

## Injectable Naloxone: the wave of the future...and the past

This document addresses some of the frequently raised concerns and questions about **0.4mg/mL intramuscularly injectable naloxone** and is geared towards programs who are:

- Introducing choice of product to their participants or responding to demand for injectable naloxone
- Struggling to meet demand and scale-up to saturation with more expensive nasal products
- Exploring the purchase of low-cost generic naloxone for higher volume distribution

#### Introduction:

No currently available naloxone product is perfect, so this document is not intended to claim that one is. Until a naloxone product is developed, packaged, made affordable and accessible to people who use drugs, with input from people who use drugs–none will be.

People who use drugs are those who *experience* overdose and who *witness and reverse* the most overdoses, and yet, have no input into the development of drugs that will be sold to, distributed to, used on, and used by them. Until people have access to the systems of power and innovation that impact their daily lives and survival, we will continue to struggle to find products that work, work well, minimize suffering and discomfort while restoring life, and are accessible to *all* people who use drugs.

Naloxone is also just one piece of the puzzle, it is not a solution. It is a band-aid on an open wound that the drug war has created and continues to exacerbate. The unregulated and dangerous drug supply–a direct result of prohibition, US imperialism and the racist war on drugs–will not be fixed with naloxone. We need systemic change, resources and innovative solutions.

Remedy Alliance/For the People provides access to large volumes of low-cost and free naloxone to harm reduction programs, but does this within the context of a broader call for systemic change that includes but is not limited to the following:

- Immediate implementation of <u>safe supply</u>
- Expansion of accessible, advanced drug-checking technologies
- An end to the racist war on drugs and mass incarceration of people who use and sell drugs
- Robust low-threshold funding and resource allocation to harm reduction and mutual aid projects who are providing access to life-saving material resources to people who use drugs
- Support for innovative supply distribution strategies such as mail-order, vending machine and peer-based models that get material resources into the hands of people who do not have access to traditional brick and mortar programs

This document is specifically focused on dispelling myths and misunderstandings about injectable naloxone, and is a call to action to expand the volume of naloxone distributed and increase autonomy and choice for people who use drugs and others likely to witness an overdose. As harm reduction work (and especially naloxone distribution) has increasingly migrated from its original radical context of bodily autonomy and the liberation of medicine and supplies from medical-legal gatekeeping, we hope this document serves to reorient us back to some of the fundamental principles of material resource access.

#### Injectable naloxone basics:



The generic injectable naloxone vials that are distributed by harm reduction programs are primarily made by Pfizer pharmaceuticals (orange caps, left), Hikma pharmaceuticals (purple caps, middle), Somerset (blue caps, right), Aurobindo (not pictured) or other generic manufacturers.

The vials of naloxone most commonly distributed are **0.4mg/1ml**, which means there is **0.4mg** of the drug naloxone suspended in **1ml of fluid**. For reference, this is 1/10th the amount of drug in nasal Narcan and generics by Teva, Sandoz and Padagis, which contain **4mgs** of the drug in **0.1ml** of fluid.

Naloxone vials for injection do not contain the equivalent amount of the drug as in the nasal devices. Here's a chart showing the equivalents:

Narcan & generics by Teva, Sandoz and Padagis 4mg (nasal) = 10 vials of 0.4mg injectable naloxone Kloxxado 8mg (nasal)= 20 vials of 0.4mg injectable naloxone Zimhi 5mgs (injected)= 12.5 vials of 0.4mg injectable naloxone

**These equivalents are simply measurement equivalents, because route of administration matters when talking about naloxone**—*so one 4mg nasal spray is not truly the equivalent of injecting someone with 10 vials of naloxone* because the drug is absorbed differently depending on the route of administration. However, with the Zimhi product, since it is also an intramuscular injection, the 5mgs is the *equivalent* to the amount of naloxone in 12.5 vials of naloxone since it has the same route of administration.

0.4mg/1ml naloxone is a standard dose to begin the overdose reversal process, but it is important to administer the whole dose–please do not "microdose" injectable naloxone by injecting only a quarter or half of the vial, this amount of drug (0.1mg or 0.2mg) is not likely enough naloxone to successfully reverse an overdose.

### A very brief history of injectable and nasal naloxone access in the US:

Naloxone hydrochloride, the antidote to an opioid overdose, has been distributed by harm reduction programs since <u>1996 in the US</u>. Until 2015, the majority of naloxone distributed to people who use drugs was generic injectable naloxone. In a few higher-resourced early adoption states such as NY, NM and MA–the <u>off-label</u> <u>nasal naloxone</u> was distributed in addition to injectable.

In 2015, nasal <u>Narcan® was approved by the FDA</u> and Adapt Pharma/Emergent Biosolutions has achieved market dominance and high product visibility over the last seven years. In 2021, during the injectable naloxone shortage which devastated harm reduction programs across the US and created a sudden and unanticipated 1.5+ million dose deficit in the supply,<sup>1</sup> Emergent Biosolutions made <u>\$434 million</u> dollars on their nasal naloxone product, a 50% increase in sales over the previous year.

Many harm reduction programs across the country continue to distribute generic injectable naloxone largely due to its low cost and their high-volume needs, and in many cases, participant preference. In 2020, harm reduction programs in the US distributed over <u>1.3 million doses of generic injectable</u> naloxone to people who use drugs and others likely to witness an overdose. Many programs distribute both forms of naloxone so they can meet the demand for high-volume distribution, and offer participants a choice in product based on preference and comfort level.

For many newer programs who began distributing nasal Narcan® in the last seven years, or states where the <u>off-label use of the former nasal naloxone</u> previously dominated, program staff and participants may be unfamiliar and uncomfortable with the use of generic injectable naloxone.

As drug use trends continue to shift and the supply becomes increasingly dangerous to more people, there has also been a movement away from focusing naloxone distribution to people who inject drugs. Nasal products are often more available or desirable to people who have no experience using injectables. We will address this later in this document.

Hopefully this document can answer some commonly asked questions and provide a deeper understanding of the different naloxone products that are available.

<sup>&</sup>lt;sup>1</sup> This is an estimate based on Buyers Club programs' distribution volume in 2020 (1.3 million doses) and the approximate amount of naloxone that was also procured from Direct Relief, who also provided access to Pfizer-manufactured generic injectable naloxone.

## Generic intramuscular 0.4mg/1ml naloxone is effective in reversing opioid overdoses– *including fentanyl overdoses*.

With the increased presence of fentanyl in the <u>drug supply</u> since 2013-2014, there has been <u>concern</u> over generic 0.4mg/1ml injectable naloxone's effectiveness in reversing fentanyl overdoses. Titrated<sup>2</sup> 0.4mg naloxone (via IV) is still the standard of care in hospital settings for the reversal of <u>fentanyl</u> used during anesthesia and other procedures that necessitate fentanyl administration.

While the "illicitly" manufactured fentanyl supply does not consist of diverted pharmaceutical fentanyl, it is the same basic drug, and responds to naloxone if administered in enough time. Due to the potency, inconsistency, and unpredictability of the street drug supply and the rapid nature of fentanyl overdoses, it is common to hear about the need for multiple doses of naloxone in overdose events. This has led to the belief that these overdose events "required" the high dosage of naloxone administered, but this is a possible misinterpretation of the events and a misunderstanding about how naloxone works in general.

A recently published peer reviewed journal <u>article</u> delves into this further (emphasis ours):

Advocates for more powerful opioid antagonists often cite two retrospective studies which found that emergency medical services (EMS) providers responding to a suspected opioid overdose were more likely to administer multiple doses of naloxone in 2015 (18.2%) compared to 2012 (14.5%) (Faul et al., 2017) and in 2016 (21.4%) compared to 2013 (15.0%) (Geiger, Smart, & Stein, 2020). However, these studies did not describe the route or dose of these administrations. IN naloxone administrations were likely rare as trained clinicians often prefer to carefully titrate IV dosing and may also administer IM. The significance of a modest increase in multiple administrations of unknown IV and IM doses is difficult to ascertain. Given widespread news reports describing the increased prevalence of potent synthetic opioids, often accompanied by alarmist misinformation about passive exposure risk, it is plausible that the increase in multiple naloxone administrations among EMS is an artifact of availability bias with multiple doses of naloxone administered out of an abundance of caution rather than based on clinical signs and symptoms. Patients treated for a suspected opioid overdose may also appear to need more naloxone due to intentional concomitant use of opioids and other sedating drugs (e.g., alcohol, benzodiazepines) and contamination of the illegal opioid supply with non-opioid depressants (e.g., xylazine, barbiturates).

Three other studies, two in emergency departments and one in a syringe services program, provide superior insight regarding the hypothesized need for more powerful opioid antagonists. An analysis of prehospital and emergency department naloxone administration was conducted in Atlanta from 2017 to 2018 (*Carpenter et al., 2020*). This study included naloxone dosing information and urine drug screen results, and it found that the median dose of naloxone administered in successful reversals did not differ significantly based on the presence or absence of fentanyl (0.8 mg IV vs

<sup>&</sup>lt;sup>2</sup> To "titrate" means to adjust the dose based on response. Titration is a way to limit potential side effects by taking time to see how the body will react to a drug. In titration, the medication is started at a low dose and then increased until the maximum effective dose has been achieved or side effects occur.

0.56 mg IV, p = 0.79). A study conducted in Boston from 2017 to 2018 compared blood fentanyl concentrations to naloxone doses administered among patients experiencing a non-fatal opioid-related overdose (*Krotulski et al.*, 2021). All 20 subjects reported use of heroin, and fentanyl was detected in 19. No relationship between blood fentanyl concentration and naloxone dose administered was identified. Data collected from clients of a syringe services program in Pittsburgh, Pennsylvania from 2013 to 2016 corroborate these results (*Bell, Bennett, Jones, Doe-Simkins, & Williams, 2019*). While the proportion of opioid overdose deaths testing positive for fentanyl in the county increased from 3.5% to 68.7% during this timeframe, the reported naloxone doses used by clients to effectively reverse opioid overdoses did not change. **Notably, the program distributed relatively low-dose 0.4 mg vials for IM administration, and a mean of only 1.56 doses per reversal were required.** 

One common misunderstanding about the administration of naloxone is that a higher dose or administering multiple doses in quick succession makes the naloxone *work faster* or that the overdose reversal was only successful based on the number of doses that were reportedly used. This misunderstanding is exploited by manufacturers of higher-dose naloxone products. All formulations and potencies of naloxone take 1-3 minutes (average) to begin to take effect–*sometimes longer*–and any form of naloxone may possibly require a subsequent dose after the first few minutes, depending on the overdose. If you administer more than one dose of naloxone within the first few minutes, there is no way to know if one dose would have worked on its own, and it is impossible to claim or infer that the overdosing person "needed" multiple doses if they are administered concurrently.

It is important to try to understand what happened during the overdose reversal as clearly as possible, as misinterpretation of these events has led to misinformation and misunderstandings about how naloxone works and how overdoses happen. Understanding what happened during an overdose event is complicated, and there are many ways to better gather information about what occurred.

#### Considerations for an overdose event analysis:

- How experienced is the overdose rescuer?
- How well does the overdose rescuer know the overdosing person?
- Did the overdose rescuer know exactly how much the overdosing person took of the substance(s) that caused the overdose?
- Was the overdosing person mixing substances? Do they or the rescuer know what substances?
- Were there unusual or particularly scary aspects to this overdose? Did the person gulp, gasp, clutch at their throat? Did they turn blue/gray quickly?
- How quickly after the overdosing person became unresponsive did the rescuer administer naloxone doses? How do they know this?
- Did the rescuer perform rescue breathing?
- How many people were present and involved in the rescue?
- How many doses of naloxone were available to use?
- How long did the rescuer wait between doses?
- How prevalent are non-opioid additives in your opioid supply (for example- etizolam, xylazine)?

• Do you know how long the person had been overdosing for?

There is no significant difference in how fast the different forms of naloxone work to reverse respiratory depression. A comparative <u>study</u> in Canada between intranasal and intramuscular naloxone used to reverse an overdose showed that IM naloxone worked *marginally* faster than nasal. For example, if you give 4 doses of nasal Narcan® (16 mgs) in rapid succession during an overdose, it does not make it work any faster than if you give one dose of nasal Narcan® (4mg) or one dose of injectable naloxone (0.4mg), wait, perform rescue breathing, and administer a second dose if needed after several minutes.

However, when the naloxone reaches *peak* concentration (approximately 30 mins for 4mg nasal and 25 mins for IM) an opioid dependent person may feel varying intensity of withdrawal symptoms depending on the quantity of naloxone administered.

Notice in the table below from the Hill, et al. <u>paper</u>, the Cmax (this is the concentration of naloxone in the bloodstream) is substantially higher with the 4mg and 8mg nasal products, but takes almost the same amount of time to reach peak concentration.

Drug	Route	Dose	Cmax ng/mL	Tmax hours	AUC (ng h/mL)
Naloxone	IM	0.4mg	0.9	0.4	1.8
Naloxone	IN	2mg	3.1	0.3	4.7
Naloxone	IN	4mg	5.3	0.5	8.5
Naloxone	IN	8mg	10.3	0.3	15.8
Nalmefene	IN	3mg	4.45	0.25	15.2

Pharmacokinetics of opioid antagonists in healthy volunteers (Krieter et al., 2016; Krieter et al., 2019).

Cmax indicates the maximum plasma concentration achieved. tmax indicates the amount of time elapsed prior to achieving Cmax.

AUC represents the total drug exposure.

*The severity of withdrawal symptoms matters* for people who use drugs who are dependent on opioids and people taking opioids for chronic pain management. Extreme withdrawal experiences are potentially dangerous, painful and traumatizing. It can result in negative feelings towards naloxone and people who administered it, or result in more concealment of drug use to avoid having naloxone administered:

Precipitated opioid withdrawal is a known risk of naloxone for opioid-tolerant individuals, producing symptoms such as hyperalgesia, diarrhea, and vomiting, particularly at higher doses (<u>Purssell et al., 2021</u>). Aversion to being administered naloxone and experiencing opioid withdrawal symptoms was thoroughly documented in an ethnographic study conducted in Scotland from 1997 to 1999 (<u>Neale & Strang, 2015</u>).

Nearly all subjects who were familiar with naloxone described it negatively and indicated it should be avoided, and many expressed mistrust of health professionals' judgment regarding when to administer it.[...]In one study, 10 adults reporting to an emergency department in Boston with an opioid-related chief complaint were interviewed (Lai et al., 2021). All were familiar with naloxone and had received training in its administration, and they generally reported positive perceptions of it. However, the eight subjects who had previously received naloxone each reported experiencing severe opioid withdrawal symptoms they were eager to avoid in the future. In another study, 20 adults who use opioids in New York were interviewed to identify reasons they do or do not carry naloxone (Bennett, Freeman, Des Jarlais, & Aronson, 2020). A major reported theme from these interviews was a fear of misrecognizing the need for naloxone and inducing or experiencing prolonged opioid withdrawal symptoms. Significantly, an 8 mg naloxone product has not yet been marketed, so these qualitative findings are in the context of 4 mg IN being the highest single-dose naloxone product available. The introduction of an 8 mg IN naloxone product and the potential future introduction of a similarly potent nalmefene product with longer duration of action could plausibly lead some people who use opioids to avoid carrying it.

# *All* forms of naloxone may take longer/be less effective with poly-drug overdoses.

Complicating factors in overdose events that can impact the efficacy of *any* form of naloxone are the addition of other drugs, especially benzodiazepines, alcohol or some substances that are now more frequently found in the street fentanyl supply, like xylazine.

*Naloxone has always had its work cut out for it in poly-substance overdose events, especially ones that contain benzodiazepines.* It is common for responders to report administering multiple doses of naloxone along with requiring airway management and rescue breathing–a crucial component to any overdose reversal, but especially when the response time is longer and it is more difficult to revive someone.

#### Intramuscular syringes.

Legally speaking, the syringes included in an injectable naloxone kit are the *prescribed devices needed to administer a medication*, and therefore are exempted from laws prohibiting "paraphernalia to inject illegal drugs"—they fall in the same legal category as the syringes needed to inject insulin, IVF or HRT.

The syringes included in an IM naloxone kit should be between 1'-1.5" long, hold between 1-3ml of liquid and be at least 25g-21g. *The IM syringes should be a large enough gauge to go through clothing, and long enough to reach through the skin and fat layers to the muscle layer in any sized body*.

In the early days of naloxone distribution (late 90s-early 2010s) naloxone was almost exclusively distributed via <u>syringe access programs</u>. These programs were already working directly with people who use drugs, focused primarily on people using syringes and provided access to sterile syringes in addition to the IM syringes needed

for naloxone. As naloxone distribution has migrated out of the syringe services program context into more diverse venues and reaching more populations, there are more issues with distributing the injectable form of naloxone in places where there is syringe scarcity and where naloxone is being distributed to people other than those who are already familiar with injected drugs.

Access to sterile syringes is still inadequate and limited in most places in the US. In areas where there is no access to syringe services programs or pharmacies that are willing and able to sell syringes without a prescription, this poses a challenge to programs distributing injectable naloxone kits. Syringe scarcity can result in the included IM syringes being used to inject other drugs in a moment of no other option, leaving the kit incomplete in the event the naloxone is needed. Restrictive paraphernalia laws can place people carrying an injectable naloxone kit at risk if law enforcement is unaware or unwilling to acknowledge the legality of the IM syringes as medical devices and instead consider them paraphernalia.

#### This is a syringe scarcity problem, a problem with paraphernalia laws at the state level and/or a misunderstanding of them at the local level, a law enforcement problem, a war on drugs problem, and a problem with inadequate access to harm reduction services in the majority of the US.

If you are distributing injectable naloxone to people who use drugs in an environment where there is inadequate or zero access to other harm reduction services, it is important to advocate for expansion of harm reduction services in tandem with your naloxone distribution, including syringe access. You can also include explicit information on the naloxone kit targeted to law enforcement explaining that the syringes are medical devices for the administration of a life saving medication and not paraphernalia. These strategies are not guaranteed to keep people who use drugs or who are carrying naloxone safe, but they can mitigate some of the risk.

People who use drugs and especially people who use drugs who are Black, Indigenous, Latinx, sex workers, trans and gender non-conforming are over-policed and the targets of prohibition and the war on drugs. Possessing drugs, syringes, other paraphernalia and even nasal or injectable naloxone for aiding another person in distress puts people at great risk of bodily harm or death at the hands of law enforcement. <u>Hesitancy to carry naloxone</u> by Black people has been well documented, as the dangers of responding to an overdose or being found in possession of naloxone may carry more risk than someone is able to safely take on. Context matters, and as rates of overdose especially among Black and Indigenous people in the US continue to rise, the over-policing of communities of color has the direct added consequence of limiting safe access to naloxone and other life-saving services.

#### Preferences, nasal vs injectable.

Preference for one form of naloxone over another depends entirely on the person, the program, the community experience, familiarity with both forms of naloxone and accessibility of different products. In areas where injectable naloxone has always been available, the introduction of nasal Narcan® has been met with resistance and skepticism. In places that have only had nasal Narcan® access, you may hear the opposite, that no one wants, or can use injectable. In places where both options are offered, people often have strong preferences for

one over the other, or a preference for both for different situations or different drugs or different people. You may hear people say the nasal is too strong or the nasal is too weak—the injectable doesn't work, the nasal doesn't work. The nasal makes people sicker, the injectable makes people sicker. The injectable doesn't work on fentanyl, the nasal doesn't work on fentanyl.

The experience of witnessing and responding to overdose events, sometimes repeatedly, can inform preference for either product or one over the other, along with provider bias influencing attitudes about either form of naloxone. It is common to hear providers speaking on behalf of participants of programs, saying that "no one likes" this one form of naloxone or the other, but this can be informed by their own experience and comfort with the different products. In places where only injectable naloxone is distributed, providers can influence the preference for injectable and contribute to the resistance to nasal Narcan®–conversely, in places where only nasal Narcan® is available, providers can influence attitudes against injectable naloxone. Harm reduction providers are often trusted members of a community and wield considerable influence. Even subtle endorsements of one product over the other can influence people's choices community-wide.

Ideally, all people who use drugs should have choice, and they should have access to enough naloxone of either or both forms to support peer distribution and have enough on hand for any overdoses they are likely to witness. If you can scale up your distribution to meet this need with one form or the other-that is ideal and that will get closer to saving the most lives. However, if you cannot do this with one form of naloxone-it is highly encouraged to seek out multiple sources and forms of naloxone to ensure that you have an adequate supply.

# Benefits and challenges associated with the different available forms of naloxone:

Form/dosage of naloxone:	Benefits	Challenges
0.4mg/1ml intramuscular (IM) naloxone vial and syringe	<ul> <li>Lowest dose needed to reverse OD</li> <li>Least severe withdrawal symptoms</li> <li>Autonomy and ability to titrate doses</li> <li>Higher bioavailability than nasal (nasal is approx 50% bioavailable compared with IM)</li> <li>Adaptable kits, can include any number of vials/syringes based on participant request</li> <li>Low or no cost, ability to purchase large volumes to bring to scale</li> <li>FDA approved for opioid</li> </ul>	<ul> <li>Kits require multiple components and assembly</li> <li>Syringe scarcity, no harm reduction services access, stigma and paraphernalia laws make carrying injectable med riskier for PWUD</li> <li>Requires more training (but still only minutes)</li> <li>Provider bias against injectable form of naloxone, misinformation</li> <li>Participant preference</li> </ul>

Form/dosage of naloxone:	Benefits	Challenges
	<ul> <li>overdose reversal</li> <li>Preparing injection creates natural pause between dosing, decreases the chance of excessive administration of naloxone</li> <li>Available through low-barrier, harm reduction-informed and ethical distribution source</li> </ul>	<ul> <li>for nasal</li> <li>Vials are glass and can be subject to breakage or other damage</li> <li>Labeling does not explicitly state for layperson use</li> </ul>
Narcan® & generics by Teva, Sandoz and Padagis nasal sprays (4mg per dose)	<ul> <li>Pre-packaged and labeled kits</li> <li>No assembly required</li> <li>Easy to use with little instruction</li> <li>Preferred by some people with no injection experience</li> <li>No syringe involved, less stigmatized and easier in areas with strict paraphernalia laws and syringe scarcity</li> <li>Explicit FDA approval for layperson use</li> </ul>	<ul> <li>High cost per 2 dose box, prohibitive for scaling to saturation and supporting robust peer distribution</li> <li>Participant preference for IM</li> <li>Cannot titrate, less autonomy</li> <li>Frequent reports of more than 2 doses needed to reverse overdose</li> <li>Plastic applicator can be subject to breakage or other damage</li> </ul>
Kloxxado® nasal spray (8mg per dose)	<ul> <li>Could be effective with non-opioid dependent people who are experiencing an overdose</li> <li>Pre-packaged and labeled kits</li> <li>Easy to use with little instruction</li> <li>No assembly required</li> <li>Preferred by some people with no injection experience</li> <li>No syringe involved, less stigmatized and easier in areas with strict paraphernalia laws and syringe scarcity</li> <li>Explicit FDA approval for layperson use</li> </ul>	<ul> <li>High-dose not supported by robust evidence</li> <li>Could likely result in severe precipitated withdrawal in opioid dependent people</li> <li>Limited reports from opioid dependent people</li> <li>High cost per 2 dose box, prohibitive for scaling to saturation and supporting peer distribution</li> <li>Participant preference for IM or existing nasal naloxone</li> <li>Cannot titrate, less autonomy</li> </ul>

Form/dosage of naloxone:	Benefits	Challenges
		• Plastic applicator can be subject to breakage or other damage
Zimhi® auto injector (5 mgs)	<ul> <li>Could be effective with non-opioid dependent people who are experiencing an overdose</li> <li>Pre-packaged and labeled kits</li> <li>No assembly required</li> <li>Explicit FDA approval for layperson use</li> </ul>	<ul> <li>Extremely high dose (equivalent of 12.5 vials of 0.4mg naloxone), not supported by robust evidence</li> <li>Could likely result in extremely severe precipitated withdrawal in opioid dependent people</li> <li>No use reports from opioid dependent people</li> </ul>

## So WHY increase distribution of injectable naloxone?

As the drug supply becomes increasingly dangerous and unstable and we lose over 100,000 people a year to preventable overdose death—one thing that we know for sure is that *nowhere in the US* is <u>enough naloxone</u> <u>being distributed</u>, especially directly to people most likely to witness overdoses.

#### Injectable naloxone is affordable.

Massive resource misallocation in the last few years has resulted in huge volumes of naloxone purchased with federal and state dollars going to law enforcement, prohibitionist anti-drug coalitions and other more "acceptable" organizations who do not provide robust access to people who use drugs nor do they operate within a harm reduction framework.

Harm reduction and mutual aid groups remain under-resourced and are still struggling to get access to the true volumes of naloxone that they need to distribute to their communities. The cost-prohibitive nature of nasal naloxone products and their dominance in the public funding domain has effectively created a volume limit on naloxone distribution and has indirectly resulted in a deeply rooted resource-scarcity mentality.

In order for harm reduction programs to truly be able to scale up distribution towards "saturation," and needs-based distribution of naloxone, an affordable product *must be considered*. Currently, the only affordable product is injectable generic naloxone, so it is imperative that resources and attention be directed back to this well-tested resource.

#### Intramuscular naloxone is easy to use.

The harm reduction community has over 26 years of experiential evidence that injectable naloxone is acceptable and usable in an overdose situation. In the early days of naloxone distribution, programs were primarily focused on getting naloxone to people who inject drugs, so there was a high likelihood that people may already have experience with using syringes and preparing injections.

However, with the rise in overdoses from drugs consumed by smoking, snorting or taken orally, the recipient of naloxone may not have experience using syringes. Similarly, for concerned friends and family, or the general public who may be receiving naloxone in case of witnessing an overdose, there may be less familiarity and comfort using an injected product. Nasal naloxone is a good choice for people with no experience administering naloxone or extreme discomfort with the idea of injecting a medication. *However, if access to nasal naloxone is limited or unavailable altogether, it has been demonstrated that people will be open to the injectable option with some training and support, rather than carry no naloxone at all.* 

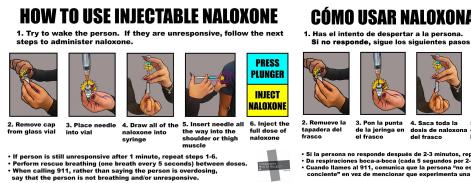
There is an abundance of stigma associated with injected drugs, and that has come to include injectable naloxone because of its association with reversing overdoses among people who use drugs like fentanyl, heroin or other opioids obtained from the street market. There is an often repeated belief that only a person who injects drugs can use injectable naloxone. Nasal Narcan $\mathbb{R}$  is often marketed as being more "acceptable" to friends, family and people prescribed opioids and this marketing contributes to the added stigma directed towards people who inject drugs and injectable naloxone.

However, less-stigmatized injectable medicines are extremely common in out-of-hospital settings and a routine part of our healthcare system---i.e. insulin, In Vitro Fertilization (IVF) treatment or Hormone Replacement Therapies (HRT). <u>Over 8 million Americans require insulin to regulate their blood glucose levels</u>. Some patients in the US are even sent home to administer IV medications through <u>PICC lines</u> and ports on their own without medical supervision (much more risky than administering an intramuscular injection through the clothing). Instructing an individual with little to no experience doing an injection takes only a few minutes, and is routinely done in the US health care setting during a brief overview with a pharmacist or through written materials.

Epinephrine (Epi-Pens) are another parallel example where an emergency medicine must be injected, and sometimes it is necessary for another person to administer the injection to the person experiencing anaphylaxis. While Epi-Pens come in an auto-injector form instead of a separate vial and syringe, there are easy instructions available for <u>parents</u> of children who have allergies, caregivers and even strangers—on how to administer this medicine (which carries a significantly higher risk profile than naloxone).

In the context of community-based naloxone distribution, instructing someone with no experience with injectables on how to draw up the naloxone and inject it intramuscularly can also be done in minutes.

Here are some examples of simple instructions on IM naloxone administration from Community Health Project in Los Angeles, CA.



#### COMO USAR NALOXONA INYECTABLE



5. Inserta la jeringa 6. Injecta en el músculo del toda la de brazo o el muslo de naloxo

ii la persona no responde después de 2-3 minutos, repite los pasos 2 a 6. la respiraciones boca-a-boca (cada 5 segundos por 2-3 minutos) entre cad cuando llames al 911, comunica que la persona "no está respirando y/o no conciente" en vez de mencionar que experimenta una sobredosis.

### It is legal to distribute injectable naloxone, and injectable naloxone is an FDA-approved product for use in community distribution programs.

There is no prohibition on the distribution of injectable naloxone from any federal agency. The FDA issued a clarifying statement in 2019 that generic "vial and syringe" naloxone was an FDA-approved product for the treatment of overdose reversal. In 2020, SAMHSA even issued a COVID-19-specific guidance that encourages the use of injectable naloxone during an overdose emergency if the responder feels that nasal naloxone administration poses additional COVID risk. Federal funds may be used to purchase injectable naloxone and are used this way in many states.

If you are being told that state and federal funds cannot be used to purchase injectable naloxone, or that community-based naloxone distribution programs are prohibited from distributing injectable naloxone, this is untrue. Please contact us and we can assist in clearing this up.

### Distributing IM naloxone does not increase the risk of needlesticks.

There is no evidence that providing people likely to witness an overdose event with injectable naloxone results in an increase in needlestick injuries.

#### Are there materials and resources available about IM naloxone?

Yes! There are several decades worth. There are stickers and comics and posters and brochures, and videos and animations–all showing how to administer injectable naloxone. However, as with anything in harm reduction practice, the best materials are made by people who use drugs and people in your own community-where you can adapt to your particular needs, experiences and context. We strongly recommend adapting any of the available materials if you can, and if you cannot, try downloading some of the available materials that you like the best and make sure to credit the original artist or program. Keep it simple, accurate, clear and relevant to your community.

This document was written by Remedy Alliance/For the People with contributions and edits by our friends at <u>NEXT Distro</u> and <u>Confluence HRKC</u>. Thank you to <u>Lucas Hill</u>, PharmD for giving this document a once-over to make sure we accurately summarized the science.