



HARM REDUCTION AND OVERDOSE PREVENTION Fact Sheet

Legality of Expired Naloxone in Missouri

Background


Drug overdose is a nationwide epidemic that claimed the lives of over 100,000 people in the United States in the past year alone.¹ Opioids, either alone or in combination with other drugs or alcohol, were responsible for approximately 75% of these deaths. Many of those 75,000 people would be alive today if they had been administered the opioid antagonist naloxone and, where needed, other emergency care.² In light of the ongoing crisis, all fifty states and the District of Columbia have modified their laws to increase access to naloxone, the standard first-line treatment for opioid overdose.³

While these laws have been successful in increasing access to this lifesaving medication, few explicitly address the legality of distributing and administering naloxone that is past its expiration date.⁴ As many governmental and non-governmental organizations increasingly have stocks of such expired naloxone, it is important to determine whether that naloxone may be distributed to individuals or organizations that are able to utilize it. This is especially true considering the unprecedented shortage of injectable naloxone that has been plaguing the country since early 2021.⁵

This fact sheet briefly discusses the efficacy of expired naloxone and examines whether Missouri law permits the distribution and administration of such naloxone. We conclude that, while Missouri law limits or prohibits the distribution of expired medications by pharmacies and some other organizations, it is silent on the distribution of expired naloxone by harm reduction organizations and the administration of expired naloxone by laypersons. Further, we find that the criminal and civil immunity provided in the state's naloxone access law likely applies to the provision and use of expired naloxone to the same extent it applies to non-expired naloxone.

Efficacy of Expired Naloxone

Numerous studies have demonstrated that naloxone retains its potency long past its expiration date, even when kept in less-than-ideal conditions. In perhaps the most comprehensive study on the subject, expired naloxone samples – some which expired as early as the early 1990's - were obtained from fire departments, emergency medical services and law enforcement agencies.⁶ Upon testing, it was discovered that these samples, which had mostly been stored in ambulances, police cars, and similar environments, retained nearly



all of their active ingredient even after nearly 30 years in storage. Only one sample, which was more than 25 years past its expiration date, had fallen to below 90% of its original strength.⁷

While that study was conducted with naloxone vials designed for injection with a needle and syringe, similar results have been obtained with Evzio, an auto-injector device, and Narcan, a nasal spray. Testing on several of these products that were at least one year past their listed expiration date revealed that they all retained greater than 100% of their labeled naloxone concentration. The researchers who conducted that study noted that the data suggests “extending the shelf life of these products” to “aid in avoiding the significant expense of replacing them every two years and also increase the availability” of naloxone in communities.⁸

Even extremes of heat and cold seem to do little to impact the efficacy of naloxone. In another study, ampoules of naloxone were cycled through repeated heating and cooling cycles for 28 days. These samples, which had been either repeatedly cooled to around -70 degrees Fahrenheit or heated to around 176 degrees Fahrenheit, “remained at comparable concentrations as ampoules stored at room temperature.”⁹

Summary of Relevant Missouri Law

Missouri has taken several steps to increase access to naloxone. First, state law permits the director of the department of health and senior services to issue a statewide standing order for an opioid antagonist,¹⁰ which he has done.¹¹ Licensed pharmacists are permitted to sell and dispense an opioid antagonist (such as naloxone) under either a physician protocol or the statewide standing order.¹² Both pharmacists who, acting in good faith and with reasonable care, sell or dispense an opioid antagonist as well as a physician that writes a protocol for it to be dispensed are immune from criminal liability, civil liability, and disciplinary action for any outcomes related to those actions.¹³

Notwithstanding any other law or regulation to the contrary, any person may possess naloxone or another opioid antagonist,¹⁴ and any person or organization acting under a standing order may store and dispense an opioid antagonist so long as they do not collect a fee or compensation for dispensing it.¹⁵ An organization that is permitted to obtain an opioid antagonist under the law is permitted to store it without “being subject to the licensing and permitting requirements” of the chapter that regulates pharmacists and pharmacies.¹⁶ Any person, acting in good faith and with reasonable care, is immune from criminal prosecution, disciplinary actions from his or her professional licensing board, and civil liability due to the administration of the opioid antagonist to another person whom they believe to be suffering an opioid-related overdose.¹⁷

Missouri law does contain several provisions explicitly related to expired and out of date medications. For example, regulations governing residential care and assisted living facilities,¹⁸ long-term care facilities,¹⁹ and hospice facilities²⁰ require the disposal or return of expired drugs. The state’s drug depository program, which permits the donation of unused drugs, supplies, and medical devices to uninsured and underinsured patients in the state, requires participating organizations to only accept drugs that are not within six months of their expiration date.²¹

The Board of Pharmacy has also promulgated several regulations related to expired drugs. Perhaps most importantly, the pharmacist-in-charge must ensure that “no outdated drugs are dispensed or maintained within the active inventory of the pharmacy, including prescription and related nonprescription items.”²² Additionally, registered pharmacies must separate drugs and devices that are “maintained as part of the pharmacy inventory or are being processed for dispensing or other distribution purposes ... from... drugs that are ... outdated.”²³ The label of dispensed prescription drugs is required to include the expiration date of the drug.²⁴



Legal Analysis

Missouri law imposes several restrictions on the acquisition, distribution, storage, and use of expired medications, including naloxone. However, these restrictions apply only to specific entities such as pharmacies and other regulated facilities. There are no laws prohibiting the distribution of expired naloxone from harm reduction organizations and similar outlets. Further, Missouri law permits individuals and organizations acting under a standing order to store and dispense an opioid antagonist “[n]otwithstanding any other law or regulation to the contrary”.²⁵

“Opioid antagonist” is defined as “naloxone hydrochloride that blocks the effects of an opioid overdose...”²⁶ As noted above, naloxone retains its ability to block the effects of opioid overdose well after its listed expiration date. This language could therefore reasonably be read as permitting those entities to distribute expired naloxone even if doing so would otherwise be prohibited.

While there are no relevant cases on the question, due to the demonstrated negative consequences associated with opioid overdose and the strong evidence that naloxone, even when expired, reverses the effects of opioids, it is likely that the civil and criminal immunity provisions of the naloxone access law would apply to expired naloxone to the same extent that they apply to non-expired naloxone.²⁷ Further, it is likely that a person who received naloxone via prescription or standing order would be protected from civil and criminal liability for administering the expired naloxone.

Conclusion

Certain regulated facilities in Missouri, including pharmacies, are prohibited from using or dispensing expired medications, including naloxone. However, no law prevents harm reduction organizations from distributing expired naloxone to the same extent they are permitted to distribute non-expired naloxone, and laypeople who possess expired naloxone can likely administer it in the event of an overdose without fear of legal repercussions.

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¹ National Center for Health Statistics. Vital Statistics Rapid Release: Provisional Drug Overdose Death Counts. 2021; <https://www.cdc.gov/nchs/nvss/vsrr/drug-overdose-data.htm>. Accessed January 18, 2022.

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- ² Opioid overdose is caused by excessive depression of the respiratory and central nervous systems. Naloxone, a κ - and δ , and μ -opioid receptor competitive antagonist, works by displacing opioids from these receptors, thereby reversing their depressant effect. See Chamberlain JM, Klein BL. A comprehensive review of naloxone for the emergency physician. *Am J Emerg Med.* 1994;12(6):650-660.
- ³ For a comprehensive list of state naloxone access laws, see Network for Public Health Law, Legal Interventions to Reduce Overdose Mortality: Naloxone Access Laws. <https://www.networkforphl.org/wp-content/uploads/2021/04/NAL-FINAL-4-12.pdf>.
- ⁴ Colorado is a notable exception. There, state law explicitly extends immunity protections to individuals who furnish or administer expired naloxone. See Colo. Rev. Stat. § 13-21-108.7(3)(a); Colo. Rev. Stat. § 18-1-712(2)(a). The Colorado Consortium for Prescription Drug Abuse Prevention has created an Expired Naloxone Program toolkit that walks agencies through the process of donating expired naloxone. See Colorado Consortium for Prescription Drug Abuse Prevention, Expired Naloxone Donation program, <https://corxconsortium.org/projects/expired-naloxone/>.
- ⁵ See Kornfeld M. Affordable naloxone is running out, creating a perfect storm for more overdose deaths, activists say. *Washington Post.* August 11, 2021, available at <https://www.washingtonpost.com/health/2021/08/11/naloxone-demand/>.
- ⁶ Pruyn S, Frey J, Baker B, et al. Quality Assessment of Expired Naloxone Products from First-Responders' Supplies. *Prehosp Emerg Care.* 2019;23(5):647-653.
- ⁷ The potency of that sample, which expired in May 1992, was approximately 89% of that when it was new.
- ⁸ Mohammad Hossain, et al., Evaluation of Chemical Stability of Naloxone Products beyond Their Labeled Expiration Dates, American Association of Pharmaceutical Scientists presentation at PharmSci 360 Conference (November 6, 2018).
- ⁹ The study reported the temperatures in Celsius (-20 and 80 degrees Celsius). Lai D, Pham AT, Nekkar Rao PP, Beazely MA. The effects of heat and freeze-thaw cycling on naloxone stability. *Harm Reduct J.* 2019;16(1):17. Similar results were obtained from a previous study. See Johansen RB, Schafer NC, Brown PI. Effect of extreme temperatures on drugs for prehospital ACLS. *Am J Emerg Med.* 1993;11(5):450-452.
- ¹⁰ This authorization is limited to circumstances in which the director is a licensed physician; where the director is not, the department is authorized to contract with a licensed physician to issue the statewide standing order. Mo. Rev. Stat. §195.206(2).
- ¹¹ Missouri Department of Health and Senior Services Director's Naloxone Standing Order, April 20,2021, <https://pr.mo.gov/boards/pharmacy/NaloxoneStandingOrder.pdf>.
- ¹² Mo. Rev. Stat. §195.206(4).
- ¹³ Mo. Rev. Stat. §195.206(3).
- ¹⁴ Mo. Rev. Stat. §195.206(5).
- ¹⁵ Mo. Rev. Stat. § 338.205(1).
- ¹⁶ Mo. Rev. Stat. § 338.205(1).
- ¹⁷ Mo. Rev. Stat. §195.206(6).
- ¹⁸ "All other medications, including all controlled substances and all expired or otherwise unusable medications, shall be destroyed within thirty (30) days." 19 Mo. Code Regs. 30-86.042(60)(F). "Medications may be returned to the pharmacy that dispensed the medications ... or returned pursuant to the Prescription Drug Repository Program.... All other medications, including all controlled substances and all expired or otherwise unusable medications, shall be destroyed within thirty (30) days." 19 Mo. Code Regs. 30-86.047(56)(E).
- ¹⁹ "Unwanted controlled substances that have been expired, discontinued, or are otherwise unwanted shall be disposed of" 19 Mo. Code Regs. 30-1.078(2)(B).
- ²⁰ "Other expired or nonusable medications shall be destroyed within five (5) days." 19 Mo. Code Regs. 30-35.020(3)(5)(E).
- ²¹ 19 Mo. Code Regs. 20-50.025(2)(E)
- ²² 20 Mo. Code Regs. 2220-2.090(2)(V).
- ²³ 20 Mo. Code Regs. 2220-2.010(6).
- ²⁴ Mo. Rev. Stat. § 338.059(2).
- ²⁵ Mo. Rev. Stat. § 338.205(1).
- ²⁶ Mo. Rev. Stat. §195.206(1)(1).
- ²⁷ Mo. Rev. Stat. §195.206(6).