

January 17, 2023

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Food and Drug Administration  
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**Re: Docket No. FDA-2022-N-2673 for “Safety and Effectiveness of Certain Naloxone Hydrochloride Drug Products for Nonprescription Use; Request for Comments.”**

On behalf of the nation’s nearly 3,000 local health departments, the National Association of County and City Health Officials (NACCHO) appreciates the opportunity to respond to the request for comments regarding the safety and effectiveness of certain naloxone hydrochloride drug products for nonprescription use. NACCHO appreciates FDA’s efforts to increase potential naloxone availability in the community and supports improving access to naloxone as an important tool to reducing fatal opioid overdoses. NACCHO is pleased to provide comment on the three areas requested by FDA to help inform additional approaches to facilitate access to naloxone.

**1. Data to support the safe and effective use of nonprescription naloxone hydrochloride injection for intravenous, intramuscular, or subcutaneous use.**

Currently, there are two FDA-approved injectable naloxone formulations: 1) traditional intra-muscular (IM) naloxone hydrochloride and 2) auto-injector naloxone. The FDA’s preliminary assessment is that only the auto-injector formulation (along with nasal-administered naloxone) is safe and effective for nonprescription use, but available data suggests FDA should consider nonprescription status for traditional injectable formulations as well.<sup>i</sup>

NACCHO is not able to finance the purchase of naloxone due to funding restrictions by the Centers for Disease Control and Prevention (CDC) but does support naloxone distribution programs and naloxone trainings at many local health department partners. Layperson distribution programs through local health departments and community programs have distributed hundreds of thousands of doses of injection-administered naloxone without adverse issues. Individuals and organizations may prefer one formulation type over another due to a variety of factors including cost, familiarity with administration method, or ease of use. A wider array of naloxone formulations available for nonprescription use would facilitate greater community availability of this important tool, which is consistently in high demand. Notably, the most frequent naloxone related request made by partners to NACCHO is to discuss the lifting of funding restrictions by CDC to increase access to and community saturation of naloxone.

**2. Data to support the safe and effective use of higher dose nonprescription naloxone hydrochloride products, such as naloxone hydrochloride, nasal spray greater than 4 mg.**

While higher dose naloxone itself is chemically safe, evidence suggests that generally a single 4mg dose is sufficient to treat individuals who have overdosed. The National Highway Traffic Safety Administration’s Office of Emergency Medical Services National EMS Information System dashboard



shows that the average number of naloxone administrations per overdose is 1.1.<sup>ii</sup> While the presence of fentanyl in the drug supply is often cited as a reason for promoting high-dose naloxone, another study demonstrated no change in naloxone dose required to reverse overdose during a period when the local drug supply transitioned from heroin to stronger fentanyl.<sup>iii</sup>

If more naloxone is required to treat an overdose, a second 4mg dose can be administered a few minutes after the first dose. Many current naloxone kits come standard with two 4mg doses. Higher dose naloxone is more likely to trigger precipitated withdrawal, which can cause extreme discomfort and affect willingness for revived individuals to remain in place to receive further medical care. This could put the individual at risk, as naloxone has an elimination half-life far shorter than most opioids, and individuals who are not monitored following naloxone administration may face adverse side effects due to recurrent opioid toxicity.

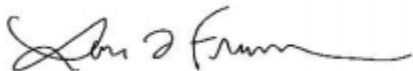
**3. Any potential consequences of a switch from prescription to nonprescription status for naloxone products, and actions that FDA could consider to address them, including but not limited to, impacts on community-based naloxone distribution programs and consumers, drug shortages, and the distribution and supply of naloxone.**

In NACCHO's experience working with local health departments and their partners, prescription status is not the only barrier to naloxone saturation. While a switch to nonprescription status would be welcomed by NACCHO, our members cite cost, particularly as it relates to nasal and auto-injector naloxone, as a major barrier to access. Without support to reduce the costs borne by local health departments to procure naloxone, a switch to over-the-counter (OTC) status is likely to have limited impact on overall capacity to distribute naloxone widely in communities.

Notably, traditional injectable naloxone costs significantly less than autoinjector and nasal spray. Furthermore, NACCHO is concerned that by not considering traditional injectable (as opposed to auto-injector) naloxone for OTC status, the FDA may be sending the incorrect message that this method of naloxone administration poses risks. NACCHO encourages FDA to consider traditional injectable naloxone for OTC status in addition to auto-injector.

Thank you for the consideration of these comments. For additional information, please contact Adriane Casalotti, Chief of Government and Public Affairs, at [acasalotti@naccho.org](mailto:acasalotti@naccho.org).

Sincerely,



Lori Freeman, MBA  
Chief Executive Officer

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<sup>i</sup> <https://pubmed.ncbi.nlm.nih.gov/26086633/>

<sup>ii</sup> <https://nemsis.org/opioid-overdose-tracker/>

<sup>iii</sup> <https://pubmed.ncbi.nlm.nih.gov/29558283/>