on contamination rates in actual or simulated office-based practice environments may be of use in drafting future regulations.

Acknowledgments

This piece received no specific grant from any funding agency in the public, commercial, or not-for-profit sectors. Dr Forrest’s efforts were funded in part by National Institutes of Health grants NCI 1R01CA173292 and FDA 1U01FD005285.

References

1. Hruza, GJ. Anesthesia. In: Bologna, JL.; Jorizzo, JL.; Schaffer, JV., editors. *Dermatology*. China: Elsevier Limited; 2012. p. 2343-2352.
2. Huether, MJ.; Weinberger, CH.; Brodland, DG. Local anesthetics. In: Wolverton, SE., editor. *Comprehensive Dermatologic Drug Therapy*. New York (NY): Elsevier; 2013. p. 637-651.
3. Soriano, TT.; Breithaupt, A.; Chestnut, C. Anesthesia and analgesia. In: Robinson, JK.; Hanke, CW.; Siegel, DM.; Fratila, A., editors. *Surgery of the Skin: Procedural Dermatology*. London (United Kingdom): Elsevier Inc; 2015. p. 43-63.
4. US Food and Drug Administration. Compounding and the FDA: questions and answers. Washington, (DC): Available from: URL: <http://www.fda.gov/Drugs/>

[GuidanceComplianceRegulatoryInformation/PharmacyCompounding/ucm339764.htm](https://www.fda.gov/oc/ohrt/GuidanceComplianceRegulatoryInformation/PharmacyCompounding/ucm339764.htm). Accessed January 14, 2016

5. Stewart JH, Cole GW, Klein JA. Neutralized lidocaine with epinephrine for local anesthesia. *J Dermatol Surg Oncol*. 1989; 15:1081–1083. [PubMed: 2794204]
6. Larson PO, Ragi G, Swandby M, et al. Stability of buffered lidocaine and epinephrine for local anesthesia. *J Dermatol Surg Oncol*. 1991; 17:411–414. [PubMed: 2030202]
7. The United States Pharmacopeial Convention. Learn about US Pharmacopeial Convention. Available from: <http://www.usp.org/about-usp>. Accessed February 23, 2016
8. US Pharmacopeial Convention Inc. General chapter <797>: pharmaceutical compounding of sterile preparations. *United States Pharmacopeia 38th rev and National Formulary*. 33rd. Rockville (MD): United States Pharmacopeial Convention; 2015. p. 567-611.